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Journal of Clinical Oncology®

An American Society of Clinical Oncology Journal

2020 ASCO Annual Meeting Proceedings

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American Society of Clinical Oncology

2020 Annual Meeting Proceedings

(a supplement to *Journal of Clinical Oncology*)

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Letter From the Editor

The *2020 ASCO Annual Meeting Proceedings* (a supplement to *Journal of Clinical Oncology*) is an enduring record of the more than 2,400 abstracts selected by the ASCO Scientific Program Committee for presentation as part of the ASCO Annual Meeting. Publication-only abstracts are included in the online supplement to the May 20 issue of *Journal of Clinical Oncology* at JCO.org. Abstracts can be also accessed online through the ASCO Meeting Library (meetinglibrary.asco.org). Online abstracts include the full list of abstract authors and their disclosure information.

All abstracts carry *Journal of Clinical Oncology* citations, for example:

J Clin Oncol 38:15s, 2020 (suppl; abstr 1)

Should you have any questions or comments about this publication, we encourage you to provide feedback by contacting us at abstracts@asco.org.

Michael A. Carducci, MD, FACP, FASCO
Editor, *ASCO Annual Meeting Proceedings*

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In the unlikely event that ASCO publicly releases an abstract in advance of the scheduled time, the release will be publicly announced on ASCO.org.

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LBA1 **Plenary Session, Sun, 1:00 PM-4:00 PM**

Maintenance avelumab + best supportive care (BSC) versus BSC alone after platinum-based first-line (1L) chemotherapy in advanced urothelial carcinoma (UC): JAVELIN Bladder 100 phase III interim analysis. *First Author: Thomas Powles, Barts Cancer Institute, Experimental Cancer Medicine Centre, Queen Mary University of London, St Bartholomew's Hospital, London, United Kingdom*

The full, final text of this abstract will be available at abstracts.asco.org at 5:00 p.m. ET on Thursday, May 28.

LBA2 **Plenary Session, Sun, 1:00 PM-4:00 PM**

A randomized phase III trial of systemic therapy plus early local therapy versus systemic therapy alone in women with de novo stage IV breast cancer: A trial of the ECOG-ACRIN Research Group (E2108). *First Author: Seema Ahsan Khan, Northwestern Memorial Hospital, Chicago, IL*

The full, final text of this abstract will be available at abstracts.asco.org at 5:00 p.m. ET on Thursday, May 28.

LBA3 **Plenary Session, Sun, 1:00 PM-4:00 PM**

Carfilzomib, lenalidomide, and dexamethasone (KRd) versus bortezomib, lenalidomide, and dexamethasone (VRd) for initial therapy of newly diagnosed multiple myeloma (NDMM): Results of ENDURANCE (E1A11) phase III trial. *First Author: Shaji Kumar, Mayo Clinic, Rochester, MN*

The full, final text of this abstract will be available at abstracts.asco.org at 5:00 p.m. ET on Thursday, May 28.

LBA4 **Plenary Session, Sun, 1:00 PM-4:00 PM**

First-line therapy of pembrolizumab versus standard of care (SOC) in microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase III, KEYNOTE-177 study. *First Author: Thierry Andre, Sorbonne University and Saint-Antoine Hospital, Paris, France*

The full, final text of this abstract will be available at abstracts.asco.org at 5:00 p.m. ET on Thursday, May 28.

LBA5 **Plenary Session, Sun, 1:00 PM-4:00 PM**

Osimertinib as adjuvant therapy in patients (pts) with stage IB–IIIA EGFR mutation positive (EGFRm) NSCLC after complete tumor resection: ADAURA. *First Author: Roy S. Herbst, Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT*

The full, final text of this abstract will be available at abstracts.asco.org at 5:00 p.m. ET on Thursday, May 28.

100 Clinical Science Symposium, Sat, 1:00 PM-2:30 PM

Phase I study of teclistamab, a humanized B-cell maturation antigen (BCMA) x CD3 bispecific antibody, in relapsed/refractory multiple myeloma (R/R MM). *First Author: Saad Zafar Usmani, Levine Cancer Institute, Atrium Health, Charlotte, NC*

Background: Teclistamab (JNJ-64007957) is a bispecific BCMA x CD3 antibody that induces T cell-mediated cytotoxicity against BCMA-expressing myeloma cells. Initial results from an ongoing study of teclistamab in RRMM (NCT03145181) are presented. **Methods:** Pts have MM and are RR to standard therapies. Primary objective for part 1 is to identify a recommended phase 2 dose(s). Multiple intravenous (iv) doses ± priming doses were explored. Adverse events (AEs) were graded per CTCAE v4.03 and cytokine release syndrome (CRS) per Lee *et al* 2014. Response was investigator-assessed using IMWG criteria; minimal residual disease (MRD) in bone marrow was assessed by next generation sequencing. **Results:** As of 31 Jan 2020, 66 pts had received iv teclistamab (0.3–270 μg/kg). Median age was 64 y (24–82), median prior therapies was 6 (2–14), 97% triple-class exposed, 83% triple-class refractory, and 38% penta-drug refractory. Most common treatment-related AEs (all grade) were CRS (56%), neutropenia (26%), and anemia (23%). CRS events were all grade 1–2 and generally confined to initial doses. 8% of pts had treatment-related neurotoxicity (3% grade ≥3), and 9% had infusion related reaction. Infection-related AEs were reported in 61% of pts (21% grade ≥3). 2 dose-limiting toxicities were reported: grade 4 delirium (resolved after 16 days) and grade 4 thrombocytopenia (resolved after 1 day). 36% of pts had treatment-related grade ≥3 AEs; neutropenia (20%) and anemia (14%) were most frequent. Only 1 grade 5 AE was reported (respiratory failure in the setting of pneumonia deemed unrelated by the investigator). PK results indicate that the half-life of teclistamab supports weekly dosing. On-target pharmacodynamic activity (T cell redistribution and activation along with transient release of cytokines) was observed at doses ≥9.6 μg/kg. Cytokine production was modulated with step-up dosing while T cell activation was maintained. 65 pts were evaluable for response. Activity was observed starting at treatment doses ≥38.4 μg/kg, with 20/52 (38%) pts achieving a response. At the highest dose, 7/9 (78%) pts responded (1 response pending confirmation). Of MRD-evaluable pts who had complete response, 2/2 were MRD negative at 10^{-6} with treatment ongoing > 12 mo. **Conclusions:** Teclistamab has manageable safety across all doses explored. A 78% overall response rate was observed at the highest weekly treatment dose in pts with advanced RRMM, supporting further evaluation of teclistamab in expansion cohorts. Clinical trial information: NCT03145181. Research Sponsor: Janssen R&D.

101 Clinical Science Symposium, Sat, 1:00 PM-2:30 PM

Safety and clinical activity of gene-engineered T-cell therapy targeting HPV-16 E7 for epithelial cancers. *First Author: Christian S. Hinrichs, National Cancer Institute at the National Institutes of Health, Bethesda, MD*

Background: Genetically engineered T-cell therapy has shown remarkable clinical activity in hematologic malignancies. It is not known if this type of treatment can be applied effectively to epithelial cancers, which account for 80% to 90% of human malignancies. **Methods:** We conducted a phase I clinical trial with a 3 + 3 dose escalation in which patients with metastatic HPV-16+ epithelial cancers were treated with a one-time infusion of genetically engineered T cells expressing a T-cell receptor targeting an HLA-A*02:01-restricted epitope of HPV-16 E7 (E7 TCR-T cells). A lymphocyte-depleting conditioning regimen was administered before cell infusion, and high-dose systemic aldesleukin was administered after cell infusion. **Results:** Twelve patients, previously treated with a median of 4 (range, 3 to 7) anticancer agents, were treated. The cell dose was not limited by toxicity. Six patients demonstrated objective clinical responses, which included regression of bulky tumors and complete elimination of some tumors. Responses occurred in patients with vulvar, anal, head and neck, and cervical cancer. Four patients who previously received PD-1-based therapy responded. Response duration ranged from 3 to 9 months. Sustained, high-level engraftment of E7 TCR-T cells in peripheral blood was observed (median after approximately 6 weeks, 66% of total T cells, range 1% to 88%) and correlated with cell dose but not with clinical response. Infused T cell characteristics did not correlate strongly with response. Of the 4 resistant tumors that were studied, 3 demonstrated genetic defects in *HLA-A*02:01* or *B2M* (necessary components of the target complex) and 1 demonstrated copy loss with decreased expression of antigen presentation and interferon response molecules (i.e. *TAP1, TAP2*, *IFNGR1*, *IFNGR2*). Of the 3 sensitive tumors studied, 0 showed genetic defects in these molecules. **Conclusions:** E7 TCR-T cells demonstrated safety and clinical activity in the treatment of highly refractory metastatic HPV-16+ cancers. Treatment resistance was linked to definitive genetic defects in the targeted peptide-HLA complex and to manifold defects in antigen processing and interferon response. Clinical trial information: NCT02858310. Research Sponsor: NIH, Pharmaceutical/ Biotech Company.

102 Clinical Science Symposium, Sat, 1:00 PM-2:30 PM

Phase I dose escalation and expansion trial to assess the safety and efficacy of ADP-A2M4 SPEAR T cells in advanced solid tumors. *First Author: David S. Hong, MD Anderson Cancer Center, Houston, TX*

Background: MAGE-A4 is a cancer/testis antigen with expression in many solid tumors promoting cell growth by preventing cell cycle arrest and apoptosis. This study (NCT03132922) evaluated safety and efficacy of SPEAR T-cells directed against the MAGE-A4 peptide expressed in 9 tumor types. **Methods:** This Phase I dose-escalation, expansion trial evaluated patients (pt) who were HLA-A*02 positive with advanced cancers that expressed the MAGE-A4 protein. Autologous T-cells from eligible patients were isolated, transduced with a lentiviral vector containing the MAGE-A4^{c1032} TCR, and expanded. Prior to ADP-A2M4 infusion, pts received a lymphodepletion regimen of cyclophosphamide and fludarabine. Cohorts 1, 2, 3, and expansion were to receive transduced cell doses of up to: 0.12×10^9, 1.2×10^9, 6×10^9, and 10×10^9, respectively. **Results:** As of 23 October 2019, 9 pts were treated in dose escalation with no DLTs; 25 pts were treated in expansion. Median age was 56.5 yr (range: 31-78). All pts received prior chemotherapy. Most common (> 30%) AEs ≥Grade 3 were lymphopenia, leukopenia, neutropenia, anemia, thrombocytopenia, and febrile neutropenia. Two pts had trial-related deaths (aplastic anemia and CVA) leading to modification of the lymphodepletion regimen and eligibility criteria. In Cohort 3/expansion (28 pts), Best Overall Response was PR (7), SD (11), PD (5), non-evaluable (5). All PRs, at the time of data cut-off, were in patients with synovial sarcoma. Transduced T-cells were detectable in all patients. Tumor infiltration of SPEAR T-cells was detectable in several cohort 3/ expansion pts. **Conclusions:** The Phase I single agent ADP-A2M4 trial will complete enrollment shortly and updated data will be presented. ADP-A2M4 shows promising efficacy and a manageable safety profile at a dose range of $1.2 - 10 \times 10^9$. Clinical activity in various tumors has led to a separate ongoing low dose radiation sub-study of this trial, a Phase II trial in sarcoma (SPEARHEAD-1, NCT04044768), and a Phase I trial (SURPASS, NCT04044859) with ADP-A2M4CD8, a next-generation SPEAR T-cell targeting MAGE-A4. Clinical trial information: NCT03132922. Research Sponsor: Adaptimmune Therapeutics plc.

103 Clinical Science Symposium, Sat, 3:30 PM-5:00 PM

NOMINATOR: Feasibility of genomic testing of rare cancers to match cancer to treatment. *First Author: Damien Kee, Peter MacCallum Cancer Centre, Melbourne, Australia*

Background: Rare cancers (RCs) often lack proven treatments and consequently have poorer outcomes. Identification of molecular biomarkers can facilitate treatment selection and trials access for RC patients (pts) where histology-based trials are not feasible. We assessed the potential for next-generation sequencing (NGS) to impact RC care. **Methods:** Pts with a rare histology, poor-prognosis solid-tumor and no standard of care therapy underwent NGS genomic profiling of paired FFPE tumor and blood (PMCC comprehensive cancer panel; 391 genes). A virtual molecular tumour board (MTB) reviewed curated results regarding diagnosis, actionability (OncoKB) and treatment recommendations. **Results:** Between July 2017 and Nov 2019, 121 pt were prospectively enrolled across 4 Australian sites. 109 (91%) pts had a tumour with an incidence of < 1/100,000 person/years with 83 diverse RC histologies represented. 100 (83%) cases were successfully sequenced. The most commonly aberrant genes (> 10%) were: TP53 (45%), CDKN2A/B, RB1, PTEN and NF1. 51 (51%) had at least one potentially actionable finding, with 27 matched to a clinically validated drug (OncoKB level 3 or better) [Table]. In 6 cases NGS resulted in a revised diagnosis (includes 4 with FDA approved therapy). Actionable germline mutations were detected in 3 individuals of which 2 were previously known. The majority of pts remain in follow-up, however, 8 died prior to or within 28 days of NGS result availability. Drug access remains a limitation with only 12 receiving therapy based on NGS/MTB guidance. Clinical trial information: ACTRN12616001000493. **Conclusions:** NGS in RCs is feasible with potential impact in half of cases. Earlier testing and improved off-label/trial drug access is necessary to increase the likelihood that RC patients may benefit from molecularly guided therapy. Research Sponsor: Melbourne Health, Other Government Agency.

OncoKB Level (Best result per tumour)	N (100)	Genetic biomarker/Diagnosis
No findings	5	
Currently not actionable	44	Includes: TP53, RB1, APC, ARID1A, KMT2D, FAT1, NF2, ATM, ATRX, PBRM1, SMAD4
4 or clinical trial biomarker	24	CDKN2A/B, EGFR amp, MAPK1, NF1, PTEN, RAF1-fusion, SMARCA4/B1, TMB high, XPO1
3	8	AKT, FGFR2-fusion, HRAS, PIK3CA, PTCH1
2	12	ERBB2 amp, BRAF, gBRCA1/2, IDH2, TSC1/2
1	7	BRAF, MSH2/6, Melanoma[#] (4)
#Revised diagnosis	6	RHM > ASTB, DLMGNT > DNT, MEL (4)
Germline	13	ATM, BRCA1/2, CYP2D6, ERCC2, FANCA, FH, MUTYH, NF1, SDHC

104 Clinical Science Symposium, Sat, 3:30 PM-5:00 PM

Different response to ALK inhibitors in EML4-ALK positive mediastinal cancer of unknown primary. *First Author: Chunhong Hu, Department of Oncology, The Second Xiangya Hospital, Central South University, Changsha, China*

Background: With the development of next-generation sequencing (NGS) and precision medicine, targeted therapy especially molecule-driven therapy irrespective of tumor site may play an important role in cancer patients with druggable targets. Cancer of unknown primary (CUP) especially mediastinal CUP (MCUP) has poor prognosis with empirical chemotherapy but may harbor targetable genetic alterations. In the study, we evaluate the response to ALK inhibitors in ALK-positive MCUP. **Methods:** We queried the cancer database of the Second Xiangya hospitalfrom 2018.10 to 2019.12 for patients with ALK-positive cancers regardless of tumor site.Then we selected ALK-positive MCUP patients treated with ALK inhibitors, on which both NGS and programmed death-ligand 1 (PD-L1) testing were performed. **Results:** Forty-eightpatients with ALK-positive cancers were registered in the database. Two MCUP patients were found and showed different response. The first MCUP patient obtaining remarkable response to alectinib harbored ALK/TP53 co-mutation and TERT wild type accompanied by low PD-L1 expression, while the second one showing stable disease with crizotinib carried ALK/TP53/TERT co-mutation and high PD-L1 expression. **Conclusions:** We reveal for the first time that ALK inhibitors are applied to MCUP as first-line therapy and alectinib is firstly reported to treat MCUP patients. ALK inhibitor alectinib is expected to improve outcomes of patients with ALK-positive MCUP. NGS and PD-L1 testing should be recommended for MCUP to get more information about therapy and efficacy. Research Sponsor: None.

Published cases with ALK-positive mediastinal carcinomas of unknown primary.

Year	Age	Sex	Smoke	Histology	Tumor sites	Gene alterations	Therapy	Follow-up (months)	Outcome
2014	55	Female	No	ADC	Mediastinum, neck LNs, breast	ALK fusion	Chemo, crizotinib	>3	Alive without progression
2016	45	Female	No	ADC	Mediastinum, hilar, pleural, adrenal, brain	EML4-ALK fusion	CRT, crizotinib	>40	Alive with recurrence
2016	52	Male	Yes	PDC	Mediastinum	EML4-ALK fusion	Surgery	36	Alive without recurrence
2016	26	Female	Yes	ADC	Ovarian, mediastinal, neck LNs, rib	EML4-ALK fusion	CRT	44	Alive with recurrence
2016	78	Female	Yes	PDC	Mesenteric, pretracheal LNs, bone	EML4-ALK fusion	Symptomatic care	N/A	N/A
2019	31	Female	N/A	ADC	Lung, mediastinum, liver, muscle, skeleton	EML4-ALK fusion	Chemo, crizotinb, brigatinib	6	Alive with progression

Note: eTMs elevated tumor markers, N/A not available, ADC adenocarcinoma, PDC poorly differentiated carcinoma, LNs lymph nodes, Chemo chemotherapy, CRT chemoradiotherapy.

105 Clinical Science Symposium, Sat, 3:30 PM-5:00 PM

Utility of circulating cell-free DNA (cfDNA) analysis in patients with carcinoma of unknown primary (CUP) in identifying alterations with strong evidence for response or resistance to targeted therapy. *First Author: Caroline Weipert, Guardant Health, Redwood City, CA*

Background: CUP is a rare, heterogeneous group of cancers with an overall poor prognosis; the standard treatment remains chemotherapy. The OncoKB database is a curated list of somatic molecular alterations. Alterations with the highest classification must be an FDA-recognized biomarker associated with response to an FDA-approved drug (Level 1), be recommended by major guidelines or expert panels as predictive of response to an FDA-approved drug (Level 2) or be predictive of resistance to an FDA-approved drug (R1). We explored the landscape of alterations classified as Level 1, 2 or R1 based on the OncoKB scale in a large cohort of CUP patients tested via a well-validated cfDNA assay. **Methods:** We queried consecutive samples from advanced cancer patients with a listed diagnosis of CUP who underwent testing via a commercially available liquid biopsy assay (Guardant360) between November 2016 and November 2019. The cfDNA assay included targeted next-generation sequencing of 73- to 74-genes specifically curated to include genes with potential targeted therapy options. Alterations were classified based on their ranking in the OncoKB database as of January 2020. **Results:** In total we identified 2,022 samples with a diagnosis of CUP, and 90.0% of these samples had >1 cfDNA alteration detected. The median age of patients was 68 years and 51% were female. Overall, 20.7% of patients had a Level 1 alteration, 9.5% had a Level 2 alteration, and 23.9% had an R1 alteration (select alterations outlined in Table). **Conclusions:** cfDNA analysis of patients with advanced CUP identified a significant number of patients with alterations associated with strong evidence for either response or resistance to treatment based on the OncoKB classification schema. While many of these alterations are associated with approvals in specific cancer types, the identification of these alterations suggests many CUP patients may have targeted therapy options. We will present case examples illustrating patient outcomes from CUP patients who received targeting therapy based on cfDNA results. Research Sponsor: None.

Alteration	# of Patients (%)
Total Level 1 Alterations	361 (20.7)
***BRAF* V600E**	36 (2.1)
***BRCA1/2* (Loss of Function)**	73 (4.2)
Microsatellite Instability High	20 (2.4)
Total Level 2 Alterations	166 (9.5)
***ERBB2* Activating**	37 (2.1)
***MET* Exon 14 Skipping**	11 (0.6)
Total R1 Alterations	416 (23.9)
***KRAS* G12C**	63 (3.6)

106 Clinical Science Symposium, Sat, 3:30 PM-5:00 PM

NivoCUP: An open-label phase II study on the efficacy of nivolumab in cancer of unknown primary. *First Author: Junko Tanizaki, Kishiwada City Hospital, Kishiwada, Japan*

Background: CUP has a poor prognosis with a median survival of less than 12 months. Given the recent approval of immune checkpoint inhibitors in several cancer types, we performed a multicenter phase II study of nivolumab in CUP patients (pts). **Methods:** The main population of this study is CUP pts who were previously treated with more than one line of systemic chemotherapy. Previously untreated CUP pts were also enrolled for exploratory analysis. Pathological examination (including IHC), CT, FDG-PET, gastroscopy and colonoscopy and medical examination were mandatory for diagnosis of CUP before enrollment. CUP pts belonging to favorable prognosis groups were excluded from the trial. Nivolumab (240 mg/body) was delivered as an intravenous infusion every 2 weeks for up to 52 cycles until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) according to RECIST 1.1 by an Independent Endpoint Review Committee in previously treated pts. The secondary objectives include investigator-assessed ORR, progression-free survival (PFS), overall survival (OS), safety and the association between the efficacy of nivolumab and PD-L1 expression. **Results:** A total of 56 CUP pts, 45 previously treated and 11 previously untreated pts, were enrolled in this trial. The median age was 65.5 years, 22 pts were male. Median follow-up was 8.05 mo (range, 0.1 to 20.7 mo). Of 45 previously treated pts, 2 and 9 had an investigator-assessed complete response and partial response (ORR 24.4%, 95% CI: 12.9-39.5%), with a median PFS (mPFS) and OS (mOS) of 5.4 mo (95% CI: 2.6-6.9) and 15.1 mo (95% CI: 8.3-NR), respectively. Among 11 previously untreated pts, 1 pt had partial response (ORR 9.1%, 95% CI: 0.2-41.3%). The mPFS was 3.9 mo and the mOS was not reached in untreated pts (95% CI: 1.1-5.6, and 95% CI: 2.6-NR, respectively). Nivolumab demonstrated a mPFS of 5.1mo (95% CI: 2.7-5.6) and a mOS of 15.9 mo (95% CI: 8.4-NR) in an overall population. Immune-related adverse events occurred in 57% of overall pts with 5% of grade 3 or higher, and the most common were rash (27%), hypothyroidism (16%), and diarrhea/colitis (16%). No treatment related death was observed. **Conclusions:** In pts with previously treated and untreated CUP, nivolumab demonstrated durable antitumor activity with a manageable safety. Clinical trial information: UMIN000030649. Research Sponsor: ONO PHARMACEUTICAL CO., LTD.

107 Clinical Science Symposium, Sun, 10:30 AM-12:00 PM

Updated entrectinib data in children and adolescents with recurrent or refractory solid tumors, including primary CNS tumors. *First Author: Ami Vijay Desai, University of Chicago Medical Center, Chicago, IL*

Background: The phase 1/2 STARTRK-NG trial (NCT02650401) is evaluating entrectinib, a CNS-penetrant oral inhibitor of TRK, ROS1 and ALK tyrosine kinases, in children and adolescents < 21 years old with recurrent/refractory solid tumors, including primary CNS tumors. **Methods:** After determining the recommended dose as 550mg/m^2/day in all-comers, expansion cohorts with gene-fusion-positive CNS/solid tumors (*NTRK1/2/3* and *ROS1*) are being enrolled. **Results:** As of 1 July 2019 (data cut-off), 34 patients (4.9 months to 20 years old; median age 7 years) have been evaluated for response to treatment with entrectinib. Responses were classified as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD) using RANO for CNS tumors, RECISTv1.1 for solid tumors, or Curie score for neuroblastomas. Responses in fusion-positive patients were assessed by blinded independent central review (BICR), and occurred at doses ≥400mg/m^2. Best responses in patients with fusion-positive CNS tumors (n = 8) were four CR (*ETV6-NTRK3, EML1-NTRK2, GOPC-ROS1,* and *TPR-NTRK1*), two PR (*KANK1-NTRK2* and *EEF1G-ROS1*), and two PD (*EML4-ALK* and *PARP6-NTRK3*). In patients with fusion-positive solid tumors (n = 6) best responses were three CR (*DCTN1-ALK, ETV6-NTRK3,* and *ETV6-NTRK3*), and three PR (*TFG-ROS1, EML4-NTRK3,* and *KIF5B-ALK*). Responses (Investigator-assessed) in patients with non-fusion tumors (n = 20) were one CR (*ALK F1174L* mutation), four SD, ten PD, and five patients were unevaluable or had no data. The objective response rate (defined as the total number of CR and PR) in fusion-positive patients was 86% (12/14) versus 5% (1/20) in non-fusion patients. Similarly, PFS was 17.5 months (95% CI 7.4–NE) in fusion-positive patients versus 1.9 months (1.8–5.7; p = 0.0002) in non-fusion patients. Most commonly reported treatment-related adverse events included weight gain (n = 14 [5 Grade 3/4]), elevated creatinine (n = 13), anemia (n = 13), nausea (n = 11), increased ALT (n = 10 [1 Grade 3/4]), increased AST (n = 10 [1 Grade 3/4]), decreased neutrophils (n = 9 [6 Grade 3/4]), and bone fractures (n = 7, of which 4 were treatment related). **Conclusions:** In children and adolescents < 21 years old, entrectinib has produced striking, rapid, and durable responses in solid tumors with target gene fusions, especially in high-grade CNS neoplasms. Clinical trial information: NCT02650401. Research Sponsor: Hoffmann-La Roche.

108 Clinical Science Symposium, Sun, 10:30 AM-12:00 PM

FOENIX-CCA2: A phase II, open-label, multicenter study of futibatinib in patients (pts) with intrahepatic cholangiocarcinoma (iCCA) harboring *FGFR2* gene fusions or other rearrangements. *First Author: Lipika Goyal, Massachusetts General Hospital, Boston, MA*

Background: Patients (pts) with intrahepatic cholangiocarcinoma (iCCA) have a 5-year survival rate of 24%. There is no standard treatment for advanced disease after first-line chemotherapy. Fibroblast growth factor receptor-2 (*FGFR2*) gene fusions occur in 10% to 20% of pts with iCCA, offering a promising therapeutic avenue for this disease. Futibatinib is a highly selective irreversible FGFR1-4 inhibitor given as a continuous once-daily (QD) oral regimen. This phase 2 registrational trial was initiated because of results from a phase 1 dose escalation/expansion study showing tolerability and preliminary efficacy of futibatinib in pts with iCCA with *FGFR2* fusions. **Methods:** FOENIX-CCA2 (NCT02052778), a single-arm multicenter phase 2 study, enrolled pts with locally advanced/metastatic unresectable iCCA harboring *FGFR2* gene fusions or other rearrangements, disease progression after ≥1 line of systemic therapy (including gemcitabine plus platinum-based chemotherapy), no prior FGFR inhibitor treatment, and an ECOG performance status of 0 or 1. Pts received futibatinib 20 mg QD until disease progression/unacceptable toxicity. The primary endpoint is objective response rate (ORR) based on independent central radiology review. Secondary endpoints include disease control rate (DCR), duration of response (DOR), and safety. **Results:** A total of 103 pts were enrolled. For this interim analysis, data are reported for the 67 pts (65%) with ≥6 months of follow-up. Of these, 82.1% of pts had tumors harboring an *FGFR2* fusion. One, 2, or ≥3 prior therapies were received by 44.8%, 28.4%, and 26.9% of pts, respectively. ORR was 34.3% (all partial response, n = 23), and DCR was 76.1%; assessment was pending for 8 pts. Median time to response was 1.6 months (range, 1.0-4.9), and median DOR was 6.2 months (range, 2.1-14.2). The most common treatment-related adverse events (AEs; all grade, grade ≥3) were hyperphosphatemia (79.1%, 25.4%), diarrhea (37.3%, 0%), and dry mouth (32.8%, 0%). Any-cause grade ≥3 AEs were reported in 73.1% of pts. Dose delay or dose reduction was required in 65.7% and 53.7% of pts, respectively; 6.0% of pts discontinued treatment because of AEs. **Conclusions:** Preliminary assessment of these phase 2 data indicate efficacy and tolerability of futibatinib for treatment of pts with iCCA harboring *FGFR2* fusions or other rearrangements who have progressed after chemotherapy. Continued analysis of the study population is underway. Clinical trial information: NCT02052778. Research Sponsor: Taiho Oncology, Inc.

109 Clinical Science Symposium, Sun, 10:30 AM-12:00 PM

Clinical activity of the RET inhibitor pralsetinib (BLU-667) in patients with RET fusion+ solid tumors. *First Author: Vivek Subbiah, Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: RET gene fusions are targetable oncogenic drivers in multiple tumor types, including up to 20% of papillary thyroid cancers (PTC). Pralsetinib is an investigational, highly potent, selective inhibitor of oncogenic RET alterations. In the registration-enabling Phase 1/2 ARROW study (NCT03037385), pralsetinib demonstrated an overall response rate (ORR; response-evaluable patients [REP], central review) of 73% (19/26) in treatment-naïve patients and 61% (49/80; 2 pending confirmation) in platinum-exposed patients with RET fusion+ non-small cell lung cancer (NSCLC) and was well tolerated (data cut-off November 18, 2019). We provide an update on the clinical activity of pralsetinib in other RET fusion+ solid tumor types. **Methods:** ARROW consists of a phase 1 dose escalation (30–600 mg once [QD] or twice daily) followed by a phase 2 expansion (400 mg QD) in patients with advanced RET-altered solid tumors. Primary objectives were ORR and safety. **Results:** As of November 18, 2019, 29 patients with metastatic solid tumor types other than NSCLC (16 PTC, 1 undifferentiated thyroid, 3 pancreatic, 3 colon, 6 other) bearing a RET fusion have received pralsetinib. Efficacy data are presented for REP enrolled by July 11, 2019. In patients with thyroid cancer that is RET fusion+, ORR (investigator assessment) was 75% (9/12; all confirmed). Median (range) duration of response (DOR) was 14.5 (3.7+, 16.8) months (mo), with 67% of responding patients continuing treatment. Two patients with stable disease were continuing treatment at 11.5+ and 19.3+ mo. In other RET fusion+ cancers, ORR was 60% (3/5; all confirmed) with partial responses in 2/2 patients with pancreatic cancer (DOR 5.5, 7.4+ mo) and 1 patient with intrahepatic bile duct carcinoma (DOR 7.5 mo). Two patients with colon cancer had stable disease for 7.3 and 9.3 mo. Responses were observed across multiple fusion genotypes. In the entire safety population (all patients treated with 400 mg QD pralsetinib, regardless of diagnosis; n = 354), most treatment-related adverse events (TRAEs) were grade 1-2, and included increased aspartate aminotransferase (31%), anemia (22%), increased alanine aminotransferase (21%), constipation (21%) and hypertension (20%). Only 4% of patients in the safety population discontinued due to TRAEs. **Conclusions:** Pralsetinib demonstrated broad and durable antitumor activity across multiple advanced solid tumor types, regardless of RET fusion genotype, and was well tolerated. The study is ongoing and still enrolling patients in this cohort. Clinical trial information: NCT03037385. Research Sponsor: Blueprint Medicines Inc.

LBA110 Clinical Science Symposium, Sat, 4:30 PM-5:30 PM

Clinical impact of COVID-19 on patients with cancer: Data from the COVID-19 and Cancer Consortium (CCC19). *First Author: Jeremy Lyle Warner, Vanderbilt-Ingram Cancer Center, Nashville, TN*

The full, final text of this abstract will be available at abstracts.asco.org at 5:00 p.m. ET on Thursday, May 28.

LBA111 Clinical Science Symposium, Sat, 4:30 PM-5:30 PM

Thoracic Cancers International COVID-19 Collaboration (TERAVOLT): Impact of type of cancer therapy and COVID therapy on survival. *First Author: Leora Horn, Department of Medicine, Vanderbilt Ingram Cancer Center, Nashville, TN*

The full, final text of this abstract will be available at abstracts.asco.org at 5:00 p.m. ET on Thursday, May 28.

500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Primary analysis of KAITLIN: A phase III study of trastuzumab emtansine (T-DM1) + pertuzumab versus trastuzumab + pertuzumab + taxane, after anthracyclines as adjuvant therapy for high-risk HER2-positive early breast cancer (EBC). *First Author: Nadia Harbeck, Brustzentrum der Universität München (LMU), Munich, Germany*

Background: The standard of care for HER2-positive EBC is chemotherapy plus one year of HER2-directed therapy. However, recurrence—particularly in high-risk populations—remains a problem, as does systemic chemotherapy-associated toxicity. In KAITLIN, we aimed to improve efficacy and reduce toxicity by replacing taxanes and trastuzumab with T-DM1. **Methods:** KAITLIN (NCT01966471) is a phase 3, randomized, open-label study that enrolled 1846 patients with adequately excised, centrally confirmed HER2-positive EBC either node-positive (LN+); or node-negative, HR-negative, and tumor size > 2.0 cm. Within 9 weeks of surgery, patients were randomized 1:1 to 3-4 cycles of anthracycline-based chemotherapy followed by 18 cycles of T-DM1 3.6 mg/kg + pertuzumab 420 mg q3w (loading dose [LD] 840 mg) (AC-KP) or taxane (3-4 cycles) + concurrent trastuzumab 6 mg/kg (LD 8 mg/kg) + pertuzumab 420 mg q3w (LD 840 mg) (AC-THP). Patients were stratified by world region, nodal status, HR status, and anthracycline type. Adjuvant radiotherapy and/or endocrine therapy was administered after 4 cycles of HER2-targeted therapy when indicated. The co-primary endpoints were invasive disease-free survival (IDFS) in the LN+ and in the ITT populations applying a hierarchical testing procedure. Secondary endpoints included overall survival (OS), patient-reported outcomes (PROs), and safety. **Results:** KAITLIN did not meet its co-primary endpoints. In LN+ patients (n = 1658), there was no significant difference between arms in IDFS event risk (stratified hazard ratio = 0.97; 95%CI 0.71–1.32). Three-year IDFS was 94.1% with AC-THP and 92.7% with AC-KP. Results were similar in the ITT population (stratified hazard ratio = 0.98; 95%CI 0.72–1.32; 3-year IDFS: 94.2% vs 93.1%). OS data are immature with an event rate of ~4%–5% in each arm. During the study overall, there was a similar incidence of grade ≥3 AEs (55.4% vs 51.8%) and SAEs (23.3% vs 21.4%) with AC-THP and AC-KP, respectively. More patients receiving AC-KP than AC-THP discontinued T-DM1 or trastuzumab, respectively, because of AEs (26.8% vs 4.0%). PRO data will be presented. **Conclusions:** Replacing adjuvant taxane and trastuzumab with T-DM1 did not result in significantly improved efficacy or overall safety. Nonetheless, in this high-risk population, a favorable IDFS outcome was achieved in both study arms. HP + chemotherapy remains the standard of care for patients with high-risk HER2-positive EBC. Clinical trial information: NCT01966471. Research Sponsor: F. Hoffmann-La Roche.

501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Three-year follow-up of neoadjuvant chemotherapy with or without anthracyclines in the presence of dual HER2-blockade for HER2-positive breast cancer (TRAIN-2): A randomized phase III trial. *First Author: Anna van der Voort, Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: The multicenter phase III TRAIN-2 study showed high pathological complete response (pCR) rates after neoadjuvant chemotherapy with and without anthracylines plus dual HER2-blockade in stage II-III HER2-positive breast cancer patients (67% vs 68%, p = 0.95) (NCT01996267). Here we report 3-year efficacy and safety outcomes. **Methods:** Patients were randomly assigned (1:1) to receive 3 cycles 5-fluoruoracil (500mg/m^2), epirubicin (90mg/m^2), and cyclophosphamide (500mg/m^2) followed by 6 cycles paclitaxel (80mg/m^2 day 1 and 8) and carboplatin (AUC = 6mg/ml·min) (FEC-PC) or 9 cycles paclitaxel and carboplatin (PC). Both regimens were combined with trastuzumab (T; 6mg/kg, loading dose 8mg/kg) and pertuzumab (Ptz; 420mg, loading dose 840mg). Patients completed one year of trastuzumab, radiotherapy and endocrine therapy as indicated. The primary endpoint pCR was previously reported. Secondary efficacy endpoints reported here are event-free-survival (EFS) defined as time from randomization to first event (disease progression resulting in inoperability, recurrence [contralateral DCIS excluded], secondary primary malignancies, or death) and overall survival (OS), both in the intention-to-treat population. Safety endpoints are reported for patients treated with at least one dose of study medication. **Results:** 438 patients were randomized (219/arm) and evaluable for long-term efficacy endpoints. After a median follow-up of 48.8 months 23 EFS events occurred in the FECT-PTC-Ptz-arm and 21 in the PTC-Ptz-arm (HR 0.90; 95% CI 0.50-1.63). Three-year EFS estimates were 92.7% (95% CI: 89.3-96.2) for FECT-PTC-Ptz and 93.6% (95% CI: 90.4-96.9) for PTC-Ptz. Three-year OS estimates were 97.7% (95% CI: 95.7-99.7) for FECT-PTC-Ptz and 98.2% (95% CI: 96.4-100) for PTC-Ptz. These results were irrespective of hormone receptor and nodal status. LVEF decline ≥10% from baseline and < 50% was more common in patients who received anthracyclines than in the PTC-Ptz arm (8.6% vs. 3.2%, p = 0.021). Two patients in the FECT-PTC-Ptz arm developed acute leukemia. No other new safety concerns were seen. **Conclusions:** The 3-year follow-up of the TRAIN-2 study confirms the results of the primary outcome that anthracylines do not improve efficacy and are associated with clinically relevant toxicity. A neoadjuvant carboplatin-taxane based regimen with dual HER2-blockade can be considered in all stage II-III breast cancer patients, regardless of hormone receptor and nodal status. Clinical trial information: NCT01996267. Research Sponsor: Roche.

502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Biomarker data from KATHERINE: A phase III study of adjuvant trastuzumab emtansine (T-DM1) versus trastuzumab (H) in patients with residual invasive disease after neoadjuvant therapy for HER2-positive breast cancer. *First Author: Carsten Denkert, Philipps University Marburg, Marburg, Germany*

Background: The phase 3 KATHERINE study (NCT01772472) compared adjuvant T-DM1 versus H in patients with residual invasive breast cancer after neoadjuvant chemotherapy plus HER2-targeted therapy. Here we report exploratory analyses of the relationship between invasive disease-free survival (IDFS) and biomarkers potentially related to response. **Methods:** Formalin fixed paraffin-embedded tissue samples were collected before neoadjuvant treatment and/or at surgery. Surgical samples were used for analyses, except when only pre-treatment samples were available (~20% of cases). DNA was derived to identify *PIK3CA* hotspot mutations and gene expression (RNA) analysis was used to detect HER2, PD-L1, CD8 and predefined immune signatures including 3-gene, 5-gene, Teffector, chemokine signaling, and checkpoint inhibitor signatures. RNA analysis was adjusted for tumor content and expression levels were dichotomized at the median into low (≤) and high (>) groups. The effect of treatment and biomarkers on IDFS was assessed. **Results:** *PIK3CA* mutation (mut) status was available from 1363 (91.7%) patients. T-DM1 IDFS benefit was independent of *PIK3CA* mut status (mut: HR 0.54; 95%CI 0.23–0.90; non-mut: HR 0.48; 95% CI 0.35–0.65) and no impact of *PIK3CA* mut was observed within either treatment arm. Gene expression data were available from 1059 (71.3%) patients. Similar gene expression levels were observed between treatment arms, but, unlike the surgical samples (n = 815), the pre-treatment samples (n = 244) were not representative of the ITT population. Thus, subsequent analyses were based on surgical samples (H n = 398; T-DM1 n = 417). Consistent treatment benefit with T-DM1 vs H was observed across the single-gene and immune gene-signature subgroups as in the ITT population. High vs low HER2 expression was associated with worse outcome (HR 2.02; 95% CI 1.32–3.11) within the H arm, but not within the T-DM1 arm (HR 1.01; 95% CI 0.56–1.83). High vs low PD-L1 expression was associated with better outcome within the H arm (HR 0.66; 95% CI 0.44–1.00) but not within the T-DM1 arm (HR 1.05; 95% CI 0.59–1.87). Similar trends were observed in the checkpoint inhibitor subgroups. **Conclusions:** These exploratory analyses provide the first data on the relationship between biomarker expression in residual disease after HER2-targeted therapy and outcomes. *PIK3CA* mut status did not influence outcomes with H or T-DM1. T-DM1 benefit appeared to be independent of all biomarkers assessed. Clinical trial information: NCT01772472. Research Sponsor: F. Hoffmann-La Roche Ltd.

503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Chemotherapy (CT) de-escalation using an FDG-PET/CT (F-PET) and pathological response-adapted strategy in HER2[+] early breast cancer (EBC): PHERGain Trial. *First Author: Javier Cortes, IOB Institute of Oncology, Hospital Quirónsalud, Medica Scientia Innovation Research, and Vall d'Hebron University of Oncology, Barcelona, Spain*

Background: Dual trastuzumab plus pertuzumab (HP) has shown promising pathologic complete response (pCR) rates in HER2[+] EBC although lower to CT regimens. Identification of new markers of sensitivity to HP could help to de-escalate CT. PHERGain assessed early metabolic response by F-PET to neoadjuvant HP and the opportunity of CT de-escalation with a response-adapted strategy in patients (pts) with HER2[+] EBC. **Methods:** PHERGain randomized (1:4 ratio) centrally-confirmed HER2[+] stage I-III EBC pts to receive either docetaxel (T), carboplatin (C), and HP (cohort A) or HP ± endocrine therapy (ET) (cohort B). Randomization was stratified by hormone receptor (HR) status. Pts with subclinical metastases by F-PET were included in a different cohort (cohort C). Centrally-reviewed F-PET was performed prior to randomization and after 2 cycles of TX (cohorts A/B). Cohort A pts completed a total of 6 cycles regardless of F-PET results. Cohort B/PET-responder (RX) pts continued with HP ± ET for 6 cycles, while PET-non-RX pts were switched to receive 6 cycles of TCHP. After surgery, cohort B/PET-RX pts who did not achieve a pCR received 6 cycles of TCHP and all pts from cohorts A/B completed 18 cycles of HP. Cohort C pts received 6 cycles of TCHP. Co-primary endpoints were breast/axilla pCR rate (ypT0/isN0) among cohort B/PET-RX pts and 3-year invasive disease-free survival (iDFS) in pts allocated to cohort B. **Results:** A total of 376 pts were included (71 pts in cohort A, 285 pts in cohort B, and 20 pts in cohort C). In cohort B, median age was 50 years, 49.2% had node-positive disease, and 67.4% had HR+ tumors. pCR in cohort A was achieved in 41 pts (57.7%, 95% CI 47.4-69.4%) and it was observed in 101 pts included in cohort B (35.4%, 95% CI 29.9-41.3%). Among cohort B pts, 227 (79.6%) were PET-RX; 86 of them (37.9%, 95% CI 31.6-44.5%) obtained a pCR. Among PET-non-RX pts, 15 (25.9%, 95% CI 15.3-39%) achieved a pCR after adding CT (TCHP). PET-RX pCR by HR status was 44.3% for HR[-] and 35% for HR[+] (p = 0.184). The incidence of commonly reported adverse events (AEs) was higher in pts allocated to cohort A (grade≥3 AEs 58.8 vs 12%; serious AEs 29.4 vs 4.6%). The rate of pts with a ≥10% global health status decline in cohorts A and B were 40.8 and 23.5%, respectively. **Conclusions:** F-PET identify pts with HER2[+] EBC who are more likely to benefit from CT-free dual HER2-blockade with HP. Follow-up is ongoing for iDFS endpoint. Depending on the results of this second co-primary endpoint, this strategy could select a group of HER2[+] EBC pts who would not need CT. Clinical trial information: NCT03161353. Research Sponsor: F. Hoffmann-La Roche Ltd.

504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

ALTERNATE: Neoadjuvant endocrine treatment (NET) approaches for clinical stage II or III estrogen receptor-positive HER2-negative breast cancer (ER+ HER2- BC) in postmenopausal (PM) women: Alliance A011106. *First Author: Cynthia X. Ma, Washington University School of Medicine in St. Louis, St. Louis, MO*

Background: For PM patients (pts) with locally advanced ER+ HER2- BC, NET improves breast conservation surgery (BCS) rates, and modified preoperative endocrine prognostic index (mPEPI) 0, defined as pT1-2 pN0 Ki67< 2.7%, or pathologic complete response (pCR: no invasive disease in breast or lymph node) is associated with low risk of recurrence without adjuvant chemotherapy (CT). The ALTERNATE trial was initiated to assess if the endocrine-sensitive disease rate (ESDR: number of mPEPI 0 pts/number of eligible pts initiating NET) with fulvestrant (F) or F+anastrozole (A) is improved relative to A alone (reported here) and if the 5-year (yr) recurrence-free survival (RFS) rate for pts with mPEPI 0 on A alone without CT is ≥ 95% (awaits further follow-up). **Methods:** PM pts with clinical stage II/III ER+ HER2- BC were randomized 1:1:1 to 1 mg A po daily, 500 mg F IM every 4 week (wk)s after loading dose, or A+F for 6 months. Ki67 was tested centrally on biopsies acquired prior to NET, wk 4, wk 12 and at surgery. Pts with Ki67 >10% at wk 4 or 12 were recommended to go off protocol-directed ET and switch to CT. Pts with mPEPI 0 at surgery were recommended to continue assigned ET for 1.5 yrs followed by A for a total of 5 yrs ET (and not to receive CT). The primary endpoint of the neoadjuvant phase was ESDR. ESDR of each F arm was compared to that of the A alone arm. With 425 pts per arm, a one-tailed alpha = 0.025 chi-square test of two independent proportions has 84% power to detect an increase of ≥10% in ESDR for F or F+A compared to the A arm, assuming ESDR ≤30% in A. **Results:** 1362 pts (A 452; F 454; A+F 456) were enrolled Feb 2014 to Nov 2018. 63 pts were excluded (did not start NET). Of the remaining 1299 pts (A 434; F 431, A+F 434), 42% were cN1-3 and 73% were considered candidates for BCS. ESDR was 18.6% (95%CI: 15.1-22.7%) with A, 22.7% (95%CI: 18.9-27.0%) with F, and 20.5% (95%CI: 16.8-24.6%) with A+F. No significant difference in ESDR was found between A and F (p=0.15) or A and A+F (p=0.55). Among the 825 pts with wk 4 Ki67 < 10% who completed NET and surgery, ESDR and the BCS rate were 27.7% and 70.3% with A; 29.6% and 68.1% with F, and 26.8% and 69.9% with A+F, respectively. **Conclusion:** Neither F nor F+A significantly improved ESDR compared to A alone in PM pts with locally advanced ER+ HER2- BC. RFS data are awaited. Support: U10CA180821, U10CA180882, U24CA196171, https://acknowledgments.alliancefound.org; NCI BIQSFP, BCRF, Genentech, AstraZeneca. Clinical trial information: NCT01953588. Research Sponsor: U10CA180821, U10CA180882, U24CA196171; Alliance Foundation, NCI Biomarker, Imaging and Quality of Life Studies Funding Program (BIQSFP), Breast Cancer Research Foundation, Genentech, AstraZeneca, https://acknowledgments.alliancefound.org.

505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Letrozole + ribociclib versus letrozole + placebo as neoadjuvant therapy for ER+ breast cancer (FELINE trial). *First Author: Qamar J. Khan, University of Kansas Medical Center, Westwood, KS*

Background: Ribociclib (R) + letrozole (L) is superior to L in metastatic breast cancer (BC). Preoperative endocrine prognostic index (PEPI) score 0 after neoadjuvant endocrine therapy (NET) is associated with low risk of relapse without chemotherapy in ER+ BC. On-therapy change in Ki-67 predicts adjuvant recurrence. FELINE is a biomarker-based multicenter randomized trial comparing changes in Ki-67 and PEPI between L+ Placebo (P) & L+R. **Methods:** Postmenopausal women with >2 cm or node+ ER+ HER2- BC were randomized 1:1:1 between L+P, L+R 400 mg continuous dose (Rc) and L+R 600 mg, 3 weeks on/1 week off - intermittent dose (Ri). Treatment was continued for six 28-day cycles. Core biopsies, blood samples were obtained at baseline, Day 14 cycle 1 (D14C1), and surgery. Clinical measurement, mammogram and US were obtained at baseline, surgery; MRI at baseline, week 8. Primary endpoint was rate of PEPI score 0 between L+P and L+R (i+c combined). Other endpoints were change in centrally performed Ki-67, complete cell cycle arrest (CCCA): Ki-67 <2.7%, clinical/imaging response, and difference in response & toxicity between the two R (Rc and Ri) arms. **Results:** From 2/2016 to 8/2018, 120 women were enrolled at 9 US centers. Thirty-eight were randomized to L+P and 82 to L+R groups (41 in Ri and Rc). Treatment groups were balanced at baseline. PEPI score of 0 was equal (25%) in L+P & L+R groups. CCCA at D14C1 was observed in 52% vs. 92% in L+P, L+R respectively ($p < 0.0001$). CCCA at surgery was observed in 63.3% vs. 71.4% in L+P, L+R respectively (p = NS). A significant increase in Ki-67 was observed between D14C1 and surgery in 66% vs. 33% in L+R, L+P respectively (p = 0.006). There was no difference in clinical, mammographic, US or MRI response between L+P and L+R. CCCA at D14C1 and surgery was similar in Ri & Rc arms. Grade >3 AEs were observed in 4 (10%) patients in L+P, 23 (56%) in L+Ri, 19 (46%) in L+Rc arms. **Conclusions:** Addition of R to L as NET did not result in more women with a PEPI score of 0. At D14C1 twice as many women on L+R had CCCA compared to L+P (92% vs 52%). However, significantly more women on L+R had increased proliferation between D14C1 and surgery, resulting in similar CCCA at surgery. Correlative studies are being performed to determine mechanisms of on-therapy acquired resistance to ribociclib. Continuous and intermittent doses of R have similar efficacy, toxicity. Clinical trial information: NCT02712723. Research Sponsor: Novartis.

	L+P	L+R	p-value
PEPI 0 (%)	25.8	25.4	0.96
D14C1-Ki-67 > 10% (%)	17.2	4.0	0.025*
CCCA at D14C1 (%)	51.7	91.9	< 0.0001*
CCCA at surgery (%)	63.3	71.4	0.42
Ki-67 increase D14C1 to surgery (%)	33.3	65.7	0.006*

506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

MINDACT: Long-term results of the large prospective trial testing the 70-gene signature MammaPrint as guidance for adjuvant chemotherapy in breast cancer patients. *First Author: Fatima Cardoso, Champalimaud Clinical Center/Champalimaud Foundation, Lisbon, Portugal*

Background: The 70-gene signature MammaPrint has been shown to identify breast cancer patients for whom adjuvant chemotherapy (CT) could be safely omitted even in the presence of unfavorable standard clinical-pathological criteria. The MINDACT primary endpoint at 5 years median follow-up was met in 2016 (Cardoso et al, NEJM 2016) with a distant metastasis free survival (DMFS) rate at 5 years of 94.7% (95% CI: 92.5-96.2) in clinical high (C-High) / genomic low (G-Low) risk patients who received no CT. Longer follow-up is now available. **Methods:** 6693 patients were enrolled in the prospective phase III randomized MINDACT study (EORTC 10041/BIG3-04) between 2007-2011. We assessed the DMFS rate at 5 years in the primary test (PT) population of C-High / G-Low patients who were randomized to receive no CT (n = 644). As secondary analysis, we evaluated DMFS and overall survival (OS) in the intention to treat (ITT) population of the C-High / G-Low group randomized to CT vs no CT (n = 749 and 748 respectively). Comparisons between CT and no CT groups are low-powered. We used Kaplan-Meier estimates for time to event endpoints and hazard ratios (HR) with 95% CI from cox-regression models adjusted for stratification factors used for the randomization. **Results:** The median follow-up is 8.7 years, resulting in an updated 5-year DMFS rate for the PT population of C-High / G-Low patients with no CT of 95.1% (95% CI 93.1-96.6). The updated outcomes of the ITT population of C-High / G-Low patients are shown in the table. Further analyses will update the suggested age-dependent effect of CT omission for luminal breast cancer seen at 5 years in pre- versus post-menopausal women as in Tailor-X (Piccart et al, SABCS 2019). **Conclusions:** The primary DMFS endpoint at 5 years continues to be met in CT untreated C-High / G-Low risk women, confirming MINDACT as a positive de-escalation study. With longer follow-up and in line with the natural history of luminal breast cancer, more distant relapses do occur but the estimated gain of 2.6% for CT administration in C-High / G-Low patients remains small in light of CT harmful effects. The level IA evidence for the clinical utility of the 70-gene signature for adjuvant CT decision making is maintained. Clinical trial information: NCT00433589. Research Sponsor: MINDACT was supported by grants from the European Commission Framework Programme VI (FP6-LSHC-CT-2004-503426, "TRANSBIG Network of Excellence"), the Breast Cancer Research Foundation, the U.S. National Cancer Institute, the European Breast Cancer Council-, Pharmaceutical/Biotech Company, U.S. National Institutes of Health.

C-High / G-Low patients (ITT population): updated outcomes		
	DMFS with CT	**DMFS without CT**
At 5 years (95% CI)	95.7% (93.9-96.9)	94.8% (92.9-96.2)
At 8 years (95% CI)	92.0% (89.6-93.8)	89.4% (86.8-91.5)
	OS with CT	OS without CT
At 8 years (95% CI)	95.7% (93.9-97.0)	94.3% (92.2-95.8)

507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase III trial of metronomic capecitabine maintenance after standard treatment in operable triple-negative breast cancer (SYSUCC-001). *First Author: XI Wang, Departments of Breast Oncology, Sun Yat-Sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, China*

Background: Triple-negative breast cancer (TNBC) has a relatively high relapse rate and poor outcome after standard therapy among all subtypes of breast cancer. Effective strategies to reduce risk of relapse and death are unmet medical needs. **Methods:** In this phase III trial, patients with operable TNBC were randomly assigned to receive metronomic capecitabine (650 mg/m^2 twice daily continuously for one year) as maintenance therapy or observation after standard local and systemic treatment for curative intent. The primary end point was disease-free survival (DFS). Secondary end points included distant disease-free survival (DDFS), overall survival (OS) and safety. **Results:** A total of 434 patients were randomly assigned to capecitabine group (n = 221) or observation group (n = 213). At a median follow-up of 56.5 months, 5-year DFS was significantly better in capecitabine group than in observation group (83% vs. 73%, HR, 0.63; 95% CI, 0.42 to 0.96; $p = 0.027$). 5-year DDFS was also significantly better in capecitabine group than in observation group (85% vs. 76%, HR, 0.56; 95% CI, 0.37 to 0.90; $p = 0.016$). However, 5-year OS was not significantly different between two groups (85% vs. 81%, HR, 0.74; 95% CI, 0.47 to 1.18; $p = 0.203$). Two hundred and two (91.4%) of patients completed one year of capecitabine therapy as planned. The most common capecitabine-related adverse events were hand-foot syndrome (46%), leukopenia (24%), Hyperbilirubinemia (13%), gastrointestinal pain (7%) and elevated serum transaminases (5%). **Conclusions:** Maintenance therapy with metronomic capecitabine for one year following standard treatment significantly improved DFS in operable TNBC, which was safe and well tolerated. (SYSUCC-001, ClinicaltTrials.gov number, NCT01112826). Clinical trial information: NCT01112826. Research Sponsor: the Sun Yat-sen University Clinical Research 5010 Program (Grant No. 2012014).

508 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Primary results of NRG Oncology / NSABP B-43: Phase III trial comparing concurrent trastuzumab (T) and radiation therapy (RT) with RT alone for women with HER2-positive ductal carcinoma in situ (DCIS) after lumpectomy. *First Author: Melody A. Cobleigh, NRG Oncology, and Rush University Cancer Center, Chicago, PA*

Background: Preclinical studies report that T can boost RT effectiveness. The primary aim of this trial assessed the efficacy of concurrent T + RT vs RT alone in preventing recurrence of ipsilateral breast cancer, ipsilateral skin cancer, or ipsilateral DCIS (IBTR) in women with DCIS. **Methods:** Eligibility: Women ≥18 yrs, ECOG performance status 0 or 1, DCIS resected by lumpectomy, and clear margins. Whole-breast RT after randomization was with 25+ fractions or accelerated with 16-17 fractions. RT boost was allowed. Centralized HER2 testing and ER and/or PR were required before entry. Stratification was by menopausal status, adjuvant endocrine therapy plan, and nuclear grade. T was given at 8 mg/kg IV within 1 wk before and 5 days after RT began (Dose 1) and at 6 mg/kg IV 3 wks after Dose 1 (Dose 2). Definitive intent-to-treat primary analysis was to be conducted when either 163 IBTR events were recorded or when all accrued pts were on study for ≥5 yrs. **Results:** 2014 pts were randomized (11/9/08 to 12/8/14);1998 (99.2%) had follow-up information. Median follow-up time on 12/31/19 was 79.2 mos. 2001 pts had RT information, 1965 (98.2%) completed RT: 988 (98.3%) in the RT arm and 977 (98.1%) in the RT+T arm. 996 pts had T compliance information in the RT+T arm, 939 (94.3%) completed two doses of T, 25 (2.5%) had one dose of T, and 32 (3.2%) did not receive T. At primary definitive analysis, 114 IBTR events occurred: 63 in the RT arm and 51 in the RT+T arm (HR = 0.81 [95% CI: 0.56-1.17], p-value = 0.26). 38 were invasive: 18 in the RT arm and 20 in the RT+T arm (HR = 1.11 [95% CI: 0.59-2.10], p-value = 0.74). 76 were DCIS: 45 in the RT arm and 31 in the RT+T arm (HR = 0.68 [95% CI: 0.43-1.08], p-value = 0.10). Annual IBTR event rates were 0.99%/yr in the RT group and 0.80%/yr in the RT+T group. There were 288 events of any kind [iDFS-DCIS] (DFS): 155 in the RT arm and 133 in the RT+T arm (HR = 0.84 [95% CI: 0.66-1.05], p-value = 0.13) and 48 deaths: 26 in the RT arm and 22 in the RT+T arm (OS HR = 0.85 [95% CI: 0.48-1.51], p = 0.59). The study did not reach the 163 protocol-specified events, so the definitive analysis was triggered by all pts having been on study for ≥5 years. **Conclusions:** The addition of T to RT did not achieve the protocol objective of 36% reduction in the IBTR rate but did achieve a modest, statistically non-significant reduction of 19%. Support: U10-180868, -180822, UG1-189867; Genentech. The authors thank Elaina Harper and Marlon Jones for data management. Clinical trial information: NCT00769379. Research Sponsor: U.S. National Institutes of Health, Genentech.

509 Poster Discussion Session; Displayed in Poster Session (Board #1), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Immune phenotype and response to neoadjuvant systemic therapy (NAST) in triple negative breast cancer (TNBC). *First Author: Clinton Yam, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: In TNBC patients (pts) receiving NAST, increasing tumor infiltrating lymphocytes (TILs) is associated with higher pathologic complete response (pCR) rates. However, since the presence of TIL do not consistently predict pCR, the current study was undertaken to more fully characterize the immune cell response and its association with pCR. **Methods:** T cell receptor (TCR) sequencing, PD-L1 immunohistochemistry and multiplex immunofluorescence were performed on prospectively collected pre-NAST tumor samples from 98 pts with stage I-III TNBC enrolled in ARTEMIS (NCT: 02276443). TCR clonality was calculated using Shannon's entropy. PD-L1+ was defined as ≥1% immune cell staining. Response to NAST was defined using the residual cancer burden (RCB) index. Associations between TCR clonality, immune phenotype, and response were examined with the Wilcoxon rank sum test, Spearman's rank correlation and multivariable logistic regression using stepwise elimination (threshold $p > 0.2$), as appropriate. **Results:** The pCR rate was 39% (38/98). pCR was associated with higher TCR clonality (median = 0.2 [in pts with pCR] vs 0.1 [in pts with residual disease], p = 0.05). Notably, the association between pCR and higher TCR clonality was observed in pts with ≥5% TIL (n = 61; p = 0.05) but not in pts with < 5% TIL (n = 37; p = 0.87). Among pts with ≥5% TIL, TCR clonality emerged as the only independent predictor of response in a multivariable model of tumor immune characteristics (odds ratio/0.1 increase in TCR clonality: 3.0, p = 0.021). PD-L1+ status was associated with higher TCR clonality (median = 0.2 [in PD-L1+] vs 0.1 [in PD-L1-], p = 0.004). Higher TCR clonality was associated with higher CD3+ (rho = 0.32, p = 0.0018) and CD3+CD8+ (rho = 0.33, p = 0.0013) infiltration but lower expression of PD-1 on CD3+ (rho = -0.24, p = 0.021) and CD3+CD8+ cells (rho = -0.21, p = 0.037). **Conclusions:** In TNBC, a more clonal T cell population is associated with an immunologically active microenvironment (higher CD3+ and CD3/8+ T cell; lower PD-1+CD3+ and PD-1+CD3/8+ T cell; PD-L1+) and favorable response to NAST, especially in pts with ≥5% TIL, suggesting a role for deep immune phenotyping in further refining the predictive value of TILs. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology, MD Anderson Breast Cancer Moonshot Program.

510 Poster Discussion Session; Displayed in Poster Session (Board #2), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Role of intratumoral NK cells in triple-negative breast cancer in the FinXX trial and Mayo Clinic cohort. *First Author: Saranya Chumsri, Mayo Clinic, Jacksonville, FL*

Background: Several studies have established the critical role of preexisting immune response in triple negative breast cancer (TNBC). Most studies evaluated the tumor infiltrating lymphocytes in stroma. However, limited data are available with regards to the importance of specific subtypes and spatial distribution of these immune infiltrates. **Methods:** NanoString IO360 gene expression analysis and Digital Spatial Profiling (DSP) were used. DSP was used to quantify 39 immune-related proteins in stromal and tumor-enriched segments from 44 TNBC samples from the FinXX trial (NCT00114816) and 335 samples from the Mayo Clinic (MC) cohort of centrally reviewed TNBC (Leon-Ferre BCRT 2018). In FinXX trial, 22 patients with recurrence and 22 patients without recurrence were included. In MC cohort, 217/335 patients received adjuvant chemotherapy while 118 patients had surgery only without adjuvant chemotherapy. Regions were segmented based on pancytokeratin staining. The general linear model was used for statistical analysis of differential expression with recurrence free survival (RFS) as a categorical variable (recur yes or no). Kaplan-Meier estimates and Cox regression models were also used for analysis. **Results:** In the FinXX trial, using global gene expression analysis with IO360, there was no signature significantly associated with RFS. However, using DSP, high protein expression of CD56 in the tumor-enriched segments was associated with significant improvement in RFS (HR 0.26, 95%CI 0.09-0.78, p 0.01). Nevertheless, CD56 expression in the stroma (HR 0.66, 95%CI 0.29-1.53, p 0.33) and all segments (HR 0.53, 95%CI 0.23-1.25, p 0.14) was not significantly associated with improved outcome. We further validated these findings in the MC TNBC cohort where intratumoral CD56 expression was associated with a significant improvement in RFS (HR 0.23, p 0.002) but not stromal CD56 (p 0.79). Interestingly, when evaluating the MC TNBC cohort according to receipt of chemotherapy, intratumoral CD56 was associated with improved outcome only in patients who received chemotherapy (p 0.02 vs. 0.07). In both cohorts, higher expressions of intratumoral PD-L1, HLA-DR, and CD8 were associated with improved outcome. **Conclusions:** Using an in-depth analysis with spatially defined context, we identify that intratumoral CD56-positive NK cells are associated with improved outcome in TNBC. Our study highlights the potential role of NK cells in TNBC and future implications for biomarkers and therapeutic targets.Support: W81XWH-15-1-0292, P50CA116201-9, P50CA015083. Clinical trial information: NCT00114816. Research Sponsor: Department of Defense, U.S. National Institutes of Health.

511 Poster Discussion Session; Displayed in Poster Session (Board #3), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Association of T- and B-cell receptor repertoires with molecular subtypes and outcome in HER2+ breast cancer: An analysis of the NeoALTTO clinical trial. *First Author: Mattia Rediti, Breast Cancer Translational Research Laboratory J.-C. Heuson, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium*

Background: Clinicopathological and molecular features, including estrogen receptor (ER) status and PAM50 subtypes, have shown an association with immunogenicity and tumor-infiltrating lymphocyte (TIL) levels in breast cancer (BC). To investigate the complexity of the immune response in HER2+ BC, we explored the association of T- and B-cell receptor (TCR and BCR) repertoires with clinicopathological characteristics, PAM50 subtypes and outcome in the NeoALTTO phase III trial. **Methods:** RNA sequencing (RNAseq) data from baseline tumor biopsies were available for 254 out of the 455 patients enrolled. TCR and BCR repertoires were extracted from RNAseq data using the MiXCR software. Repertoire and diversity measures (read counts, number of clones, evenness, Gini index, Shannon entropy, length of the complementarity-determining region 3 [CDR3], top and second top clone proportions) were estimated. PAM50 subtypes were computed from RNAseq data. Univariate and multivariate (adjusted for clinicopathological characteristics, TIL levels dichotomized using the median value of 12.5% and treatment arm) Cox proportional hazard models were used for survival analysis, while logistic regressions were used for pathological complete response (pCR), defined as ypT0/is. All results reported had a false discovery rate (FDR) <0.05. **Results:** Higher BCR read counts, number of clones and Gini index were significantly associated with ER-negative as well as grade 3 tumors. Among the PAM50 subtypes, HER2-enriched (HER2-E) showed significantly higher BCR read counts, number of clones and Gini index along with lower evenness compared to luminal A and B, as well as higher length of CDR3 than luminal A. Of note, basal-like showed similar BCR diversity measures to HER2-E. No significant differences were noted for TCR diversity measures. In multivariate analyses, neither TCR nor BCR features were associated with pCR, while BCR evenness (HR 1.5; 95%CI 1.1-2.1) and Gini index (HR 0.66; 95%CI 0.5-0.88) were associated with event-free survival. **Conclusions:** BCR repertoire measures suggest a clonal expansion in HER2-E and basal-like PAM50 subtypes. Furthermore, the implementation of BCR-derived biomarkers can help to identify patients with an improved clinical outcome after neoadjuvant anti-HER2 treatment. Our findings highlight the heterogeneity of the immune response within HER2+ BC and provide support for biomarker-driven treatment strategies including immunotherapy in this BC subtype. Further validation is required. Clinical trial information: NCT00553358. Research Sponsor: NeoALTTO study was funded by GSK and later Novartis. The RNA sequencing on which the analyses described in this abstract are based was funded by GSK., Other Foundation.

512 Poster Discussion Session; Displayed in Poster Session (Board #4), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Breast cancer index (BCI) predicts benefit of two-and-a-half versus five years of extended endocrine therapy in HR+ breast cancer patients treated in the ideal trial. *First Author: Gerrit-Jan Liefers, Leiden University Medical Center, Leiden, Netherlands*

Background: For postmenopausal women with hormone receptor positive (HR+) breast cancer, the optimal duration of extended endocrine therapy (EET), after completing 5 years of initial aromatase inhibitor (AI)–based adjuvant therapy, remains unclear. BCI [HOXB13/IL17BR (H/I)] is a gene expression-based biomarker that has been demonstrated to predict EET benefit in the MA.17 and Trans-aTTom studies in patients treated with adjuvant tamoxifen. The current study examined the ability of BCI (H/I) to predict endocrine benefit from 2.5 vs. 5 years of extended letrozole in the IDEAL trial. **Methods:** All patients with available tumor specimens were eligible for this blinded prospective-retrospective study. The primary endpoint was Recurrence-Free Interval (RFI). Median follow-up was 9.1 years from randomization. Kaplan-Meier and Cox proportional hazards regression analysis were used to analyze the differential benefit of EET with statistical significance of the interaction between BCI (H/I) and treatment assessed by likelihood ratio test. **Results:** 908 HR+ patients (73% pN+, median 59y, 45% pT1, 48% pT2, disease free at 2.5 years) were included, with 88% and 68% receiving prior treatment with an AI or chemotherapy, respectively. BCI by H/I status (High vs. Low) was significantly predictive of response from extended letrozole in the overall (N = 908) and pN+ (N = 664) cohorts. Notably, BCI (H/I) predicted EET benefit in patients that received any primary adjuvant therapy with an AI (N = 794). Treatment to biomarker interaction was significant in the overall (p = 0.045), pN+ (p = 0.029) and any prior AI (p = 0.025) cohorts, adjusted for age, pT stage, grade, nodal status, prior endocrine therapy and prior chemotherapy. **Conclusions:** Novel findings from this study demonstrate that BCI predicts endocrine benefit from extended letrozole in postmenopausal patients treated with primary adjuvant AI. These results support the growing body of evidence that BCI by H/I status predicts preferential endocrine response in distinct subgroups of patients, and further support its role as an important genomic tool to inform the risk-benefit regarding duration of extended endocrine therapy. Clinical trial information: NTR3077, BOOG 2006-05, Eudra-CT 2006-003958-16. Research Sponsor: Biotheranostics, Inc.

Study Cohort	Relative Risk Reduction (HR)	P Value
Overall (N = 908)	H/I-High: 0.42 (0.21 – 0.84)	0.011
	H/I-Low: 0.95 (0.58 – 1.56)	0.835
pN+ (N = 664)	H/I-High: 0.30 (0.12 – 0.77)	0.008
	H/I-Low: 0.88 (0.50 – 1.53)	0.644
Prior endocrine therapy with an AI (N = 794)	H/I-High: 0.34 (0.16 – 0.73)	0.004
	H/I-Low: 0.90 (0.53 – 1.55)	0.712

513 Poster Discussion Session; Displayed in Poster Session (Board #5), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Validation of MAF biomarker for response prediction to adjuvant bisphosphonates in 2 clinical trials: AZURE and NSABP-B34. *First Author: Alexander H. G. Paterson, Tom Baker Cancer Center, Calgary, AB, Canada*

Background: An Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis indicates that adjuvant bisphosphonates increase time to bone recurrence and survival in postmenopausal breast cancer patients, but results of individual trials have been inconclusive. Retrospective analyses of AZURE, a trial of adjuvant zoledronic acid, showed MAF (a transcription factor of the AP-1 family) amplification status predicted bisphosphonate benefit independently of menopause for invasive disease-free survival (IDFS) and overall survival (OS). Validation of MAF amplification status as a potential companion diagnostic for adjuvant bisphosphonates was confirmed using NSABP-B34 specimens. **Methods:** The randomized, placebo-controlled NSABP B-34 study of women with stage 1-3 breast cancer were assigned to adjuvant systemic therapy plus oral clodronate 1600 mg daily or placebo for 3 years. The primary endpoint was disease-free survival (DFS) with overall survival (OS) as a secondary outcome. MAF amplification was assessed by fluorescence in-situ hybridization on anonymized sections of breast tumor tissue in all patients with tumor samples and performed in a laboratory blind to treatment assignment. Protocol and analysis plans were pre-specified. Disease outcomes were analysed using intention to treat principles. **Results:** 2496 B-34 patients contributed tumor samples (from 2001-2004), of whom 1883 (75%) were evaluable (947 placebo and 936 clodronate). 1515 (80%) tumors were MAF negative (766 placebo and 749 clodronate) and 368 were MAF positive. At median follow-up of 108 months, MAF was prognostic for DFS, OS and bone-metastasis-free survival in the control group (MAF-positive vs MAF-negative: HRDFS=1·39, 95%CI 1·01-1·92; p=0.045; HROS=1·59, 95%CI 1·08-2·33; p=0.018; HRBM=2·03, 95%CI 1·13-3·68; p=0.016). In patients with MAF-negative tumors, clodronate gave higher DFS and OS than controls at 60 months (HRDFS=0·70, 95%CI 0·51-0·94; p=0.020 and HROS=0·59, 95%CI 0·37-0·93; p=0.024), the latter maintained through follow-up (HROS=0·74, 95%CI 0·54-1.00; p=0.047), but not in patients with MAF-positive tumors - consistent with previous AZURE results. **Conclusions:** MAF benefit prediction from adjuvant bisphosphonates was confirmed using specimens from 2 randomized clinical trials (AZURE and NSABP-B-34) conducted and analyzed in similar manner using the same validated tests and clinical endpoints. These results are evidence towards introducing MAF testing into clinical practice. Research Sponsor: Inbiomotion, NSABP.

514 Poster Discussion Session; Displayed in Poster Session (Board #6), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Response to neoadjuvant chemotherapy and the 21-gene breast recurrence score in young women with estrogen receptor-positive early breast cancer. *First Author: Tal Sella, 450 Brookline Ave, Boston, MA*

Background: The *21-gene Breast Recurrence Score* predicts benefit from adjuvant chemotherapy in estrogen receptor positive (ER+), HER-2 negative (-) breast cancer (BC). We aimed to examine whether the 21-gene assay predicts response to neoadjuvant chemotherapy (NAC). **Methods:** We identified patients with stage I-III ER+/HER2− BC treated with NAC from the Young Women's Breast Cancer Study, a prospective cohort of women diagnosed with BC at age ≤ 40 years. The 21-gene assay was performed on tumor specimens removed prior to NAC either as part of clinical care or retrospectively for research. Pathologic complete response (pCR) was defined as no residual invasive tumor (ypT0/is ypN0). The relationship between Recurrence Score result (RS) and pCR was evaluated using logistic regression modeling. **Results:** 76 women in the cohort had undergone NAC for ER+, HER2- BC and were eligible for this analysis: 5 had undergone clinical 21-gene assay testing, 71 had banked specimens retrospectively tested. Median age at diagnosis was 36.7 (24.3-40). Most tumors were of ductal histology (78%), high grade (51%), progesterone receptor (PgR) positive (86%), ≥T2 (88%), clinically node positive (74%), and anthracycline and taxane containing protocols were administered in 86% of cases. RS ranged between 5-75 with 50% > 25 and only 4 < 11. Mean RS was significantly higher among tumors achieving pCR vs. non-pCR response (51.9 vs. 26.6, $p_{wilcoxon}$= 0.0005). pCR rate in patients with RS > 25 was 21% (8/38) vs. 5% in patients with RS < 25 (2/38), with both pCRs in the <25 group in patients with RS 21-25. In univariable analysis, PgR negativity (odds ratio (OR) 5.62, 95% confidence interval (CI) 1.27-24.89, p = 0.02), high grade (OR 9.03, 95%CI 1.07-76.32, p = 0.04) and higher RS as a continuous variable (OR 1.08, 95%CI 1.04-1.13, p = 0.0003) were associated with a greater likelihood of pCR. In multivariable analysis only RS remained significantly associated with pCR (OR: 1.07, 95%CI 1.01-1.12, p = 0.01): a 7% increase in the odds of pCR for every 1-point increase in RS. **Conclusions:** In young women with ER+, HER2- BC who received NAC, higher pretreatment RS was associated with an increased likelihood of pCR. Genomic expression profiling assays may have a role in decision-making in young women in need of neoadjuvant therapy. For women with low likelihood of benefiting from NAC, alternative approaches are clearly warranted. Given the demonstrated efficacy of neoadjuvant endocrine therapy in post-menopausal women, further evaluation in young women should be pursued. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology, Other Foundation, Pharmaceutical/Biotech Company.

515 Poster Discussion Session; Displayed in Poster Session (Board #7), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

De-escalated chemotherapy versus endocrine therapy plus pertuzumab+ trastuzumab for HR+/HER2+ early breast cancer (BC): First efficacy results from the neoadjuvant WSG-TP-II study. *First Author: Oleg Gluz, Breast Center Niederrhein, University Clinics Cologne and West German Study Group, Moenchengladbach, Germany*

Background: HR+/HER2+ breast cancer (BC) is a distinct entity associated with better prognosis compared to HR-/HER2+ BC. However, combination of chemotherapy (CT) with (dual) anti-HER2 blockade is standard in HER2+ early BC (EBC), irrespective of HR-status. Despite of some promising data on combination of endocrine therapy (ET) with dual anti-HER2 blockade in EBC and metastatic HR+/HER2+ BC, no prospective comparison of neoadjuvant CT vs. ET + dual HER2-blockade has yet been performed. **Methods:** In the prospective WSG TP-II phase II-trial (NCT03272477; Sponsor: Palleos GmbH, Wiesbaden, Germany), 207 patients (pts) (257 screened; 40 centers) with centrally confirmed HR+/HER2+ EBC were randomized to 12 weeks of standard ET (n=100) vs. paclitaxel 80 mg/m^2 weekly (n=107) +trastuzumab+pertuzumab q3w for all pts. Primary endpoint was pCR (ypT0/is/ypN0). Secondary endpoints include safety, disease-free and overall survival, translational research, and quality of life (QoL). Omission of further CT was allowed in all pts with pCR; dual HER2-blockade was administered in the adjuvant setting in all pts. **Results:** Baseline characteristics were well balanced between the arms. Median age was 53 years; 58% had cT2-4, 28% had cN+; 43% had G3 tumors. pCR data were available in 198 pts (ET: n=96; Pac: n=102). pCR was observed in 24% (95% CI: 16-34%) with ET+T+P vs. 57% (95% CI: 47-67%) with Pac+T+P (OR 0.24, 95% CI: 0-0.46, p<0.001). In multivariable logistic regression analysis and corresponding sensitivity analysis (bootstrap/subsample inclusion frequencies and lasso regression) including study arm, BMI, menopausal, cT, and cN status, histological grade, HER2-status, Ki67, ER, PR as continuous variables, only study arm and HER2 3+ status were significantly associated with pCR. Neoadjuvant treatment was well tolerated in both study arms and completed per protocol in 93/92 (ET+P+T/Pac+P+T) patients. Only 9/13 SAEs (ET+P+T/Pac+P+T) were reported during neoadjuvant therapy. PAM50 and QoL analysis are ongoing. **Conclusions:** WSG TP-II is the first randomized prospective trial comparing two neoadjuvant de-escalation treatments in HR+/HER2+ EBC. The excellent pCR rate of 57% after only 12 weeks of Pac+P+T was clearly superior to the still promising 24% pCR rate in pts treated by ET+P+T. In both arms, treatment efficacy was most pronounced in HER2 3+ tumors. Survival results need to be awaited before definite recommendations for a de-escalated regimen in HR+/HER2+ EBC can be made. Clinical trial information: 2016-005157-21. Research Sponsor: Roche.

516 Poster Discussion Session; Displayed in Poster Session (Board #8), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

GAIN-2: Neo-/adjuvant phase III trial to compare intense dose-dense chemotherapy (CT) to tailored dose-dense CT in patients (pts) with high risk early breast cancer (EBC): Results on safety and interim invasive disease-free survival (iDFS). *First Author: Volker Moebus, Internal Medicine II, Dept. of Hematology & Oncology University of Frankfurt, Frankfurt, Germany*

Background: GAIN-2 (NCT01690702) compared efficacy and safety of intense, dose-dense epirubicin, nab-paclitaxel, and cyclophosphamide (iddEnPC) vs dose-dense, dose-tailored epirubicin/ cyclophosphamide followed by dose-dense, dose-tailored docetaxel (dtEC-dtD) as adjuvant or neoadjuvant CT for node-positive or high risk node-negative EBC. Here, we report safety results and interim analysis (IA) of the primary endpoint iDFS. **Methods:** Pts (luminal A ≥N2; luminal B N+; HER2+ and TNBC) were randomized between iddEnPC (E 150 mg/m2, nP 330 mg/m2, C 2000 mg/m2, all q2w x 3) or dtEC-dtD (dtEC q2w x 4 followed after 1 week rest by dtD q2w x 4). Primary objective was to compare iDFS. 797 events are needed to detect a hazard ratio of 0.819 with a 2-sided log-rank-test with 80% power and α=0.05. The IA of iDFS was planned after 50% of the events have occurred. Safety and compliance were secondary objectives. **Results:** Between 10/2012 and 09/2018, 2887 pts were randomized and 2857 started treatment (iddEnPC 1429; dtEC-dtD 1428). Median age was 51 (range 18-75) years. Overall, 18.1% were luminal A, 31.5% luminal B/HER2-, 18.8% hormone-receptor (HR)+/HER2+, 8.5% HR-/HER2+ and 23.2% TNBC. Overall, 88.1% of pts completed all treatment in both arms. 66.8% with iddEnPC vs 58.8% with dtEC-dtD delayed CT dose ($p<0.001$). Grade 3-4 non-hematological adverse events (AEs) were more frequent with iddEnPC (iddEnPC 50.8% vs dtEC-dtD 45.1%, p=0.002). Grade 3-4 leukopenia, neutropenia, febrile neutropenia, arthralgia, and peripheral sensory neuropathy were significantly higher with iddEnPC. There were 1464 serious AEs (iddEnPC 870 vs dtEC-dtD 594) and 26 (9 vs 17) predefined AEs of special interest (anaphylaxis, any AE affecting cranial nerves, macula edema). Two deaths occurred during dtEC-dtD. After a median follow-up of 45.8 months, there was no difference in iDFS between arms (log-rank p=0.9102, hazard ratio iddEnPC vs dtEC-dtD 1.01, 95% CI 0.83-1.23). **Conclusions:** No new safety concerns were observed. Use of both iddEnPC and dtEC-dtD appears feasible in the (neo)adjuvant treatment of high risk EBC. Clinical trial information: NCT01690702. Research Sponsor: None.

517 Poster Discussion Session; Displayed in Poster Session (Board #9), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Comprehensive profiling of androgen receptor-positive (AR+) triple-negative breast cancer (TNBC) patients (pts) treated with standard neoadjuvant therapy (NAT) +/- enzalutamide. *First Author: Bora Lim, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: The luminal androgen receptor (LAR) subtype of TNBC has a low pathologic complete response (pCR) rate after NAT. We determined the pCR rate of the enzalutamide and paclitaxel (ZT) regimen for pts with anthracycline-insensitive AR^+ TNBC (NCT02689427), and related biomarkers. **Methods:** ARTEMIS (NCT02276443) is a non-randomized trial to determine if NAT can be used to personalized therapy. Pts received 4 cycles of doxorubicin-based NAT (AC). Pts with insensitive disease by imaging were offered clinical trials as the second phase of NAT based upon molecular profiling of pre-treatment biopsies. Immunohistochemistry (IHC) of $AR^+ \geq 10\%$ was the threshold for selecting ZT (enzalutamide 160 or 120 mg PO qD + paclitaxel 80 mg/m^2 qW for 12 cycles). pCR was determined by surgery after NAT. Trial had two-stage Phase II design, and we report the completed first stage. We evaluated the concordance between Vanderbilt LAR subtype by molecular profiling (microarray and RNAseq) and IHC %AR^+ cells. Frequency of PI3K pathway alterations within the LAR subtype was assessed. **Results:** 267 pts had tumors profiled by IHC, 220 by microarray, 187 by RNAseq and 197 by whole exome sequencing. 96 pts had post-AC RNAseq. LAR scores from both RNAseq and microarray profiling (n = 139) were highly concordant (R = 0.89, $P < 0.001$) and identified ~10% of TNBCs tested as LAR. The %AR^+ cells from IHC correlated with LAR subtype scores according to RNAseq (R = 0.6, $P < 0.001$), with a cut-point of $\geq$30% AR^+ having the best concordance with LAR subtype. Unlike other subtypes, by serial profiling, LAR TNBCs did not change subtype signatures after exposure to AC. LAR TNBCs had low rates of pCR (23%) and high rates of PI3K pathway activating aberrations (85%); however PI3K aberrations did not correlate with pCR. Seventeen patients with AC-insensitive TNBC received ZT. Five of 15 patients (33.3%) had responses (pCR or RCB-I). Toxicities are Grade (Gr) 4 syncope (n = 1), Gr3 abnormal liver function (n = 2), Gr3 neutropenia (n = 4). IHC & LAR subtype scores did not statistically associate with response to ZT (P = 0.8, P = 0.9). However, all responders to ZT had an upregulated androgen response pathway (ssGSEA $Z > 1$) as measured by transcriptomic analysis in pre-treatment biopsies analysis (P = 0.05, ppv = 0.56, npv = 1). **Conclusions:** The LAR TNBC subtype has a low pCR rate to NAT. Among pts with AC-insensitive TNBC, baseline upregulated androgen response pathway and LAR subtype may benefit from the ZT regimen, potentially by PI3K targeting. Clinical trial information: NCT02689427. Research Sponsor: Pfizer, MD Anderson Cancer Center.

518 Poster Discussion Session; Displayed in Poster Session (Board #10), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Defining the mutational landscape of 3,217 primary breast cancer transcriptomes through large-scale RNA-seq within the Sweden Cancerome Analysis Network: Breast Project (SCAN-B; NCT03430492). *First Author: Christian Brueffer, Lund University, Division of Oncology, Lund, Sweden*

Background: Breast cancer is a disease of genomic alterations, of which the complete panorama of somatic mutations and how these relate to molecular subtypes and therapy response is incompletely understood. The Sweden Cancerome Analysis Network-Breast project (SCAN-B; ClinicalTrials.gov NCT02306096) is a multi-center population-based ongoing prospective observational study elucidating the global transcriptomic profiles for thousands of patients and tumors using RNA sequencing. Since September 2010, over 15,000 patients with breast cancer have been enrolled at 9 hospitals across a wide geography of Sweden, comprising greater than 90% of all eligible patients in the catchment area. **Methods:** Within SCAN-B, we developed an optimized bioinformatics pipeline for detection of single nucleotide variants and small insertions and deletions from RNA-seq data. From this, we describe the mutational landscape of 3,217 primary breast cancer transcriptomes, and relate it to patient overall survival in a real-world setting (median follow-up 75 months, range 2-105 months). **Results:** We demonstrate that RNA-seq can be used to call mutations in important breast cancer genes such as PIK3CA, TP53, ESR1, and ERBB2, as well as mutation status of key molecular pathways and tumor mutational burden, identify mutations in one or more potentially druggable genes in 85.3% percent of cases, and reveal significant relationships to patient outcome within specific treatment groups. To make this rich and growing mutational portraiture of breast cancer available for the wider research community, we developed an open source interactive web application, SCAN-B MutationExplorer, publicly accessible at http://oncogenomics.bmc.lu.se/MutationExplorer. **Conclusions:** These results add another dimension to the use of RNA-seq as a potential clinical tool, where both gene expression-based signatures and gene mutation-based biomarkers can be interrogated simultaneously and in real-time within one week of tumor sampling. Research Sponsor: Mrs. Berta Kamprad Foundation, Other Foundation, Other Government Agency.

519 Poster Discussion Session; Displayed in Poster Session (Board #11), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Ipsilateral invasive cancer risk after diagnosis with ductal carcinoma in situ (DCIS): Comparison of patients with and without index surgery. *First Author: Marc D Ryser, Duke University School of Medicine, Durham, NC*

Background: Most women diagnosed with ductal carcinoma in situ (DCIS) undergo surgical resection, potentially leading to overtreatment of patients who would not develop clinically significant breast cancer in the absence of locoregional treatment. We compared the risk of ipsilateral invasive breast cancer (iIBC) between DCIS patients who received breast conserving surgery (BCS) for their index diagnosis of DCIS (BCS group) and patients who did not receive any locoregional treatment within 6 months of diagnosis (surveillance [SV] group). **Methods:** A treatment-stratified random sample of patients diagnosed with screen-detected and biopsy-confirmed DCIS in 2008-14 was selected from 1,330 Commission on Cancer-accredited facilities (20/site). Excluding patients who received a mastectomy ≤6 months, the final analytic cohort contained 14,245 (88.2%) BCS and 1,914 (11.8%) SV patients. Subsequent breast events were abstracted up to 10 years after diagnosis. Primary outcome was the 8-year absolute difference in iIBC risk between BCS and SV; a subgroup analysis was performed for grade I/II patients. A propensity score (PS) model for treatment was fitted with sampling design (SD) weighting and random effects for patients within facilities. Absolute risk differences were estimated using PS-SD-weighted Kaplan Meier estimators. **Results:** Overall, median age at diagnosis was 61 years (IQR: 52-69) and median follow-up was 5.8 years (95% CI 5.7-6.1). The majority of patients were Caucasian (81.9%), with estrogen receptor-positive (80.6%), and nuclear grade I/II (54.5%) DCIS. The fraction of patients with a Charlson comorbidity score of ≥2 was higher in SV (14.2%) compared to BCS (6.4%, $p < 0.001$). The 8-year risk of iIBC was 3.0% (95% CI: 2.4%-3.6%) for BCS and 7.7% (95% CI: 4.9%-10.5%) for SV, with an absolute risk difference of 4.7% (95% CI: 4.5%-4.9%; log-rank $p < 0.001$). Among patients with grade I/II tumors, the 8-year risk of iIBC was 3.1% (95% CI: 2.3%-4.0%) for BCS and 6.1% (95% CI: 2.5%-9.8%) for SV; difference: 3.0% (95% CI: 2.7%-3.2%; p = 0.005). **Conclusions:** Despite an increased risk of iIBC in SV patients compared to BCS patients, the 8-year risk did not exceed 10% in either group. The risk of recurrence in BCS patients was comparable to previously reported estimates. These data demonstrate a considerable degree of overtreatment among patients with non-high grade DCIS. Prospective clinical trials will help determine the tradeoffs between universally directed as opposed to selectively applied surgery for low risk DCIS. Research Sponsor: PCORI/PCS-1505-30497.

520 Poster Discussion Session; Displayed in Poster Session (Board #12), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Towards data-driven decision-making for breast cancer patients undergoing mastectomy and reconstruction: Prediction of individual patient-reported outcomes at two-year follow-up using machine learning. *First Author: André Pfob, PROVE Center, Harvard Medical School & Brigham and Women's Hospital, Boston, MA*

Background: Post-surgical satisfaction with breasts is a key outcome for women undergoing cancer-related mastectomy and reconstruction. Current decision making relies on group-level evidence, which may not offer optimal choice of treatment for individuals. We developed and validated machine learning algorithms to predict individual post-surgical breast-satisfaction. We aim to facilitate individualized data-driven decision making in breast cancer. **Methods:** We collected clinical, perioperative, and patient-reported data from 3058 women who underwent breast reconstruction due to breast cancer across 11 sites in North America. We trained and evaluated four algorithms (regularized regression, Support Vector Machine, Neural Network, Regression Tree) to predict significant changes in satisfaction with breasts at 2-year follow up using the validated BREAST-Q measure. Accuracy and area under the receiver operating characteristics curve (AUC) were used to determine algorithm performance in the test sample. **Results:** Machine learning algorithms were able to accurately predict changes in women's satisfaction with breasts (see table). Baseline satisfaction with breasts was the most informative predictor of outcome, followed by radiation during or after reconstruction, nipple-sparing and mixed mastectomy, implant-based reconstruction, chemotherapy, unilateral mastectomy, lower psychological well-being, and obesity. **Conclusions:** We reveal the crucial role of patient-reported outcomes in determining post-operative outcomes and that Machine Learning algorithms are suitable to identify individuals who might benefit from alternative treatment decisions than suggested by group-level evidence. We provide a web-based tool for individuals considering mastectomy and reconstruction. importdemo.com. Clinical trial information: NCT01723423. Research Sponsor: U.S. National Institutes of Health.

Evaluation of algorithms trained to predict significant changes compared to baseline in satisfaction with breasts at two-year follow up.

		Satisfaction lower than baseline	Satisfaction greater than baseline
Regularized Regression	Accuracy	.90	.83
	(95%CI)	(.86 – .92)	(.79 – .86)
	AUC	.87	.78
	(95%CI)	(.83 – .91)	(.73 – .83)
Regression Tree	Accuracy	.90	.83
	(95%CI)	(.87 – .92)	(.79 – .86)
	AUC	.77	.67
	(95%CI)	(.70 –.83)	(.61 – .73)
SVM	Accuracy	.89	.82
	(95%CI)	(.86 – .92)	(.78 – .86)
	AUC	.84	.73
	(95%CI)	(.78 – .89)	(.67 – .79)
Neural Network	Accuracy	.90	.84
	(95%CI)	(.87 – .92)	(.80 – .87)
	AUC	.87	.78
	(95%CI)	(.82 – .92)	(.72 – .83)

521 Poster Session (Board #13), Fri, 8:00 AM-11:00 AM

Dementia risk among post-menopausal women treated with endocrine therapy for early-stage breast cancer in Ontario, Canada. *First Author: Phillip S. Blanchette, London Regional Cancer Program, Western University, London, ON, Canada*

Background: The association between anti-estrogen therapy and risk of dementia remains controversial. We performed a population-based real-world study investigating the association between endocrine therapy use and dementia. **Methods:** We used health administrative data collected from post-menopausal women (aged ≥66 years) who were diagnosed with breast cancer and started on adjuvant endocrine therapy from 2005-2012. Patients were classified by use of either an aromatase inhibitor or tamoxifen and followed to measure an unadjusted cumulative incidence of developing dementia. A multivariable analysis adjusting for age, income quintile, medical comorbidities, and duration of endocrine therapy was completed using a Cox-proportional hazards model. **Results:** We identified 12,077 patients of whom 73% were treated with an aromatase inhibitor and 27% with tamoxifen. The median age was 73 years (IQR 69-78), 64% of patients were treated with lumpectomy, and 19% received adjuvant chemotherapy. The unadjusted event rate for developing dementia was Hazard Ratio (HR)= 0.70 (95% confidence interval (CI)=0.63-0.78, p-value<0.0001) among patients receiving an aromatase inhibitor versus tamoxifen and the 5-year dementia incidence rate was 7.4% versus 9.2% respectively. Our multivariable analysis showed a significant decrease in the rate of dementia in patients treated with an aromatase inhibitor compared to tamoxifen (HR=0.88, 95% CI 0.78-0.98, p-value=0.02) with a median of 5.9 years of follow-up. Factors associated with the development of dementia included older age, previous history of ischemic heart disease, diabetes, hypertension and stroke. Duration of endocrine therapy and previous use of adjuvant chemotherapy were not associated with dementia in our study. **Conclusions:** This investigation indicates that use of aromatase inhibitors compared to tamoxifen is associated with a lower risk of developing dementia among post-menopausal breast cancer patients. Further prospective studies investigating the neurocognitive effects of endocrine therapy are warranted. Research Sponsor: Divison of Medical Oncology Research Fund, London Regional Cancer Program, Other Government Agency.

522 Poster Session (Board #14), Fri, 8:00 AM-11:00 AM

HER2 status and prediction of extended endocrine benefit with breast cancer index (BCI) in HR+ patients in the adjuvant tamoxifen: To offer more? (aTTom) trial. *First Author: John Bartlett, Ontario Institute for Cancer Research, Toronto, ON, Canada*

Background: BCI is a validated gene expression-based assay that stratifies patients based on risk of overall (0-10y) and late (post-5y) distant recurrence (DR) and predicts likelihood of benefit from extended endocrine therapy (EET). The Trans-aTTom study established Level1B validation for BCI (H/I) to predict benefit from EET.[1] In this updated Trans-aTTom analysis including HER2 status, BCI (H/I) and prediction of endocrine benefit were further characterized. **Methods:** Centralized HER2 was determined for all cases according to current ASCO/CAP guidelines. Kaplan-Meier and Cox proportional hazards regression were conducted to assess primary and secondary endpoints of Recurrence-Free Interval (RFI) and Disease-Free Interval (DFI), respectively. A three-way interaction using likelihood ratio testing, which included treatment, BCI (H/I) and HER2, was performed to assess the effect of HER2 on BCI (H/I) prediction of EET benefit. **Results:** Of 789 N+ patients, 90% (N = 711) and 9% (N = 72) were HR+/HER2- and HR+/HER2+, respectively. In the HER2- subset, BCI (H/I)-High (48%) showed significant benefit from 10y vs. 5y of tamoxifen (9.4% RFI: HR = 0.35 [95% CI 0.15-0.81]; P = 0.047) while BCI (H/I)-Low patients did not (-2.1% RFI; HR = 1.15 [95% CI 0.78-1.69]; P = 0.491). For DFI, BCI (H/I)-High patients also showed significant benefit (10.3% DFI; HR = 0.41 [95% CI 0.18-0.91]; P = 0.047) while BCI (H/I)-Low patients did not (-1.7% DFI; HR = 1.10 [95% CI 0.75-1.62] P = 0.612). As demonstrated in the overall N+ cohort, significant interaction between BCI (H/I) and treatment was shown in the HER2- subset (RFI P = 0.045; DFI P = 0.044). Notably, three-way interaction evaluating BCI (H/I), treatment and HER2 status was not statistically significant (P = 0.85), indicating the ability of BCI (H/I) to predict benefit of EET activity was not significantly affected by HER2 status. **Conclusions:** In this updated Trans-aTTom analysis with HER2 data, BCI (H/I) showed similar predictive performance for EET response in the HER2- subset when compared to the overall N+ cohort. These data further support the clinical utility of BCI (H/I) as a predictive biomarker for informing EET benefit in HR+/HER2- and HR+/HER2+ disease. Clinical trial information: NCT00003678. Research Sponsor: Biotheranostics, Inc., Other Foundation, Ontario Institute for Cancer Research.

Treatment hazard ratios of 10y vs. 5y tamoxifen for BCI H/I-high patients.

	RFI (HR [95% CI])	DFI (HR [95% CI])
Overall HR+, N+ (N = 789)	0.33 (0.14 – 0.75)	0.43 (0.20 – 0.92)
HR+, N+, HER2- subset (N = 711)	0.35 (0.15 – 0.81)	0.41 (0.18 – 0.91)

[1]Bartlett JMS et al, Annal Oncol. 2019.

523 Poster Session (Board #15), Fri, 8:00 AM-11:00 AM

Does chemotherapy affect survival of breast cancer (BC) patients with recurrence score 26-30? *First Author: Sowmya Goranta, Hurley Medical Center/Michigan State University, Flint, MI*

Background: The Oncotype-DX recurrence score (RS) allows providers to identify hormone receptor positive and HER2-negative breast cancer (BC) patients that may benefit from adjuvant chemotherapy (AC). The TAILORx Trial showed no benefit of AC among patients with RS of 11-25, except for patients younger than 50 years. There are, however, limited studies examining any benefit of AC among those with RS of 26-30. We sought to examine the effect of AC on BC-specific survival among these patients utilizing a national database. **Methods:** We queried the Surveillance, Epidemiology, and End Results database for newly diagnosed female BC patients between 2010-2015. We included patients with T1-T3, hormone receptor positive, HER2-negative, and lymph node-negative BC with RS of 26-30. Patients with tumors 5 mm or less and with incomplete records were excluded. Cox Proportional-Hazards Model was done to examine the effect of AC on BC-specific survival. A sub-group analysis was performed for patients younger than 50 years to examine the effect of AC on BC-specific survival. **Results:** We included 2,982 patients, of whom 1,686 (56.5%) received AC. Administration of AC was associated with lower age (56.5 [9.2] vs 61.8 [9.7], $p < 0.001$), Grade III&IV (39.7% vs 30.2%, $p < 0.001$), married or patients with partners (66.5% vs 61.5%, $p < 0.001$), and T stage > 1 (31.3% vs 26.8%, p = 0.03). AC was not associated with insurance status, race, and histology. Overall 5-year BC-specific survival was 97.3% (96.2-98.3%). After adjustment through cox regression, AC was found to not have an effect on survival (HR: 0.54 [0.27-1.10], p = 0.09). There were 579 (19.4%) patients that were younger than 50 years, and AC did not have an effect on survival among these patients (HR: 0.44 [0.08-2.44], p = 0.35). Similarly, among the 2,403 (80.6%) patients aged 50 or older, AC did not have an effect on survival (HR: 0.49 [0.22-1.11], p = 0.09). **Conclusions:** In this retrospective analysis, administration of AC was associated with lower age, higher grade, marital status, and T stage. AC did not affect BC-specific survival among patients with a RS of 26-30. Subgroup analysis did not show any benefit of AC among patients younger than 50 years or among those 50 or older. Further prospective randomized trials are warranted to identify subgroups that may potentially benefit from AC. Research Sponsor: None.

524 Poster Session (Board #16), Fri, 8:00 AM-11:00 AM

Statistical machine learning model to predict Oncotype DX risk category in women over age 50. *First Author: Kate R. Pawloski, Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: The 21-gene Oncotype DX Breast Recurrence Score multigene assay (RS) identifies women with ER positive, HER negative, axillary node-negative breast cancer (BC) for whom chemotherapy provides no invasive disease-free survival benefit compared to endocrine therapy alone. International adoption of RS testing is limited by cost and resource availability. We created a supervised statistical machine learning model using standard clinicopathologic data to predict RS risk category in women $>$ 50 years old. **Methods:** From 2012 to 2018, women with ER positive, HER2 negative, pathologically node-negative BC of all ages were retrospectively identified from a prospective institutional database. Standard clinicopathologic data and RS were collected. Per institutional protocol, RS are ordered for all early-stage, ER positive tumors $>$ 5 mm. Data were randomly split into training (n=3755) and validation sets (n=1609). A random forest model with 500 trees was developed on the training set, then evaluated on the validation set. Model predictors included age, tumor size, histologic subtype, hormone receptor status, lymphovascular invasion, and overall grade. The model was used to predict RS category (low risk: RS $\leq$ 25, high risk: RS $>$ 25) in women $>$ 50 years old. **Results:** 5364 unique tumors in 5189 women were identified. 3731 (70%) of tumors were identified in women $>$ 50 years; median age was 63 years (IQR 57-69). In women $>$ 50, median tumor size was 12 mm (IQR 9-17). Most tumors were invasive ductal (79%), low or intermediate grade (79%), and LVI was absent in 82% of tumors. Median ER staining by IHC was 95%; 28% of tumors had negative or weakly positive PR staining (1-20%). The model correctly classified 96.8% of patients as low risk (95% CI: 95.7-97.7). Negative predictive value for identifying low risk category was also high (92.3%, 90.7-93.6). Sensitivity for identifying high-risk women was 44.7% (37.4-52.1) and positive predictive value was 67.2% (58.2-75.3). A classification table on the validation set includes tumors with complete data available, including predictors and RS. **Conclusions:** Our model was highly specific (96.8%) for identifying women $>$ 50 with RS $\leq$ 25 who do not benefit from adjuvant chemotherapy. This model may be utilized in lieu of RS testing if cost and availability are prohibitive. True RS $>$ 25 was not as well predicted. The model will be refined following pathologic review of discordant cases to reduce false negatives. Research Sponsor: U.S. National Institutes of Health.

Classification table on the validation set [n=1467].

	True RS > 25	True RS ≤ 25
Model predicted RS > 25	84	41
Model predicted RS ≤ 25	104	1238

525 Poster Session (Board #17), Fri, 8:00 AM-11:00 AM

Early-stage breast cancer (BC) patients: Factors associated with aromatase inhibitor-induced musculoskeletal symptoms. *First Author: Simran Arora Elder, University of Maryland Greenebaum Comprehensive Cancer Center, Baltimore, MD*

Background: Hormone receptor positive (HR+) breast cancer comprises the largest subgroup of breast cancer. Aromatase Inhibitors (AI) are a key treatment for HR+ BC patients (pts) and reduce mortality. Aromatase Inhibitor-Associated Musculoskeletal Symptoms (AIMSS), defined as myalgias, arthralgias, or joint stiffness, occur in up to 50% of pts leading to low adherence to and often discontinuation of therapy. Little is known of the mechanism of AIMSS or its predisposing risk factors. This study aims to identify risk factors associated with AIMSS development in BC patients on AI therapy. **Methods:** We conducted a medical record review of pts with non-metastatic HR+ BC on adjuvant AI therapy between January 2009 and June 2017 at the University of Maryland Comprehensive Cancer Center. This study included 194 ptswho were free of arthralgia prior to AI therapy. We analyzed pts' demographics, lifestyle factors, reproductive history, tumor characteristics, medications, cancer treatment, co-morbidities, AI type, onset and severity of AIMSS. Severe AIMSS was defined as requiring change in AI therapy or discontinuation. Multivariable-adjusted logistic regression was used to identify risk factors for severe AIMSS. **Results:** The mean age of participants was 61. The mean BMI at diagnosis was 30 kg/m^2. 41% of pts were White, 40% were Black, 7% other and 12% unknown. Most (79%) did not have a history of tamoxifen and 16% were on GnRH agonists. Most (71%) used letrozole as initial AI therapy; 18% anastrozole; and 11% exemestane. 56% experienced AIMSS while on AI therapy and 20% required change or hold of AI therapy. 4% permanently discontinued AI due to AIMSS severity. BMI at diagnosis was significantly positively associated with risk of AIMSS. Multivariate odds ratio (95% confidence intervals) comparing the highest to lowest tertile of body mass index (BMI) at diagnosis was 4.01 (1.07-10.90; P_{trend}: 0.05). There were no significant associations with race, smoking, reproductive factors, type of AI therapy, tamoxifen use prior to AI therapy, medication use, experience of other cancer treatments, and tumor characteristics. **Conclusions:** 56% of BC pts on adjuvant AI therapy experienced AIMSS. 24% of these changed, held or discontinued AI regimen due to severe AIMSS. Higher BMI at diagnosis was associated with a higher risk of AIMSS. Our results confirm clinical significance of AIMSS among BC pts on AI therapy and suggest BMI as a modifiable factor for AIMSS. A larger study is warranted to replicate our findings and seek other possible risk factors for AIMSS. Research Sponsor: None.

526 Poster Session (Board #18), Fri, 8:00 AM-11:00 AM

CX-2009, a CD166-directed probody drug conjugate (PDC): Results from the first-in-human study in patients (Pts) with advanced cancer including breast cancer (BC). *First Author: Valentina Boni, START Madrid, CIOCC, Madrid, Spain*

Background: CX-2009 is a PROBODY drug conjugate (PDC) directed against CD166 (ALCAM) and conjugated to DM4, a potent microtubule inhibitor (MTI). CD166 is overexpressed in carcinomas but is also ubiquitously expressed in normal epithelium and thus has not been previously considered a viable target for a traditional antibody drug conjugate. PDCs have a peptide mask that blocks normal tissue binding and can be removed by tumor-associated proteases, thereby limiting off-tumor/on-target binding. CX-2009 demonstrated preclinical activity in multiple solid tumor models. Here we report results of the first in human study in patients with advanced cancer. **Methods:** In this phase I multi-part dose-escalation study, pts with advanced solid tumors received CX-2009 0.25–10 mpk IV every 14 or 21 days (Q2W or Q3W). Tumor types were selected based on expected high CD166 expression and MTI sensitivity. **Results:** The dose-escalation phase of the trial enrolled 43 pts; 49 additional pts were subsequently enrolled between 4–10 mpk to collect biomarker data and define the recommended phase II dose (RP2D), for a total of 92 pts as of 30 Nov 2019 (39 pts with breast cancer [BC], 22 ovarian [OC], 12 non-small cell lung [NSCLC], 9 head/neck squamous cell [HNSCC], 10 other) with a median of 6 (range 1–19) prior therapies. Median number of CX-2009 doses was 2 (range, 1–15). For Q3W dosing, one dose limiting toxicity (DLT; grade 3 vomiting) was observed at 8 mpk; MTD was not reached up to 10 mpk. The RP2D for Q3W schedule was 7 mpk based on safety, dose-response, and population pharmacokinetic simulations. Q2W dosing continues; DLTs were observed at 6 mpk. Common treatment-related adverse events (TRAEs) at 7 mpk (n=9) were nausea (44%), fatigue, infusion-related reactions (both 33%), vomiting and arthralgias (both 22%). Grade 3 TRAEs occurred in 2 pts (nausea/vomiting; peripheral neuropathy). No pts discontinued at 7 mpk due to TRAEs. Ocular toxicity was dose dependent; mild to moderate reversible keratitis/blurred vision was seen in 3 pts at 7 mpk and mitigated by ocular prophylaxis. Partial responses were seen in 8 pts (2 confirmed, both HR+/HER2- BC) treated between 4–10 mpk, including BC (n=5), OC (n=2), and HNSCC (n=1). SD ($\geq$1 on-study scan) was observed in 21 pts, 5 had SD $\geq$3 mos. **Conclusions:** CX-2009 at 7 mpk is the RP2D on Q3W schedule. Phase II expansion has begun in pts with HR+/HER2- BC. The Q2W schedule will continue to enroll pts to define the RP2D. CX-2009 will also be studied in combination with CX-072, a PD-L1 PROBODY therapeutic (NCT03149549) Clinical trial information: NCT03149549. Research Sponsor: CytomX Therapeutics, Inc.

527 Poster Session (Board #19), Fri, 8:00 AM-11:00 AM

Adherence to extended adjuvant endocrine therapy following Breast Cancer Index (BCI) testing in women with early-stage hormone receptor (HR)-positive breast cancers. *First Author: Julia Foldi, Yale Cancer Center, New Haven, CT*

Background: Evidence suggests continuing endocrine therapy (ET) beyond 5 years (yr) may reduce breast cancer recurrence in early stage HR+ breast cancers. Given the modest benefit and potentially serious adverse effects of extended ET (EET), improved approaches to identify patients who are at increased risk of late distant recurrence and who derive benefit from EET are critical. Guidelines recommend shared decision-making between oncologists and patients. The adherence rate to EET by 5 yr is only 50-60%. BCI is a gene-expression assay used to predict late distant recurrence and is predictive of benefit from EET. We assessed adherence to EET in women who had BCI testing. **Methods:** Women with stage I-III HR+ breast cancer s/p 3.5 yr of adjuvant ET and had BCI testing at our institution (8/2013-7/2015) were included. Pts who had $<$ 4 yr of follow-up since BCI testing were excluded. Information including demographics, tumor characteristics, treatment history, number DXA scans, history of osteopenia/osteoporosis were collected. Data on medication adherence was based on prescriptions in the electronic health record. **Results:** 102 pts were included in our analysis. The median age was 61yr (46-89 yr). The majority of pts had stage I (63%), N0 (77%) and HER2- (90%) disease. 50 pts (46%) received chemotherapy. 44 (43%) received tamoxifen and 79 (77%) had an aromatase inhibitor. BCI categorized 61 (60%) pts as low risk, 26 (25%) as intermediate, and 15 (15%) as high risk for late distant recurrence. 61 (60%) and 41 (40%) pts were predicted to have low and high likelihood of benefit from EET, respectively. All 15 (100%) pts categorized as high risk for late recurrence were predicted to have a high likelihood to benefit from EET; all were recommended to continue EET by their oncologist and all 15 elected EET. 11 (73%) completed 10 yr or were on EET at last follow-up. Of the 4 (27%) pts who stopped before 10 yr, 1 pt had metastatic recurrence and 3 had intolerable side effects. Pts on EET underwent an avg of 1.91 DXA scans, compared with 1.23 for those who stopped ET at 5 yr ($p = 0.003$). At a median follow-up of 10 yr from diagnosis, there were 2 metastatic (1/15 in the high risk and 1/26 in the intermediate risk group) and 1 local recurrence (1/61 in the low risk group). **Conclusions:** In pts who continued ET beyond 5 years based on BCI testing and discussion with their oncologist, the rates of adherence and persistence to EET were higher than those previously published. EET may increase the number of DXA scans performed. Research Sponsor: Biotheranostics Inc.

528 Poster Session (Board #20), Fri, 8:00 AM-11:00 AM

Safety and efficacy of single-agent adjuvant trastuzumab in older women with early-stage breast cancer. *First Author: Cynthia Owusu, Case Western Reserve University School of Medicine, Cleveland, OH*

Background: Older adults with multiple comorbidities and poor functional status may not be appropriate candidates for chemotherapy. We conducted a phase II trial to examine the safety and efficacy of single-agent Trastuzumab for older women with early stage Human Epidermal Growth Factor Receptor Type 2 (Her2)-positive breast cancer. **Methods:** This was a single-arm open label multi-institutional clinical trial of adjuvant single-agent Trastuzumab in women aged ≥ 60 years with stage I-III Her2-positive breast cancer who had either declined chemotherapy or were not chemotherapy candidates. Patients received Trastuzumab monotherapy, (8 mg/kg) for cycle 1 followed by (6 mg/kg) every 3 weeks for 12 months. The primary end point was one-year cumulative incidence of symptomatic congestive heart failure with reduced ejection fraction (HFrEF). Secondary endpoints were disease free survival (DFS) and overall survival (OS) at 5 years. **Results:** Fifty-six patients were enrolled across four centers with a median follow-up period of 5.0 years, (range 0-6.5). The median age was 72.5 years (range 60-90), 64% had stage I disease, 77% had estrogen-receptor positive disease and 82% had node-negative breast cancer. Only two patients had symptomatic congestive HFrEF with a one-year cumulative incidence of 3.6%; (95% confidence interval [CI], 0.09 to 13.8). Five patients had asymptomatic declines in ejection fraction with a one-year cumulative incidence of 9.1%; (95% CI, 3.9 to 20.1). The 5-year DFS was 86.4%; (95% CI, 73.6 to 93.3). Among seven relapses seen, two were due to distant metastatic breast cancer. The 5-year rate of overall survival was 90.2%; (95% CI, 78.1 to 95.8). Among five deaths, one was due to distant metastatic breast cancer. **Conclusions:** Among older women with stage I-III HER2-positive breast cancer who decline chemotherapy or are not chemotherapy candidates, treatment with her2 targeted therapy only without chemotherapy may offer a reasonable treatment option without an inordinate rate of cardiac toxicity. Clinical trial information: NCT00796978. Research Sponsor: Genentech.

529 Poster Session (Board #21), Fri, 8:00 AM-11:00 AM

Value of clinical treatment score post-5 years (CTS5) for late relapse risk assessment in patients with early-stage HER2+ breast cancer (BC) in the north central cancer treatment group (NCCTG) N9831 (Alliance) trial. *First Author: Tanmayi Pai, Mayo Clinic Florida, Jacksonville, FL*

Background: Multiple prognostic models exist to predict late relapse risk in early stage hormone receptor-positive (HR+) breast cancer (BC). The CTS5 is one such model that has been validated in HR+ HER2-negative BC. The value of this model in HR+ HER2+ has not been established. Here, we assessed CTS5 in patients (pts) with early stage HER2+ BC treated in the NCCTG N9831 (Alliance) trial. **Methods:** Pts with stage I-III HER2+ HR+ BC who survived ≥ 5 years were included. The online CTS5 calculator was used to determine CTS5 score and risk group (low, intermediate, and high) based on age, tumor size, grade, and number of involved nodes. Kaplan-Meier (KM) estimates, Cox regression models, and C index were used for analysis. **Results:** From 3,130 pts, 1,204 pts met the criteria and were included. Median age was 49 (22-79) years and median tumor size was 2.4 (0.1-12) cm. 63.6% had grade 3 tumors, 33.6% grade 2, and 2.8% grade 1. Median follow up was 10.89 (5.01-15.32) years. Based on CTS5, 821 (68.2%) pts were classified as high risk, 289 (24%) as intermediate risk, and 94 (7.8%) as low risk. Overall, using univariate Cox regression analysis, there was no statistically significant difference in recurrence free survival (RFS) among pts with intermediate vs. low (HR 0.47 95%CI 0.18-1.22, p = 0.12) and high vs. low (HR1.23 95%CI0.57-2.67, p = 0.6) with the C index of 0.58. Among pts who received concurrent trastuzumab (H) with HR+ BC, there was also no statistical difference in RFS between high vs. low (HR 0.68 95%CI0.24-1.97, p = 0.48) with the C index of 0.55. Paradoxically, pts with intermediate risk had better RFS than low risk (HR 0.18 95%CI0.03-0.97, p = 0.05). As a continuous variable, there is also no significant improvement in RFS per 1 unit increase in CTS5 score (HR 1.19 95%CI 0.73-1.96, p = 0.49) with the C index of 0.54. After 5 years, 7.06% (n = 30/425) of HR+ pts treated with concurrent H recurred. **Conclusions:** The CTS5 model is not prognostic in pts with early stage HR+ HER2+ BC receiving adjuvant H. While most HR+ HER2+ pts are classified as high risk by CTS5, the recurrence between years 5-10 was low in pts who received adjuvant H. This study highlights the need to develop a new predictive model for risk of late relapse in this specific group of pts to enable clinicians to determine which pts would benefit from extended adjuvant endocrine therapy. Support: BCRF-19-161, U10CA180821, Genentech. https://acknowledgments.alliancefound.org Clinical trial information: NCT00005970. Research Sponsor: U.S. National Institutes of Health, Other Foundation, Pharmaceutical/Biotech Company.

530 Poster Session (Board #22), Fri, 8:00 AM-11:00 AM

The predictive potential of the spatial signature of lymphocytes in breast cancer patients. *First Author: Nora Balint-Lahat, Chaim Sheba Medical Center, Tel-Hashomer, Israel*

Background: Tumor-infiltrating lymphocytes in breast cancer have emerged as both a prognostic and a potentially predictive immunotherapy biomarker. Advancements in artificial intelligence can extract pathology-based spatial immune fingerprints for use as treatment decision support tools. **Methods:** We examined 908 primary breast cancer patients with whole slide images (WSI) available from TCGA database. Digital structuring of WSIs included automated detection of lymphocytes, tumor and tumor adjacent stroma, using deep learning-based semantic segmentation. Prognosis was defined as progression free interval (PFI). A Cox Survival analysis was used to detect prognostic spatial features. We used principal component analysis (PCA) to reduce and decorrelate significant features. The resulting PCA features were used to fit the final model. The model was then validated on an independent database of WSI of breast lumpectomies, from two tertiary hospitals in Israel. **Results:** The analysis included 908 WSI. The average age was 58.4 years old, with a majority of early stage breast cancer (76.7%, stage I and II). The detection performance for tumor area and lymphocytes reached F1 scores of 99% and 97% respectively, in comparison to human annotation. In the Kaplan Meier (KM) analysis of 414 early stage luminal breast cancers, a high number of lymphocyte clusters (LC) and a high ratio between stromal lymphocyte density and tumor lymphocyte density (LD-S/LD-T) were significantly associated with longer PFI (p = 0.005 and p = 0.038, respectively). Based on these features, two continuous PCA features were added to the multivariate model, and remained significantly associated with PFI after adjusting for age (HR = 1.19, 95% CI 1.05-1.35; HR = 1.26 95% CI 1.03-1.55). The validation set was underpowered (n = 79) and data is still being collected. In a preliminary KM analysis of 37 early stage luminal breast cancer cases from the validation set, LD-S/LD-T was significantly associated with longer PFI (p = 0.046). **Conclusions:** In our study, LC and LD-S/LD-T, presumably surrogate measures of peritumoral lymphocytes, were found significantly associated with longer PFI. Research Sponsor: Nucleai.

531 Poster Session (Board #23), Fri, 8:00 AM-11:00 AM

Phase II study of adjuvant endocrine therapy with CDK 4/6 inhibitor, ribociclib, for localized ER+/HER2- breast cancer (LEADER). *First Author: Laura Spring, Massachusetts General Hospital, Boston, MA*

Background: Given the success of CDK 4/6 inhibitors for ER+/HER2- metastatic breast cancer, there is much interest in exploring these agents in early breast cancer to potentially reduce recurrence risk. However, tolerability and adherence are important considerations in the adjuvant setting. We evaluated the tolerability and adherence of adjuvant endocrine therapy with the CDK 4/6 inhibitor, ribociclib, in two different schedules, in a prospective phase II clinical trial. **Methods:** Eligible patients were those with localized stage I-III ER+ (≥ 10%), HER2- breast cancer who had completed surgery and were on adjuvant endocrine therapy with at least one year or more of treatment remaining. Patients were randomized to receive continuous ribociclib (400 mg daily of 28-day cycle; arm 1) or intermittent ribociclib (600 mg daily on days 1-21 of 28-day cycle; arm 2) for one year, in addition to an aromatase inhibitor (plus GnRH agonist if premenopausal). Toxicities were evaluated using CTCAE version 4.03. Adherence was monitored by review of patient diaries and pill count. **Results:** Of the 81 patients enrolled, 24 discontinued early. The table shows the current status of the patients based on treatment arm (data cut-off as of 1/31/20; updated results will be presented at meeting). A total of 8 serious adverse events (AEs) have occurred thus far: grade 3 transaminitis (1), grade 4 transaminitis (3), grade 3 colitis (1), grade 3 infection (2), and grade 4 lymphopenia (1). The most common grade 3 or greater AEs leading to study discontinuation thus far were transaminitis (8.6%), neutropenia (2.5%), and fatigue (2.5%). No patients discontinued early due to prolonged QTc. Adherence results will be reported at the meeting. **Conclusions:** Interim results demonstrate that while serious AEs with one year of adjuvant ribociclib are low, a number of patients discontinued adjuvant CDK 4/6 inhibitor. Tolerability and adherence patterns will need to be carefully considered with CDK 4/6 inhibitors in the adjuvant setting. Clinical trial information: NCT03285412. Research Sponsor: Novartis.

	Arm 1 (400 mg continuous)	Arm 2 (600 mg)
Enrolled	41	40
Completed per protocol	13	11
Active treatment	15	18
Discontinued early	13	11
Discontinued early due to AE	10	8
-No. with grade 3 or greater toxicity	9	7

532 Poster Session (Board #24), Fri, 8:00 AM-11:00 AM

Estimation of absolute benefit of S-1 postoperative therapy for ER-positive, HER2-negative breast cancer: Exploratory analysis of the phase III potent trial. *First Author: Masahiro Takada, Department of Breast Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan*

Background: Estimation of risk of recurrence is critical for adjuvant therapy decision making in patients with primary breast cancer. The POTENT trial examined outcomes associated with standard postoperative endocrine therapy with/without S-1 in patients with estrogen receptor (ER)-positive and human epidermal growth factor receptor 2 (HER2)-negative primary breast cancer (Toi et al, San Antonio Breast Cancer Symposium 2019). The aim of this study was to investigate absolute treatment effect across recurrence risk score to individualize indication for the concurrent administration of standard postoperative endocrine therapy with S-1. **Methods:** The POTENT trial included 1930 patients with ER-positive and HER2-negative breast cancer. The primary end point was invasive disease-free survival (iDFS). A continuous, composite measure of recurrence risk for each patient was determined from a Cox model incorporating age, tumor size, nodal status, grade, estrogen receptor, and Ki-67 expression levels. Absolute treatment effect of S-1 was estimated in each risk group defined by the composite risk score. **Results:** Of 1930 patients, we included the data from 1897 patients without unavailable data. Tumor grade, ER expression, and Ki-67 expression were available from central assessment. A Cox proportional hazards model for iDFS was estimated in standard endocrine therapy only group (N = 954). Age was excluded from the model because it did not add prognostic information. 5-year iDFS estimates were 91.6%, 82.0%, and 67.2% for low, intermediate, and high composite risk group, respectively. Absolute improvement in 5-year iDFS by the addition of S-1 to standard endocrine therapy were 0.9%, 6.7%, and 8.1% for low, intermediate, and high composite risk group, respectively. Hazard ratio for S-1 in each risk group were 0.86 (95%CI: 0.45-1.63, P = 0.642), 0.51 (95%CI: 0.34-0.78, P = 0.001), and 0.71 (95%CI: 0.49-1.02, P = 0.064), respectively. Continuous value of composite risk was also prognostic in a Cox proportional hazards model stratified by S-1 and neoadjuvant/adjuvant chemotherapy use (HR 2.58, 95%CI: 2.13-3.11, P $<$ 0.0001). **Conclusions:** Patients with ER-positive and HER2-negative disease, and intermediate to high risk, defined by clinicopathological factors, experienced absolute improvement of about 7-8% in 5-year iDFS with addition of S-1 to standard endocrine therapy, while improvement was minimal in those at low risk. Clinical trial information: 000003969. Research Sponsor: Taiho Pharmaceutical Co., Ltd.

533 Poster Session (Board #25), Fri, 8:00 AM-11:00 AM

Factors associated with adjuvant endocrine therapy adherence in non-metastatic breast cancer. *First Author: Joan Marie Neuner, Medcl Coll of Wisconsin, Milwaukee, WI*

Background: Over 50% of breast cancer patients prescribed adjuvant endocrine therapy (ET) are nonadherent during the recommended 5-year course of therapy. We investigated the role of cancer medication delivery on adherence, including mail order pharmacy use, number of pharmacies and copays. **Methods:** We conducted a retrospective cohort study of 15,769 commercially insured breast cancer patients age 18-64 with newly diagnosed breast cancer in 2007-2015 that initiated ET. Incident breast cancer was identified by a validated algorithm which identifies mainly non-metastatic breast cancer. We examined the association between 12-month AET adherence (proportion of days covered by fills $\geq$0.80) and mail order pharmacy use, number of pharmacies, and AET copays. We used Poisson regression to estimate nonadherence risk ratios and adjusted for demographics (age, income, race, urbanicity), comorbidities, total medications, primary cancer treatments (surgery, radiation, chemo, and ET initiated), and generic AI availability. Sensitivity analyses were conducted using alternate specifications for independent variables. To test whether any observed differences were due to self-selection, we also conducted a negative control analysis. **Results:** Most patients were white (74.4%) and age 55-64 (43.3%). Only 16% of patients used a mail order pharmacy for ET fills, most patients only used one pharmacy (58.8%) and 25.2% had a co-pay of $20 or more. In the primary analysis, mail order patients were more likely to be adherent to their ET (aRR 1.21; 95% CI 1.18-1.24), patients using one pharmacy were more likely to be adherent (1 vs 3+: aRR 1.09; 95% CI 1.06-1.13), and patients with lower copays were more likely to be adherent (quartile 1 vs 4: aRR 1.04; 95% CI 1.01-1.08). Results were consistent across sensitivity analyses, and there was no association between mail order and copays and the negative control outcome of any pneumonia diagnoses. **Conclusions:** Medication delivery factors are associated with adherence to breast cancer AET. Future work should investigate whether interventions to streamline medication delivery could improve adherence for this population. Research Sponsor: U.S. National Institutes of Health.

534 Poster Session (Board #26), Fri, 8:00 AM-11:00 AM

Disparities in receipt of and time to adjuvant therapy after lumpectomy. *First Author: Irene Dankwa-Mullan, IBM Watson Health, Bethesda, MD*

Background: Adjuvant treatment after breast conserving surgery (BCS) has been shown to improve outcomes, but the degree of uptake varies considerably. We sought to examine factors associated with post-BCS receipt of and time to treatment (TTT) for adjuvant radiation therapy (ART), cytotoxic chemotherapy (ACT) and endocrine therapy (AET) among women with breast cancer. **Methods:** IBM MarketScan claims data were used to select women diagnosed with non-metastatic invasive breast cancer from 01/01/2012 to 03/31/2018, who received primary BCS without any neoadjuvant therapy, and who had continuous insurance eligibility 60 days post-BCS. Logistic and quantile regressions were used to identify factors associated with receipt of adjuvant therapy (ART, ACT, AET) and median TTT in days for ART (rTTT), ACT (cTTT), and AET (eTTT), respectively, after adjustment for covariates including age, year, region, insurance plan type, comorbidities, and a vector of ZIP3-level measures (e.g., community race/ethnicity-density, education level) from the 2019 Area Health Resource Files. **Results:** 36,270 patients were identified: 11,996 (33%) received ART only, 4,837 (13%) received ACT only, 3,458 (10 %) received AET only, 5,752 (16%) received both ART and AET, and 9,909 (27%) received no adjuvant therapy within 6 months of BCS. (318) 1% of patients received combinations of either ART, AET or ACT. Relative to having no adjuvant therapy, patients $>$ 80 years were significantly less likely to receive ART only (relative risk ratio [RRR] 0.65), ACT only (RRR 0.05), or combination ART/AET (RRR 0.66) but more likely to receive AET alone (RRR 3.61) (all $p < .001$). Patients from communities with high proportions of Black (RRR 0.14), Asian (RRR 0.13), or Hispanic (RRR 0.45) residents were significantly less likely to receive combination ART and AET (all $p < .001$). Having HIV/AIDS (+11 days; $p = .01$) and residing in highly concentrated Black (+8.5 days; $p = .01$) and Asian (+12.2 days; $p = .04$) communities were associated with longer rTTT. Longer cTTT was associated with having comorbidities of cerebrovascular disease (+6.0 days; $p < .001$), moderate to severe liver disease (+12.3 days; $p < .001$) and residing in high-density Asian communities (+18.0 days; $p < .001$). Shorter eTTT (-11.4 days; $p = .06$) and cTTT (-14.8 days; $p < .001$) was observed in patients with comorbidities of dementia. **Conclusions:** Results from this cohort of privately insured patients demonstrate disparities in receipt of post-BCS adjuvant radiation and systemic therapy along multiple demographic dimensions and expose opportunities to promote timely receipt of care. Research Sponsor: None.

535 Poster Session (Board #27), Fri, 8:00 AM-11:00 AM

Real-world patterns of treatment and recurrence by frailty status among older women with HR-positive, HER2-negative early breast cancer. *First Author: Gregory Sampang Calip, University of Illinois at Chicago, College of Pharmacy, Chicago, IL*

Background: Frail health status impacts clinical decision making for older cancer patients and their families, and frailty is independently associated with increased risks of mortality. Our objective was to describe differences in treatment and rates of recurrence by frailty status among older women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer. **Methods:** We performed a large, population-based retrospective cohort study of women aged 65 years and older diagnosed with first primary stage I-III HR+/HER2- breast cancer using the Surveillance, Epidemiology, and End Results Medicare-linked database between 2007 and 2015. Using administrative health claims, we ascertained information on breast cancer treatment and utilized validated claims-based algorithms to determine frailty status (robust, pre-frail, and frail) and identify subsequent invasive breast cancer recurrences. Relative hazards of recurrence were determined using Fine and Gray competing risks regression models with estimated subdistribution hazard ratios (SHR) and robust 95% confidence intervals (CI). **Results:** From an overall cohort of 46,027 women, most women (56%) were classified as robust at breast cancer diagnosis, whereas 37% and 7% were identified as pre-frail and frail, respectively. Compared to robust patients, frail patients were more likely to have stage III disease (10% vs. 7%) and receive mastectomy (27% vs. 18%), and less likely to receive radiation (35% vs. 57%) or chemotherapy (5% vs. 9%). Five-year cumulative incidences of recurrence were 15%, 18% and 22% among robust, pre-frail, and frail women, respectively. In multivariable competing risks models adjusted for age, race, stage, and treatment, frail (SHR 1.28, 95%CI 1.17-1.41) and pre-frail (SHR 1.15, 95%CI 1.09-1.21) women had a significantly increased risk of breast cancer recurrence. **Conclusions:** Independent of differences in treatment, frailty was associated with increased breast cancer recurrence risk in this population-based cohort of older women. However, the vast majority of older women living with HR+/HER2- early breast cancer were not identified as frail. These study results suggest that age alone is not an adequate indicator of physical resilience and underscores the need to consider additional factors when assessing the benefits and risks of treatments for the prevention of recurrence among HR+/HER2- early breast cancer patients. Research Sponsor: Pfizer Inc.

536 Poster Session (Board #28), Fri, 8:00 AM-11:00 AM

Trends in utilization of hypofractionated whole breast radiation in breast cancer: An analysis of the National Cancer Database. *First Author: Steven Gerard Woodward, Thomas Jefferson University Hospital, Philadelphia, PA*

Background: Utilization of hypofractionated radiation (HR) as a component of breast conserving treatment (BCT) in breast cancer is lacking in the U.S. despite studies demonstrating its efficacy and guidelines supporting its use from the American Society for Radiation Oncology (ASTRO) in 2011 and 2018. Little is known regarding national trends in uptake and factors associated with uptake of HR in the U.S. since the 2011 ASTRO guidelines. **Methods:** We performed a retrospective review of the National Cancer Data Base (2012-2016) on patients undergoing BCT. Logistic regression modeling was used to identify relationships between patient, hospital, and tumor factors with the use of HR or traditional radiation (TR). **Results:** A total of 360,834 cases of BCT were identified with 65% (n=235,783) undergoing TR and 35% (n=125,051) undergoing HR. The odds of utilization of HR increased with year of diagnosis, patient age, higher median income, private insurance, treatment at an academic center, travel distance to treatment >20 miles, smaller tumors, lymph node negative disease, and without use of chemotherapy (p-values <0.0001, Table). **Conclusions:** Despite studies demonstrating the efficacy of its use and the support of ASTRO, HR utilization in the U.S. is still lacking. By understanding which patient populations are still not receiving the benefit of this therapy we can improve our utilization of HR in the U.S. leading to reduced healthcare costs and patient satisfaction. Research Sponsor: None.

Odds ratio estimates of undergoing hypofractionated RT compared to conventional RT.

Effect	Category (OR Estimates)					P value
Year of Diagnosis [% use per year]	2012 (Reference) [17.96%]	2013 (1.502) [24.19%]	2014 (2.377) [32.22%]	2015 (3.932) [42.57%]	2016 (5.889) [50.38%]	<0.0001
Patient Age in Years	<50 (0.469)	50-59 (0.801)	60-69 (Reference)	70-79 (1.349)	80+ (2.197)	<0.0001
Median Income of Zip Code	<$40,227 (reference)		$40,227-$50,353 (1.071)	$50,353-$63,332 (1.136)	>$63,332 (1.236)	<0.0001
Insurance Type	Private (Reference)	Medicaid (0.874)	Other Government (0.895)	Medicare (0.984)	Not Insured (0.997)	<0.0001
Facility Type	Academic (Reference)		Community (0.499)	Comprehensive Community (0.576)	Integrated Network (0.757)	<0.0001
Distance to Treatment Center (Miles)	<10 (Reference)		10-20 (1.028)		>20 (1.139)	<0.0001
Tumor Size (mm)	<5 (Reference)	5-10 (1.002)	10-20 (0.964)	20-50 (0.961)	>50 (0.832)	<0.0001
Lymph Node Status	Negative (Reference)			Positive (0.310)		<0.0001
Chemotherapy Use	None (Reference)			Administered (0.558)		<0.0001

537 Poster Session (Board #29), Fri, 8:00 AM-11:00 AM

Impact of delays in initiation of adjuvant endocrine therapy and survival among patients with breast cancer. *First Author: Kimberley Lee, Johns Hopkins School of Medicine, Baltimore, MD*

Background: Time to adjuvant endocrine therapy concerns patients and clinicians, but its impact on overall survival is not clear. There are no population level studies that address this question. Our primary objective is to describe the relationship between time from diagnosis of breast cancer to start of adjuvant endocrine therapy and overall survival. **Methods:** This is a population-based cohort study using prospectively collected population level data from the National Cancer Database (NCDB). The NCDB prospectively collects data on incident cancer cases from over 1500 Commission on Cancer-accredited facilities nationally. NCDB captures approximately 70% of incident cases of cancer in the United States. The participants are women with Stage II and III estrogen or progesterone receptor positive, human epidermal receptor 2 negative, invasive breast cancer who underwent definitive surgical treatment. **Results:** Of the 391,594 women in this study, 12,162 (3.1%) began treatment with adjuvant endocrine therapy more than 12 months after initial diagnosis of hormone receptor positive, invasive breast cancer. Mean age at diagnosis was 59.7 years (SD 13.4). Predictors of delayed initiation of adjuvant endocrine therapy include Black race or Hispanic ethnicity (adjusted odds ratio [aOR] of Black vs White, 1.57; 95% CI, 1.48-1.66; $P < .001$, Hispanic vs White, aOR 1.22, 95% CI 1.13-1.32; $P < .001$), Insurance other than private insurance (Medicare vs Private, aOR 1.09, 95% CI 1.01-1.17; $P = .007$, Medicaid vs Private, aOR 1.36, 95% CI 1.28-1.45; $P < .001$), higher stage of disease at diagnosis (Stage III vs II, aOR 1.24, 95% CI 1.19-1.30; $P < .001$), and delayed surgery or chemotherapy (Delayed surgery vs On-time lumpectomy, aOR 2.76, 95% CI 2.60-2.93; $P < .001$ and Delayed chemotherapy vs no chemotherapy, aOR 11.5, 95%CI 10.6-12.5). With median follow-up of 63.2 months, 67,335 (17.2%) patients died by the end of follow-up. Delayed initiation of AET resulted in no change in the hazard of death (HR, 1.00; 95% CI, 0.95-1.05; $P = .97$) compared to initiation within 12 months of diagnosis after adjusting for age, race and ethnicity, insurance type, urban vs rural residence, neighborhood income and education, comorbidity, cancer grade, stage, and receipt of timely or delayed surgery, chemotherapy, and/or radiation therapy. **Conclusions:** These results suggest that there may be no detriment to survival if initiation of adjuvant endocrine therapy occurs 12 to 24 months after initial diagnosis compared to within 12 months of diagnosis, as currently recommended. Research Sponsor: U.S. National Institutes of Health.

538 Poster Session (Board #30), Fri, 8:00 AM-11:00 AM

Genome-wide association study of steady-state letrozole concentration in patients with breast cancer. *First Author: Daniel Louis Hertz, University of Michigan College of Pharmacy, Ann Arbor, MI*

Background: Letrozole is a non-steroidal aromatase inhibitor (AI) used to treat hormone receptor positive (HR+) breast cancer. Variability in letrozole efficacy and toxicity may be partially attributable to variable systemic drug exposure, which may be influenced by germline variants in the enzymes responsible for letrozole metabolism, including CYP2A6. The objective of this genome-wide association study (GWAS) was to identify genetic variants that affect steady state letrozole concentrations. **Methods:** The Exemestane and Letrozole Pharmacogenetics (ELPh) Study randomized 503 post-menopausal patients with HR+ non-metastatic breast cancer to exemestane or letrozole treatment. Germline DNA was collected pre-treatment and blood samples were collected after 1 or 3 months of treatment to measure steady-state letrozole concentration via HPLC/MS. Genome-wide genotyping was conducted on the Infinium Global Screening Array to the Haplotype Reference Panel (> 2 million variants). The association of each polymorphism with square-root transformed letrozole concentration was tested in self-reported white patients via linear regression using the standard alpha for genome-wide significance ($\alpha = 5x10^{-8}$) assuming an additive genetic model and correcting for age and body mass index. **Results:** 228 patients met inclusion criteria and had all necessary data. Each variant allele of rs7937 a patient carried increased their letrozole concentration ~22.9 ng/mL (standard error = 4.01, $p = 3.51x10^{-8}$, Table) and this variant explained 13% of the variability in letrozole concentrations. rs7937 is located ~50 kB upstream of *CYP2A6*, and has previously been identified in GWAS of CYP2A6-related phenotypes, including nicotine metabolism and lung cancer. **Conclusions:** This GWAS confirmed that steady-state letrozole concentrations are partially determined by germline polymorphisms affecting CYP2A6 activity. If letrozole concentrations affect treatment efficacy or toxicity, CYP2A6 genetics may be useful to individualize letrozole dosing to improve clinical outcomes in patients with HR+ breast cancer. Research Sponsor: Breast Cancer Research Foundation.

	Wild-type (n = 62)	Heterozygous (n = 118)	Homozygous variant (n = 48)
Mean (ng/mL) (±std dev) letrozole concentration	74.6 (35.8)	98.3 (43.2)	120.4 (46.4)

539 Poster Session (Board #31), Fri, 8:00 AM-11:00 AM

Is hypofractionated radiation associated with improved timely completion of adjuvant radiation in breast conserving therapy? A National Cancer Database study. *First Author: Steven Gerard Woodward, Thomas Jefferson University Hospital, Philadelphia, PA*

Background: Timely completion (TC) of adjuvant radiation therapy following breast conservation therapy (BCT) has been associated with improved mortality and disease-free survival (DFS). Little data exists comparing TC of hypofractionated radiation (HR) and traditional radiation (TR). **Methods:** We performed a retrospective review of the National Cancer Data Base (2012-2016) on patients undergoing BCT. A multivariable logistic regression model was used to compare TC of HR (within 5 weeks of initiation) and TR (within 7 weeks of initiation) with interaction terms to look at within treatment effects of patient, tumor, and facility characteristics. **Results:** A total of 360,834 patients who underwent BCT were identified with 65% (n=235,783) undergoing TR and 35% (n=125,051) undergoing HR. TC of HR was achieved in 93.5% of patients and 74.2% of TR patients (p<0.0001). Across categories of year of diagnosis, age, race, median income, facility type, distance to treatment, T-stage, chemotherapy use, and lymph node status it was found that rate of TC was greater in HR compared to TR. The effect on TC by these factors was different in HR patients compared to TR in all categories except median income, distance to treatment, and T-stage (table). **Conclusions:** The decision between use of HR or TR in BCT is an essential component in treatment of breast cancer patients. Providers may improve mortality and DFS by identifying patients who are more likely to finish HR or TR on time based on patient, facility, and tumor factors. Research Sponsor: None.

Adjusted proportions of completing RT on time for hypofractionated compared to traditional RT.

Effect	Category (HR %/TR%)					Interaction P-value
Year of Diagnosis	2012 (89%/72%)	2013 (92%/73%)	2014 (94%/74%)	2015 (96%/77%)	2016 (96%/78%)	<0.0001
Patient Age (Years)	40-49 (91%/74%)	50-59 (94%/74%)	60-69 (95%/75%)	70-79 (96%/75%)	80+ (96%/75%)	<0.0001
Race/Ethnicity	White (95%/75%)		Black (93%/72%)	Hispanic (94%/74%)	Other (96%/76%)	<0.0001
Median Income of Zip Code	<$40,227 (94%/73%)		$40,227-$50,353 (94%/74%)	$50,353-$63,332 (95%/74%)	>$63,332 (95%/76%)	0.0978
Facility Type	Academic (95%/78%)		Community (93%/71%)	Comprehensive Community (94%/72%)	Integrated Network (95%/77%)	<0.0001
Distance to Treatment Center (Miles)	<10 (95%/75%)		10-20 (95%/75%)		>20 (95%/75%)	0.2231
Tumor Size (mm)	<5 (95%/76%)	5-10 (95%/76%)	10-20 (95%/75%)	20-50 (95%/74%)	50+ (94%/74%)	0.3699
Chemotherapy Use	No (95%/75%)			Yes (93%/75%)		<0.0001
Lymph Node Status	Negative (95%/75%)			Positive (88%/75%)		<0.0001

540 Poster Session (Board #32), Fri, 8:00 AM-11:00 AM

Real-world analysis of clinical and economic impact of 21-gene recurrence score (RS) testing in early-stage breast cancer (ESBC) in Ireland. *First Author: Lynda M McSorley, Galway University Hospital, Galway, Ireland*

Background: Treatment of hormone receptor positive (HR+) ESBC is evolving. The use of chemotherapy (CT) is declining with use of the 21-gene RS assay. This validated tool predicts the likelihood of adjuvant CT benefit in HR+ ESBC. Results from the TAILOR-x study suggest up to 70% of HR+ node negative ESBC patients (pts) may avoid CT with RS ≤25. Our objectives were to assess the clinical and economic impact of RS testing on treatment decisions using real-world data. **Methods:** From October 2011 to February 2019, a retrospective, cross-sectional observational study was conducted of HR+ node negative ESBC pts who had RS testing in Ireland. A survey of Irish breast medical oncologists provided the assumption for the decision impact analysis that grade (G) 1 pts would not receive CT pre RS testing and G2/3 pts would receive CT. Using TAILOR-x results, pts were classified low risk (RS ≤ 25) and high risk (RS > 25). Data was collected via electronic patient records. Descriptive statistics were used. Cost data was obtained via the National Healthcare Pricing Regulatory Authority. The economic analysis was adjusted for changing treatment and assay costs over the study period. **Results:** 963pts were identified. Mean age 56 years. Mean tumour size 1.87cm. 114 (11.8%), 636(66%), 211(22%), 2(0.2%) pts had G1, G2, G3 and unknown G respectively (resp). 797pts (82.8%) had low RS, 159 (16.5%) had high RS, and 7pts(0.7%) unknown RS. 251pts(26%) were aged < 51 at diagnosis. Of these, 45(17.9%), 145(57.8%), 58(23%), 3(1.2) had G1, G2, G3 and unknown G resp. 208pts(82.9%) had RS ≤ 25, 39pts(15.5%) had RS > 25 and 4pts(1.6%) unknown RS. In the RS ≤ 25 group, 111pts(44%) had RS 0-15, 59(23.5%) had RS16-20, and 38(15.1%) had RS21-25. Post RS testing 595pts(61.8%) had a change in CT decision; 586 changed to hormone therapy (HT) alone, and 9 from HT to CT. In total, 227pts(23.5%) received CT, and 3pts(0.3%) declined. Of pts treated with CT; 9(4%) had RS 0-15, 89(39.2%) had RS16-25**,** 129(56.8%) had RS > 25. The most common CT regimen was docetaxel and cyclophosphamide(TC), administered to 121pts(53%). RS assay use achieved a 69% change in treatment decision among G2/3 pts and a net 61% reduction in CT use. This resulted in savings of over €4 million in treatment costs. Deducting the assay cost, net savings of over one million euro was achieved. **Conclusions:** Ireland was the first public healthcare system to approve reimbursement for RS testing. Over the 8 year period of the study, a net 61% reduction in CT use in Irish pts with HR+ ESBC was achieved with conservative net savings of over €1,000,000. Research Sponsor: None.

541 Poster Session (Board #33), Fri, 8:00 AM-11:00 AM

CanAssist breast: An affordable breast cancer prognostic test validated on Asian patients. *First Author: Poonam Patil, Manipal Hospital, Bangalore, India*

Background: Treatment decisions for early stage HR+/HER2neu- breast cancer patients in the West routinely depend on prognostic tests that predict risk of recurrence. However, such tests are rarely used in Asia due to prohibitive costs and lack of validation data on Asian patients. Chemotherapy is thus often a default treatment leading to physiological and financial toxicity. To address these, we have developed CanAssist Breast (CAB) as an affordable IHC-based prognostic test, retrospectively validated on ~1400 patients, 63% South Asians and rest Caucasians. To date CAB has been prescribed by 180+ doctors across 30 cities in India for ~600 patients in clinics, enabling personalized treatment decisions. **Methods:** Primary surgical FFPE blocks and clinical follow-up data were obtained from hospitals. GraphPad Prism and MedCalc were respectively used for Kaplan-Meier survival analyses and Cox logistic regression to calculate hazard ratios. **Results:** The median age of diagnosis in the validation cohort was 56 years, 63% patients with stage II disease and 60% node negative tumors. Distant Metastasis Free Survival (DMFS) in the low-risk category of the validation cohort was 95%, and 84% in high-risk (P < 0.0001). Similar results were obtained with the Caucasian subgroup, as also with the chemotherapy-naive subgroup (30% of the cohort), demonstrating that risk stratification by CAB is unaffected by race or chemotherapy. Next, the performance of CAB was compared with Oncotype DX (ODX). 83% patients stratified as low risk by ODX (RS 0-25) in a sub-cohort of 109 were also stratified as low-risk by CAB. To assess the impact of CAB in treatment decision making, we assessed the data of 589 patients who have undergone CAB testing so far, 288 were identified as low-risk. 93% of these CAB low-risk patients were not given chemotherapy, demonstrating the clinical impact of CAB. **Conclusions:** CAB is the first test of its kind to be retrospectively validated in Asia. It shows high concordance with ODX in risk stratification of patients. CAB has been in clinical practice in India and near-India markets for 2 years and is helping clinicians and patients in making affordable treatment decisions. Research Sponsor: OncoStem Diagnostics.

542 Poster Session (Board #34), Fri, 8:00 AM-11:00 AM

Association of intraoperative opioids with improved recurrence-free survival in triple-negative breast cancer. *First Author: Giacomo Montagna, Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Opioid-induced immunomodulation may be of particular importance in triple negative breast cancer (TNBC) where an immune response is associated with improved outcome and response to immunotherapy. We evaluated the association between intraoperative opioids and outcomes in a large TNBC cohort. **Methods:** Consecutive patients with stage I-III primary TNBC treated between 03/2010 and 12/2016 were identified from our prospectively maintained database. Total intraoperative opioid dose was extracted from anesthetic records and converted to oral morphine milligram equivalents (MME) (10 MME = 50 mcg fentanyl IV). Univariable and multivariable (MVA) Cox proportional hazards analysis (adjusting for relevant clinicopathological features, (neo)adjuvant therapy, anesthesia technique and morbidity score), were performed to quantify the association between opioid exposure and recurrence-free survival (RFS) and overall survival (OS). **Results:** 1143 patients were included. Median age was 54 years (IQR 45, 64). 911 (80%) had ductal histology, 359 (31%) had nodal metastases, and 1070 (94%) were poorly differentiated. 781 (68%) received adjuvant chemotherapy and 313 (27%) received neoadjuvant chemotherapy. 525 (46%) received total intravenous anesthesia and 618 (54%) had general anesthesia. Median intraoperative opioid dose was 30 MME (IQR 20, 60). 5-year RFS was 81% (95% CI 79%-84%), 5-year OS was 86% (95% CI 84%-88%). In MVA, higher opioid administration was associated with favorable RFS but did not significantly affect OS (Table). **Conclusions:** Our study is the first to directly evaluate intraoperative opioid administration in TNBC and suggests a protective effect on RFS. Future work will focus on elucidating the underlying mechanism for this effect, including possible modulation of endogenous opioid signaling pathways and immunologic correlates. Research Sponsor: None.

	HR RFS	95% CI	p-value	HR OS	95% CI	p-value
Intraoperative opioid dose (per 10 MME)	0.94	0.89 – 1.00	0.048	0.97	0.91 – 1.03	0.3
LVI (Ref. no LVI)	1.62	1.18 – 2.22	0.003	1.39	0.95 – 2.03	0.087
N1 stage (Ref. N0)	1.40	0.92 – 2.12	0.11	1.31	0.80 – 2.15	0.3
N2 stage (Ref. N0)	1.90	1.04 – 3.47	0.036	2.02	1.02 – 3.99	0.044
N3 Stage (Ref. N0)	3.44	1.84 – 6.41	< 0.001	3.44	1.72 – 6.90	< 0.001
No response to NAC (Ref. No NAC)	2.15	1.40 – 3.30	< 0.001	2.12	1.28 – 3.51	0.003
Mastectomy (Ref. lumpectomy with WBI)	1.07	0.65 – 1.78	0.8	1.11	0.61 – 2.01	0.7
Lumpectomy without WBI (Ref. lumpectomy with WBI)	4.25	2.39 – 7.55	< 0.001	2.75	1.25 – 6.02	0.012
Van Walraven Score (per 1 point increase)	1.03	1.00 – 1.07	0.058	1.07	1.03 - 1.12	< 0.001

545 Poster Session (Board #37), Fri, 8:00 AM-11:00 AM

PD-1 protein and gene expression in early breast cancer: Prognostic implications. *First Author: Ioannis Zerdes, Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden*

Background: We have previously shown the prognostic value of PD-L1 protein and gene expression in early breast cancer (BC), however, the prognostic role of PD-1 expression remains unclear. **Methods:** The prognostic value of PD-1 in early BC was investigated using three different approaches: i) evaluation of PD-1 at the protein (IHC, immunohistochemistry in tissue microarrays) and mRNA levels in a retrospective patient cohort of 586 patients treated for early BC in Stockholm, Sweden between 1997-2005, ii) systematic review and trial-level meta-analysis of studies published in Medline, Embase, Cochrane Library and Web of Science Core Collection libraries on the prognostic value of PD-1 IHC expression, and iii) pooled analysis of transcriptomic data from 39 publicly available datasets for the prognostic capacity of PD-1 gene expression. Univariate and multivariable Cox regression models were used. **Results:** In the retrospective study cohort, PD-1 protein was significantly associated with biologically high-risk characteristics. PD-1 protein, but not gene expression, was correlated with improved overall survival (OS) (adjusted HR = 0.73, 95% CI 0.55 – 0.96, p = 0.023 and adjusted HR = 0.88, 95% CI 0.68 – 1.13, p = 0.307, respectively). In the trial-level meta-analysis, 4736 entries were initially identified and 15 studies, including our original cohort, fulfilled the predefined eligibility criteria. PD-1 IHC expression was not prognostic in unselected patients. However, a significant correlation to improved disease-free survival was seen within the triple-negative subtype (pooled multivariate HR = 0.57, 95% CI 0.29 – 0.90, p = 0.02). In the pooled gene expression analysis, PD-1 gene expression was associated with improved OS in the entire population (adjusted HR = 0.89, 95% CI 0.80 – 0.99, p = 0.025) and in basal-like (adjusted HR = 0.77, 95% CI 0.63 – 0.95, p = 0.014) tumors. **Conclusions:** PD-1 expression at the RNA and protein levels represent promising prognostic factors, especially in the triple-negative and basal-like subtypes. Standardization and further validation are needed prior to clinical implementation. Research Sponsor: Swedish Cancer Society, Cancer Society in Stockholm, Swedish Breast Cancer Association.

546 Poster Session (Board #38), Fri, 8:00 AM-11:00 AM

Tumor-infiltrating lymphocytes in ipsilateral breast tumor recurrences predict prognosis. *First Author: Axel Stenmark Tullberg, Sahlgrenska University Hospital, Västra Frölunda, Sweden*

Background: The antitumoral immune response is dynamic and changes with tumor progression. Previous studies show that immunohistochemical (IHC) assessment of TILs in local recurrences can predict prognosis. It is not clear how adjuvant radiotherapy (RT) can alter the local immune response or if gene expression analyses of TILs in recurrences can provide prognostic information. **Methods:** Matched biopsies from primary tumors and ipsilateral breast tumor recurrences (IBTRs) from the randomized SweBCG91RT trial were assessed for TILs. Analyses were performed using gene expression (86 matched pairs) and IHC assessment (126 matched pairs). **Results:** The median time to IBTR was 8.0 years among irradiated patients and 3.6 years among unirradiated patients. In the gene expression analyses, higher absolute values of CD8+ T cells, CD4+ effector memory and CD8+ effector memory T cells in the recurrence could significantly predict a decreased risk of subsequent distant metastasis. In addition, a net increase of these cells in the IBTR compared to the primary tumor was associated with a significantly lower risk of metastasis. TILs did not change significantly between the matched tumors for the whole group or among irradiated patients versus unirradiated patients in the gene expression or IHC analyses. Surprisingly, the group with unchanged TILs levels as measured by IHC had the lowest risk of metastasis while an increase or a decrease in TILs was significantly associated with an increased risk. **Conclusions:** Cytotoxic and memory T cells in the recurrence protect against subsequent distant metastasis although IHC measurement of TILs could not confirm these results. No significant differences in TILs infiltration between irradiated versus unirradiated patients could be determined in the recurrences. Further analyses including changes of subtypes between the primary tumor and the recurrence will be presented. Research Sponsor: Supported by the Swedish state under the agreement between the Swedish government and the county councils, ALF-agreement Grant No. ALFGBG-716711, the Swedish Cancer Society Grant No. Can-2016/ 485, the King Gustav V Jubilee Clinic Foundation Grant No. 201.

548 Poster Session (Board #40), Fri, 8:00 AM-11:00 AM

A novel biosignature to assess residual risk in ductal carcinoma in situ (DCIS) patients after standard treatment. *First Author: Troy Bremer, PreludeDx, Laguna Hills, CA*

Background: There is an unmet need to identify women diagnosed with DCIS with elevated risk after standard treatment for whom enhanced treatment strategies should be considered. A response type (RSt) signature has been assessed in women treated with breast conserving surgery (BCS) with or without radiotherapy (RT), or with mastectomy. **Methods:** Women diagnosed with pure DCIS and treated with BCS or, BCS with whole breast RT were consecutively collected in Sweden, 1986-2004 and the USA, 1999-2008. A third cohort treated with mastectomy was collected in Sweden from 1986-2004. Patients with FFPE tissue were included unless they had prior or simultaneous invasive breast cancer (IBC). The RSt and DCISionRT biosignatures were calculated using biomarkers (p16/INK4A, Ki-67, COX-2, PgR, HER2, FOXA1, SIAH2), scored by board certified pathologists. Pathology and clinical data were collected from medical records. Only women at elevated risk by DCISionRT (DS $>$ 3) and negative margins were included in analysis. Total breast event risk included either ipsilateral DCIS or IBC. Multivariate Cox proportional hazards and survival analysis were used to assess cumulative incidence risk differences, hazard ratios, and 10-year risks adjusted for year of diagnosis. **Results:** Women with a poor RSt were all HER2 positive and remained at particularly elevated risk after BCS and RT (23% 10-yr risk, $p < 0.0001$, Table), with a risk profile similar to women treated with BCS without RT (RSt not evaluated). The distribution of age and size were not statistically different for good versus poor RSt, but poor RSt were more commonly Grade 3. In a small cohort of women treated with mastectomy, those women with a poor RSt were still at elevated risk after surgery, comparered to women with a good RSt (HR = 5.4, p = 0.014). The 10-year risk profile for women with a good RSt treated with BCS plus RT or mastectomy, was low (table). **Conclusions:** A novel biosignature identified women with a good and poor RSt, where the good RSt identified women with an apparent substantial benefit from RT, as well as women with a poor RSt who remained at particularly elevated risk after RT, and for whom enhanced treatment strategies should be considered. Additional validation studies are ongoing. Research Sponsor: PreludeDx, Other Government Agency.

Elevated DCISionRT Risk, DS > 3 and Negative Margins	Patients	Events	10-year Risk (95% CI) *
BCS with no RT	106	29	22% (10-32)
BCS+RT; Good RSt	141	5	4% (0-8)
BCS+RT; Poor RSt	19	8	23% (2-49)
Mastectomy; Good RSt	44	3	5% (0-12)
Mastectomy; Poor RSt	13	4	30% (0-49)

*Adjusted for Year of Diagnosis ≥ 1996

549 Poster Session (Board #41), Fri, 8:00 AM-11:00 AM

Novel association of pre-chemotherapy immune cell profiles with functional decline and resilience in women with breast cancer receiving chemotherapy. *First Author: Nikesha Gilmore, University of Rochester Medical Center, Rochester, NY*

Background: Chemotherapy adversely affects physical function. While many patients recover after treatment (i.e. are resilient), some are unable to return to their pre-treatment function (i.e. are non-resilient). Since immune dysfunction may play a role in functional decline, we assessed the relationship of pre-chemotherapy immune cell profiles with functional decline and resilience in women with breast cancer receiving chemotherapy. **Methods:** This study was based on a large nationwide cohort study in women with stage I-III breast cancer. Physical function was measured by the Functional Assessment of Cancer Therapy: General – Physical subscale (FACT-PWB) ≤7 days before chemotherapy (T1), ≤1 month after chemotherapy (T2), and 6 months after T2 (T3). Functional decline at T2 and T3 was defined as $>$ 1 point decrease (clinically meaningful difference) in FACT-PWD score from T1. Patients were considered non-resilient if they had T2 functional decline and did not return to within 1 point of their baseline FACT-PWB score by T3. Immune cell counts, neutrophil:lymphocyte ratio (NLR), and lymphocyte:monocyte ratio (LMR) were obtained at T1. Multivariate logistic regressions were used to determine whether immune cell counts and ratios were associated with functional decline and being non-resilient controlling for baseline FACT-PWD, age, race, education, and marital status. **Results:** One-third of patients (178/529; mean age 53, range 22-81) had functional decline from T1-T3. Of the 59% (n = 310) of patients with functional decline at T2, 50% (n = 147) did not recover by T3 (i.e. were non-resilient). Patients with a low ($<$ median) NLR at T1 were twice as likely to have functional decline by T3 than those with a high (≥ median) NLR [Adjusted Odds Ratio (AOR) 1.8, 95% CI: 1.2-2.8, $p < 0.01$]. Similarly, in patients with functional decline at T2, those with a low NLR at T1 were twice as likely to be non-resilient than those with high NLR (AOR: 1.9, 95% CI: 1.1-3.2, p = 0.01). Conversely, patients with high T1 lymphocytes were twice as likely to be non-resilient than those with low lymphocytes (AOR: 1.8, 95% CI: 1.1-3.1, p = 0.02). **Conclusions:** One-third of women with breast cancer have clinically meaningful, persistent functional decline six months after completing chemotherapy. Higher pre-chemotherapy lymphocytes and lower NLR may be useful to identify which women are at increased risk of functional decline and reduced ability to regain baseline physical function. These findings can inform interventions to ameliorate this decline. Research Sponsor: U.S. National Institutes of Health.

550 Poster Session (Board #42), Fri, 8:00 AM-11:00 AM

Expanding criteria for prognostic stage IA disease in HR+ breast cancer. *First Author: Olga Kantor, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA*

Background: The 8th ed AJCC staging system incorporated grade, receptor status and the Oncotype DX Recurrence Score (RS) result into staging. Based on TAILORx trial data and evidence of utility for RS results in node positive disease, this study was undertaken to determine if staging should incorporate expanded RS criteria. **Methods:** Patients (pts) with T1-3N0-3 HR+HER2- disease undergoing surgery 2010-15 were identified in the SEER database. 5yr DSS was estimated based on T and N category, grade and RS result; differences were compared between pts with path prognostic stage IA disease and all other groups. **Results:** 154,054 pts were identified; median follow up was 49 mo (range 0-83). RS results were obtained in 60,886 (39.5%); RS $<$11 in 13,570 (22.3%) and RS 11-25 in 39,240 (64.5%). The table details 5yr DSS rates. 5yr DSS for path prognostic stage IA pts (n=114,675, 73.4%) was 98.2%. Among all pts with RS $<$11, 5yr DSS was excellent and not significantly different than for path prognostic stage IA pts. For those with RS 11-25 not receiving chemo, 5yr DSS was inferior to path prognostic stage IA disease for T1-2N1 pts and for those with T2-3N0 disease although among N0 pts the differences were numerically small (1.4%-2.5% vs overall path prognostic stage IA). **Conclusions:** Pts with Recurrence Score $<$11 have excellent 5yr DSS regardless of T and N category or grade suggesting further modification of the AJCC staging system using this cutoff. Additional study is required to optimize staging for patients with Recurrence Score 11-25. Research Sponsor: None.

	Recurrence Score <11			Recurrence Score 11-25 without chemo			Recurrence Score 11-25 with chemo		
	N	5yr DSS %	p-value*	N	5yr DSS %	p-value*	N	5yr DSS %	p-value*
8th ed AJCC stage IA^									
T1N0 grade 1-3	8894	99.5		22368	99.6		2831	99.6	
T2N0 grade 1-2	2362	99.2		4496	99.0		896	99.0	
T3N0 grade 1	44	99.5		79	98.2		11	99.3	
T1N1mi grade 1-3	604	99.7		1283	99.6		416	97.6	
T2N1mi grade 1	54	99.9		107	99.8		32	92.4	
T1N1 grade 1-2	704	98.7		1307	97.6		587	99.0	
T2N1 grade 1	129	99.0		160	99.3		87	99.6	
Not stage IA by 8th ed AJCC									
T2N0 grade 3 or grade 1-2 and RS >11	--	--	--	1204	96.8	<0.01	460	97.1	0.25
T3N0 grade 2-3	112	99.9	0.40	242	95.7	<0.01	119	99.9	0.36
T2N1mi grade 2-3	178	99.9	0.29	389	98.2	0.83	173	97.9	0.50
T3N1mi grade 1-3	19	99.9	0.69	26	99.8	0.66	33	95.7	0.14
T1N1 grade 3	52	99.9	0.53	194	93.8	<0.01	166	94.4	0.07
T2N1 grade 2-3	307	98.5	0.16	642	96.3	0.01	512	95.2	<0.01
T3N1 grade 1-3	48	99.9	0.58	86	99.9	0.42	78	96.0	0.08
T1-3N2-3 grade 1-3	63	99.9	0.51	72	91.1	<0.01	184	96.5	0.50

*vs stage IA
^ p-value not determined; already path prognostic stage IA

552 Poster Session (Board #44), Fri, 8:00 AM-11:00 AM

Distinct genomic profiles of 589 Chinese early-stage breast cancer. *First Author: Ning Liao, Department of Breast Cancer, Cancer Center, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China, Guangzhou, China*

Background: Extensive efforts by The Cancer Genome Atlas (TCGA) Network had provided much of our current understanding of the molecular profile of various solid tumors including breast tumors; however, Asian patients were underrepresented in this cohort. In this study, we aimed to elucidate the comprehensive genetic alteration profile of early-stage breast tumors among Chinese patients. **Methods:** Surgical tissue samples from 589 Chinese women with stage I-III breast cancer with various histology and molecular subtype consecutively diagnosed at Guangdong Provincial People's Hospital were sequenced using a panel targeting 520 cancer-related genes spanning 1.64Mb of the human genome. Clinical and genomic data from our cohort was compared with publicly-available data from 1,046 stage I-III breast cancer patients from the TCGA dataset. **Results:** Based on the analysis of the genetic alteration profile from our cohort, at least one genetic alteration was observed from 98% of the tumor samples, with *TP53* (47%), *PIK3CA* (45%), *ERBB2* (30%), and *CDK12* (18%) as the most commonly altered genes. The most common genetic alteration types were copy number amplification (43.6%) and missense mutations (36.8%). As compared with the TCGA dataset, our cohort is mostly composed of women 50 years and younger (59.1% vs. 30.4%, $P< 0.001$), with significantly fewer patients with lobular carcinoma histology (2.4% vs. 19.0%, $P< 0.001$), and significantly more patients with pathologic stage I tumors (23.3% vs. 17.3%, $P= 0.012$). Consistently, genetic alterations detected from our cohort affected genes involved in PI3K (63% vs. 56%, $P= 0.009$) and cell cycle (23% vs. 35%, $P< 0.001$) pathways, with statistically different genetic alteration rates as compared with the TCGA dataset. Comparison of genetic alteration profile between the two cohorts revealed that our cohort had more frequent genetic alterations in genes including *PIK3CA* ($P< 0.001$), *TP53*, particularly in hotspot mutations Q192* ($P< 0.001$) and A307V/del ($P= 0.02$), and *ERBB2* amplification ($P< 0.001$). **Conclusions:** Our study contributes to the understanding of the key pathways and specific genetic alterations harbored by Chinese patients with early-stage breast cancer that could potentially be developed as markers of treatment response to targeted therapeutics. Research Sponsor: This study was supported by funding from National Natural Science Foundation of China (Grant No.81602645),Guangdong Provincial Natural Science Foundation (Grant No.2016A030313768).

553 Poster Session (Board #45), Fri, 8:00 AM-11:00 AM

Next-generation sequencing (NGS) identifies a new breast cancer subtype with HER2 low-amplification status as a candidate for targeted therapy. *First Author: Guo-Chun Zhang, Department of Breast Cancer, Cancer Center, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou, China*

Background: HER2 expression or amplification qualify patients to receive targeted therapeutics against HER2; however, traditional methods of quantifying HER2 amplification using fluorescence in situ hybridization (FISH) do not include a reliable definition for low level amplification. With the promising response rate of patients with low HER2 amplified-metastatic breast cancer to subsequent-line trastuzumab deruxtecan (DS-8201a) therapy, there is a need to improve the existing criteria to accurately identify patients with low HER2. In our study, we investigate whether HER2 amplification quantified by NGS could provide a method to stratify patients into subgroups. **Methods:** A total of 774 patients diagnosed with breast cancer from Guangdong Provincial People's Hospital (GDPH) who underwent targeted NGS using 520 or 33 cancer-related genes and had their HER2 status evaluated with either FISH or IHC were included in this study. HER2 status were defined as per 2018 ASCO/ACP guidelines. **Results:** Our results demonstrate that NGS could quantify HER2 amplification with high sensitivity and specificity, with area under the curve of 0.990 [95%CI: 0.982-0.999]. The receiver operating curve indicated an optimal cut-off of 2.62 copy number (CN) for identifying IHC/FISH HER2-negative status with 97.8% specificity. Meanwhile, the cut-off of $\geq$ 3.62 CN identified patients with IHC/FISH HER2-positive status with 99.8% specificity. Among the 774 patients, 65.8% (n = 509) had HER2 CN of $\leq$ 2.62 and were classified as HER2 non-amplified, while 25.8% (n = 199) had HER2 CN of $\geq$ 3.62, classified as HER2-amplified. The remaining 66 patients (8.5%) had HER2 CN between 2.62 and 3.62, and were the patients with heterogeneous IHC/FISH results, classified using NGS as HER2 low-amplified. Patients with low-amplified (49.0% vs. 38.8%, $P < 0.001$) and amplified (50.3% vs. 38.8%, $P < 0.001$) HER2 had significantly more number of copy number amplifications in other gene, including CDK12, RARA, and SPOP ($P < 0.001$, $P < 0.001$) than patients with HER2 non-amplified, indicating distinct mutation profile. **Conclusions:** Our results demonstrate that NGS could provide a more accurate stratification of patients based on their HER2 amplification levels. Patients with low levels of HER2 amplification has a distinct mutation profile, suggesting that NGS could serve as a robust tool to identify patients with HER2 amplification, whether high or low, who could benefit treatment with targeted agents designed against heterogeneous HER2 expression. Research Sponsor: This study was supported by funding from National Natural Science Foundation of China (Grant No.81602645), Guangdong Provincial Natural Science Foundation (Grant No.2016A030313768).

554 Poster Session (Board #46), Fri, 8:00 AM-11:00 AM

Somatic and germline mutation profiles of Chinese breast cancer patients younger than 35. *First Author: Ning Liao, Department of Breast Cancer, Cancer Center, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China, Guangzhou, China*

Background: Limited studies have investigated the molecular underpinnings driving breast cancer development in Chinese younger women. Based from our previous data, more Chinese women are diagnosed with early-onset breast cancer than in the West. In our study, we aim to investigate the comprehensive mutational profile of Chinese women 35 years old and younger ($\leq$35y) diagnosed with breast cancer. **Methods:** Targeted sequencing was performed on surgically-removed tumor tissues and blood samples collected from 589 women diagnosed with stage I-III breast cancer of various molecular subtypes at the Guangdong Provincial People's Hospital (GPDH) using a gene panel interrogating 520 cancer-related genes. We compared the data of 53 women aged $\leq$35y from our cohort to the data from 33 breast cancer patients aged $\leq$35y included in The Cancer Genome Atlas (TCGA) dataset. **Results:** Among the women aged $\leq$35y with early-stage breast cancer from both cohorts, our cohort had more number of hormone receptor-positive (HR+) patients (GPDH, 72% vs. TCGA, 61%, $P< 0.001$). Analysis revealed an overall mutation detection rate of 98% in our cohort, with mutations affecting genes involved in the PI3K pathway (47%) and cell cycle pathway (23%). *TP53* and *PIK3CA* were the most commonly mutated genes, with mutation rates of 51% and 25% from our cohort. No statistical difference in mutation profile was found between GPDH and TCGA cohorts. Moreover, germline mutations considered as pathogenic and likely pathogenic (P/LP) in breast cancer susceptibility genes including *BRCA1* (n = 4), *BRCA2* (n = 2), *PALB2* (n = 1), *PMS2* (n = 1), *PTEN* (n = 1), and *ATM* (n = 1) were detected from 18.9% (10/53) of the patients from our cohort. Women aged $\leq$35y had significantly more germline *BRCA1* mutations than patients $>$ 35y from our cohort (7.5%, 4/53 vs. 2.1%, 11/536 $P= 0.049$). **Conclusions:** Our study has identified the involvement of PI3K and cell cycle as the two key pathways in the early development of breast tumors in younger women. In addition, our results also support the role of P/LP germline mutations in breast oncogenesis in Chinese patients with early-onset breast cancer, indicating the need to include a more comprehensive germline mutation screening in our population. Research Sponsor: This study was supported by funding from National Natural Science Foundation of China (Grant No.81602645), Guangdong Provincial Natural Science Foundation (Grant No.2016A030313768).

555 Poster Session (Board #47), Fri, 8:00 AM-11:00 AM

Modulation by treatment of tumor infiltrating lymphocytes (TILs) and PDL1 expression in triple-negative breast cancer in the ETNA trial. *First Author: Giampaolo Bianchini, IRCCS San Raffaele Hospital, Milan, Italy*

Background: We assessed TILs and PDL1 expression before, during and after neoadjuvant treatment in TNBC patients enrolled in the ETNA study, and investigated associations with clinical outcome. **Methods:** In ETNA patients randomly received paclitaxel or nab-paclitaxel followed by 4 cycles of an anthracycline regimen, including 219 centrally confirmed TNBC. We successfully measured stromal and intratumoral TILs (sTILs, iTILs) and PDL1 status (Ventana SP142, IC$\geq$1%) on biopsies before [n = 186/213 (84.9%)], on d1 cycle 2 (d1c2) of therapy [n = 41/186 (22.0%)], and at surgery [SX, n = 65/129 (34.9%)]. We investigated the expression and modulation over time of TILs and PDL1 and their association with pCR and event-free survival (EFS). **Results:** Prevalence of PDL1+ was 35.5% (baseline), 20.6% (d1c2) and 30.1% (SX). At each time-point sTILs and iTILs were higher in PDL1+ cases ($p\leq0.01$). An effect of age of the tumor blocks (5-7.5 years) or pre-analytical issues could not be ruled out for the relatively low rate of PDL1 positivity. Paired PDL1 at baseline and d1c2 showed conversion in 25.7% (pos to neg [11.4%] or neg to pos [14.3%]). Comparing PDL1 at baseline and SX, the conversion rate was 30% (pos to neg [8.3%] or neg to pos [21.6%]). sTILs and iTILs significantly increased at cycle 2, more significantly in pCR ($p\leq0.001$) than in RD ($p\leq0.05$) cases, and a not significant trend of decrease was observed at surgery PDL1+ tumors had a higher pCR rate (54.7% vs 32.5%, p = 0.004). PDL1 retained significance (OR 2.00 [1.04-3.88], p = 0.039) after adjustment for sTILs (OR 1.21 [1.03-1.42], p = 0.021). High iTILs and sTILs at d1c2, but not PDL1 status, were predictive of pCR. Notably, adjusting for sTILs, PDL1+ tumors at d1c2 showed a trend for association with lower pCR rate (OR 0.06 [0.01-1.15], p = 0.062). sTILs at cycle 2 was the most informative variable (OR 1.61 [1.28-1.61], p = 0.004) and provided independent information to baseline biomarkers. Baseline PDL1 and biomarkers at cycle 2 were not associated with EFS. In surgical samples with RD, higher sTILs, but not iTILs and PDL1 status, were associated with a trend for a lower risk of recurrence (HR 0.19 [0.02-1.39], p = 0.068). **Conclusions:** sTILs assessment on core biopsies after one cycle of taxane is a promising early biomarker of pCR. PDL1, as well as sTILs and iTILs, provided independent prediction of pCR and were strongly modulated by treatment. The modulation of PDL1 expression should be considered whenever PDL1 is assessed in view of identifying candidates to atezolizumab in 1st line advanced setting. Research Sponsor: AIRC (Associazione Italiana per la Ricerca sul Cancro), BCRF (Breast Cancer Research Foundation), Fondazione Michelangelo.

556 Poster Session (Board #48), Fri, 8:00 AM-11:00 AM

Basal subtype and clinical estrogen receptor status of genomically basal breast tumors in Caucasian, African American, and Latin American patients. *First Author: Virginia G. Kaklamani, University of Texas San Antonio MD Anderson Cancer Center, San Antonio, TX*

Background: Genomically basal-type breast cancer is a heterogenous subtype that occurs at higher frequencies in non-Caucasian patients. Triple negative breast cancer (TNBC) has been refined into distinct transcriptomic groups including the basal-like immunoactive (BLIA), basal-like immunosuppressed (BLIS), luminal androgen receptor (LAR), and mesenchymal (MES) subtypes. Here we report the distribution of triple negative subtypes in genomically basal cancers from Caucasian (CA), African American (AA), and Latin American (LA) patients and the association of clinical estrogen receptor (ER) status. **Methods:** The FLEX Registry (NCT03053193) is an ongoing, prospective study evaluating primary tumors from patients with stage I-III breast cancer who receive the 70-gene signature and 80-gene signature (80-GS) molecular testing and consent to clinically annotated full transcriptome data collection. This sub-analysis evaluated 143 80-GS Basal type tumors from patients with self-reported ethnicity (60 CA, 59 AA, 24 LA). TNBC subtypes BLIA, BLIS, LAR, and MES were derived using an adjusted version of the 80-gene centroid signature published by Burstein and colleagues (2015). Differences in clinical ER expression between ethnicities were assessed by Fisher's exact test. **Results:** Basal indices from 80-GS were not influenced by patient ethnicity (one-way ANOVA, p = 0.182). The frequency of BLIA, BLIS, LAR, and MES subtypes did not vary significantly by ethnicity (Fisher's exact test, p = 0.671). The majority of tumors in all ethnic groups were BLIS (67% CA, 75% AA, 63% LA), followed by BLIA (22% CA, 22% AA, 25% LA), with low frequency of LAR (5% CA, 1.7% AA, 8.3% LA) and MES (5% CA, 1.7% AA, 4.2% LA) subtypes. Nearly one third (31%) of Basal type tumors were defined by IHC as ER positive and were present in all TNBC subtypes (39% BLIA, 29% BLIS, 33% LAR, and 20% MES); ER receptor expression ranged from 1-90% and was not associated with specific basal subtype (p = 0.8) nor ethnicity (P = 0.76). Progesterone receptor expression ranged from 1-50%. **Conclusions:** This analysis demonstrated that genomic Basal type tumor classification by 80-GS encompasses all TNBC subtypes evaluated regardless of ethnicity. Additionally, we show that IHC ER positive tumors occur in all TNBC subtypes assessed. These findings confirm the heterogeneous nature of basal breast tumors in CA, AA, and LA patients and highlight the clinical need to delineate basal biology in the ER+ cohort to advance treatment for basal-like tumors. Clinical trial information: NCT03053193. Research Sponsor: Agendia.

557 Poster Session (Board #49), Fri, 8:00 AM-11:00 AM

The quantitation of thioredoxin 1 from serum as a novel means to detect breast cancer (BC). *First Author: Kyoung Hoon Suh, E&S Healthcare, Daejeon, South Korea*

Background: Breast cancer (BC) is the most common cancer and the second leading cause of cancer death in women. Enormous effort has been conducted without success to develop a means to detect BC using the blood. We have reported that the level of thioredoxin 1 (Trx1) in serum could be a novel standard to evaluate the risk of BC. Therefore, we have investigated the clinical utility of Trx1 as a biomarker to detect BC by testing sera from normal women, women with BC, women with five other types of cancer. **Methods:** We have developed an ELISA kit that quantitates Trx1 in sera. The level of Trx1 was determined in each serum from normal healthy women (n = 114), as well as patients with BC (n = 106), cervical cancer (n = 17), lung cancer (n = 14), stomach cancer (n = 9), and thyroid cancer (n = 4). BC patients were recruited according to their age and cancer stage. Each test was duplicated more than three times, and test results were analyzed by ROC analysis, one-way ANOVA tests, and unpaired t-tests. **Results:** The mean value of Trx1 from normal women was 5.60±4.39(±SD) and that from BC was 22.25±7.07. The Trx1 level was effective to distinguish BC serum from healthy serum with a sensitivity of 94.3% and specificity of 93.9% (AUC 0.985, $p < 0.001$). The levels of Trx1 from BC patients were higher than the cut-off value of 14.13 U/ml regardless of age, stage, histological grade, type, ER/PR/HER2 expression profile, and proliferation activity of BC cells. The levels of Trx1 from the other five types of cancers (2.34±1.82 - 3.64±2.99) were low enough to be distinguishable from BC. Especially, Trx1 levels could rescue patients whose mammography resulted in a false judgement. **Conclusions:** These results indicated that the blood level of Trx1 is an effective and accurate method to detect breast cancer, and particularly as a complement to mammography. Research Sponsor: E&S Healthcare Co., Ltd.

558 Poster Session (Board #50), Fri, 8:00 AM-11:00 AM

Next generation sequencing reveals CCNE1 amplification as an independent prognostic factor for triple negative breast cancer (TNBC) patients. *First Author: Xin Huang, Peking Union Medical College Hospital, Beijing, China*

Background: Triple negative breast cancer (TNBC) has the worst prognosis among breast cancer due to the heterogeneity as well as lack of better therapeutic approach. It remains controversial whether *BRCA* status is the predictor of survival in TNBC. Besides, both germline and somatic mutation may contribute to the prognosis. This study is to explore the potential predictors and therapeutic targets based on genetic data and clinicopathological parameters. **Methods:** Seventy-five TNBC patients were enrolled with approximately 2:1 based on *BRCA* status. Genetic data was analysed by comprehensive genomic profiling 508 key cancer related genes. DAVID was applied to perform pathway enrichment analysis of significant enriched genetic alterations. Cox regression model was applied to evaluate disease-free survival (DFS) and overall survival (OS). Immuno-chemistry (IHC) was used to validate clinically meaningful genetic alteration. **Results:** In this study, 27 germline mutations were detected, including 26 homologous recombination repair (HRR) pathway gene mutations and 1 mismatch repair gene mutation among them 16 *BRCA1* mutations and 5 *BRCA2* mutations were found. Germline HRR including *BRCA1/2* mutation marginally affected DFS ($p = 0.0624$ and 0.15, respectively). We found 480 somatic genetic alterations including 110 copy number variations (CNV). The median value of TMB was determined to be 4.1 Muts/Mb which divided 74 TNBC patients into TMB-low (TMB-l) and TMB-high (TMB-h) group. TMB-l group had inferior DFS to TMB-h ($p = 0.0457$). *CCNE1* (with 5% frequency) copy number gain was specifically enriched in TMB-l group but mutually exclusive with *BRCA1/2* mutation. TNBC with *CCNE1* gain displayed worse DFS ($p < 0.0001$). Cox multivariate regression analysis indicated *CCNE1* gain was an independent risk factors for DFS [HR = 13.48 (95% CI 2.62-69.23), $p = 0.002$)]. Pathway analysis indicated *CCNE1* harmed prognosis through regulation of transcription in G1/S phase. Expression of cyclin E1 was validated by IHC, which would be presented later. **Conclusions:** Comprehensive genomic profiling disclosed various potential prognostic markers for TNBC by integrating clinical characters. Especially, amplified *CCNE1* may be a potential prognostic marker and therapeutic target. Research Sponsor: None.

CCNE1	DFS			OS		
Kaplan-Meier univariate		$p < 0.0001$			$p = 0.166$	
Cox multivariate regression	HR	CI	*p* value	HR	CI	*p* value
	13.48	2.62-69.23	0.002	9.64	2.62-69.23	0.034

560 Poster Session (Board #52), Fri, 8:00 AM-11:00 AM

Novel estrogen receptor beta agonist S-equol decreases tumor proliferation in patients with triple negative breast cancer (TNBC). *First Author: Kate Ida Lathrop, The University of Texas San Antonio Mays Cancer Center, San Antonio, TX*

Background: Patients with TNBC breast cancer have inferior treatment outcomes compared to other breast cancer subtypes and targeted therapies are lacking. S-equol is a novel oral Estrogen Receptor (ER) Beta agonist with preclinical data showing suppression of TNBC cellular proliferation. We therefore conducted an early phase window of opportunity trial to evaluate the impact of S-equol on Ki-67 change in patients with TNBC. **Methods:** This neoadjuvant window trial enrolled 39 patients with confirmed TNBC on diagnostic core needle biopsy. Cohort A (20 patients) received a daily dose of 50 mg daily and Cohort B (19 patients) received a higher dose of 150 mg daily. Paired biopsies were evaluable for 36 patients. Both cohorts were treated for a duration of 10-21 days. Primary outcome was change from pre- to post-treatment Ki-67 evaluated by paired t-test. All tests were 2-sided with a significance level of 0.05. Statistics were conducted within an accountable data analysis process in R (ADAPR). Secondary outcomes included toxicity and correlative biomarkers. **Results:** The mean (SD) pre-treatment was 68% (21.99) and post-treatment 59% (20.62). The average decrease in Ki-67 was 8% (P = 0.00206, 95% CI -13.46 to -3.26). A Ki-67 decrease of at least 20% from baseline was observed in 28% of the patients. S-equol was well tolerated with the most common toxicities being nausea, constipation, diarrhea, and headache. All toxicities were grade one. Treatment compliance was greater than 95%. Planned correlative studies included RNA-seq. A total of 161 genes are differentially expressed with fold change $> = 2$ and p value < 0.05. The top genes of the differential expression list include BMP5, S100A7, FABP7, SCGB2A2, CH507-338C24.1, and DUSP1. Gene Set Enrichment Analysis (GSEA) indicates that top enriched gene modules are related to interferon function and immune response, most of which are downregulated in the post-treatment group. **Conclusions:** S-equol is a novel well tolerated oral ER-Beta agonist with inhibition of proliferation in patients with TNBC as measured by a decrease in Ki-67. RNA-seq data supports potential immune activation during this short period of drug exposure. Future studies aim to evaluate S-equol as an immune activating agent for combination with immunotherapies such as checkpoint inhibitors in TNBC. Clinical trial information: NCT02352025. Research Sponsor: Ausio Pharmaceuticals.

561 Poster Session (Board #53), Fri, 8:00 AM-11:00 AM

Incidence of PI3K pathway alteration and response to neoadjuvant therapy (NAT) in triple negative breast cancer (TNBC) subtypes. *First Author: Reva K Basho, Cedars-Sinai Medical Center, Houston, TX*

Background: Limited cell line and human data suggest that TNBCs characterized as mesenchymal and luminal androgen receptor (LAR) commonly have alterations in the PI3K pathway. More data is needed to better characterize the role of the PI3K pathway across TNBC subtypes. **Methods:** Pre-treatment tumor biopsies were collected from operable TNBC patients (pts) enrolled on a clinical trial of genomically tailored NAT (ARTEMIS; NCT02276443). Tumors were categorized into 5 groups using the Pietenpol criteria: basal-like (BL) comprised of BL-1 and BL-2, mesenchymal and mesenchymal stem-like (M), immunomodulatory (IM), LAR, or unspecified (UNS). Using whole exome sequencing data, variants (single nucleotide polymorphisms and insertions/deletions) and copy number variations (CNVs) were identified in 32 genes known to activate the PI3K pathway. **Results:** Tumor subtyping and pathologic response to NAT was available in 127 pts (clinical stage I: 9; II: 84; III: 34). PI3K pathway alteration defined as a variant in one of the evaluated genes and/or deletion of PTEN was seen in 76 (60%) tumors. The most frequent alterations were: PTEN deletion (21%), PIK3CA variant (11%), and PIK3R1 variant (8%). PI3K alteration and residual cancer burden (RCB) rates across TNBC subtypes are shown in the table. There was a significant difference in pathologic complete response (pCR)/RCB 0 rate after NAT across TNBC subtypes (chi^2 test; P = 0.02). There was a significant difference in the incidence of PI3K pathway alteration across TNBC subtypes (chi^2 test; $P < 0.01$). Overall, the presence of PI3K alteration was not associated with pCR (Fisher exact test; P = 0.85). Pts with M tumors had a higher rate of substantial residual disease (RCB II-III) after NAT. Presence of PI3K pathway alteration was common in the M subtype and associated with RCB II-III (82% in PI3K-altered vs 33% in wild-type tumors; Fisher exact test; P = 0.02). Presence of PI3K pathway alteration was common but not associated with response in the LAR subtype. **Conclusions:** The incidence of PI3K pathway alteration varied by TNBC subtype but was not associated with pathologic response to NAT with the exception of increased substantial residual disease (RCB II-III) in the M subtype. Research Sponsor: MD Anderson MoonShot, Conquer Cancer Foundation of the American Society of Clinical Oncology.

Subtype	N	PI3K Altered N (%)	RCB 0 N (%)	RCB 0 if PI3K-Altered N (%)	RCB II-III N (%)	RCB II-III if PI3K-Altered N (%)
All	127	76 (60)	47 (37)	29 (38)	64 (50)	40 (53)
BL	34	22 (65)	14 (41)	10 (45)	16 (47)	9 (41)
M	31	22 (71)	5 (16)	3 (14)	21 (68)	18 (82)
IM	28	9 (32)	16 (57)	6 (67)	9 (32)	2 (22)
LAR	13	11 (85)	3 (23)	3 (27)	7 (54)	6 (55)
UNS	21	12 (57)	9 (43)	7 (58)	11 (52)	5 (42)

562 Poster Session (Board #54), Fri, 8:00 AM-11:00 AM

Impact of metastases directed radiation therapy on CDK4/6 inhibitors dose reduction and treatment discontinuation for metastatic HR+/HER2- breast cancer (MBC). *First Author: Icro Meattini, Radiation Oncology Unit-Oncology Department, University of Florence, Florence, Italy*

Background: Cyclin-Dependent Kinase 4/6 inhibitors (CDK4/6i) represent the standard I-II line for hormonal receptors positive/human epidermal growth factor receptor 2 negative metastatic breast cancer (MBC) patients. Metastases directed radiotherapy (RT) for these patients is commonly used with palliative or radical schedules during systemic treatment. Although encouraging preliminary results were published, there is still a lack of robust data on the safety concerning RT during CDK4/6i treatment. **Methods:** we analyzed at Our Institution 85 consecutive patients treated in I (n=47) and II line (n=38) for MBC with CDK4/6i between April 2017 and September 2019 (22 ribociclib, 63 palbociclib). Overall, 25 (29.4%) patients received metastases directed RT during CDK4/6i treatment, including 14 concomitant (16.5%) and 11 sequential (12.9%). Estimated CDK4/6i half-life is 26 and 30 hours for palbociclib and ribociclib, respectively. Five half-lives are required to reduce drug concentration by 95-97%; thus, we also analyzed CDK4/6i treatment as non-concomitant or sequential to RT. Main endpoints of our analysis were impact of RT on CDK4/6i dose reduction and discontinuation, overall adverse events rate (any grade and grade ≥2), and neutropenia grade ≥2 as per CTCAE scale version 5.0. **Results:** at a median follow up of 12 months (range 3-29), we observed a CDK4/6i dose reduction in 35 patients (41.2%) and 5 patients (5.9%) discontinued treatment due to adverse events; 82 patients (96.5%) experienced any grade of toxicity, 72 (84.7%) a grade ≥2 and 70 patients (82.4%) neutropenia grade ≥2. We did not observe significant difference in terms of CDK4/6i dose reduction or discontinuation, any grade or grade ≥2 toxicity, neutropenia grade ≥2 in the comparison between patients receiving RT *versus* no RT and between patients receiving concomitant RT versus sequential RT versus no-RT (Table). **Conclusions:** our results showed that the prescription of a metastases directed RT during treatment with a CDK4/6i as I-II line for MBC did not significantly impact on dose reduction or discontinuation caused by an exceeding in adverse event rate. Although these promising results, caution should be used and cooperative initiatives strongly encouraged. Research Sponsor: None.

Endpoint	RT (n=25) *vs* No-RT (n=60), P-value	Concomitant RT (n=14) *vs* Sequential RT (n=11) *vs* No-RT (n=60), P-value
CDK4/6i dose reduction	1.0	0.88
CDK4/6i discontinuation	1.0	0.56
Adverse events, any grade	1.0	0.47
Adverse events, grade ≥2	0.096	0.14
Neutropenia, grade ≥2	0.057	0.087

563 Poster Session (Board #55), Fri, 8:00 AM-11:00 AM

Clinical utility of 18F-FDG-PET/CT in staging localized breast cancer prior to initiating preoperative systemic therapy. *First Author: Heidi Ko, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY*

Background: 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET/CT) is recommended as an optional study in current National Comprehensive Cancer Network (NCCN) guidelines after computerized tomography and bone scan (CTBS) in patients with stage IIA-IIIC breast cancer. We evaluated our experience with use of PET/CT in this setting prior to beginning primary systemic therapy (PST) before planned surgery. **Methods:** We performed medical record abstractions to identify all adult female patients with clinical stage IIA to IIIC breast cancer diagnosed at Montefiore Medical Center from January 1, 2014 to January 1, 2019 who underwent PET/CT. We calculated the proportion of patients upstaged after PET/CT, stratified by their initial clinical stages and use of PST, and examined the cost and radiation exposure associated with PET/CT compared with CTBS. **Results:** 227 patients with 230 breast cancers (bilateral disease in 3) met the study inclusion criteria. PET/CT was the only staging done in 195 patients (86%); 32 patients had PET/CT based on suspicious findings from prior CTBS. Among these 195 patients with 196 breast cancers (bilateral disease in 1) that had PET/CT as the only staging done, the overall upstaging rate for regional nodal and/or distant metastasis was 37% (73/196), including 24% for stage IIA (9/38), 39% for IIB (31/79), 54% for IIIA (22/41), 27% for IIIB (8/30), and 37% for IIIC (3/8). The overall upstaging rate to stage IV was 14% (27/196), including 0% for stage IIA, 13% for IIB (10/79), 22% for IIIA (9/41), 17% for IIIB (5/30), and 37% for IIIC (3/8). The sensitivity and specificity of PET/CT in detecting distant metastasis was 100% and 94%, respectively. Our institution's total Medicare reimbursement rate of PET/CT is $1604.37 whereas CTBS is $1679.94. Radiation dose for PET/CT is 14 mSv whereas CTBS is 21 mSv. **Conclusions:** Approximately 37% of patients with clinical stage IIA-IIIC breast cancer who underwent PET/CT prior to PST showed more extensive disease, including 23% with more extensive regional nodal metastases and 14% with distant metastasis. Given the high detection rate, comparable cost, lower radiation dose and greater convenience, PET/CT should be considered as an alternative to CTBS rather than "optional" after CTBS, especially in patients who require an efficient and expeditious work up prior to initiating PST. Research Sponsor: None.

564 Poster Session (Board #56), Fri, 8:00 AM-11:00 AM

Can sentinel node biopsy after neoadjuvant systemic chemotherapy (NAC) be safely omitted in selected patient with early breast cancer? *First Author: Atsushi Yoshida, St. Luke's International Hospital, Tokyo, Japan*

Background: There is a recent trend of performing minimum axillary surgery considering the prognostic value and fewer complications for primary breast cancer patients since the results of ACOSOG Z011. Nodal status after NAC is not be useful for postoperative treatment in most of cN0 patients. Therefore, sentinel node biopsy (SNB) may be omitted if ypN0 after NAC can be predicted in cN0 patients. We assessed clinicopathological factors associated with ypN0 after NAC in cN0 primary breast cancer patients. **Methods:** Two-institutional retrospective cohort study of clinically N0 breast cancer patients before NAC and who underwent breast surgery was conducted, including 419 consecutive patients between 2009 and 2016 in St. Luke's International Hospital and St. Marianna University School of Medicine hospital. Each institutional review board approved this study. In the patients with or without nodal metastasis on SNB after NAC, we compared clinicopathological factors including Estrogen Receptor (ER), Progesterone Receptor (PgR), human epidermal growth factor receptor 2 (HER2), Ki-67 on needle biopsy specimens, and tumor size before and after NAC on MRI findings. **Results:** Of the 419 patients, 380 patients (90.7%) were ypN0 and 39 patients (9.3%) were ypN+ after NAC. In univariate analysis, clinical complete response of primary tumor on MRI findings (MRI-CR) ($p<0.01$), ER-negative ($p<0.01$), PgR-negative ($p<0.01$), and high-Ki-67 >30% ($p<0.01$) were significantly associated with ypN0 on SNB after NAC. In multivariate analysis, MRI-CR (HR 5.12, $p<0.01$) and high-Ki-67 (HR 2.86, $p<0.01$) were independent predictive factors of ypN0 after NAC.According to breast cancer subtype, only one of 72 ER-negative and HER2-positive had significantly low risk of ypN+ (1.3%) comparing other subtypes ($p<0.01$). **Conclusions:** Achieving cCR of primary tumor after NAC and high-Ki67 in cN0 patients, especially in HER2 type breast cancer, might have ypN0. We are conducting prospective study to omit SNB for these populations based on these results, Research Sponsor: None.

565 Poster Session (Board #57), Fri, 8:00 AM-11:00 AM

Artificial intelligence to accurately identify breast cancer patients with a pathologic complete response for omission of surgery after neoadjuvant systemic therapy: An international multicenter analysis. *First Author: André Pfob, Department of Obstetrics and Gynecology, University Hospital Heidelberg, Heidelberg, Germany*

Background: Neoadjuvant systemic treatment elicits a pathologic complete response (pCR) in up to 80% of women with breast cancer. In such cases, breast surgery, the gold standard for confirming pCR in the breast, may be considered overtreatment. So far, no approach alone – e.g. imaging, vacuum-assisted biopsy (VAB) – has accurately detected and excluded residual disease without surgery in multicenter prospective trials. We evaluated the ability of Artificial Intelligence algorithms to securely identify patients with residual tumor in the breast to safely select patients who might be spared from surgery. **Methods:** We collected multicenter, international data from 570 women who were included in prospective trials with initial stage I-III breast cancer of all biological subtypes and at least partial response on imaging, undergoing VAB before guideline-adherent surgery. We trained an ensemble of algorithms (including Regularized Regression, Support Vector Machines, and Neural Network) using 27 patient, tumor and VAB variables. Data were randomly partitioned into training and test sample with a 3:1 ratio and developed with 10-fold cross-validation. Primary endpoint was the sensitivity to diagnose residual disease by algorithm compared to surgery. Diagnostic performance of the algorithm was further evaluated on an external, independent dataset. **Results:** The algorithm was able to reliably identify women with residual disease before surgery (see table): Sensitivity for the internal test set was 96.9% (94 of 97; 95%CI 91.2-99.4%) and for the external, independent dataset 96.2% (26 of 27; 95%CI 80.4-99.9%). Most informative predictor of residual disease were tumor cells diagnosed in the VAB specimen, DCIS in the initial diagnostic biopsy, grading, and largest diameter on imaging after neoadjuvant treatment. **Conclusions:** Safely selected patients without residual disease as assessed by our algorithm may be spared by breast surgery in future trials. Research Sponsor: DFG (German Research Foundation).

Evaluation of algorithm to diagnose residual disease in the breast.

	Internal test set		External dataset	
	Residual disease by algorithm	No residual disease by algorithm	Residual disease by algorithm	No residual disease by algorithm
Residual disease by surgery	94	3	26	1
No residual disease by surgery	38	38	13	10
Sensitivity (95% CI)	96.9%	(91.2-99.4)	96.2%	(80.4-99.9)

566 Poster Session (Board #58), Fri, 8:00 AM-11:00 AM

The impact of age on early breast cancer after breast conserving therapy: Results of a subanalysis from the accelerated partial breast irradiation IMRT Florence trial. *First Author: Icro Meattini, Radiation Oncology Unit-Oncology Department, University of Florence, Florence, Italy*

Background: The impact of age on local recurrence rate of patients affected by early breast cancer is still unclear. The standard of care for older adult largely varies depending on patient- and tumor-related features, but also on national guidelines. We recently presented the 10 years median follow update of the APBI-IMRT Florence phase III trial. The primary aim of the present analysis is to identify the potential relationship between age and ipsilateral breast tumor recurrence (IBTR) in this setting of patients. **Methods:** This retrospective analysis was performed on the whole series of 520 patients who were enrolled in the trial after breast conserving surgery and randomized to receive APBI or whole breast irradiation. We analyzed patients stratified by age (70+ vs 40-69 years). **Results:** At a median follow up time of 10.7 years, we recorded 15 IBTR events. Four hundred and three patients (77.5%) were aged less than 70 years old (11 IBTR) and 117 patients (22.5%) were aged 70 years or older (4 IBTR). At the univariate analysis the age (70+ vs 40-69 years) was not significantly correlated with IBTR occurrence (HR 1.33, 95% CI 0.42-4.17; p=0.63). The only significant prognostic factor was adjuvant endocrine therapy, also at the multivariable analysis (HR 0.26, 95% CI 0.07-0.94; p=0.041). Main results are summarized in the table. Within the luminal-like patients (n=437; 12 IBTR events), the age did not impact on the IBTR rate (HR 0.91, 95% CI 0.19-4.31; p=0.91) and adjuvant endocrine therapy lost its significance (HR 0.32, 95% CI 0.09-1.11; p=0.072). **Conclusions:** Our trial subanalysis did not demonstrate a significant effect of age on IBTR rate for early breast cancer patients receiving a breast conserving therapy. Due to the low number of events, the benefit of adjuvant endocrine therapy is unclear and calls for further investigations. Clinical trial information: NCT02104895. Research Sponsor: None.

		Univariate		Multivariable	
Variable	Events	HR (95% CI)	p-value	HR (95% CI)	p-value
Age (70+ vs <70)	4/11	1.33 (0.42-4.17)	0.63	1.32 (0.37-4.74)	0.67
Tumor size (2.1+ vs <2 cm)	2/13	2.78 /0.63-12.31)	0.18	3.44 (0.61-19.42)	0.16
Grade (3 vs 1-2)	4/11	3.11 (0.99-9.75)	0.052	2.52 (0.41-15.5)	0.32
Nodal status (positive vs negative)	2/12	1.45 (0.32-6.46)	0.63	2.46 (0.46-13.28)	0.30
Hormone receptor status (negative vs positive)	2/13	3.90 (0.88-17.26)	0.07	1.37 (0.15-12.26)	0.78
Endocrine therapy (yes vs no)	6/9	**0.33 (0.12-0.94)**	**0.038**	**0.26 (0.07-0.94)**	**0.041**
APBI vs WBI	6/9	1.56 (0.55-4.37)	0.40	1.69 (0.56-5.17)	0.35

567 Poster Session (Board #59), Fri, 8:00 AM-11:00 AM

Factors associated with axillary conversion after neoadjuvant chemotherapy in initially node positive breast cancer patients: A transSENTINA analysis. *First Author: Hans-Christian Kolberg, Marienhospital, Bottrop, Germany*

Background: Current study concepts in early breast cancer after neoadjuvant chemotherapy (NAT) are aiming at reducing morbidity by omission of axillary surgery in selected patients. Selection criteria for this strategy have to include the probability of conversion from cN1 to ycN0. We analyzed the association of clinical/pathological parameters and axillary conversion with data from arms C and D of the SENTINA trial (Kühn T et al., Lancet Oncol 2013). **Methods:** Patients were recruited to Arms C/D of the SENTINA trial in case they presented with clinically positive nodes before NAT. Based on their response to NAT they were then assigned to either arm C (clinically conversion to ycN0) or arm D (no clinical conversion (ycN+). In both the pre- and post-NAT scenarios, clinically involved lymph nodes were defined as palpable and/or suspect by ultrasound. Univariate logistic regression analyses were carried out to evaluate the association between clinical/pathological parameters and axillary conversion after NAT. **Results:** Of the 892 patients in arms C and D of the SENTINA trial 716 were evaluable for this analysis. After NAT, 593 patients converted to ycN0 and were therefore assigned to arm C; in contrast, 123 patients still had involved lymph nodes after NAT (ycN+) and were assigned to Arm D. Arms C and D were compared regarding the clinical/pathological parameters tumor diameter by ultrasound before and after NAT, grading, multifocality, ER status, PR status, HER2 status, pathological complete remission in the breast (breast pCR), morphology, lymphovascular invasion (LVI) and hemangiosis. Only small tumor diameter after NAT ($p = 0.0038$), achievement of breast pCR ($p = 0.0001$) and lack of LVI ($p = 0.0009$) were positively associated with axillary conversion from cN1 to ycN0 after NAT. **Conclusions:** Because of the small patient number in arm D, we were not able to identify an association between parameters of tumor biology (ER, PR, HER2 and TN status) and axillary conversion. However, favorable response of the primary tumor (represented both clinically by tumor diameter after NAT and pathologically by pCR in the breast) were positively associated with conversion from cN1 to ycN0. These results justify including patients with clinical and pathological response of the primary tumor in trials investigating de-escalation of axillary surgery after NAT. Research Sponsor: Brustkrebs Deutschland e.V. - Prognose Leben.

568 Poster Session (Board #60), Fri, 8:00 AM-11:00 AM

Validation of nomograms to predict non-sentinel lymph node metastasis after positive sentinel lymph node in breast cancer: Indian cohort background. *First Author: Asha Reddy, Tata Memorial Centre, Parel, India*

Background: Axillary lymph node metastasis is still the important prognostic factor in the management of breast cancer (BC). Where we have moved towards axillary conservation in clinically node negative (cN0), the debate on what after 1-2 sentinel lymph nodes positive (SLN+ve) still continues. The ideal situation would be wherein we can accurately predict which patient has a risk of additional non SLN+ve. Several nomograms have been developed to predict the risk of NonSLN+ve. But in view of the differences in tumor size and nodal burden between our patients and the western data, we conducted a study to validate some of these nomograms in our cohort of early BC with positive LN on Low axillary sampling (LAS). **Methods:** Clinicopathological data was collected for operable BC (OBC) with cN0 who underwent upfront SLNB or AS. This was entered into the various nomograms and the probability of the Non SLN+ve was calculated. Nomograms with AUC of greater than 0.7 were pre-defined as considerable discrimination. **Results:** From 2013 to 2018, 2350 women with cN0 OBC underwent LAS. Of which, 670 (28.5%) had a positive node on LAS. Median pT size was 3 cm with 327 (48%), LVI +ve 152 (77%) ENI +ve, 525 (78.4%) Hormone receptor +ve and 485 (72.4%) grade 3 tumors. Of 670, 239 (35.7%) had a NonSLN+ve on completion axillary dissection. The AUC values for nomograms included,ie. MSKCC, MDAnderson, Tenon, Cambridge, Shanghai, Mayo clinic and Turkish were 0.769, 0.77, 0.55, 0.74, 0.65, 0.529, 0.563 respectively. Only three nomograms, MDA, MSKCC and Cambridge had an AUC of more than 0.7. However, they were associated with poor sensitivity and specificity and high FNR (Table) making them clinically unreliable for this cohort. **Conclusions:** All 7 nomograms were not validated in our study. The larger T size and higher nodal burden of our cohort may be responsible for the same. We thus need to develop an Indian nomogram to predict the risk of non SLN+ve for our patients. Research Sponsor: None.

Nomogram	AUC	Sensitivity	Specificity	FNR
MSKCC	0.769	62.3%	84.5%	37.7%
MD Anderson	0.774	56.1%	86%	43.9%
Cambridge	0.74	60.7%	72.4%	27.6%

569 Poster Session (Board #61), Fri, 8:00 AM-11:00 AM

Breast cancer patient reported outcomes, depression, and objective measures of breast cosmesis. *First Author: Shauna McManus, Department of Biostatistics, Rollins School of Public Health, Emory University, Atlanta, GA*

Background: Patient-reported outcomes (PROs) of cosmesis after breast-conserving therapy (BCT) are increasingly emphasized as meaningful treatment endpoints but little is known about the relationship between objective measures, mood, and PROs following radiation (XRT). We hypothesized that pre-XRT depression, assessed by Inventory of Depressive Symptomatology Self-Report (IDS-SR), would influence PROs of breast cosmesis 1-year post-XRT independent of objective measures of breast asymmetry. **Methods:** 98 women were enrolled on two prospective longitudinal studies of breast cosmesis. Percentage breast retraction assessment (pBRA) was used as an objective measure of breast asymmetry pre- and 1 year post-XRT. At the same time points, pBRA was measured and compared with two different PRO ratings of cosmetic outcome (0-10 scale): 1) happiness with cosmesis and 2) perceived differences in treated vs. untreated breast. We performed univariate and multivariate analysis to evaluate the relationship between PROs, pBRA, IDS-SR scores, clinical, tumor, and treatment characteristics. **Results:** Among subjects, 50% were African American. Mean age was 56.45 years. At 1 year, 65.3% of patients were happy with their cosmetic outcome (Score $>$ 8) although 59.5% noted moderate to severe differences in the treated vs. untreated breast (Score $<$ 6). Mean pBRA increased from 7.20 (SD 3.88) pre-XRT to 9.69 (SD 6.22) confirming more breast asymmetry 1-year post-XRT. Prior to XRT, 23% of patients had moderate-to-severe depression (IDS-SR scores $>$ 26). In multivariate analyses, 1 year PROs of happiness with cosmetic outcome did not correlate with pBRA ($p = 0.3$) but were strongly correlated with pre and post-XRT depression (all $p < 0.05$). Patients were more likely to perceive differences in breast texture or asymmetry (i.e. lower PRO ratings of asymmetry) if they had higher pBRA measurements at 1 year (all $p = 0.004$). Neither pre- nor post- XRT depression were associated with specific PRO ratings of breast asymmetry in multivariate analysis. **Conclusions:** Our study suggests that PROs may not always reflect the effects of cancer treatment. For patients treated with BCT, baseline depression strongly influenced patient reported happiness with overall cosmetic outcome 1 year post-XRT. Perceived differences in the treated vs. untreated breast correlated with objective measures of breast asymmetry. Our data suggests that this PRO may be more indicative of treatment-related toxicities than patient ratings of overall satisfaction and happiness with cosmetic outcome. Clinical trial information: NCT03167359. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

570 Poster Session (Board #62), Fri, 8:00 AM-11:00 AM

Psychosocial outcomes following surgery in women with unilateral, nonhereditary breast cancer. *First Author: David Wai Lim, Womens College Hospital, Toronto, ON, Canada*

Background: Rates of bilateral mastectomy continue to rise in average-risk women with unilateral breast cancer. We aim to characterize psychosocial predictors of surgical procedure and how psychosocial outcomes change over time after surgery for breast cancer. **Methods:** A prospective cohort of women with unilateral, nonhereditary breast cancer were recruited at University Health Network in Toronto, Canada between 2014-2017. Women completed validated psychosocial questionnaires (BREAST-Q) pre-operatively, and 6 and 12 months after surgery. Outcomes were assessed between three surgical groups (unilateral lumpectomy, unilateral mastectomy, bilateral mastectomy). Predictors of surgical procedure were identified using a multinomial logistic regression model. Change in psychosocial scores over time according to procedure was assessed using linear mixed models. All models control for age, stage, reconstruction and treatment. *P* values $<$ .05 were considered statistically significant. **Results:** 506 women underwent surgery as follows: 216 unilateral lumpectomy (43%), 181 unilateral mastectomy (36%) and 109 bilateral mastectomy (22%). In the multinomial regression model, younger age ($p <$ .01), and lower chest physical ($p = .03$) and sexual well-being ($p = .02$) predicted having bilateral mastectomy over unilateral lumpectomy while younger age ($p <$ .01) and lower disease stage ($p = .02$) predicted bilateral mastectomy over unilateral mastectomy. The mixed model demonstrates that breast satisfaction follows a non-linear pattern of change over time, with 6- but not 12-month scores being significantly different from baseline ($p = .015$). Procedure predicts baseline satisfaction ($p = .016$), with bilateral mastectomy having worse satisfaction than unilateral lumpectomy. Procedure also predicts change in satisfaction, with unilateral and bilateral mastectomy having lower scores across time than lumpectomy. While a significant improvement in psychological well-being is detected by 12 months ($p = .02$), those with unilateral and bilateral mastectomy have worse psychological well-being over time compared to lumpectomy. Women having mastectomy start with worse physical well-being than those in the lumpectomy group, but their physical well-being does not decline as much as the lumpectomy group over time ($p <$ .01). **Conclusions:** Definitive surgical procedure affects the trajectory of psychosocial functioning over time. This emerging data may be used to further facilitate surgical decision-making in women considering contralateral prophylactic mastectomy. Research Sponsor: None.

571 Poster Session (Board #63), Fri, 8:00 AM-11:00 AM

Radioparp: A phase I of olaparib with radiation therapy (RT) in patients with inflammatory, locoregionally advanced or metastatic triple-negative breast cancer (TNBC) or patient with operated TNBC with residual disease—Preliminary results. *First Author: Youlia M. Kirova, Institut Curie, Paris, France*

Background: Preclinical studies have shown that cell lines and murine models of TNBC phenotype are more sensitive to PARP1 inhibitors. This evidence provides strong rationale for developing a new therapeutic approach to TNBC based on targeting the DNA-repair defects via PARP inhibition. **Methods:** The purpose of this study was to report the Maximal Tolerated Dose (MTD) of Olaparib (O) administered concurrently with locoregional RT and evaluate the Dose-Limiting Toxicity (DLT). **Results:** Twenty-four pts with performance status 0-1 were enrolled between 09/2017 and 11/2019. Of them, 21 underwent adjuvant RT-O because poor response to NAC, and 3 received preoperative RT+O because of progression after NAC. The patients' profile is given in table. All patients received full course RT-O, as following: 4 pts at dose 50mg bid; 8 at 100x2; 7 at 150x2, and 5 at 200x2. No DLT was observed. Two pts (8.7%) experienced acute grade 3 dermatitis no grade 4 toxicities related to the RT were observed. The O-related toxicity was acceptable with mostly grade 1-2 symptoms. The only grade 3-4 hematological toxicity was lymphopenia in 11 cases. **Conclusions:** Dose of O was escalated to the target dose of 200 mgx2, without DLT. Further follow up is needed to evaluate the late toxicities. Clinical trial information: NCT03109080. Research Sponsor: Astra Zeneca.

Characteristics	N_o. (%)
Age	46 (25-74)
EE grade	
II	5 (22)
III	18 (78)
Not done	1
Clinical T stage	
T1	4 (17)
T2	14 (58)
T3	4 (17)
T4	1 (4)
T4D	1 (4)
Clinical N stage	
N0	13 (54)
N1	10 (42)
N2	1 (4)
Clinical M stage	
M0	20 (83)
Mx	4 (17)

572 Poster Session (Board #64), Fri, 8:00 AM-11:00 AM

Impact of axillary lymph node dissection (ALND) on survival in patients with ypN1 breast cancer that receive regional nodal irradiation (RNI): A national cancer database (NCDB) analysis. *First Author: Michael Kharouta, Uni-University Hospitals Cleveland Medical Center, Seidman Cancer Center, Cleveland, OH*

Background: The innovation of sentinel lymph node biopsy (SLNB) has allowed many patients with invasive breast cancer to forego ALND. However, the benefit of ALND is unclear in patients with pathologic N1 disease detected on SLNB following neoadjuvant chemotherapy, particularly in patients who receive adjuvant regional nodal irradiation. **Methods:** The National Cancer Database (NCDB) was queried for women ages 18-75 with cT1-3N1, and ypT0-T3N1M0 invasive breast cancer who underwent definitive surgical resection with axillary staging and also received adjuvant RNI. Patients treated from 2012 – 2015 were included to allow for appropriate coding of extent of axillary surgery. Overall survival (OS) was estimated using the Kaplan-Meier method and compared between patients who received SLNB alone and ALND with or without SLNB utilizing log rank testing. Propensity matching was performed to reduce the impact of potential confounders and balance sample bias. Cox proportional hazards regression was used to identify predictors of overall survival. **Results:** A total of 1411 women were identified who met inclusion criteria. The median age was 52 (23-75) years. 206 (15%) women had SLNB alone and 1205 (85%) had ALND with or without SLNB. Five year OS was 73% in patients who underwent ALND compared to 76% in those who had SLNB alone ($p = 0.39$). Following propensity matching by age, race, Charlson Deyo Comorbid Condition score, pT stage, grade, ER status, and HER2 status, 5 year OS was 79% in patients who underwent SLNB alone vs. 69% in patients who had ALND performed ($p = 0.33$). On Cox regression analysis, none of the variables predicted for 5 year OS. **Conclusions:** ALND in addition to RNI did not improve survival in patients with cT1-3N1M0 and ypT0-3N1M0 breast cancer compared to SLNB and RNI. We await results of the Alliance 011202 randomized trial for prospective validation of ALND omission in a similar subset of patients. Research Sponsor: None.

Baseline characteristics.

	SLNB (n=206)	ALND (n=1205)
Median Age	52	52
Grade 1 (n, %)	14 (6.7%)	52 (4.3%)
Grade 2 (n, %)	70 (34.0%)	360 (29.9%)
Grade 3 (n, %)	100 (48.8%)	648 (53.8%)
cT1 (n, %)	28 (13.6%)	198 (16.4%)
cT2 (n, %)	116 (56.3%)	677 (56.2%)
cT3 (n, %)	62 (30.1%)	330 (27.4%)
ER-positive (n, %)	118 (57.3%)	642 (53.3%)
HER2-positive (n, %)	26 (12.6%)	139 (11.5%)
Median # of Nodes Examined	3	12

573 Poster Session (Board #65), Fri, 8:00 AM-11:00 AM

4R Program results in breast cancer: the impact of 4R Care Delivery Model on timing and sequence of guideline recommended care. *First Author: Christine B. Weldon, Northwestern University Feinberg School of Medicine, Chicago, IL*

Background: We previously proposed a 4R care delivery model which enables patients and care teams to manage timing and sequence of interdependent, time sensitive care with a novel multimodality 4R Care Sequence plan (NCI ASCO Teams Project; Trosman, JOP 2016). We report final results of a program which tested 4R at 10 US centers (4 academic and 6 non-academic) from 2016 to 2019. **Methods:** 4R Sequences were provided to stage 0-III breast cancer patients (4R cohort, N = 422) at participating centers. Analyses of clinical and patient-reported data compared the 4R cohort to a historical control cohort of patients who received care pre-4R at the same centers (N = 466). **Results:** We significantly improved 5 guideline recommended referral metrics and 4 referral completion metrics indicating receipt of care by patients who were referred (Table). Although significantly increased, referrals to dental visit and smoking cessation before treatment remained low (< 20% and < 10% respectively). Patient survey comments indicated that insufficient lead time to quit smoking or obtain fertility consult before cancer treatment was a key barrier for completing these referrals. **Conclusions:** 4R markedly improved referral and receipt of interdependent guideline recommended breast cancer care for most metrics. Future 4R program should optimize the timing of referrals within the 4R Care Sequence to allow sufficient time for smoking cessation and fertility care before treatment initiation. Research Sponsor: None.

Metric	Guideline	% of patients referred: 4R cohort (N = 422) vs control (N = 466), p value	% of referral completion by referred patients: 4R cohort vs. control, p value (N = referrals for respective cohort and metric)
PCP visit before treatment	NCCN OAO	34% vs 28%, .05	67% (N = 143) vs 44% (N = 129), .0002
Genetic consult before surgery	NCCN BR/OV	43% vs 35%, .01	66% (N = 183) vs 53% (N = 163), .02
Flu shot before treatment	NCCN INF	39% vs 28%, .008	67% (N = 163) vs 53% (N = 130), .02
Dental visit before treatment	ADA	19% vs 5%, .0001	71% (N = 81) vs 57% (N = 23), .03
Smoking cessation before treatment	NCCN SC	5% vs 2%, .02	55% (N = 20) vs 44% (N = 9), NS
Fertility consult before treatment	NCCN BC, AYAO	8% vs 5%, .NS	59% (N = 34) vs 32% (N = 22), NS

574 Poster Session (Board #66), Fri, 8:00 AM-11:00 AM

Predicting nodal positivity in women with hormone receptor-positive (HR+), early stage breast cancer (ESBC). *First Author: Emily Miller Ray, UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC*

Background: Omission of axillary surgery is appropriate in some patients with clinically node-negative (cN0), HR+ ESBC; however, there are no pre-operative tools to predict pathologic node positivity (pN+) in these women. We propose a clinically validated predictive model to inform treatment decisions regarding axillary evaluation. **Methods:** We constructed a cohort of adult women with ESBC (clinical T1/T2, N0, M0) diagnosed 2012-2016, who underwent lumpectomy or mastectomy and lymph node surgery without neoadjuvant therapy using the National Cancer Database breast cancer dataset. The dataset was non-randomly split into training (2012-2015) and testing (2016) for development and validation. Stepwise logistic regression was used to identify predictors of pathologic node positivity (pN0 vs pN+) in the training dataset. Potential predictors included: age, race, ethnicity, comorbidity score, histologic type, clinical T, ER positivity, PR positivity, HER2 positivity, and grade. Predictor variables required a bivariate p-value <0.30 to be entered into model, and an adjusted p-value <0.35 to stay in model. A partial score method was used to develop a lymph node prediction score (LNPS) by assigning a weighted value to each strong predictor variable (OR >1.5) and adding together the values for each included variable. LNPS was treated as a linear variable for prediction in validation dataset. **Results:** 423,068 women were included (2012-2015: 334,778; 2016: 88,290). Pathologic node positivity was 17% in 2012-2015 and 2016. All variables were included in the final stepwise model. Strong predictors were age, histologic type, clinical T, and grade. Scores ranged from 0-11. In the validation dataset, predicted pN+ by LNPS was very similar to actual pN+ (Table). A 1-point increase in LNPS was associated with a 3.3% increase in absolute risk of pN+. **Conclusions:** A novel lymph node prediction score can be used in HR+ cT1-T2 cN0 breast cancers to estimate the probability of pN+ and guide decisions regarding axillary surgical evaluation. Research Sponsor: None.

Predicted and actual probability of pN+ in the testing dataset.

LNPS[a]	N	Predicted pN+ (%)	Actual pN+ (%)	Difference (%)
0	1,507	6.5	3.2	3.3
1	871	7.9	5.0	2.9
2	128	9.6	7.8	1.8
4	30,217	14.1	14.9	-0.8
6	1,381	20.2	18.2	2.0
8	4,194	28.0	31.2	-3.2
10	3,722	37.4	32.9	4.5
11	78	42.6	46.2	-3.6

[a]LNPS included: age (18-59 years: 1 point; ≥60 years: 0), histologic type (lobular: 4; ductal: 3, other subtypes: 0), clinical T (T1mi/T1a: 0; T1b: 1; T1c: 3; T2: 7; T1 unspecified: 2), and grade (grade I/II: 0; grade III/IV: 1)

575 Poster Session (Board #67), Fri, 8:00 AM-11:00 AM

Sentinel-Lymphnode Biopsy in primary breast cancer: 99mTc versus ICG—A prospective, randomized trial. *First Author: Peter Kern, University Duisburg-Essen, University Hospital of Essen, West-German Cancer Center, Women´s Department, Herten, Germany*

Background: Sentinel-Lymphnode Biopsy (SLNB) is the standard procedure in primary breast cancer, routinely performed with 99mTechnetium radioactive tracers. Awareness of nuclear waste, costs and time consumption lead to the desire of breast surgeons to find safe and effective alternative options for detection of sentinel lymph nodes (SLN) in breast cancer and melanoma. Indocyaningreen is a tracer which emits fluorescence with near-infrared light of 780-810 nm when injected in the peritumoral or periareolar region, enabling surgeons to detect SLN and lymphatic pathways at the breast. **Methods:** We performed a prospective, randomized trial with patients with primary breast cancer. Both detection methods have been applied to patients of the study cohort comparing the preparation time, time to identify, concordance of the two methods and costs. Reference method was preoperative lymphszintigraphy. **Results:** 55 patients have been analyzed in this first report. Preparation time was 75,8 min (range 60-120 min) for 99mTc-tracer and a standard of 20 min for ICG. Time to identify SLN at a mean of 3,8 min(range 1-15 min) for 99mTc and 3 min (range 1-8 min) for ICG. Concordance rates were 98,2 % for the 1st SLN, 93,8 % both for 2nd and 3rd SLN. After neoadjuvant chemotherapy, all SLN have been been detected by both techniques, in 3 patients additional SLN have been found by ICG. Costs have been cut down to 1/10 with the use of ICG, coming up to saving of 27 000 US-$ per each 100 SLNB procedures performed. **Conclusions:** We report a high concordance rate between the 2 techniques - 99mTechnetium and ICG with near-infrared - for detection of SLN in breast cancer. Preparation time is cut down to less than 30 %, and costs to less the 10 % of radioactive labelling. Clinical trial information: 18-8054-BO. Research Sponsor: University of Duisburg-Essen.

576 Poster Session (Board #68), Fri, 8:00 AM-11:00 AM

Re-excision rates among older breast cancer patients undergoing breast-conserving surgery (BCS): Impact of the SSO-ASTRO consensus guideline on margins. *First Author: Mariana Chavez-MacGregor, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: BCS has been historically associated with a high re-excision rate, driven in part by the need of obtaining negative margins. The SSO-ASTRO consensus guideline on invasive margins, defined a negative margin as no ink on tumor. In this large population-based study of older breast cancer patients undergoing BCS for invasive breast cancer we evaluate the guideline impact on re-excision rates. **Methods:** Female patients diagnosed with stage I-II breast cancer between 2012-2015 were identified in the SEER-Medicare database. Patients were >66 years and underwent BCS. Patients treated with neoadjuvant chemotherapy were excluded. We defined the following time periods: pre-guideline (January 2012-September 2013); peri-guideline (October 2013-March 2014) and post-guideline (April 2014-December 2016). Re-excision was defined as a resection, BCS or mastectomy identified using ICD-9 or CPT codes between 4 and 90 days after initial BCS. Overall re-excision rates and 95%CI were calculated and groups compared using X^2test. Within subgroups we calculated re-excision rates for the pre and post-guideline periods and report the relative percent change. Regression model evaluated the association between time periods and re-excision while adjusting for important covariates, risk ratios (RRs) and 95%CI are presented. **Results:** 17001 patients were included. 6762 of them had BCS in the pre, 1786 in the peri, and 8453 in the post-guideline periods. Overall 22.6% of the patients had a re-excision. The rate decreased from 24.8% pre-guideline to 20.3% post-guideline (P < 0.001). The relative change in re-excision varied according to region (Midwest 3-7.3%, Northeast -20%, West -16.5% and South -13.5%) Differences in the relative change according to race/ethnicity were also seen (Whites -19.2, Blacks -15.3% and Hispanics -9.9%). In the multivariable model, BCS in the post-guideline period was associated with a decreased risk of re-excision (RR = 0.83; 95%CI 0.79-0.88). Lobular histology was associated with a higher risk of re-excision (RR = 1.31; 95%CI 1.21-1.42); greater surgeon volume was associated with lower risk of re-excision (RR = 0.89; 95%CI 0.82-0.95). **Conclusions:** There has been a statistically significant decrease in the re-excision rate after BCS associated with the dissemination of the SSO-ASTRO consensus guideline on invasive margins. Our study confirms the impact that guidelines have modifying patterns or practice, reducing the frequency of unnecessary interventions. Research Sponsor: Susan G. Kome, CIPRIT.

577 Poster Session (Board #69), Fri, 8:00 AM-11:00 AM

Neoadjuvant chemotherapy (NACT) and HER2 double inhibition including biosimilar trastuzumab (ONTRUZANT) for HER2-positive early breast cancer (EBC): Population-based real world data from the Danish Breast Cancer Group (DBCG). *First Author: Michael Andersson, Department of Oncology, Rigshospitalet University Hospital, Copenhagen, Denmark*

Background: Increasingly, HER2-positive early breast cancer (EBC) is treated by NACT combined with trastuzumab and pertuzumab followed by surgery. Ontruzant is registered as a biosimilar trastuzumab based on the totality of evidence including a randomized phase III study of NACT+Herceptin versus NACT+Ontruzant demonstrating similar pCR-rates (Pivot et al. J Clin Oncol 2018;36:968). However, no data exist for the efficacy of the combination of NACT with pertuzumab+Ontruzant (p+O). This investigator-initiated study was conducted to assess real world efficacy in HER2-positive EBC patients treated with NACT+p+O based on data from DBCG. DBCG has since 1977 provided guidelines for treatment of breast cancer and collected data from Danish hospital departments of surgery, pathology, and oncology prospectively on NACT, date and type of surgery and patho-anatomic findings. **Methods:** From the DBCG database, information was extracted for consecutive patients with unilateral early HER2-positive breast cancer registered to have received NACT+p+O from September 1, 2018 to August 31, 2019. pCR was defined as absence of residual invasive tumor in the breast and axillary lymph nodes (ypTO/Tis ypN0(i-)). **Results:** 215 patients received NACT+p+O. Median age was 54.8 years (range 24-81). NACT used, in combination with concurrent p+O, was cyclophosphamide+epirubicin followed by paclitaxel (62% on 6 cycles and 35% on 8 cycles) or other chemotherapy followed by paclitaxel (3%). Overall, 56% of patients achieved a pCR (Table). 68% of node-positive patients before receiving NACT+p+O had tumor-free axillary nodes after completing NACT+p+O. **Conclusions:** Real-world data from a nationwide population based study demonstrated a pCR-rate with NACT+p+O comparable to that seen in clinical studies with NACT+p+Herceptin (Chen et al. BMC Cancer 2019;19: 973). pCR-rate was highly dependent on estrogen receptor (ER)-status and malignancy grade but not on clinical nodal status and tumor size. 68% of patients with cN+ converted to ypN0(i-). Research Sponsor: Samsung Bioepis.

Baseline characteristics and treatment outcomes.

	pCR-Yes N(%)	pCR-No N(%)	pCR-Unknown N
Clinical nodal status			
Positive	47(55)	39(45)	2
Negative	68(58)	50(42)	9
Clinical tumor size			
<5cm	92(59)	64(41)	8
≥5cm	22(47)	25(53)	2
Unknown	1	0	1
ER status*			
0%	49(72)	19(28)	4
1-9%	10(77)	3(23)	1
10-100%	56(46)	67(54)	6
Malignancy grade*			
I	2(20)	8(80)	0
II	73(61)	46(39)	6
III	34(52)	31(48)	2
Unknown	6	4	3
Total	115(56)	89(44)	11

*χ2-test $p<0.05$

578 Poster Session (Board #70), Fri, 8:00 AM-11:00 AM

Four-year follow-up of a phase III study comparing SB3 (trastuzumab biosimilar) and reference trastuzumab in HER2-positive early or locally advanced breast cancer in neoadjuvant setting. *First Author: Xavier Pivot, CHRU de Besançon–IRFC, Besançon, France*

Background: SB3 was approved in the US and EU as a biosimilar of reference trastuzumab (TRZ). Here, we report 4-year cardiac safety and survival outcomes. **Methods:** After completing neoadjuvant-adjuvant therapy in patients with HER2 positive early breast cancer, patients from selected countries participated in a 5-year follow-up study of a phase III trial (Pivot et al. Eur J Cancer 2019). The aim was to observe long-term cardiac safety and survival. EFS and OS were analyzed in subgroups by ADCC status within TRZ in ad-hoc analyses. **Results:** Of 875 patients randomized in the phase III trial, 367 patients (SB3, N=186; TRZ, N=181) were enrolled in the follow-up study. The median follow-up was 53 months. During the follow-up, the incidence of asymptomatic significant left ventricular ejection fraction (LVEF) decrease was low (SB3, n=1; TRZ, n=2), with all patients recovering with LVEF ≥ 50%. No cases of symptomatic congestive heart failure, cardiac death, or other significant cardiac condition were reported. 4-year EFS rates were 83.4% for SB3 and 80.7% for TRZ with a HR of 0.77 [95% CI 0.47, 1.27]. 4-year OS rates were 94.3% for SB3 and 89.6% for TRZ with a HR of 0.53 [95% CI 0.24, 1.16]. From ad-hoc analysis, a difference in EFS and OS was seen between Non-drifted TRZ and Drifted TRZ; Difference between SB3 and Non-drifted TRZ was not statistically significant. **Conclusions:** In a subset of patients from the phase III trial, comparable long-term cardiac safety and survival at 4-year supports biosimilarity between SB3 and TRZ. Ad-hoc analysis results by ADCC status suggest a possible correlation between ADCC and clinical efficacy. Further follow-up is needed. Clinical trial information: NCT02771795. Research Sponsor: Samsung Bioepis Co., Ltd.

Survival results.

	SB3 N=186	TRZ All N=181	Non-drifted TRZ N=55	Drifted TRZ N=126	HR [95% CI] (SB3/TRZ)	HR [95% CI] (SB3/Non-drifted TRZ)[a]	HR [95% CI] (Drifted TRZ/Non-drifted TRZ)[a]
EFS, n (%)							
Patients with event	29(15.6)	35(19.3)	5(9.1)	30(23.8)	0.77 [0.47, 1.27] p=0.306	1.60 [0.58, 4.40] p=0.362	5.50 [1.81, 16.65] p=0.003
Recurrence	26(14.0)	32(17.7)	4(7.3)	28(22.2)			
Progression	1(0.5)	1(0.6)	1(1.8)	0(0.0)			
Deaths	2(1.1)	2(1.1)	0(0.0)	2(1.6)			
OS, n (%)							
Patients with death	10(5.4)	18(9.9)	1(1.8)	17(13.5)	0.53 [0.24, 1.16] p=0.112	0.97 [0.11, 8.50] p=0.975	15.35 [1.78, 132.69] p=0.013

Non-drifted TRZ, patients never exposed to any vials from an ADCC-drifted TRZ lot during neoadjuvant period; Drifted TRZ, patients exposed to at least one vial from an ADCC-drifted TRZ lot during neoadjuvant period. [a]HR was estimated with bpCR as a covariate.

579 Poster Session (Board #71), Fri, 8:00 AM-11:00 AM

Establishing analytical and clinical similarity between HD201 and herceptin. *First Author: Jocelyn Hii, Prestige Biopharma Pte Ltd, Singapore, Singapore*

Background: Trastuzumab, an approved prescription drug by EMA and FDA under the name Herceptin has become the key treatment in patients with HER2$^+$positive breast cancer. HD201, developed by Prestige Biopharma Pte Ltd is a biosimilar candidate to Herceptin. The biosimilarity of HD201 was established based on systematic stepwise comparisons between HD201 and reference product, Herceptin. In order to confirm clinical similarity of HD201 to Trastuzumab, two clinical studies were undertaken. **Methods:** First, in a double-blind, randomised and parallel group study, 101 randomised healthy human subjects were subjected to a single 6 mg/kg IV dose by body weight over 90-min infusion of either HD201, EU- and US-Herceptin group by assessing pharmacokinetic (PK) and safety (TROIKA-I). The second study was a randomised, double-blind, parallel group, equivalence, multicentre clinical phase III trial (TROIKA) designed to compare the efficacy based on total pathological complete response rate (tpCR), safety, and pharmacokinetics of HD201 to EU-Herceptin in patients with HER2 positive early breast cancer. Each group of ~250 subjects were administered with either HD201 or EU-Herceptin in combination with chemotherapy in neoadjuvant followed by the antibody alone in the adjuvant phase. **Results:** TROIKA-I study demonstrated that HD201 was safe and well tolerated with comparable PK as EU- and US-Herceptin. Based on the neoadjuvant data from TROIKA study, the tpCR rate in the HD201 and Herceptin treatment groups was comparable and the 95% CI was included within the pre-defined margins of equivalence (Table). The incidence and severity of reported TEAEs did not imply any significant safety concerns and were comparable between both groups. In addition, the comparison of steady-state C_{trough} between both arms in TROIKA study has established equivalence. **Conclusions:** The overall comparison exercise demonstrated the equivalence of HD201 to Herceptin. Clinical trial information: 2016-0040019-11. Research Sponsor: Private funding.

Primary endpoint: (tpCR) (Local assessment).

PPS	HD201 arm	Herceptin arm	Difference (HD201-Herceptin)
Responders (%)	111/238 (46.6%)	109/236 (46.2%)	0.5% [-8.6%, 9.6%]
95% CI	[40.2%, 53.2%]	[39.7%, 52.8%]	Pre-defined equivalence margin is [-15%, 15%].

Onset of Cycle 8: Ctrough concentration profiles

	HD201 arm	Herceptin arm	Difference (HD201-Herceptin)
Responders (%)	145/250 (58.0%)	144/252 (57.1%)	4.0% [-2.6%, 10.6%]
Mean (SD)	53.72 (18.13)	51.64 (17.00)	Pre-defined equivalence margin is [10%, 10%].

580 Poster Session (Board #72), Fri, 8:00 AM-11:00 AM

Influence of denosumab on disseminated tumor cells (DTC) in the bone marrow of breast cancer (BC) patients with neoadjuvant treatment: A GeparX translational substudy. *First Author: Pauline Wimberger, Department of Gynecology and Obstetrics, University Hospital Carl Gustav Carus, TU Dresden, Dresden, Germany*

Background: DTCs in the bone marrow are observed in up to 30% at primary diagnosis of BC and their presence is an independent prognostic factor for reduced survival. It was shown that antiresorptive therapy eradicates DTCs and improves prognosis in DTC-positive BC patients (pts). In the GeparX phase III prospective randomized trial, denosumab (a monoclonal IgG2-anti-RANKL-antibody) was investigated as add-on treatment to neoadjuvant chemotherapy (NACT) with two different nab-paclitaxel schedules in early high-risk primary BC. In a translational substudy, we analyzed for the first time the influence of short-term denosumab treatment (24 weeks) on the presence of DTCs. **Methods:** A total of 167 pts from the GeparX trial were analyzed for DTCs at baseline by immunocytochemistry using the pan-cytokeratin antibody A45-B/B3. Initially DTC-positive pts were re-analyzed for DTCs after NACT±Denosumab. **Results:** Overall, 60/167 pts (35.9%) treated with NACT±Denosumab had a pathological complete response (pCR; 55.4% in TNBC, 43.3% in HER2+, 15.3% in HR+/HER2-). At baseline, 43/167 pts (25.7%) were DTC-positive and 41 of those were available for re-analysis of DTCs after NACT±Denosumab. DTC eradication was observed in 77.8% after NACT+Denosumab and in 69.6% after NACT alone (p = 0.726). Due to the limited number of pts eligible for DTC-re-analysis after NACT, a subtype specific analysis for the effect of denosumab was not possible. There was no significant association between pCR and i) the presence of DTCs at baseline (37.1% DTC-negative vs 32.6% positive, p = 0.71) or ii) the eradication of DTCs after NACT±Denosumab (36.7% vs 27.3%, p = 0.72). Notably, in TNBC, we observed a tendency that DTC-positivity at baseline or DTC-persistence after NACT could be associated with reduced pCR rate (40.0% in DTC-positive vs. 66.7% in DTC-negative pts, p = 0.16; 25% in DTC-persistent pts vs. 50% in DTC-eradicated pts, p = 0.59). **Conclusions:** Denosumab in addition to NACT does not improve pCR, but the suspected effect of denosumab on DTC eradication should be further analyzed in TNBC. Key words: GeparX trial, denosumab, disseminated tumor cells, bone marrow, neoadjuvant chemotherapy. Funding: GeparX and DTC substudy were financially supported by Amgen and Celgene. Clinical trial information: NCT02682693. Research Sponsor: Amgen, Celgene.

581 Poster Session (Board #73), Fri, 8:00 AM-11:00 AM

The impact of pattern of tumor response and other post-treatment histologic features on local recurrence in patients treated with neoadjuvant chemotherapy and breast conservation. *First Author: Alison Laws, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA*

Background: Residual disease after neoadjuvant chemotherapy (NAC) is a poor prognostic factor. The relationship between the pattern of tumor response and other post-treatment histologic features on local recurrence (LR) is not well studied. **Methods:** We identified 380 patients (pts) treated with NAC, breast-conserving surgery and radiation from 2002-2014. Pts with available surgical slides underwent detailed pathology review. Pathologic complete response (pCR) was defined as no invasive or in situ disease in the breast or axilla. Pattern of tumor response was defined as: none, scattered, or concentric. The degree of treatment effect was categorized as: absent, mild or marked. Univariate (UVA) and multivariate analyses (MVA) were performed to identify factors associated with LR. **Results:** 243 (64%) cases had complete slides available and formed the study cohort. 76 (31%) were ER+/HER2-, 90 (38%) ER-/HER2- and 77 (31%) HER2+. 98% of HER2+ pts received neoadjuvant trastuzumab; 89% of ER+ pts received adjuvant endocrine therapy. At median follow-up of 75 months, 10/243 (4.1%) pts had LR and 5-yr LR-free survival was 95.7%. LR occurred in 1/76 (1.3%) pts with breast pCR, 1/19 (5.2%) with residual DCIS, and 8/148 (5.4%) with residual invasive disease; including 6/78 (7.7%) with scattered tumor response, 2/46 (4.3%) with concentric response and 0/24 with no response. On UVA, age (OR $<$ 50 vs $\geq$50 5.9, p = 0.03) and residual DCIS with comedonecrosis (OR 8.2, $p < 0.01$) were significantly associated with LR. Presence of tumor bed at the margin (OR 4.6, p = 0.06) approached significance. The odds of LR were higher with scattered regression (OR 1.83 vs. concentric, p = 0.47) and lower with breast pCR (OR 0.23, p = 0.17), but these results were not statistically significant. Multicentric disease, receptor status, ypT, ypN, RCB score, degree of treatment effect, high-grade residual invasive disease, margin status of residual disease and lymphovascular invasion were not associated with LR (all $p > 0.05$). Age (OR $<$ 50 vs $\geq$50 7.4, p = 0.04) and residual DCIS with comedonecrosis (OR 7.5, p = 0.02) remained significant on MVA. **Conclusions:** With modern systemic therapy, LR rates after NAC, breast-conserving surgery and radiation are low, with less than 5% of patients experiencing a LR after a median follow-up of over 6 years. Young age and residual DCIS with comedonecrosis were associated with LR, but not pattern of tumor response. Research Sponsor: None.

582 Poster Session (Board #74), Fri, 8:00 AM-11:00 AM

Survival analysis of the prospective randomized Cher-Lob study evaluating the dual anti-HER2 treatment with trastuzumab and lapatinib plus chemotherapy as neoadjuvant therapy for HER2-positive breast cancer (BC). *First Author: Valentina Guarneri, Department of Surgery, Oncology and Gastroenterology, University of Padua and Medical Oncology 2, Istituto Oncologico Veneto IRCCS, Padua, Italy*

Background: The CHER-LOB randomized phase II study showed that the combination of lapatinib and trastuzumab plus chemotherapy increases the pathologic complete response (pCR) rate compared with chemotherapy plus either trastuzumab or lapatinib. Here we report the results of survival analysis according to treatment arm and pCR. **Methods:** The CherLOB study randomized 121 HER2-positive, stage II-IIIA breast cancer patients to anthracyclines/taxane-based chemotherapy plus trastuzumab, lapatinib, or both. After surgery, patients received adjuvant trastuzumab for up to 1 year. The primary end point of the study was met, with a relative increase of 80% in the pCR rate achieved with chemotherapy plus trastuzumab and lapatinib compared with chemotherapy plus either trastuzumab or lapatinib (Guarneri, J Clin Oncol 2012). Relapse-free survival (RFS) was calculated from randomization to breast cancer recurrence (locoregional or distant) or death from any cause, whichever first. Overall survival (OS) was calculated from randomization to death from any cause. **Results:** At a median follow up of 8.8 years, RFS rates at 5 years were: 85.8% in the trastuzumab + lapatinib arm, 77.8% in the trastuzumab arm, 78.1% in the lapatinib arm (log-rank p = 0.160). Patients treated with dual HER2 blockade (trastuzumab + lapatinib arm) experienced numerically better RFS as compared to patients treated with single HER2 blockade (trastuzumab arm and lapatinib arm combined): 5-yr RFS 85.8% vs 78.0%, log-rank p = 0.087; HR = 0.51, 95% CI 0.23-1.12, p = 0.093. The achievement of pCR was a strong prognostic factor. 5-yr RFS rate was 97.3% for pCR patients vs 72.9% for non-pCR patients (log-rank $p < 0.001$, HR = 0.12, 95% CI 0.03-0.49, p = 0.003); similar significant results were observed in both the estrogen receptor-negative and estrogen-receptor positive subgroups. OS was also improved in pCR patients: 8-yr OS rates were 97.2% vs 80.0% for non pCR patients (log-rank p = 0.028, HR = 0.14, 95% CI 0.02-1.08, p = 0.060). **Conclusions:** In the Cher-LOB study, there was a not statistically significant signal for a better RFS for patients who received dual HER2 blockade with trastuzumab and lapatinib plus chemotherapy as compared to patients treated with single anti-HER2 agent (trastuzumab or lapatinib) plus chemotherapy. Patients achieving a pCR had longer RFS and OS as compared to non-pCR patients. Clinical trial information: NCT00429299. Research Sponsor: Ricerca Scientifica fondi quota EX 60% - Bando 2014 60A07-9077, UNIMORE - UniPD grant.

583 Poster Session (Board #75), Fri, 8:00 AM-11:00 AM

Prognostic impact of high stromal tumor-infiltrating lymphocytes (sTIL) in the absence of pathologic complete response (pCR) to neoadjuvant therapy (NAT) in early stage triple negative breast cancer (TNBC). *First Author: Nour Abuhadra, MD Anderson Hematology/Oncology Fellowship, Houston, TX*

Background: Pathologic complete response is an excellent surrogate for disease-free survival (DFS) and overall survival (OS) in TNBC. High sTIL is associated with improved pCR rates in TNBC. Recent data suggest that high sTIL is also associated with improved outcomes in patients who received no chemotherapy for early stage TNBC (Park, Annals of Oncology, 2019). Thus, we hypothesized that high sTIL may have prognostic impact in patients who do not achieve pCR to NAT. **Methods:** Pretreatment core biopsies from 182 patients with early-stage TNBC enrolled on the ARTEMIS trial (NCT02276443) were evaluated for sTIL by H&E. Patients were stratified according to sTIL (low $<$ 30%, and high $>$ 30%) and pCR (patients with pCR vs. no pCR). The primary outcome measure was DFS, defined from the date of diagnosis to the first local recurrence, distant metastases or death. Cox proportional hazards regression model was used. During follow-up 33 events for DFS were observed. **Results:** Among subjects who achieve pCR, DFS was excellent regardless of sTIL status and significantly better than those without pCR ($p < 0.05$). However, patients with high sTIL and no pCR demonstrated significantly worse DFS compared to all subjects having pCR (HR 0.18, 95% CI 0.04-0.76, p = 0.02). Additionally, we did not find a significant difference between high and low sTIL patients who did not achieve pCR. **Conclusions:** In early TNBC receiving NAT, for patients failing to achieve pCR, high sTIL was not associated with improved DFS; outcomes were comparable to those with low sTIL without pCR. Thus, high sTIL at baseline does not appear to confer an intrinsic prognostic benefit in the absence of pCR. Research Sponsor: CPRIT, MD Anderson Breast Moonshots Program.

584 Poster Session (Board #76), Fri, 8:00 AM-11:00 AM

Inhibiting fatty acid synthase in operable triple negative breast cancer. *First Author: Sagar D. Sardesai, The Ohio State University Comprehensive Cancer Center, Division of Medical Oncology, Columbus, OH*

Background: Fatty acid synthase (FASN) is overexpressed in 70% of newly diagnosed triple negative breast cancer (TNBC) and is associated with poor prognosis. *In vitro*, FASN overexpression induces drug resistance to DNA damaging agents. Proton pump inhibitors (PPI) selectively inhibit FASN activity and induce apoptosis in breast cancer cell lines with minimal effect on non-malignant cells. We report the results of a single arm phase II study of high dose omeprazole (OMP) in combination with anthracycline- taxane (AC-T) based neoadjuvant chemotherapy. **Methods:** Patients (pts) with operable TNBC independent of baseline FASN expression; and no prior PPI use within 12 months were enrolled. Pts began OMP 80 mg PO BID for 4-7 days prior to AC-T; carboplatin was allowed per physician discretion. OMP was continued until surgery. Paired biopsy samples were obtained before and after OMP monotherapy. The primary endpoint was pathologic complete response (pCR), defined as no residual invasive disease in breast or axilla, in pts with baseline FASN expression (FASN+) assessed using immunohistochemistry. Relevant secondary endpoints included pCR in the intent to treat population, change in FASN expression, enzyme activity and downstream target gene expression after OMP monotherapy; safety and limited OMP pharmacokinetics. We targeted a pCR rate of 60% in FASN+ pts (null pCR ~ 40%) with 80% power and alpha of 0.10. **Results:** A total of 42 pts were recruited from 5 US sites. Median age was 51y (28-72). Most pts had $>$cT2 (33, 79%) and $\geq$N1 (22, 52%) disease. 14 (33%) were African American. FASN expression prior to AC-T was identified in 28 (85%) samples available for analysis. The pCR rate was 71.4% (95% CI 51.3 to 86.8) in FASN+ pts and 71.8 %(95% CI 55.1 to 85.0) in all enrolled pts. Fifteen pts (36%) received carboplatin with AC-T; pCR in this subset was 73%. Peak OMP concentration was significantly higher than IC_{50} observed during preclinical testing; FASN positivity significantly decreased with OMP monotherapy from 0.53(SD 0.25) at baseline to 0.38(SD 0.30; p = 0.02). OMP was well tolerated with no known grade (G) 3 or 4 toxicities. Chemotherapy toxicity was similar to prior studies using AC-T with G3 or 4 neutropenia (19%), febrile neutropenia (7%) and peripheral neuropathy (7%) being the most common. **Conclusions:** Consistent with previous studies, FASN is frequently expressed in early stage TNBC. OMP can be safely administered in doses that inhibit FASN. The addition of high dose OMP to neoadjuvant AC-T yields a promising pCR rate without adding toxicity. Funded by the Breast Cancer Research Foundation. Clinical trial information: NCT02595372. Research Sponsor: Breast Cancer Research Foundation.

585 Poster Session (Board #77), Fri, 8:00 AM-11:00 AM

Neoadjuvant TCH (docetaxel/darboplatin/trastuzumab) versus EC-TH (epirubicin/cyclophosphamide followed by docetaxel/ trastuzumab) in patients with HER2-positive breast cancer (neoCARH): A randomised, open-label, multicenter, phase II trial. *First Author: Hong-Fei Gao, Department of Breast Cancer, Cancer Center, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, 510080, China, Guangzhou, China*

Background: The optimal neoadjuvant treatment for HER2-positive breast cancer is unknown. We wanted to compare the efficacy and safety of the anthracycline regimen EC-TH versus nonanthracycline regimen TCH in neoadjuvant setting for HER2-positive breast cancer. **Methods:** Patients with stage II or III HER2-positive breast cancer were randomly assigned to either four cycles of epirubicin/cyclophosphamide followed by four cycles of docetaxel and trastuzumab (EC-TH) every 3 weeks during all chemotherapy cycles, or six cycles of docetaxel and carboplatin plus trastuzumab (TCH) every 3 weeks. The primary endpoint was pathological complete response (defined as the absence of invasive tumour cells in breast and axilla, ypT0/is ypN0). This trial is registered with ClinicalTrials.gov, number NCT03140553. **Results:** From September 2016 to November 2019, 140 patients were randomly assigned, and 131 were evaluable for the primary end-point. The pathological complete response was recorded in 25 (38.5%, 95% confidence interval [CI] 26.6–50.2) of 65 patients in the EC-TH group and in 37 (56.1%, 44.1–68.0) of 66 in the TCH group (p=0.044). In the EC-TH group, 15 (23.1%) of 65 patients underwent breast-conserving surgery. In the TCH group, 21 (31.8%) of 66 patients underwent breast-conserving surgery. There was no difference in the proportions of patients undergoing breast-conserving surgery between the two treatment groups (p=0·262). The most common adverse events were neutropenia (in 23 [35.4%] of 65 patients in the EC-TH group vs 27 [40.9%] of 66 in the TCH group), anemia(in 33 [50.8%] of 65 patients in the EC-TH group vs 34 [51.5%] of 66 in the TCH group) and thrombocytopenia (in 5 [7.7%] of 65 patient in the EC-TH group vs 17 [25.8%] of 66 in the TCH group). **Conclusion**: This is the first multicenter prospective randomised phase II trial compare EC-TH with TCH for neoadjuvant therapy in HER2-positive breast cancer. There was a similar incidence of AEs but a higher pCR rate in TCH arm compared with the EC-TH arm. TCH regimen might be a preferred approach in patients with HER2-positive breast cancer. Long-term follow-up is required to confirm these results. Clinical trial information: NCT03140553. Research Sponsor: None.

586 Poster Session (Board #78), Fri, 8:00 AM-11:00 AM

Neoadjuvant docetaxel + carboplatin versus epirubicin+cyclophosphamide followed by docetaxel in triple-negative, early-stage breast cancer (NeoCART): Results from a multicenter, randomized controlled, open-label, phase II trial. *First Author: Liulu Zhang, Department of Breast Cancer, Cancer Center, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China*

Background: Taxane- and anthracycline-based neoadjuvant regimens have become a standard treatment for triple-negative breast cancer (TNBC). Previous studies have shown that adding carboplatin to neoadjuvant chemotherapy regimens significantly improved pCR rate in TNBC patients. The NeoCART study was designed to compare the efficacy and safety of docetaxel plus carboplatin with standard neoadjuvant chemotherapy in TNBC. **Methods:** NeoCART was designed as a multicenter, randomized controlled, open-label, phase 2 trial. The patients enrolled were at least 18 years old with previously untreated stage II-III (T1cN1-2 or T2-4N0-2) invasive TNBC who had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. All eligible patients were randomly assigned, in a 1:1 ratio, to the experimental arm (docetaxel (75 mg/m2) plus carboplatin (AUC 6) for six cycles) or the standard treatment arm (epirubicin 90 mg/m2 plus cyclophosphamide 600 mg/m2 four cycles, followed by docetaxel 100 mg/m2 for four cycles). The primary end point was the pCR rate (ypT0/is and ypN0). Secondary endpoints included event-free survival, frequency of breast-conserving surgery, and safety. **Results:** Between September 1, 2016, and December 31, 2019, 88 patients from 6 participating centers were included and randomized (44 patients to the DCb arm and 44 to the EC-D arm). In the primary end point analysis, 27 patients (61.4%, 95% CI 47.0 - 75.8) in the DCb group achieved a pCR compared with 17 patients (38·6%, 95% CI 24.3 - 53.0) in the EC-D group (odds ratio 2.52, 95% CI 2.4 - 43.1; p = 0.033). In different stage disease, the pCR rates of the DCb and the EC-D groups were 73.3% (22/30) vs 48.4% (15/31) in stage II (p = 0.046), and 35.7% (5/14) vs 15.4% (2/13) in stage III (p = 0.384). In patients with axillary lymph node involvement, the pCR rates were 45.8% (11/24) vs 30.8% (8/26) (p = 0.273); and 80.0% (16/20) vs 50.0% (9/18) with lymph node negative disease (p = 0.052). The frequency of breast-conserving surgery in the DCb and EC-D groups was 36.4% and 37.2%, respectively (p = 0·935). The grade 3/4 adverse events include anemia (4.5%), thrombocytopenia (2.3%), neutropenia (2.3%) and ALT/AST increased (2.3%) in the DCb group. **Conclusions:** Compared with the standard neoadjuvant regimen, docetaxel combined with carboplatin showed a higher pCR rate in TNBC. The higher pCR rate was more significant in patients with earlier disease stage and negative lymph node. Clinical trial information: NCT03154749. Research Sponsor: None.

587 Poster Session (Board #79), Fri, 8:00 AM-11:00 AM

Efficacy of neoadjuvant chemotherapy (NAC) in male breast cancer (MaBC) compared with female breast cancer (FBC): A National Cancer Database (NCDB) study. *First Author: Jose Pablo Leone, Dana-Farber Cancer Institute, Boston, MA*

Background: NAC is frequently used in the treatment of FBC. The efficacy of NAC in MaBC is unclear. Few studies have compared outcomes for MaBC and FBC after similar treatment. The aim of this study was to compare proportions of pathologic complete response (pCR) between MaBC and FBC according to tumor subtype (TS). Secondary aims were clinical response and overall survival (OS). **Methods:** We evaluated men and women with breast cancer treated with NAC between 2010 and 2016 with known hormone receptor (HR) status and human epidermal growth factor receptor 2 (HER2) status at NCDB centers. The proportion with pCR (ypT0/Tis ypN0) was compared for MaBC and FBC for each TS by Fisher's exact test. Logistic regression evaluated odds of pCR. OS was estimated by Kaplan-Meier and compared by log-rank test. **Results:** Of 7,721 MaBC and 859,096 FBC patients, 385 MaBC (5%) and 68,065 FBC (7.9%) underwent NAC and were included in this study. Median age for MaBC was 58 years (y) (range 23-88) and for FBC was 53 y (range 18-90). Within each TS, there were no significant differences in the distribution of tumor grade between MaBC and FBC. Clinical stage in MaBC and FBC were: Stage I: 8% v 11%, Stage II: 54% v 59%, Stage III: 38% v 30%; respectively. Median time from initiation of NAC to surgery was 143 days in MaBC and 148 days in FBC. Compared with FBC, MaBC had a lower proportion of complete clinical response (18% v 31%) and a higher proportion of no clinical response (14% v 7%); $p < 0.001$. Proportions and odds of pCR were numerically lower in MaBC compared with FBC for each TS and statistically significant for HR+/HER2- and HR+/HER2+ (table). pCR was associated with OS in both MaBC and FBC. Specifically, in MaBC who achieved pCR v not, 5 y OS was 90% v 64.7%; p = 0.02. In FBC who achieved pCR v not, 5 y OS was 91.9% v 75.3%; $p < 0.01$. Among pts receiving NAC, MaBC had worse OS at 5 y than FBC (67.1% v 79.0%; p = 0.02). **Conclusions:** Men receiving NAC achieved lower proportions of pCR than women and had significantly worse OS. However, pCR is prognostic in both MaBC and FBC. Limitations include small sample sizes for HR-/HER2+ and triple-negative TS and lack of detailed regimen information. Nevertheless, our results suggest that, compared with FBC, MaBC may be intrinsically more resistant to NAC. Research Sponsor: None.

	MaBC		FBC			
	N	pCR (ypT0/Tis ypN0) (%)	N	pCR (ypT0/Tis ypN0) (%)	p	Odds ratio (95% CI) pCR FBC v MaBC
HR+/HER2-	206	4.9	25,326	9.7	0.01	2.1 (1.1 – 4.0)
HR+/HER2+	112	16.1	15,539	33.6	<0.001	2.6 (1.6 – 4.4)
HR-/HER2+	25	44.0	8,198	53.2	0.42	1.4 (0.7 – 3.2)
Triple negative	42	21.4	19,002	32.1	0.18	1.7 (0.8 – 3.6)

588 Poster Session (Board #80), Fri, 8:00 AM-11:00 AM

Differential effects of epirubicin and docetaxel on the immune system in patients with breast cancer (BC). *First Author: Kerstin Wimmer, Department of Surgery and Comprehensive Cancer Center, Medical University Vienna, Vienna, Austria*

Background: Neoadjuvant chemotherapy (NAC) with epirubicin/cyclophosphamid (EC) followed by docetaxel (D) is currently a standard of care therapy in women with early, high-risk breast cancer (BC). New approaches aim to improve the outcome by combining chemo- with immunotherapy. It is therefore of great interest if chemotherapeutics differ in their effect on the immune system and if some substances are superior combination partners than others. **Methods:** 79 BC patients, who participated in the ABCSG-34 trial, were included. 39 patients were treated with 6 cycles of EC followed by 6 cycles of D and 40 received the reverse sequence (D→EC). Blood was collected before and after 6 cycles. The plasma levels of a variety of immune mediators were determined by multiplex bead array assay. The response to therapy was measured by Residual Cancer Burden (RCB)-score. A score of ≤1.36 was determined as good response. Lymphocyte activation was assessed after stimulation with phytohaemagglutinin (PHA) by flow cytometric analysis of IFNgamma. Additionally, lymphocytes of 6 healthy probands were stimulated with PHA and treated with E or D. The stimulation was quantified by measuring cluster formation after 5 days. Further, a human BC cell line (SK-BR3) was treated with E or D. The induced cell death was determined morphologically as well as by flow cytometry after staining of phosphatidylserine, Sub-G1 DNA and active caspase-3. **Results:** The treatment of BC patients with 6 cycles of EC resulted in a decrease of lymphocyte stimulation whereas 6 cycles of D had no effect. The plasma levels of most immune mediators decreased significantly after six cycles EC when compared to baseline. Under the influence of D, the effect was much weaker. The changes of Eotaxin and OPG during the first 6 cycles of D correlated with the RCB-score in the reverse group. A decrease in Eotaxin (p = 0.0136) or in OPG (p = 0.0487) correlated with good response. The in vitro lymphocyte stimulation assay showed that E and D have similar inhibitory effects on lymphocytes.The annexin V/PI analysis confirmed that E more often leads to apoptotic cell death in SK-BR3 cells than D (E:53% vs. D:14%). SK-BR3 cells formed more often polyploid cells when treated with D. This suggests that D induces a regulated form of necrosis whereas E apoptosis. **Conclusions:** This study is the first to compare the immunomodulatory effect of E and D in BC patients. E inhibits lymphocyte activation in vitro and in vivo and suppresses many soluble immune mediators. This suggests that it is not suited for combination with immunotherapies. D showed a much weaker effect. Research Sponsor: Georg-Stumpf-Stipendium.

589 Poster Session (Board #81), Fri, 8:00 AM-11:00 AM

Long-term outcomes of patients with HER2+ breast cancer with small-size residual disease (≤ypT1) in the absence of pathological response after trastuzumab-based neoadjuvant chemotherapy and without adjuvant T-DM1: A monocentric retrospective study. *First Author: Ludovic Doucet, ICO, Nantes Saint-Herblain, France*

Background: The Katherine trial has shown that adjuvant T-DM1 improved invasive disease free survival (iDFS) of patients with HER2+ breast cancer who did not achieve a pathological complete response (pCR) with trastuzumab-based neoadjuvant chemotherapy (NAC). However, some subgroups may benefit less from this treatment escalation. **Methods:** All HER2+ breast cancer patients treated with trastuzumab-based NAC between 2006 and 2016 were retrieved from our institution's database. Neo- or adjuvant T-DM1 was an exclusion criterion. We then selected the patients who did not achieve a pCR and analyzed the outcome (iDFS and overall survival (OS)) according to ypT, ypN and several factors analyzed in the Katherine trial. **Results:** Out of the 182 patients, 117 patients reached the inclusion criteria. Patient's characteristics were similar to the trastuzumab arm of the Katherine trial. With a median follow-up of 75.4 months (29.3–149.7), 28 events (24%) occurred, among which 22 distant relapses. In univariate analysis, ≤ypT1 vs > ypT1, ypN0 vs ypN+, no capsular rupture, signs of histological response (Sataloff not D in T or N) were associated with a better iDFS. In multivariate analysis, only ypT status remained significant. Of note, patients with ≤ypT1 (ypTis, ypT0, ypTmic, ypT1) (n = 81; 69%) had an excellent outcome: 3 years (y) and 5y iDFS rates of 90% (83.6-96.8) and 88.6% (81.9-95.9) respectively. The remaining patients (n = 36; 31%) had a significantly lower 3y and 5y iDFS: 69.2% (55.6-86.2) and 59.5% (45-78.6) respectively (p = 0.0017). OS in a multivariate analysis was also improved in pts with the smaller residual and/or node negative disease (3y OS rates of 100% (100-100) vs 92.1% (85.7-99); 5y OS rates of 96% (90.7-100) vs 81.1% (71.6-91.9); p = 0.02). **Conclusions:** In the absence of pCR after trastuzumab-based NAC, patients with pathological response scored as ≤ypT1 (ypTis,ypT0, ypTmic, ypT1) have an excellent outcome. These patients may derive less benefit from adjuvant T-DM1. Research Sponsor: None.

590 Poster Session (Board #82), Fri, 8:00 AM-11:00 AM

One-year follow-up of health-related quality of life in the Swedish PREDIX HER 2 trial, evaluating docetaxel, trastuzumab sc, pertuzumab versus trastuzumab emtansine as neoadjuvant treatment of HER2 positive breast cancer. *First Author: Yvonne Brandberg, Karolinska Institutet, Department of Oncology-Pathology (OnkPat), Karolinska University Hospital, Stockholm, Sweden*

Background: Neoadjuvant therapy combining docetaxel, trastuzumab and pertuzumab (DTP) was compared to trastuzumab emtansine (T-DM1) in the randomised phase II PREDIX HER2 trial. Patients, ≥18 years with HER2 positive breast cancer, ≥20mm or with verified lymph node metastases, were randomised to six courses of DTP (Standard group) or T-DM1 (Experimental group) before surgery. After operation patients in the Standard arm received two, and those in the Experimental arm four courses of EC. Since there were no differences in proportions of complete response at surgery and in the event-free survival between the groups, health-related quality of life (HRQoL) is of special interest. **Methods:** HRQoL was measured, using European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 + EORTC QLQ-BR23, before randomisation, after six courses before surgery, at three months and one year after surgery. **Results:** Response rate for the questionnaires varied between 87% and 99% for the 198 included patients. There were no between-group differences at baseline. Results after six courses revealed statistically significant differences (p≤0.01), favouring the Experimental group on 12 out of 21 of the EORTC QLQ-C30 and BR23 variables (Physical-, Role-, and Social- functioning, Global quality of Life, Fatigue, Dyspnea, and Diarrhea, Body image, Sexual functioning, Sexual enjoyment, Systemic therapy side effects and Upset by hair loss). Three months after surgery, however, statistically significant differences in favour of the Standard group were found for six variables (Physical functioning, Nausea/vomiting, Dyspnea, Constipation, Systemic therapy side effects, Upset by hair loss). No other between group differences were found with one exception: lower levels of Breast symptoms in the Experimental group. One possible explanation is that patients in the Experimental group were still on chemotherapy at that assessment point, whereas the majority in the Standard group had terminated their treatment. No differences were found between the groups at the one-year after surgery follow-up, where the levels on most variables had returned to baseline values. **Conclusions:** HRQoL was better in the Experimental group during neoadjuvant treatment. Three months after surgery, however, HRQoL was in favour or the Standard arm. HRQoL returned to baseline levels for most variables at the one-year follow-up and no between-group differences were found. Clinical trial information: NCT02568839. Research Sponsor: Swedish Cancer Society.

591 Poster Session (Board #83), Fri, 8:00 AM-11:00 AM

12-chemokine gene expression score in breast cancer patients treated with neoadjuvant chemotherapy. *First Author: Hatem Hussein Soliman, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Although advances in immunotherapy for the treatment of breast cancer have been minimal compared with other cancers, studies demonstrating tumor-infiltrating lymphocytes and immunomodulatory gene activation in the tumor microenvironment suggest the importance of antitumor immune responses in clinical outcomes. A 12-chemokine gene score has been shown to predict the presence of ectopic lymph node-like structures (ELN) in the tumor microenvironment and improved survival in melanoma, colon cancer, and breast cancer patients (Prabhakaran, 2017). Here, we evaluated this signature in an independent dataset of breast cancer patients treated with neoadjuvant chemotherapy. **Methods:** Tumor specimens used in this retrospective analysis (n = 92) were from breast cancer patients enrolled in either MINT (NCT0151487) or NBRST (NCT01479101) neoadjuvant registry trials from 2011 to 2016. Clinical data were captured with informed consent, and 70-gene signature (70-GS), 80-gene signature (80-GS), and full transcriptome data were generated by Agendia, Inc. Gene expression data were quantile normalized using R limma package. Principal component analysis (PCA) was performed on the normalized dataset using R princomp package. Chemokine score (CS) was defined as the first principal component values resulting from PCA. 70-GS/80-GS and clinical data were evaluated in relation to CS. CS were compared using Mann-Whitney test. **Results:** Of 92 breast tumors available for analysis, 84% were 70-GS High Risk (HR). Tumors were 39% Luminal-type, 24% HER2-type, and 32% Basal-type by 80-GS. HR tumors had higher CS than 70-GS Low Risk (LR) tumors ($p < 0.001$). 80-GS Basal-type, HER2-type, and Luminal B tumors had higher CS than Luminal A tumors ($p < 0.01$ for each comparison). High grade and ER-negative tumors seemed to have a high CS, although not significantly. Tumors from patients who achieved a pathological complete response (pCR) following neoadjuvant chemotherapy had higher CS than patients with residual cancer burden (p = 0.048). **Conclusions:** The current study demonstrated a significantly higher CS in 70-GS HR tumors and those which achieved pCR following neoadjuvant chemotherapy. Although further study is needed to evaluate the association of high CS with tumor-associated ELN, these results support previous work demonstrating that, although high CS is associated with aggressive clinical features, it also predicts superior clinical outcomes. The current study suggests validation of the 12-chemokine gene score in an independent dataset of breast cancer patients. Research Sponsor: Agendia, Inc.

592 Poster Session (Board #84), Fri, 8:00 AM-11:00 AM

Liquid biopsy of the immune environment: Evaluation of peripheral blood mononuclear cells (PBMCs) with CyTOF and response to trastuzumab (T)-based neoadjuvant chemotherapy (NAC) in HER2+ breast cancer (BC). *First Author: Roberto Antonio Leon-Ferre, Mayo Clinic, Rochester, MN*

Background: Immune responses in the tumor microenvironment have prognostic and predictive value in BC. However, the potential of immune responses observed in peripheral blood as biomarkers in BC remains unclear. We have shown that a higher frequency of circulating monocytes and a lower frequency of antigen-experienced memory CD8+ T cells are associated with response to NAC in triple negative BC (Leon-Ferre et al SABCS 2019). Here, we used cytometry by time-of-flight (CyTOF) to evaluate associations between circulating immune cells, clinical features and response to T-based NAC in HER2+ BC. **Methods:** PBMC suspensions from 36 pts with stage I-III HER2+ BC were prospectively collected prior to initiation of T-based NAC, stained with 29 metal-tagged antibodies optimized to identify major human immune cell subsets, and acquired in the Helios CyTOF instrument. Differential abundance analysis of immune cells by clinical characteristics and by NAC response was evaluated using Wilcoxon rank sum test. % of immune cell subsets is presented as % of all PBMCs. **Results:** Most pts presented with ER- tumors (56%), measuring > 5cm (64%) and with nodal metastases (78%). After NAC, 16 pts (44%) achieved pathologic complete response (pCR). Analysis of preNAC PBMCs demonstrated a significantly higher number of B cells (8% vs 5%, p = 0.05) and effector memory CD8+ T cells (CD45RA-/CCR7-, 3 vs 1%, p = 0.02) in pts with pCR compared to those with residual disease. Of the B cell subsets, naïve B cells (CD24-/CD27-) were higher in pts who achieved pCR vs not (7% vs 4%, 0 = 0.04). Regarding clinical characteristics, cN+ pts at presentation exhibited a lower number of peripheral blood T cells compared to cN- pts (47% vs 63%, p = 0.03). Of the T cell subsets, overall CD4+ and naïve CD4+ T cells (CD45RA+/CCR7+) were lower in cN+ vs cN- pts (31% vs 45%, p = 0.05; and 11% vs 24%, p = 0.04). We also observed differences in CD56+/CD16- NK cells by ER status (ER- 1% vs ER+ 3%, p = 0.01), and a moderate negative correlation between age and % circulating CD8+ T cells (rho -0.4669, p = 0.004). **Conclusions:** Distinct peripheral blood immune cell profiles are observed in HER2+ BC at diagnosis, and are associated with response to T-based NAC and initial clinical characteristics. Notably, pts who later achieved pCR had a relative abundance of B cells and effector memory CD8+ T cells at diagnosis. These data suggest that immune cell phenotyping in peripheral blood may have potential as a biomarker to predict response to NAC in BC. Research Sponsor: Wohlers Family Foundation, Other Foundation, Other Government Agency, This project was supported by CTSA Grant Number KL2 TR002379 from the National Center for Advancing Translational Science (NCATS). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

593 Poster Session (Board #85), Fri, 8:00 AM-11:00 AM

Impact of body composition on toxicity and pathological complete response in locally advanced breast cancer (BC). *First Author: Laura Sofia Munoz-Arcos, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY*

Background: Obesity, defined as body mass index (BMI) > 30 kg/m^2, has been associated with inferior outcomes in localized breast cancer (BC), including lower pathological complete response (pCR) to neoadjuvant chemotherapy (NAC). High BMI is usually associated with excess adipose tissue (AT), but also reflects skeletal muscle (SM) mass. Low SM mass (sarcopenia) has also been associated with inferior outcomes and more chemotherapy-associated toxicity. We aimed to evaluate the association of BMI, AT and SM tissue with pCR and toxicity after NAC for stage II-III breast cancer (BC). **Methods:** 191 patients with stage II-III BC received NAC, had information regarding baseline BMI, toxicity and pCR to NAC at surgery, and, had abdominal computerized tomography (CT) prior to NAC. Total AT (TAT), visceral AT (VAT), subcutaneous AT (SAT), SM area (SMA) and SM density (SMD) were measured by CT at the L3 level using the TOMOVISION software. SM index (SMI) was calculated (SMA/height) to assess for sarcopenia (SMI < 40). Association linking BMI, SAT, VAT, SMA and SMD to pCR and severe toxicity (ST ≥ grade 3) was evaluated using logistic regression models. **Results:** Patients were predominantly black (51%) with a median age of 54 years (interquartile range = 45-63). pCR was achieved in 31% (60/191) of patients. Of those, 47% (n = 28/60), 40% (n = 24/60) and 13% (n = 8/60) corresponded to HER2(+), triple negative, and hormone receptor-HR(+)/HER2(-) tumors, respectively. ST occurred in 38% (n = 73/191) of patients. Obesity and sarcopenia were present in 52% (n = 100/191) and 14% (n = 27/191) of patients, respectively. There was a statistically significant association between VAT and pCR (median VAT 95.3 cm^2 vs. 121.8 cm^2 in the pCR vs. no-pCR groups, respectively, p = 0.03). This association remained after adjusting for age, race, tumor grade, stage, BMI, SMD, HR and HER2 status (p = 0.04). There was a statistically significant association between SMA and ST (mean SMA 123 cm^2 vs. 130 cm^2 in the ST vs. no-ST groups, respectively, p = 0.03). This association disappeared after adjusting for age, race, BMI, VAT, SAT, and SMD (p = 0.21). **Conclusions:** This study provides evidence that in patients with stage II-III BC receiving NAC, excess VAT is associated with significantly lower pCR rates, and low SMA is associated with ST. Additional research is needed to elucidate the pathophysiologic mechanisms contributing to these associations. Research Sponsor: None.

594 Poster Session (Board #86), Fri, 8:00 AM-11:00 AM

Prediction of response to neoadjuvant hormonal therapy (NAHT) using upfront oncotype Dx recurrence score (RS): Results from the SAFIA phase III trial. *First Author: Khalid A Al-Saleh, King Saud University, College of Medicine, Riyadh, Saudi Arabia*

Background: While hormonal therapy (HT) is a fundamental treatment in breast cancer therapy, neoadjuvant NAHT is not considered standard. The SAFIA trial is a prospective international neoadjuvant Phase III investigating the potential role of the addition of palbociclib (P) in patients (pts) sensitive to HT. We report the results of induction Faslodex (+/- zoladex) in pts initially selected by RS < 31, in order to assess their individual HT sensitivity before double-blind randomization HT vs HT + P followed by surgery. **Materials and Methods:** A total of 308 pts (stages II and IIIA Luminal A/B HER2 negative) in 24 centers and 6 countries (Middle-East/Maghreb) underwent upfront RS to select pts for induction HT. Pts with RS < 31 received induction neoadjuvant fulvestrant (500 mg i.m Day 1, 14, 28 then q.4 weeks) + goseriline (3.6 mg s.c q.4 w for pre and peri-menopausal pts) for 4 months, followed by clinical and radiological assessment of the disease response before randomization. Response was defined as no progression: Complete Response-CR/ Partial Response-PR: > 50% and Minor Response-MR: < 50% to > 0%/ No Response-NR: progression > 0%. **Results:** A total of 70 pts (22%) with RS > 31 were excluded, leaving 238 eligible pts for NAHT, age (25-84); pre-peri/ post menopause: 135 (57%)/103 (43%); Luminal A/B: 112 (49%)/114 (51%); Stage II/IIIA: 196 (87%) / 29 (13%). One hundred and seventy-seven pts (177) have validated responses to induction NAHT: CR: 9 pts (5%) / MR: 105 pts (59%) for major response rate: 64% / MR: 56 pts (32%) / NR: 7 pts (4%); available RS 0-10: 23 pts (16%) / RS 11-18: 67 pts (47%) / RS 19-25: 34 pts (24%) / RS 26-30: 18 pts (13%). Correlations between Response to NAHT and RS are shown in the table below (not statistically significant). **Conclusions:** In our population, upfront Oncotype DX RS < 31 allowed to select pts for induction NAHT without loss of chances with a no-progression rate (CR+PR = MR) of 96%. No significant correlation was found between RS and response to NAHT. Upfront RS > 31 (22%) is selecting pts candidates for neoadjuvant chemotherapy with a potential high risk of endocrine resistance. Clinical trial information: ICRG1201. Research Sponsor: Investigator initiated trial funded by Pfizer and AstraZeneca, Other Government Agency.

595 Poster Session (Board #87), Fri, 8:00 AM-11:00 AM

Statistical modeling of a novel clinical trial design using neoadjuvant therapy (NAT) to personalize therapy in patients (pts) with triple-negative breast cancer (TNBC). *First Author: Stacy L. Moulder, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: 40-50% of pts with TNBC develop pathologic complete response (pCR) with adriamycin/cyclophosphamide (AC)àtaxane (T) NAT; thus, most pts treated in randomized trials (RCTs) adding experimental drugs (ED) to standard NAT do not benefit from trial participation. A personalized trial design that enriches for non-pCR to standard NAT would diminish toxicity from ED in pts who do not need them and enrich ED in high-risk pts that are most likely to benefit. **Methods:** ARTEMIS (NCT02276443) is a non-randomized trial to study personalization of NAT in TNBC. Tumor biopsies were performed pre-NAT and volumetric change by ultrasound (VCU) after 4 cycles of AC (or upon clinical progression) assessed response. Pts with sensitive TNBC (VCU >=70% after AC) had T as the second phase of NAT. Pts with <70% VCU were offered phase II trials. pCR was assessed at surgical resection. 273 pts had available pCR status and 222 had complete data to generate a model predictive of response using multivariate logistic regression with common clinical factors. Data was randomly divided into training (n=111) and validation (n=111) sets. **Results:** 85 pts (38%) had pCR and VCU after AC x 4 was the strongest predictor of pCR. Other factors significant on multivariate analysis and included in the model were T stage (T1-4), stromal TIL, Ki67 and PD-L1. When applied to the validation data set, the accuracy of this model for predicting pCR was 76.6%, sensitivity 78.6% and specificity 75.4%. The PPV was 66.0% and the NPV was 85.2% with a ROC curve AUC of 82.4%. Using these data, ED exposure (table) was estimated for the ARTEMIS study design vs a 1:1 or a 2:1 RCT design (with an estimated pCR in control arm=40%), with a demonstrated benefit for personalization. **Conclusions:** This modeling indicates that personalization of NAT trials has the potential to enrich ED exposure for non-responsive disease as well as diminish ED exposure in pts likely to achieve pCR with standard NAT. Improved prediction of pCR would further enhance personalized trial design. Clinical trial information: NCT02276443. Research Sponsor: MD Anderson Moon Shot.

Estimated ED exposure in 300 pts by trial design.

		Unfavorable	
No exposure to unnecessary ED	**Favorable**		
	High risk receives ED	**High risk no ED**	**Unnecessary exposure to ED**
ARTEMIS			
Predicted pCR=pCR	Predicted non-pCR=non-pCR	False positive prediction pCR	False negative predicted pCR
90	141	45	24
RCT 1:1 Randomization			
pCR on Control Arm	Non-pCR enrolled in EXP arm	Non-pCR in Control arm	Would have pCR with standard NAT but enrolled in EXP arm
60	90	90	60
RCT 2:1 Randomization			
40	120	60	80

TPS596 Poster Session (Board #88), Fri, 8:00 AM-11:00 AM

KEYLYNK-009: A phase II/III, open-label, randomized study of pembrolizumab (pembro) plus olaparib vs pembro plus chemotherapy after induction with first-line pembro plus chemotherapy in patients with locally recurrent inoperable or metastatic triple-negative breast cancer (TNBC). *First Author: Hope S. Rugo, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

Background: Combination therapy with immunotherapy + chemotherapy is a promising approach for first-line (1L) treatment of locally recurrent, inoperable TNBC or metastatic TNBC (mTNBC). However, an unmet need exists for effective and tolerable maintenance regimens in mTNBC to sustain clinical benefit after induction therapy and avoid potential toxicity or resistance in response to prolonged chemotherapy. The PARP inhibitor olaparib has demonstrated efficacy in the maintenance setting for multiple platinum-sensitive tumors, and the prevalence of *BRCA* mutations in TNBC may make these tumors particularly sensitive to DNA-damaging agents. Moreover, previous data suggest that combination therapy with olaparib and the PD-1 inhibitor pembro may have clinical benefits. KEYLYNK-009 (NCT04191135) is a phase II/III, open-label, randomized study of pembro + olaparib or pembro + chemotherapy after induction with 1L pembro + chemotherapy in patients with locally recurrent, inoperable TNBC or mTNBC. **Methods:** This 2-in-1 study design will enroll ~317 patients in phase II; if a planned efficacy boundary is met, ~615 additional patients will be enrolled in phase III. Patients eligible for induction therapy must have measurable, locally recurrent, inoperable TNBC that cannot be treated with curative intent or mTNBC previously untreated with chemotherapy in the metastatic setting. All patients will receive up to 6 cycles of induction therapy with pembro 200 mg every 3 wk (Q3W) + chemotherapy (carboplatin AUC 2 + gemcitabine 1000 mg/m^2). Patients eligible for postinduction treatment must achieve complete or partial response or maintain stable disease during induction after 4-6 treatment cycles, with ECOG PS 0/1 and no grade >1 toxicities related to induction therapy (excluding alopecia, Hb ≥9.0 g/dL, grade 2 hyper-/hypothyroidism, or grade 2 hyperglycemia). These patients will be randomized 1:1 to receive pembro 200 mg Q3W + olaparib 300 mg twice daily or continue pembro + chemotherapy (same as induction regimen). Olaparib and chemotherapy may continue until progression or unacceptable toxicity; pembro may continue for ≤35 cycles (including induction), unacceptable toxicity, or progression. Phase III dual primary endpoints are PFS per RECIST v1.1 by BICR and OS. Secondary endpoints include OS and PFS in patients with BRCAm, health-related quality of life, and safety. Enrollment is ongoing. Clinical trial information: NCT04191135. Research Sponsor: Merck Sharp & Dohme Corp.

TPS597 **Poster Session (Board #89), Fri, 8:00 AM-11:00 AM**

Randomized, phase II trial to evaluate the efficacy and safety of atezolizumab plus capecitabine adjuvant therapy compared to capecitabine monotherapy for triple receptor-negative breast cancer (TNBC) with residual invasive cancer after neoadjuvant chemotherapy (MIRINAE trial, KCSG-BR18-21). *First Author: In Hae Park, Division of Hemato-Oncology, Department of Internal Medicine, Korea University College of Medicine, Guro Hospital, Seoul, South Korea*

Background: Triple negative breast cancer (TNBC), lack of ER, PR and HER2 expression, is known to have aggressive clinical features such as early recurrence, drug resistance, and frequent distant metastasis at the diagnosis. The most effective chemotherapy combinations used for early TNBC include anthracycline, taxanes, and/or platinum agents. Achieving a pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC) provides important prognostic information and is considered as a surrogate endpoint in many clinical trials especially with TNBC. Patients with residual invasive disease after NAC have a high risk for early relapse and worse prognosis compared to those with pCR. Therefore, patients who did not get pCR could be better candidates for additional adjuvant treatment because their risk of recurrence would be higher than those with pCR. The CREATE-X (capecitabine for residual cancer as adjuvant therapy) trial howed that adjuvant capecitabine treatment improved 5-yr rate of disease free survival in TNBC subtype. A recent study indicated that immunosuppressive microenvironment had developed even in early stage of TNBC with increased T cells with a high exhaustion signature which are targets of immune modulating agents. Therefore, earlier cooperation of immune modulating drugs would be beneficial by generating a long-lasting anti-tumor immune response to micrometastatic disease, thus preventing disease relapse or recurrence. **Methods:** This study is a phase II, multicenter, randomized open label trial of atezolizumab (anti-PD-L1 antibody) and capecitabine compared with capecitabine in patients with TNBC who had residual disease after NAC. 284 patients will be enrolled from 15 sites in Korea with a primary objective to access the 5-yr invasive disease-free survival (IDFS) rate. Secondary objectives include 5-yr IDFS rate in PD-L1 positive population, distant relapse free survival (DRFS), overall survival (OS), and safety. Major inclusion and exclusion criteria are followings; 1) histologically confirmed TNBC, 2) received anthracycline and taxane based NAC followed by complete breast surgery, 3) residual disease after NAC must be $\geq$1cm in the greatest dimension, and/or have macroscopically positive lymph nodes. The study is open with 13 patients enrolled at the time of submission. Clinical trial information: NCT03756298. Research Sponsor: Roche Korea.

TPS598 **Poster Session (Board #90), Fri, 8:00 AM-11:00 AM**

Phase III randomized study of adjuvant treatment with the ANTI-PD-L1 antibody avelumab for high-risk triple negative breast cancer patients: The A-BRAVE trial. *First Author: Pier Franco Conte, Department of Surgery, Oncology and Gastroenterology, University of Padova and Medical Oncology 2, Istituto Oncologico Veneto IRCCS, Padua, Italy*

Background: Chemotherapy represents, today, the only treatment option for triple negative breast cancer (TNBC) and still a considerable proportion of pts with primary TNBC experience disease relapse. The risk is particularly high in the presence of poor prognostic features, such as more advanced stage and, for pts treated with neoadjuvant chemotherapy, failure to achieve a pCR. Recent evidence suggest that immunotherapy can play a major role in TNBC pts. **Methods:** The A-BRAVE trial is an investigator-driven trial sponsored by the University of Padova (Dept. of Surgery, Oncology and Gastroenterology). This is a phase III, multicentric, randomized adjuvant study that compares 1 year of treatment with the anti PD-L1 avelumab vs observation for pts who completed treatment with radical intent for primary TNBC including surgery and chemotherapy. The study enrolls pts in two strata: -Stratum A: primary TNBC pts who completed surgery followed by adjuvant, defined according to one of the following stage categories: if pN2, any pT; if pN1, pT $>$ 2 cm; if pN0, pT $>$ 5 cm. -Stratum B: primary TNBC pts who completed neoadjuvant chemotherapy followed by surgery who did not achieve pCR. Pts who also received additional adjuvant chemotherapy for no more than 6 months are eligible in Stratum B, after the completion of the adjuvant chemotherapy. Pts are randomized (1:1, balanced for strata A and B) to receive Avelumab 10 mg/kg I.V. q2w for 1 year or to observation. The first and second co-primary endpoints are disease-free survival (DFS) in all pts and DFS in Stratum B pts. With a planned sample size of n = 474 pts the trial has 90% power to detect a HR = 0.60 for the first co-primary endpoint (n = 172 events required). Taking into account that the percentage of patients enrolled in the stratum B could range from 70 to 80%, there will be 70-79% power to detect a HR = 0.60 at alpha allocated in this patient subgroup (second co-primary endpoint). Secondary objectives include: DFS in PD-L1 positive pts, overall survival, safety, biomarkers. Tumor tissue, plasma samples and fecal samples are collected for biomarker analysis. The study is currently recruiting across 73 sites in Italy and UK. As of February 2020, n = 349 pts have been enrolled. EUDRACT 2016-000189-45. The authors present the A-BRAVE trial in progress on behalf of Italian and UK investigators. Clinical trial information: NCT02926196. Research Sponsor: The Trial is supported by Merck KGaA.

TPS599 **Poster Session (Board #91), Fri, 8:00 AM-11:00 AM**

Phase III, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of adagloxad simolenin (OBI-822) and OBI-821 treatment in patients with early-stage triple-negative breast cancer (TNBC) at high risk for recurrence. *First Author: Hope S. Rugo, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

Background: Adagloxad simolenin (AS) is a therapeutic vaccine comprising the tumor-associated antigen Globo H linked to the carrier protein keyhole limpet hemocyanin (KLH). The KLH provides antigenic immune recognition and T-cell responses. AS is co-administered with a saponin-based adjuvant OBI-821 to induce a humoral response. A phase 2 trial showed that AS/OBI-821 exhibited a trend for superior progression-free survival vs placebo in patients whose breast cancers have higher Globo H expression. **Methods:** Patients with TNBC (ER/PR $<$ 5%, and HER2-negative) with nonmetastatic disease and either 1) residual invasive disease of $\geq$1 cm in the breast or $\geq$1 positive axillary node following neoadjuvant chemotherapy or 2) $\geq$4 axillary lymph nodes with invasive carcinoma treated with adjuvant chemotherapy are included. Patients are prescreened for Globo H expression using a validated IHC assay (H-score of $\geq$15). Patients will receive either AS (30 μg) with OBI-821 (100 μg) or volume-matched placebo (1:1), administered as SC injections. Up to 21 SC injections of study treatment (or placebo), will be administered over 100 weeks, given on the following schedule: weekly for 4 doses; every 2 weeks for 4 doses; every 4 weeks for 4 doses; and then every 8 weeks for 9 doses. Patients may terminate treatment due to disease recurrence or unacceptable toxicity, withdrawal of consent, protocol violation, loss to follow-up or death. The primary objective is to determine the effect of AS/OBI-821 treatment on invasive disease-free survival in patients with TNBC at high risk for recurrence. Secondary objectives are to determine the impact of AS/OBI-821 treatment on overall survival, quality of life (QoL), breast cancer-free interval, distant disease-free survival, safety, and tolerability. Imaging and clinical examination will be performed regularly for 5 years. QoL will be assessed using the EORTC Core Quality of Life Questionnaire (QLQ)-C30 plus the EORTC Breast Cancer-specific QLQ-BR23 questionnaire and the European Quality of Life 5 Dimensions 5 Levels (EQ-5D-5L) questionnaire. Adverse events will be graded/recorded as per National Cancer Institute CTCAE v5.0. An estimated 668 subjects will be enrolled, treated for up to 2 years and followed until occurrence of 187 events (invasive disease recurrence or death) or 3 years from last subject randomized. Survival follow-up is for 5 years from randomization of last subject. Clinical trial information: NTC03562637. Research Sponsor: OBI Pharma Inc.

TPS600 **Poster Session (Board #92), Fri, 8:00 AM-11:00 AM**

ABC trial (A011502): A randomized phase III double-blinded placebo-controlled trial of aspirin as adjuvant therapy breast cancer. *First Author: Wendy Y. Chen, Dana-Farber Cancer Institute, Boston, MA*

Background: In-vitro and in-vivo evidence suggest that aspirin may have an anti-tumor effect. Multiple epidemiologic studies have reported improved breast cancer survival among regular aspirin users compared to non-users. Pooled data from randomized trials of aspirin for cardiovascular disease have also reported a decreased risk of metastatic cancer among aspirin users. However, the exact benefits and risks for breast cancer survivors need to be confirmed in a randomized controlled trial. Even if the clinical effect were modest, the global impact would be substantial since aspirin is inexpensive and widely available. **Methods:** The primary objective is to compare the effect of 300 mg daily aspirin versus placebo upon invasive disease-free survival (iDFS) in high risk HER2 negative breast cancer patients. Secondary objectives include effects on overall survival, cardiovascular disease, toxicity, and adherence. A biospecimen repository will be created for correlative analyses including tumor collection at baseline and blood and urine samples and questionnaires assessing lifestyle factors associated with inflammation (pain, sleep, stress, and depression) at baseline and 2 years. Study design: Subjects will be randomized (1:1) to aspirin 300 mg vs placebo daily for 5 years in a double-blinded fashion. Stratification factors include hormone receptor (HR) status (positive vs negative), body mass index ($<$ or $\geq$ 30 kg/m2), and stage (II vs III). Subjects will be followed every 6 six months while on study drug, then annually for 10 years. Accrual goal is 2936 patients to reach 381 iDFS events. We have 80% power to detect HR 0.75 assuming 5-year iDFS on placebo of 77%. Eligibility: Eligible subjects include patients aged 18-70 diagnosed with a primary invasive HER2 negative breast cancer. If HR positive, tumors need to be node positive and diagnosed within the past 10 years. If HR negative, tumor can be node positive or T2-4N0 within 18 months of diagnosis. Subjects who are currently anticoagulated or those with a prior history of GI bleeding, atrial fibrillation, or myocardial infarction are excluded. Subjects who regularly use aspirin (defined as $\geq$ 5 days per week) need to stop 30 days prior to enrollment. Updated accrual numbers will be given at the time of presentation. Clinical trial information: NCT02927249. Research Sponsor: Department of Defense, U.S. National Institutes of Health.

TPS601 **Poster Session (Board #93), Fri, 8:00 AM-11:00 AM**

ADAPTcycle: Adjuvant dynamic marker-adjusted personalized therapy (ADAPT) comparing endocrine therapy plus ribociclib versus chemotherapy in intermediate-risk HR+/HER2- early breast cancer (EBC). *First Author: Nadia Harbeck, Breast Center, Dept. Obstetrics & Gynecology, University of Munich (LMU) and CCCLMU and West German Study Group, Munich, Germany*

Background: The WSG ADAPT trial program represents the concept of individualization of (neo)-adjuvant decision-making in EBC in a subtype-specific manner. The first WSG ADAPT umbrella trial aimed to establish early predictive molecular surrogate markers for response after a short 3-week induction treatment. The goals of the WSG ADAPT trial program are early response assessment and subtype-specific therapy tailoring to those patients who are most likely to benefit. **Methods:** WSG-ADAPTcycle is a prospective, multi-center, interventional, two-arm, open-label, (neo)adjuvant, non-blinded, randomized, controlled phase III trial (NCT04055493). It investigates whether patients (pts.) with HR+/HER2- EBC identified during screening as intermediate risk (based on Oncotype DX and response to 3 weeks of preoperative endocrine therapy [ET]) derive additional benefit from 2 years of the CDK4/6 inhibitor ribociclib combined with ET compared to chemotherapy (CT) (followed by standard ET). Co-primary endpoints are disease-free survival (DFS) and distant DFS. It is planned to screen 5600 pts and to randomize 1670 pts in a 3:2 ratio (ribociclib + ET/CT). Study start was in July 2019 (80 sites, enrollment period 36 months) and until date of submission, 180 pts. have been screened and 40 randomized. Pts with HR+/HER2- EBC with clinically enhanced risk (cT2-4 or Ki67 20% or G3 or cN+) are eligible if they fulfill the ADAPT intermediate-risk group criteria: either Recurrence Score (RS) $\leq$25 and $Ki67_{postendocrine} > 10\%$, RS $>$25 and $Ki67_{postendocrine} < 10\%$ in p/cN0-1 pts, or RS $\leq$25 and $Ki67_{postendocrine} < 10\%$ in c/pN2-3 pts. Treatment duration is 2 years for the ribociclib + ET (premenopausal: AI + GnRH) arm and 16-24 weeks for the CT arm; treatment is possible either in the neoadjuvant (ET + ribociclib duration 16 – 32 weeks) or adjuvant setting. ePROs are collected using CANKADO; ECG monitoring is performed using a novel cardiology-supported CANKADO-based eHealth method. Translational analyses: Exploratory tissue biomarker research will be conducted to assess alterations in molecular markers. In addition, ctDNA/ctRNA from optional blood samples will be assessed for mutations and gene expression. Conclusions: ADAPTcycle seeks to evaluate whether endocrine-based therapy with ET and a CDK 4/6 inhibitor is superior to CT followed by ET in patients with luminal EBC who may be undertreated with ET alone (based on either lack of endocrine responsiveness or high tumor burden). Clinical trial information: 2018-003749-40. Research Sponsor: Novartis, Exact Science.

TPS602 **Poster Session (Board #94), Fri, 8:00 AM-11:00 AM**

Understanding and predicting fatigue, cardiovascular (CV) decline & events after breast cancer treatment (UPBEAT): A prospective multi-center wake forest NCORP research-base study. *First Author: Susan Faye Dent, Duke University School of Medicine, Durham, NC*

Background: Modern treatment for breast cancer (BC) has led to improved survival; however, this improvement can be offset by an increase in cancer therapy-related morbidity and mortality. Over one-third of early stage BC patients treated with cancer therapy experience CV injury, left ventricular (LV) dysfunction, exercise intolerance, or fatigue. CV disease is a leading cause of mortality in BC survivors. There is limited information on the time course and long-term CV health of BC survivors. UPBEAT, a multicenter study, will prospectively evaluate CV risk factors and outcomes in early stage BC patients, treated with modern anticancer therapies. This will facilitate evaluation of primary CV prevention strategies in this patient population. **Methods:** This is a prospective cohort study of 840 patients with early stage (I-III) BC treated with chemotherapy +/- radiation and 160 controls. Baseline and serial longitudinal measures will examine the influence of cancer treatment on CV function, exercise capacity and fatigue, and the future development of CV events. The comprehensive assessment includes: ascertainment of cardiac biomarkers, CV risk factors, comorbidities, functional status (e.g., disability measures, expanded short physical performance battery), neurocognitive tests, behavioral risk factors, socio-demographics, and quality of life at baseline, 3-, 12-, and 24-mos. Outcomes measured at the same time points include a deep phenotyping of CV dysfunction (via cardiac MRI assessing LV end diastolic volume, LV end systolic volume, LV ejection fraction, myocardial strain, strain rate, left atrial volumes and mass, and aortic stiffness), exercise intolerance (submaximal as 6-minute walk test and maximal as VO2 peak via cardiopulmonary exercise test), and fatigue (via FACT-F). Eligibility criteria: age $>$ 18 years; ECOG 0-2, able to walk without symptoms; receiving chemotherapy +/- HER2 targeted agent(s). To date, 244 participants are enrolled through 12 NCORP or ECOG-ACRIN sites. An additional 7 sites are onboarding and will be enrolling later in the year. Participants will be followed for 9 years with active surveillance of CV events (i.e., heart failure, myocardial infarction, stroke, all-cause and CV death). EA NCORP Grant: 2 UG1 CA189828 06; Research Base Grant: 2UG1 CA189824; RO1: 1RO1CA199167. Clinical trial information: NCT02791581. Research Sponsor: Wake Forest University Health Sciences, Other Government Agency.

TPS603 **Poster Session (Board #95), Fri, 8:00 AM-11:00 AM**

Personalized neoadjuvant strategy in luminal A breast cancer to increase breast conserving surgery (BCS) rate [PLATO study]. *First Author: Ji Gwang Jung, Seoul National University Hospital, Seoul, South Korea*

Background: The most important and well established benefit of neoadjuvant therapy for breast cancer patients is increased breast conservation rate. However, in ER-positive and HER-2 negative breast cancer, the response to neoadjuvant chemotherapy (NCT) is not as good as other subtype of breast cancer, such as HER-2 or triple-negative breast cancer. In addition, with the advancement of multi-gene assay tools for this subtype, adjuvant chemotherapy is not needed at all in significant proportion of this subtype. Through a selective neoadjuvant therapy, either chemotherapy or endocrine therapy using histopathologic markers and 70-gene assay (Mammaprint. Agendia inc.), we hypothesize that we could increase the breast conservation rate in ER-positive and HER-2 negative breast cancer. **Methods:** This study is a non-randomized, phase II, prospective study. The main inclusion criteria is women with stage I-IIIA, ER-positive and HER-2 negative breast cancer that tumor size is measurable. BCS is not feasible considering the tumor size, location, and patient's breast size. Two surgeons in each institution will judge the feasibility of BCS. Main exclusion criteria is diffuse malignant microcalcification or multicentric breast cancer. The conversion rate from BCS-ineligible to BCS-eligible with NCT was 35.8% in ER-positive and HER-2 negative breast cancer in our previous study. We assumed that with the study regimen, the rate will be increased to 50.8% (15% increase). Given these estimates, under 10% type II error rate and 90% power, 122 patients in total will be enrolled from nine tertiary hospitals in Korea. All the patients initially will be tested with Mammaprint assay. When the Mammaprint result is high risk, the patients will receive NCT. When the Mammaprint result is low risk, the patients will receive neoadjuvant endocrine therapy. Postmenopausal women receive letrozole 2.5mg per day for 16 weeks. Premenopausal women receive leuprorelin every 4 weeks with letrozole for 16 weeks. Period of neoadjuvant endocrine therapy can be prolonged maximum 24 weeks by physician's decision. The primary endpoint is conversion rate from BCS-ineligible to BCS-eligible of more than 50%. The secondary endpoint is actual breast conservation rate, pathologic complete response, clinical response rate, and disease-free survival. Clinical trial information: NCT03900637. Research Sponsor: Agendia Inc., Pharmaceutical/Biotech Company.

TPS604 **Poster Session (Board #96), Fri, 8:00 AM-11:00 AM**

A phase III trial of nivolumab with neoadjuvant chemotherapy and adjuvant endocrine therapy in ER+/HER2- primary breast cancer: CheckMate 7FL. *First Author: Sherene Loi, Peter MacCallum Cancer Institute, Melbourne, VIC, Australia*

Background: Patients (pts) diagnosed with primary estrogen receptor-positive (ER+), human epidermal growth factor 2-negative (HER2−) breast cancer (BC) of high grade and/or low ER expression are at increased risk of relapse, despite current standard of care (SoC). Promising data assessing programmed death-1 (PD-1) inhibition coupled with neoadjuvant chemotherapy for pts with high-risk ER+, HER2− BC noted improved pathologic complete response (pCR), which is identified as a valid surrogate endpoint for long-term clinical outcomes. **Methods:** CheckMate 7FL (NCT04109066) is a randomized, double-blind, placebo-controlled, multicenter, global phase 3 study evaluating nivolumab (NIVO) vs placebo (PBO) in combination with neoadjuvant chemotherapy and adjuvant endocrine therapy (ET) in pts with high-risk, ER+, HER2− primary BC. Eligible pts are male or female, aged $\geq$18 years with newly diagnosed grade 2 with ER expression of 1–9%, or grade 3, T1c-2, cN1-2 (tumor size $\geq$2 cm) or T3-T4, cN0-cN2 ER+, HER2− BC. Pts eligible for neoadjuvant chemotherapy and surgery, with adequate organ function, ECOG PS of 0 or 1, and tissue available for biomarker assessments will be enrolled. Approximately 1200 pts will be randomized 1:1 to NIVO or PBO, stratified by programmed death ligand 1 (PD-L1) expression, tumor grade (2 or 3), axillary nodal status (+ or −), and anthracycline + cyclophosphamide schedule (Q3W or Q2W). In the neoadjuvant phase, pts will receive NIVO 360 mg Q3W or PBO + paclitaxel 80 mg/m^2 QW for four 3-week cycles, followed by NIVO 360 mg Q3W (or 240 mg Q2W) or matching PBO in combination with either doxorubicin 60 mg/m^2 or epirubicin 90 mg/m^2 and cyclophosphamide 600 mg/m^2 Q3W or Q2W for 4 cycles. Pts will undergo surgery after completion of the neoadjuvant phase. Following surgery, pts will enter the adjuvant phase and receive NIVO 480 mg Q4W or PBO for 7 cycles + investigator's choice of ET per local SoC. Primary endpoints are pCR (ypT0/is, ypN0) and event-free survival. Secondary endpoints include overall survival, disease-free survival, distant-metastasis-free survival, safety, pCR (ypT0 ypN0 and ypT0/is) rates, overall response rates, residual cancer burden, and quality of life. Interim analyses are planned. The study is currently enrolling. Clinical trial information: NCT04109066. Research Sponsor: Bristol-Myers Squibb.

TPS605 **Poster Session (Board #97), Fri, 8:00 AM-11:00 AM**

PREDIX II HER2: Improving pre-operative systemic therapy for human epidermal growth factor receptor 2 (HER2) amplified breast cancer (BC).

First Author: Renske Kornalijnslijper-Altena, Karolinska University Hospital, Stockholm, Sweden

Background: Neo-adjuvant systemic therapy (NAT) is the standard of care for most patients with early HER2-amplified and triple negative breast cancer (BC). Increasing the rate of pathological complete response (pCR) is highly meaningful for those patients, as pCR is strongly predictive for improved long-term disease-related outcomes. Clinical and preclinical evidence support the hypothesis that pCR-rates may be augmented by the addition of checkpoint inhibitors, such as monoclonal antibodies targeting the Programmed Death Ligand receptor 1 (PD-L1), to standard systemic NAT. Studies in different BC patient cohorts (e.g., IMPassion130, PANACEA, KATE2) have indicated that PD-L1 protein expression on tumor-infiltrating lymphocytes (TIL's) is a predictive marker for checkpoint inhibitor efficacy. **Methods:** We have initiated a phase II open-label, 2:1 randomized clinical trial where women with early HER2-amplified, PD-L1+ BC (cT2-3 and/or cN+) are treated with standard NAT (composed of anti-HER2 antibodies with a chemotherapy backbone of sequentially taxanes + carboplatin and epirubicin + cyclophosphamide [EC]) +/- atezolizumab during EC. N = 190 patients will be accrued in nine centers in Sweden to be able to demonstrate a 20% increase in pCR-rate, with a power of 80% and a two-sided alpha of 10%. Firstly, a prescreening is performed to select patients with a PD-L1 expression of $>$ 1% on TIL's. Important exclusion criteria are significant organ dysfunction and (with some exceptions) active auto-immune diseases. Extensive translational side-studies are performed to explore predictive markers for treatment efficacy, including clinicopathologic studies, molecular imaging and microbiome analyses, as well as monitoring of acute and chronic treatment-related toxicity, objective cognitive function and quality of life. As of February 11th, 4 patients have been prescreened and 1 enrolled in the trial. The clinical trial registry number is NCT03894007. Clinical trial information: NCT03894007. Research Sponsor: Swedish Research Council, Other Foundation, Pharmaceutical/Biotech Company.

1000 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

KEYNOTE-355: Randomized, double-blind, phase III study of pembrolizumab + chemotherapy versus placebo + chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer. *First Author: Javier Cortes, IOB Institute of Oncology, Quiron Group & Vall d´Hebron Institute of Oncology (VHIO), Madrid & Barcelona, Spain*

Background: Pembrolizumab (pembro) monotherapy showed promising antitumor activity and manageable safety in patients (pts) with metastatic TNBC in KEYNOTE-012, -086 and -119. KEYNOTE-355 (ClinicalTrials.gov, NCT02819518) compared pembro + chemotherapy (chemo) vs placebo (pbo) + chemo for previously untreated locally recurrent inoperable or metastatic TNBC. **Methods:** Pts with ≥6 mo DFI were randomized 2:1 to pembro + chemo (nab-paclitaxel; paclitaxel; or gemcitabine/carboplatin) or pbo + chemo for up to 35 administrations of pembro/pbo or until progression/intolerable toxicity. Pts were stratified by chemo type (taxane vs gemcitabine/carboplatin), PD-L1 status (CPS ≥1 vs <1), and prior (neo)adjuvant treatment with same-class chemo (yes vs no). Dual primary endpoints are PFS (RECIST v1.1, blinded independent central review) and OS by tumor PD-L1 expression (CPS ≥10 and ≥1) and in all pts. PFS was estimated using the Kaplan-Meier method. Stratified log-rank tests were used to assess treatment group differences. HR and 95% CIs were based on a stratified Cox regression model. AEs were monitored throughout the study and graded per NCI CTCAE v4.0. **Results:** As of Dec 11 2019, median follow-up was 17.5 mo for pembro + chemo (n=566) and 15.5 mo for chemo (n=281). Pembro + chemo significantly improved PFS vs chemo alone in pts with CPS ≥10 tumors (Table), meeting one of the protocol-defined primary objectives. Although the boundary for a statistically significant benefit of pembro + chemo in pts with CPS ≥1 tumors was not met and formal testing in ITT was not performed, the pembro treatment effect increased with PD-L1 enrichment (Table). OS follow-up is ongoing. Grade 3-5 treatment-related AE rates were 68.1% with pembro + chemo (2 deaths) vs 66.9% with chemo (0 deaths); rates of grade 3-4 immune-mediated AEs and infusion reactions were 5.5% vs 0%. Clinical trial information: NCT02819518. **Conclusion:** Pembro combined with several chemo partners showed a statistically significant and clinically meaningful improvement in PFS vs chemo alone in pts with previously untreated locally recurrent inoperable or metastatic TNBC whose tumors expressed PD-L1 (CPS ≥10). Pembro + chemo was generally well tolerated, with no new safety concerns. Research Sponsor: Merck & Co., Inc.

Population	Treatment	Median PFS, mo	HR (95% CI)	*P*-value	*P*-value boundary
CPS ≥10	P + C (n=220) vs C (n=103)	9.7 vs 5.6	0.65 (0.49-0.86)	0.0012	0.00411
CPS ≥1	P + C (n=425) vs C (n=211)	7.6 vs 5.6	0.74 (0.61-0.90)	0.0014	0.00111
ITT	P + C (n=566) vs C (n=281)	7.5 vs 5.6	0.82 (0.69-0.97)	-	n/a

1001 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Results of a phase II randomized trial of cisplatin +/- veliparib in metastatic triple-negative breast cancer (TNBC) and/or germline *BRCA*-associated breast cancer (SWOG S1416). *First Author: Priyanka Sharma, University of Kansas Medical Center, Westwood, KS*

Background: PARP inhibitors(i) are effective in *BRCA*-mutation-associated metastatic breast cancer(MBC). However, there are no studies evaluating PARPi + platin chemotherapy in BRCA wild-type(wt) TNBC. Approximately 1/2 of *BRCA*wt TNBC demonstrate homologous recombination deficiency (HRD) resulting in a BRCA-like phenotype which might render them sensitive to PARPi. S1416 compared the efficacy of cisplatin plus PARPi veliparib (Vel) or placebo (P) in 3 groups of MBC: gBRCA+; BRCA-like; and non-BRCA-like. **Methods:** Patients (pts) with metastatic TNBC or g*BRCA1/2*-associated MBC, who had received < 1 line of prior therapy were treated with cisplatin (75mg/m2) plus Vel or P (300 mg po BID days 1-14), every 3 weeks. All pts underwent central *gBRCA* testing. *A priori* established multipronged biomarker panel was used to classify BRCAwt pts into BRCA-like and non-BRCA-like groups, and included myChoice HRD score, somatic *BRCA1/2* mutations, BRCA1 methylation and non-*BRCA1/2* HR germline mutations. Primary end-point was progression-free survival (PFS) in the three pre-defined groups; secondary end-points included objective response rate (ORR), overall survival (OS), toxicity. **Results:** 323/335 randomized pts were eligible for efficacy evaluation; 31% had received 1 prior chemotherapy for MBC. 248 pts were classified into the three groups: (1) 37 gBRCA+ (2) 101 BRCA-like; (3) 110 non- BRCA-like. Remaining 75 could not be classified due to missing biomarker information. In the gBRCA+ group (which reached 62% of its projected accrual), numerically better PFS was noted with Vel compared to P (HR=0.64; p=0.26) though this difference was not statistically significant. In BRCA-like group improved PFS was noted with Vel vs P (median PFS 5.7 vs 4.3 months HR=0.58; p=0.023, 1 years PFS 20% vs 7%). Numerically better OS (median OS 13.7 vs 12.1 months, HR=0.66; p=0.14) and ORR (45% vs 35%, p=0.38) were noted with Vel vs P in BRCA-like group. Non-BRCA-like group did not show benefit of veliparib for PFS (HR=0.85; p=0.43) neither did the unclassified group (HR=0.97). Grade 3/4 neutropenia (46% vs 19%) and anemia (23% vs 7%) occurred at higher frequency in Vel arm compared to P. **Conclusions:** Addition of Vel to cisplatin significantly improved PFS and showed a trend towards improved OS for BRCA-like advanced TNBC. Integral biomarkers used in this study identified a subgroup of BRCAwt TNBC who benefited from addition of PARPi to cisplatin; platinum plus PARPi combination should be explored further in BRCA-like TNBC. Clinical trial information: NCT02595905. Research Sponsor: U.S. National Institutes of Health, AbbVie Inc.

1002 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

TBCRC 048: A phase II study of olaparib monotherapy in metastatic breast cancer patients with germline or somatic mutations in DNA damage response (DDR) pathway genes (Olaparib Expanded). *First Author: Nadine M. Tung, Beth Israel Deaconess Medical Center and Dana-Farber Cancer Institute, Boston, MA*

Background: Olaparib, a PARP inhibitor, is approved for HER2-negative MBC in g*BRCA1/2* mutation carriers. Olaparib Expanded, an investigator-initiated study, assessed the response to olaparib in MBC patients with s*BRCA1/2* mutations or g/s mutations in DDR-pathway genes other than *BRCA1/2*. **Methods:** Eligibility included: MBC with measurable disease; progression on < 2 metastatic chemotherapy regimens. Prior PARP inhibitor or progression on platinum was not allowed. Cohort 1 included patients with germline mutations in non-*BRCA1/2* DDR-pathway genes. In Cohort 2 were those with somatic mutations in these genes or *BRCA1/2;* germline testing was required only to exclude a *gBRCA* mutation if a s*BRCA* mutation was present. Patients received olaparib 300 mg bid until progression or unacceptable toxicity. For each cohort, a single-arm Simon two-stage design was used with 13 then 14 patients in the 1st and 2nd stages, respectively. The null hypothesis within each cohort [≤ 5% objective response rate (ORR)] would be rejected if > 4 responses were seen at the end of stage 2. Secondary endpoints include clinical benefit rate, progression-free survival, and duration of response. **Results:** 54 patients enrolled from March 2018 to Jan 2020; 1 ineligible s*BRCA2* was excluded. Median age was 59 yrs (range: 30-87). 40 patients had ER+ HER2-, 3 HER2+, and 10 TNBC. 87% had a mutation in *PALB2,* s*BRCA1/2*, *ATM* or *CHEK2*. ORR was 29.6% (8/27, 90%-CI: 15.6%-47.1%) in Cohort 1 and 38.5% (10/26, 90%-CI: 22.5%-56.4%) in Cohort 2. Responses were gene specific (Table): g*PALB2* and s*BRCA* mutations predicted response; no responses were seen with only a *CHEK2* or *ATM* mutation. To date, responses as long as 16.4 months have been observed. Responses were seen in all subtypes: 5/10 TNBC, 1/3 HER2+, 12/40 ER+ HER2-. 11 responses occurred after prior CDK4/6 inhibitor. In June 2020, final data for confirmed ORR and secondary endpoints will be reported. **Conclusion:** In this proof-of-principle study, single-agent olaparib successfully met its primary endpoint in both cohorts. Activity was seen largely in patients with MBC and s*BRCA1/2* or g*PALB2* mutations but not with *ATM* or *CHEK2* mutations. Clinical trial information: NCT03344965. Research Sponsor: Astra-Zeneca.

Number of patients and responses per genes in both cohorts.

Gene/ cohort	*N*	*Germline*	*Somatic*
PALB2	**13**	**8/11**	0/2
sBRCA1^	7	0/0	**4/7**
sBRCA2	9	0/0	**4/9**
ATM#	10	0/6	0/4
CHEK2^	7	0/7	0/0
CDK12	2	0/0	**1/2**
BLM	1	0/0	**1/1**
BARD, RAD50	2	0/2	0/0
BRIP1, FANCA	2	0/0	0/2

^ 1 with g*CHEK2* and s*BRCA1* analyzed with s*BRCA1* # 2 also had g*CHEK2* mutations

1003 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Pyrotinib or lapatinib plus capecitabine for HER2+ metastatic breast cancer (PHOEBE): A randomized phase III trial. *First Author: Binghe Xu, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: Pyrotinib (an irreversible pan-ErbB inhibitor) plus capecitabine showed clinically meaningful benefits and acceptable tolerability in patients (pts) with HER2+ metastatic breast cancer (MBC) in phase 1 and 2 studies. **Methods:** This open-label, multicenter, randomized phase 3 study enrolled HER2+ MBC pts after trastuzumab and taxanes, and/or anthracyclines. Up to two prior lines of chemotherapy (chemo) for metastatic disease were allowed. Pts were randomly assigned (1:1) to receive pyrotinib 400 mg or lapatinib 1250 mg qd continuously plus capecitabine 1000 mg/m^2 bid on days 1–14 of 21-day cycles. The primary endpoint was progression-free survival (PFS) per blinded independent central review. **Results:** From Jul 2017 to Oct 2018, 267 pts were randomized to the pyrotinib (n=134) or lapatinib (n=133) arm. One pt in the lapatinib arm did not receive study treatment and was excluded from analyses. 42.5% and 34.8% of pts in the pyrotinib and lapatinib arm had no prior chemo for metastatic disease, 41.8% and 49.2% had one prior line, and 15.7% and 15.9% had two lines. At the planned interim analysis, the median PFS was 12.5 months (95% CI 9.7–not reached) with pyrotinib plus capecitabine vs 6.8 months (95% CI 5.4–8.1) with lapatinib plus capecitabine (HR 0.39 [95% CI 0.27–0.56]; P<0.0001), which met the criterion for statistical significance (≤0.0066). Among trastuzumab-resistant pts, prolonged PFS with pyrotinib plus capecitabine was also observed (12.5 months [95% CI 6.9 to not reached] vs 6.9 months [95% CI 5.4 to not reached]; HR 0.60 [95% CI 0.29 to 1.21]). Benefits in objective response rate, clinical benefit rate, and duration of response with pyrotinib plus capecitabine were also indicated (Table). The most common grade ≥3 adverse events were diarrhea (30.6% vs 8.3% in the pyrotinib vs lapatinib arm) and hand-foot syndrome (16.4% vs 15.2%). **Conclusions:** In pts with HER2+ MBC after trastuzumab and chemo, pyrotinib plus capecitabine achieved a significant better PFS than lapatinib plus capecitabine, with manageable toxicity, verifying the phase 2 findings. Clinical trial information: NCT03080805. Research Sponsor: Jiangsu Hengrui Medicine.

Tumor response.

	Pyrotinib arm (N=134)	Lapatinib arm (N=132)
Objective response rate, % (95% CI)	67.2 (58.5–75.0)	51.5 (42.7–60.3)
Difference, % (95% CI); P	15.6 (4.0–27.3); P=0.0091	
Clinical benefit rate, % (95% CI)	73.1 (64.8–80.4)	59.1 (50.2–67.6)
Difference, % (95% CI); P	14.0 (2.8–25.3); P=0.0155	
Duration of response (mo), median (95% CI)	11.1 (9.7–not reached)	7.0 (5.6–9.8)
Response ongoing, n (%)	63 (70.0)	33 (48.5)

1004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A randomized, open-label, phase III trial of pertuzumab retreatment in HER2-positive, locally advanced/metastatic breast cancer patients previously treated with pertuzumab, trastuzumab, and chemotherapy: The Japan Breast Cancer Research Group-M05 (PRECIOUS) study. *First Author: Yutaka Yamamoto, Department of Breast and Endocrine Surgery, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan*

Background: Patients with HER2-positive locally advanced/metastatic breast cancer (LA/MBC) previously treated with pertuzumab (P)-containing regimens have few therapeutic options. The efficacy of P re-treatment combined with trastuzumab (T)+chemotherapy was examined in such patients. **Methods:** Patients previously treated with P-containing regimens as 1st/2nd-line treatment for LA/MBC were randomly assigned 1:1 to two groups (P+T+chemotherapy based on physicians' choice (C) (PTC), and T+C (TC)), stratified by estrogen receptor status, previous P treatment duration, number of previous chemotherapy regimens, and site of metastasis. The primary endpoint was investigator-assessed progression-free survival (PFS). Secondary endpoints included PFS by independent review, PFS in patients treated with T-DM1 as the latest regimen (PFS after T-DM1), objective response rate (ORR), overall survival (OS), safety, and health-related quality of life (HRQoL). **Results:** Of the 219 pts enrolled, 217 (108 PTC, 109 TC) were included in the intent-to-treat analysis. At the data cutoff (July 31, 2019), PFS and OS events were 178 (82.0%) and 84 (38.7%), respectively. Median follow-up time was 14.3 months (mo). Investigator –assessed PFS was significantly better in the PTC group (median PFS 5.7 vs. 4.3 mo; HR=0.713 [95%CI, 0.529-0.961]; log-rank test p=0.025). Median PFS by independent review (4.6 vs. 4.0 mo; HR=0.740 [95%CI, 0.552–0.993]; log-rank test p=0.0428) and median PFS after T-DM1 (5.7 vs. 4.4 mo; HR=0.716 [95%CI, 0.511-1.002]; log-rank test p=0.0428) were also significantly better in the PTC group. OS tended to be longer in the PTC group, though further follow-up is needed (median 28.7 vs. 23.3 mo; HR=0.695, [95%CI, 0.451-1.073], p=0.099). The ORR with measurable disease (PTC (n=91) 20.2% vs. TC (n=92) 24.7%) did not differ between the groups. The serious adverse event rate did not differ between the groups (18.1% vs. 21.1%). There were no new safety signals included cardiac events in the groups. In the comparison of HRQoL by time to deterioration analysis, there was no significant difference between the groups in FACT-B TOI (PTC 2.8 mo vs. TC 4.3 mo; HR=1.27, p=0.2289). **Conclusions:** P re-treatment as 3rd or 4th-line chemotherapy should be considered a new standard treatment option for patients with HER2-positive LA/MBC previously treated with P. Clinical trial information: NCT02514681. Research Sponsor: Chugai Pharmaceutical.

1005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Tucatinib versus placebo added to trastuzumab and capecitabine for patients with previously treated HER2+ metastatic breast cancer with brain metastases (HER2CLIMB). *First Author: Nancy U. Lin, Dana-Farber Cancer Institute, Boston, MA*

Background: Tucatinib (TUC) is an investigational, highly selective HER2 kinase inhibitor. HER2CLIMB (NCT02614794) showed clinically meaningful and statistically significant improvements in overall survival (OS) and progression free survival (PFS) in all pts, prolongation of PFS in pts with brain metastases (BM), and objective response rate (ORR) when TUC was added to trastuzumab (T) and capecitabine (C). Primary methods and outcomes have been reported previously (Murthy NEJM 2019). We report the results of exploratory efficacy analyses in pts with BM. **Methods:** All pts with HER2+ metastatic breast cancer (MBC) enrolled in HER2CLIMB had a baseline brain MRI. Pts with BM were eligible and classified as untreated, treated stable, or treated and progressing. Pts were randomized 2:1 to receive TUC or placebo, in combination with T and C. Efficacy analyses in pts with BM at baseline were performed by applying RECIST 1.1 to the brain based on investigator evaluation. CNS-PFS (progression in the brain or death) and OS were evaluated in BM pts overall. Intracranial (IC) confirmed ORR (ORR-IC) and IC duration of response (DOR-IC) were evaluated in BM pts with measurable IC disease. After isolated brain progression, pts could continue study therapy after local treatment until second progression, and time from randomization to second progression or death was evaluated. **Results:** Overall, 291 pts (48%) had BM at baseline: 198 (48%) in the TUC arm and 93 (46%) in the control arm. There was a 68% reduction in risk of CNS-PFS in the TUC arm (HR: 0.32; 95% CI: 0.22, 0.48; $P < 0.0001$). Median CNS-PFS was 9.9 mo in the TUC arm vs 4.2 mo in the control arm. Risk of death overall was reduced by 42% in the TUC arm (OS HR: 0.58; 95% CI: 0.40, 0.85; $P = 0.005$). Median OS was 18.1 mo vs 12.0 mo. ORR-IC was higher in the TUC arm (47.3%; 95% CI: 33.7, 61.2) vs the control arm (20.0%; 95% CI: 5.7, 43.7). Median DOR-IC was 6.8 mo (95% CI: 5.5, 16.4) vs 3.0 mo (95% CI: 3.0, 10.3). In pts with isolated brain progression who continued study therapy after local treatment (n = 30), risk of second progression or death was reduced by 67% (HR: 0.33; 95% CI: 0.11, 1.02), and median PFS from randomization was 15.9 mo vs 9.7 mo, favoring the TUC arm. **Conclusions:** In pts with heavily previously treated HER2+ MBC with BM, TUC in combination with T and C doubled the ORR-IC, reduced risk of IC progression or death by two thirds and reduced risk of death by nearly half. If approved, TUC in combination with T and C has the potential to become a new standard of care in pts with HER2+ MBC with and without BM. Clinical trial information: NCT02614794. Research Sponsor: Seattle Genetics.

1006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Alpelisib (ALP) + fulvestrant (FUL) in patients (pts) with *PIK3CA*-mutated (mut) hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2–) advanced breast cancer (ABC) previously treated with cyclin-dependent kinase 4/6 inhibitor (CDKi) + aromatase inhibitor (AI): BYLieve study results. *First Author: Hope S. Rugo, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

Background: *PIK3CA* mutations (mut) occur in ~40% of pts with HR+, HER2– ABC and are associated with poor prognosis and resistance to treatment (tx). ALP, a PI3Kα inhibitor, plus FUL demonstrated efficacy in the phase 3 SOLAR-1 trial of HR+, HER2– *PIK3CA*-mut ABC. Little clinical data and few prospective studies are available to inform tx decisions for pts with HR+, HER2– *PIK3CA*-mut ABC in the post-CDKi setting. BYLieve is the first trial evaluating ALP + endocrine therapy (ET; FUL or letrozole) in pts with HR+, HER2– *PIK3CA*-mut ABC who progressed on/after prior therapy, including CDKi. In this ongoing phase 2, open-label, noncomparative study, 112 pts with centrally confirmed *PIK3CA* mut in tumor tissue are enrolled in each cohort per immediate prior tx of CDKi + AI, CDKi + FUL, or systemic chemo or ET. Enrollment is complete in prior CDKi + AI and CDKi + FUL cohorts and ongoing in prior systemic chemo or ET cohort. We report on the cohort of pts with CDKi + AI as immediate prior tx. **Methods:** Pts received ALP 300 mg/day + FUL 500 mg Q28D + C1D15. Primary endpoint was proportion of pts alive without disease progression at 6 mo per local assessment; 2-sided 95% confidence intervals (CI) were calculated using Clopper and Pearson (1934) exact method. Evidence of clinically meaningful tx effect was defined as the lower bound of the 95% CI > 30%. Safety was assessed in all patients; AEs presented by preferred term. **Results:** 127 pts whose immediate prior tx was CDKi + AI were enrolled, of whom 121 had centrally confirmed *PIK3CA* mut; median follow-up was 11.7 mo. Primary endpoint was met: proportion of pts without disease progression at 6 mo was 50.4% (95% CI, 41.2-59.6). Most frequent all-grade AEs were diarrhea (60%), hyperglycemia (58%), nausea (46%), fatigue (29%), decreased appetite (28%), and rash (28%). Most frequent grade ≥3 AEs included hyperglycemia (28%), rash (9%), and rash maculopapular (9%). Incidence of AEs leading to discontinuation was low; most frequent AEs leading to discontinuation were rash (5 pts, 3.9%), colitis, hyperglycemia, urticaria, and vomiting (2 pts, 1.6% each). **Conclusions:** With follow-up still ongoing, BYLieve shows in a large number of pts that ALP + FUL demonstrates clinically meaningful efficacy and manageable toxicity post CDKi tx. Building on findings from SOLAR-1, BYLieve further supports use of ALP + FUL for HR+, HER2– *PIK3CA*-mut ABC. Clinical trial information: NCT03056755. Research Sponsor: Novartis Pharmaceuticals Corporation.

1007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

PARSIFAL: A randomized, multicenter, open-label, phase II trial to evaluate palbociclib in combination with fulvestrant or letrozole in endocrine-sensitive patients with estrogen receptor (ER)[+]/HER2[-] metastatic breast cancer. *First Author: Antonio Llombart-Cussac, Hospital Arnau de Vilanova, Universidad Catolica, Medica Scientia Innovation Research (MedSIR), Valencia, Spain*

Background: The CDK4/6 inhibitor palbociclib (P) in combination with letrozole (L) has become a standard first-line treatment for patients (pts) with luminal metastatic breast cancer (MBC) (PALOMA-1 & 2 trials). Meanwhile, the anti-estrogen fulvestrant (F) showed to be superior to anastrozole in the same population (FALCON trial). We aimed to identify the best endocrine agent to combine with P in this first-line scenario. **Methods:** A total of 486 pts with ER [+]/HER2[-] MBC with no prior therapy in the advanced setting and endocrine sensitive criteria (relapse > 12 months [mo] after the end of adjuvant endocrine therapy or diagnosed with "de novo" metastatic disease) were randomly assigned (1:1 ratio) to receive P (oral 125 mg/day [d]; 3 wks on/1 wk off) plus F 500 mg/d (I.M Days 0, 14, 28, and then every 28 d) or PL (oral 2.5 mg/d). Pts were stratified by visceral involvement and type of disease presentation ("de novo"/recurrent). Primary endpoint was investigator-assessed progression-free survival (PFS). Secondary endpoints included overall survival (OS), overall response rate (ORR), clinical benefit rate (CBR), and safety. 254 events were needed with 80% power to detect a hazard ratio (HR) ≤0.7 in favor of PF (2-sided $\alpha = 0.05$). **Results:** By March 9th, 2020, 256 PFS events occurred. Pts characteristics were well balanced. Median age was 62 years (range: 25–90), 56.6% were ECOG 0, 40.7% had "de novo" metastatic disease, 48% had visceral disease, and 43.6% with ≥3 organ sites involved. At median follow-up of 32 mo, median PFS was 27.9 mo (95% confidence interval [CI], 24.2-33.1) with PF and 32.8 mo (95% CI, 25.8-35.9) with PL (HR: 1.1; 95% CI, 0.9-1.5; P = 0.321). No differences were observed for pts with or without visceral involvement (HR: 1.3 and HR: 0.97 respectively, interaction P = 0.275), and for "de novo" or recurrent metastatic disease (HR: 1.1 and HR: 1.1 respectively, P = 0.979). The 4-year OS rate was 67.6% in PF and 67.5% in PL arm (HR: 1; 95% CI, 0.7-1.5; P = 0.986). No differences were observed in ORR or CBR between arms. Grade ≥3 adverse events were similar in both arms, being neutropenia and leukopenia the most frequent. No treatment-related deaths were reported. **Conclusion:** This study was not able to identify an improvement in PFS for PF over PL in patients with endocrine-sensitive ER[+]/HER2[-] MBC. As both arms demonstrated comparable 4 years-OS, PF is a reasonable alternative to PL in this setting. Clinical trial information: NCT02491983. Research Sponsor: Pfizer.

1008 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Randomized trial of a collaborative palliative and oncology care intervention to improve communication about end-of-life care in patients with metastatic breast cancer. *First Author: Jennifer S. Temel, Massachusetts General Hospital, Boston, MA*

Background: Studies have demonstrated the benefits of early, integrated palliative care in improving quality of life (QOL) and end-of-life (EOL) care for patients with poor prognosis cancers. However, the optimal timing and outcomes of delivering palliative care for those with advanced cancers that have longer disease trajectories, such as metastatic breast cancer (MBC), remains unknown. We tested the effect of a collaborative palliative and oncology care model on communication about EOL care in patients with MBC. **Methods:** Patients with MBC and clinical indicators of poor prognosis (N=120) were randomized to receive collaborative palliative and oncology care or usual care between 05/02/2016 and 12/26/2018. The intervention entailed five structured palliative care visits, including a joint visit with oncology when possible, which focused on symptom management, coping, prognostic awareness, decision-making, and planning for EOL. The primary outcome was documentation of EOL care discussions in the electronic health record. Patients also completed questionnaires at baseline and 6, 12, 18, and 24 weeks regarding communication with clinicians about EOL care, QOL, and mood symptoms. **Results:** The sample included only women (100.0%) who mostly identified as white (87.5%), with a mean age of 56.91 years (SD=11.24). The rate of EOL care discussions documented in the health record was higher among intervention patients versus those receiving usual care (67.2% vs 40.7%, p=0.006), including a higher completion rate of a Medical Orders for Life Sustaining Treatment form (39.3% vs 13.6%, p=0.002). Intervention patients were also more likely to report discussing their EOL care wishes with their doctor compared to usual care patients (OR=3.10, 95% CI: 1.21, 7.94, p=0.019). Study groups did not differ in reported QOL or mood symptoms. **Conclusions:** This novel collaborative palliative care intervention significantly improved communication and documentation regarding EOL care for women with MBC. Further work is needed to examine the effect of this care model on healthcare utilization at the end of life. Research Sponsor: Pfizer.

1009 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Pooled ctDNA analysis of the MONALEESA (ML) phase III advanced breast cancer (ABC) trials. *First Author: Fabrice Andre, Gustave Roussy Université Paris Sud, Villejuif, France*

Background: Biomarker analyses have been presented separately for each Phase III ML trial, which tested efficacy and safety of ribociclib (RIB) with different endocrine therapy (ET) combination partners as first- or second-line treatment for hormone receptor–positive, HER2-negative (HR+/HER2−) ABC. Here, using the largest pooled biomarker dataset of a CDK4/6 inhibitor in ABC to date, we identify potential biomarkers of response or resistance to RIB across ML trials. **Methods:** Baseline ctDNA from 1503 patients (pts) enrolled in ML-2, 3, and 7 was assessed using next-generation sequencing with a targeted panel of 557 genes. Genes with an alteration frequency ≥2% and in ≥15 pts per treatment arm were included (83 genes). Genetic alteration was defined as presence of a mutation, short insertion/deletion, or copy number alteration. Cox proportional hazard model of progression-free survival (PFS) was fit with gene-by-treatment interaction. Genes with interaction $P < 0.10$ and genes of interest were investigated. **Results:** Pts with alterations in *FRS2* and *PRKCA* (treatment interaction $P < 0.05$) as well as *MDM2, ERBB2, AKT1, and BRCA1/2* ($P > 0.05$ but considered actionable) had a trend for increased PFS benefit of RIB vs PBO (Table). Pts with alterations in *CHD4, BCL11B, ATM*, or *CDKN2A/2B/2C* derived little to no added PFS benefit with RIB vs PBO (*P* interaction < 0.10; hazard ratio [HR] > 0.80). Data on genes implicated in the literature as potential mechanisms of resistance to ET and/or CDK4/6 inhibition (*ESR1, PTEN, FAT1, RB1*, and *NF1*) will be presented. **Conclusions:** Results of this pooled analysis of the ML-2, 3, and 7 trials, the largest biomarker analysis of any CDK4/6 inhibitor in ABC, revealed several potential biomarkers of response (*FRS2, MDM2, PRKCA, ERBB2, AKT1*, and *BRCA1/2*) or resistance (*CHD4, BCL11B, ATM*, or *CDKN2A/2B/2C*) to RIB. Clinical trial information: NCT01958021; NCT02422615; NCT02278120. Research Sponsor: Novartis.

Gene	WT RIB Median PFS, mo	WT PBO median PFS, mo	HR (95% CI)	Altered RIB Median PFS, mo	Altered PBO Median PFS, mo	HR (95% CI)	*P* Value for Gene-Treatment Interaction[a]
FRS2	n = 829 22.21	n = 629 13.24	0.60 (0.52-0.69)	n = 23 12.52	n = 22 1.87	0.26 (0.11-0.58)	.03
PRKCA	n = 830 22.14	n = 632 13.04	0.60 (0.52-0.70)	n = 22 17.18	n = 19 7.23	0.23 (0.09-0.60)	.04
BRCA1/2	n = 817 22.14	n = 631 12.98	0.60 (0.52-0.70)	n = 35 NA	n = 20 7.06	0.30 (0.15-0.61)	.06
MDM2	n = 835 22.21	n = 633 13.11	0.60 (0.52-0.69)	n = 17 11.27	n = 18 1.87	0.29 (0.12-0.70)	.06
ERBB2	n = 818 22.34	n = 632 13.24	0.59 (0.51-0.69)	n = 34 12.75	n = 19 1.99	0.33 (0.16-0.69)	.13
AKT1	n = 812 22.14	n = 630 13.04	0.60 (0.52-0.69)	n = 40 18.63	n = 21 7.56	0.39 (0.18-0.84)	.33

WT, wildtype. [a] Not corrected for multiple testing; results are exploratory.

1010 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Prognostic impact of ESR1 mutations in ER+ HER2- MBC patients prior treated with first line AI and palbociclib: An exploratory analysis of the PADA-1 trial. *First Author: Francois Clement Bidard, Centre René Huguenin, Saint Cloud, France*

Background: The question of which is the best endocrine partner to CDK4/6 inhibitors in first line for ER+ HER2- metastatic breast cancer (MBC) remains open. *ESR1* mutations might be of paramount importance, as they confer resistance to AI but not to SERD. In pts treated with first line palbociclib-AI combination (PADA-1 trial, NCT03079011), we investigated *ESR1mut* detection rate at inclusion, prior to any therapy, and their prognostic impact. **Methods:** The PADA-1 phase 3 trial (NCT03079011, UCBG-GINECO) evaluates the utility of monitoring the onset of *ESR1mut* in cell-free DNA (with a ddPCR assay [Jeannot *et al*, Oncogene 2020]) of pts receiving AI-palbociclib in first line. Included pts had no prior therapy for MBC and no overt resistance to AI. **Results:** N = 1017 ER+ HER2- MBC pts were included in 22 months from 04/2017 and had their cfDNA tested for *ESR1mut* at inclusion and during therapy. N = 33/1017 pts had a detectable circulating *ESR1mut* at inclusion (3.2%, 95%CI [2.2;4.5]), *ESR1mut* positivity being associated with a prior exposure to AI in the adjuvant setting ($p < 0.01$). N = 1 pt died after 1 month on treatment. In N = 25/32 evaluable pts (78%), *ESR1mut* became undetectable in cfDNA (AF < 0.1%) within the first 5 months on treatment, with a median time to *ESR1mut* 'clearance' of 34 days. Among these 25 pts, 14 pts (56%) had *ESR1mut* detected again during therapy; 2 pts (8%) experienced a progression with no *ESR1mut* detected; the remaining 9 patients (36%) were still both *ESR1mut* -free and progression-free at time of analysis. With a median FU time of 12.4 months (range: 0-25.3m) under AI-palbociclib, the 33 ESR1mut-positive pts had a shorter PFS (median: 17.5mo, 95%CI[10.5-NR]) than the 984 ESR1mut-negative pts (median not reached), with an estimated HR = 2.8 [1.6;5.0]. Updated data will be presented at the meeting. **Conclusions:** *ESR1mut* are rarely detected in the cfDNA of ER+ HER2- MBC patients with no overt resistance to AI. The quick 'clearance' of *ESR1mut* under treatment and the observed 17.5 months-long median PFS both suggest that the AI-palbociclib combination retain a clinical activity in this population. *ESR1mut*-positivity prior was however associated with a significantly shorter PFS, suggesting that *ESR1mut* positivity at baseline could accelerate the onset of resistance to AI-palbociclib. These findings may put into perspective the incoming results of the PARSIFAL trial. Clinical trial information: NCT03079011. Research Sponsor: Pfizer.

1011 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

A multiparameter classifier to predict response to lapatinib plus trastuzumab (LT) without chemotherapy in HER2+ breast cancer (BC). *First Author: Jamunarani Veeraraghavan, Baylor College of Medicine, Houston, TX*

Background: Several trials have shown 25-30% pathologic complete response (pCR) rates in patients with HER2+ BC treated with LT therapy (+ endocrine therapy if ER+), but no chemotherapy (CTX). We hypothesize that a multiparameter classifier, comprised of HER2 gene and protein levels, intratumor heterogeneity (ITH), HER2-enriched (E) subtype, and *PIK3CA* mutation status can identify patients whose tumors are "addicted" to HER2 signaling and are likely to achieve pCR from a CTX-sparing de-escalation strategy. **Methods:** Baseline specimens from 2 trials (TBCRC023 [NCT00999804] and PAMELA [NCT01973660]) of neoadjuvant CTX-sparing LT (+ endocrine therapy if ER+) in HER2+ BC were used. HER2 protein and ITH (scored for % 3+ by IHC), and gene amplification (HER2:CEP17 ratio and copy number (CN) by CISH) were measured on the same slide by the dual gene protein assay (GPA). HER2-E and *PIK3CA* mutation status were assessed by research-based PAM50 and MSK-IMPACT platforms, respectively. A decision tree algorithm was used to determine the GPA cutoffs and to construct the classifier of response (by pCR) in TBCRC023, which was then validated in PAMELA. **Results:** Of the evaluable patients from TBCRC023 (N = 130) and PAMELA (N = 151), GPA data were available for 121 and 94 cases, respectively. Both cohorts exhibited similar distributions for HER2 ratio, CN, and % 3+, and a strong correlation between HER2 ratio and CN ($R > 0.92$). In TBCRC023, 73 cases had data from GPA, PAM50, and IMPACT, of which 15 had pCR. Recursive partitioning identified cutoffs of HER2 ratio > 4.6 and % 3+ > 97.5% in both the GPA data cohort (N = 121) and complete data cohort (N = 73). With PAM50 and IMPACT data, the model added HER2-E and *PIK3CA* wild-type (wt). For practical reasons, the classifier was locked as HER2 ratio ≥ 4.5 AND % 3+ ≥ 90% AND *PIK3CA*-wt AND HER2-E, which yielded a PPV of 55% and NPV of 94%. Validation in PAMELA using 45 cases with data for all 3 assays yielded PPV of 44% and NPV of 82%. 29 TBCRC023 cases without IMPACT data could be predicted to be non-pCR, of which 26 were correct (NPV = 89%). In PAMELA, 66 additional cases could be predicted to be non-pCR, of which 54 were correct (NPV = 81%). **Conclusions:** We have constructed a multiparameter classifier that can predict pCR with targeted therapy alone that compare to pCR rates of CTX + dual anti-HER2 in unselected patients. Prospective validation in a clinical trial is warranted. Research Sponsor: Department of Defense Breast Cancer Research Program, NCI-SPORE, TBCRC (BCRF and Komen), Ventana.

Trial	pCR	Non-pCR	Sensitivity	Specificity	PPV	NPV
TBCRC023	**N**	**N**	80%	83%	55%	94%
Predict pCR	12	10				
Predict non-pCR	3	48				
PAMELA	**N**	**N**	62%	69%	44%	82%
Predict pCR	8	10				
Predict non-pCR	5	22				

ABSTRACT WITHDRAWN

1013 Poster Discussion Session; Displayed in Poster Session (Board #98), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Association of tumor mutational burden (TMB) and clinical outcomes with pembrolizumab (pembro) versus chemotherapy (chemo) in patients with metastatic triple-negative breast cancer (mTNBC) from KEYNOTE-119. *First Author: Eric P. Winer, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA*

Background: In the randomized, open-label, phase 3 KEYNOTE-119 study (NCT02555657), OS was not significantly different with pembro monotherapy versus chemo in second- or third-line settings for mTNBC; however, the pembro treatment effect increased with increasing PD-L1 enrichment. We evaluated the association of TMB with efficacy of pembro monotherapy versus chemo in patients with previously treated mTNBC. **Methods:** Patients with centrally confirmed TNBC and 1 or 2 prior systemic treatments for metastatic disease were enrolled. Patients were randomly assigned 1:1 to pembro 200 mg Q3W or single-agent chemo per investigator's choice of capecitabine, eribulin, gemcitabine, or vinorelbine. Association of TMB, as measured by FoundationOne CDx (Foundation Medicine), with response was an exploratory objective evaluated using receiver operator characteristic (ROC) analysis, logistic regression (ORR), and Cox regression (OS; PFS) within treatment arms; estimates of efficacy based on TMB cutpoint used a prespecified cutpoint of 10 mut/Mb. **Results:** TMB data were available for 253/601 (42.1%) treated patients (pembro, n = 132; chemo, n = 121); baseline characteristics were similar to that of the overall study population. One-sided *P* values for the association of TMB and clinical outcomes in pembro-treated patients were 0.154 for ORR, 0.014 for PFS, and 0.018 for OS; the area under the ROC curve ([AUROC] 95% CI) for predicting ORR was 0.58 (0.43-0.73). Two-sided *P* values for the association of TMB and clinical outcomes in chemo-treated patients were 0.114 for ORR, 0.478 for PFS, and 0.906 for OS; AUROC (95% CI) was 0.43 (0.27-0.59). Twenty-six patients had TMB ≥10 mut/Mb. Thus, the prevalence of TMB ≥10 mut/Mb was ~10%. Outcomes based on TMB cutpoint are reported in the Table. **Conclusions:** Data from this exploratory analysis from KEYNOTE-119 suggest a potential positive association between TMB and clinical benefit with pembro but not chemo in patients with mTNBC. Although precision is limited by sample size and the number of patients with TMB ≥10 mut/Mb, ORR and HRs for OS suggested a trend towards increased benefit with pembro versus chemo in patients with TMB ≥10 mut/Mb. Clinical trial information: NCT02555657. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	TMB ≥10, pembro (n = 14)	TMB ≥10, chemo (n = 12)	TMB < 10, pembro (n = 118)	TMB < 10, chemo (n = 109)
ORR, % (95% CI)	14.3% (4.0-39.9)	8.3% (0.4-35.4)	12.7% (7.9-19.9)	12.8% (7.8-20.4)
PFS, HR (95% CI)	1.14 (0.42-3.07)	–	1.24 (0.92-1.67)	–
OS, HR (95% CI)	0.58 (0.21-1.57)	–	0.81 (0.61-1.07)	–

1014 Poster Discussion Session; Displayed in Poster Session (Board #99), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Results of ENCORE 602 (TRIO025), a phase II, randomized, placebo-controlled, double-blinded, multicenter study of atezolizumab with or without entinostat in patients with advanced triple-negative breast cancer (aTNBC). *First Author: Joyce O'Shaughnessy, Baylor Charles A. Sammons Cancer Center, US Oncology and Texas Oncology, Dallas, TX*

Background: Chemotherapy remains as the only standard treatment option for aTNBC in second and subsequent lines. Entinostat (ENT) is an oral, class I-selective histone deacetylase inhibitor, that has shown antitumor activity in preclinical models of TNBC when combined with immune checkpoint blockade. ENCORE 602 evaluated the efficacy and safety of atezolizumab (ATEZO) + ENT vs ATEZO + placebo (P) in patients (pts.) with pretreated aTNBC. **Methods:** Pts. with previously treated aTNBC (PD-1/PD-L1 inhibitors naïve) were randomized 1:1 to receive ATEZO (1200 mg IV Q3W) + ENT (5 mg PO QW) or ATEZO+P. Treatment continued until unequivocal progressive disease or unacceptable toxicity. The primary endpoint was PFS as determined by the investigators using RECIST 1.1. The hypothesis was that the combination would improve median PFS by 3 months (hazard ratio = 0.57). Sixty events (from 70 pts.) would provide 80% power with 1-sided significance level of 0.1. Secondary endpoints were PFS per immune-related RECIST (irRECIST), ORR, clinical benefit rate (CBR), Overall Survival (OS), and safety. **Results:** 81 pts. were enrolled, median age 56 years (range 29-87), 69% received 1 prior line of therapy and 31% > 1 line. No significant difference in PFS per RECIST 1.1 was observed between ATEZO+ENT and ATEZO+P (median PFS 1.68 and 1.51 months, respectively [p = 0.64; HR 0.89, 95% CI: 0.53-1.48]), nor in any of the secondary efficacy endpoints (median PFS per irRECIST 1.68 vs 1.54 months; ORR 10.0% vs 2.4%; CBR 37.5% vs 31.7%; median OS 9.8 vs 12.4 months, respectively). Frequency of treatment-emergent adverse events (TEAEs), SAEs, discontinuations due to TEAE and TEAE with outcome death were higher in the ENT+ATEZO arm. **Conclusions:** In pts. with previously treated aTNBC, median PFS was not prolonged when ENT was added to ATEZO compared to ATEZO and placebo, and the combination resulted in greater toxicity. Clinical trial information: NCT02708680. Research Sponsor: Syndax Pharmaceutical Inc.

1015 Poster Discussion Session; Displayed in Poster Session (Board #100), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase Ib/II study of eribulin (ERI) plus pembrolizumab (PEMBRO) in metastatic triple-negative breast cancer (mTNBC) (ENHANCE 1). *First Author: Sara M. Tolaney, Dana-Farber Cancer Institute, Boston, MA*

Background: As monotherapies, both ERI (a chemotherapeutic microtubule inhibitor) and PEMBRO (a programmed death [PD]-1 blocking immunotherapy) have shown promising antitumor activity in mTNBC. Emerging data suggest that the addition of immunotherapy to traditional chemotherapy holds promise for mTNBC. This open-label, single-arm, phase 1b/2 study evaluated the safety and efficacy of ERI + PEMBRO in mTNBC. **Methods:** Patients (pts) with mTNBC and ≤2 prior systemic anticancer therapies for metastatic disease were enrolled and stratified by prior number of therapy (Stratum 1, 0; Stratum 2, 1–2). Pts received IV ERI 1.4 mg/m^2 on day (d)1 and d8 and IV PEMBRO 200 mg on d1 of a 21-d cycle. The primary objectives were safety and objective response rate (ORR per RECIST 1.1 by independent imaging review). Assessments also included efficacy outcomes by PD ligand-1 (PD-L1) expression status; PD-L1+ was defined as a combined positive score ≥1 using the PD-L1 IHC 22C3 pharmDx. **Results:** As of data cutoff (July 31, 2019), 167 pts (Stratum 1, n=66; Stratum 2, n=101) were enrolled and treated. No dose-limiting toxicities were observed. The most common treatment-emergent adverse events were fatigue (66%), nausea (57%), peripheral sensory neuropathy (41%), alopecia (40%), and constipation (37%). No deaths were considered treatment related. The overall ORR was 23.4% (95% CI: 17.2–30.5). Efficacy outcomes by PD-L1 status (PD-L1+, n=74; PD-L1-, n=75) and stratum are presented (table). **Conclusions:** ERI + PEMBRO has activity in pts with mTNBC. There was a trend toward more robust activity for the combination among patients with PD-L1+ tumors compared to PD-L1- tumors in the first-line setting (Stratum 1); whereas, in the later-line setting (Stratum 2) similar survival outcomes were observed among the PD-L1+ and PD-L1- pts. ERI + PEMBRO shows promise for mTNBC with efficacy that appears greater than historical reports of either agent alone. Clinical trial information: NCT02513472. Research Sponsor: This work was supported by Eisai Inc., Woodcliff Lake, NJ, USA; and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

ERI + PEMBRO	PD-L1+ Stratum 1	PD-L1- Stratum 1	PD-L1+ Stratum 2	PD-L1- Stratum 2
(N=149)[a]	**(n=29)**	**(n=31)**	**(n=45)**	**(n=44)**
ORR, %	34.5	16.1	24.4	18.2
(95% CI)	(17.9–54.3)	(5.5–33.7)	(12.9–39.5)	(8.2–32.7)
mOS, months	21.0	15.2	14.0	15.5
(95% CI)	(8.3–29.0)	(12.8–19.4)	(11.0–19.4)	(12.4–18.7)
mPFS, months	6.1	3.5	4.1	3.9
(95% CI)	(4.1–10.2)	(2.0–4.2)	(2.1–4.8)	(2.3–6.3)
mDOR, months	8.3	15.2	8.2	8.6
(95% CI)	(3.2–NE)	(6.5–22.2)	(5.1–25.1)	(3.5–13.2)

[a]Excludes 18 patients who had unknown tumor PD-L1 status. DOR, duration of response; m, median; NE, not evaluable; OS, overall survival; PFS, progression-free survival.

1016 Poster Discussion Session; Displayed in Poster Session (Board #101), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Randomized phase III trial of eribulin (E) versus standard weekly paclitaxel (P) as first- or second-line therapy for locally recurrent or metastatic breast cancer (MBC). *First Author: Minetta C. Liu, Mayo Clinic, Rochester, MN*

Background: The ph III EMBRACE trial of E vs physician's choice of tx led to FDA approval of E as ≥3rd-line tx for MBC pts with prior exposure to anthracyclines/taxanes. The ph III BOLD 301 trial of E vs capecitabine in advanced BC treated with anthracyclines/taxanes showed a nonsignificant trend to improved median OS for all pts; pre-planned analysis by HER2 status revealed a nominally significant benefit for HER2- pts. **Methods:** RU011201I is an investigator initiated ph III trial with 1:1 randomization to E (1.4 mg/m2 D1,8 q21days) vs P (90 mg/m2 D1,8,15 q28days) within strata defined by (neo)adjuvant taxanes (yes/no), HR status (+/-), and line of tx (1st/2nd). Pts had measurable or non-measurable disease by RECIST v1.1; new or progressive mets; peripheral neuropathy (PN) gr<2; ≤1 prior chemotx regimens for advanced or MBC. Asymptomatic brain mets with stable MRIs for >3 mos were allowed. (Neo)adjuvant taxanes were allowed if >12 mos between tx completion and disease recurrence. Radiographic studies occur q12wks. Survival data are collected q12wks after the Off-Tx Visit. Pts reported side effects weekly; post-baseline symptomatic AE rates worse than baseline were compared between arms using Fisher's exact tests. We report clinical outcomes and the primary objective related to PRO-CTCAE use. **Results:** 201 pts enrolled 3/2014 - 5/2018 with 33.8 mos median f/u; 3 are on tx as of 2/20/20 (1E, 2P). Pt characteristics were the same between E vs P: median age 62 yrs (range 27-85); 42% prior taxane; 78% ER+; 70% starting 1st line tx. Baseline lesion distribution was similar except for lung mets (37E, 53P). No difference was seen between E vs P in PFS (5.7 vs 5.9 mos; P=0.72), OS (18.1 vs 16.4 mos; P=0.75), TTF (5.3 vs 4.9 mos; P=0.82), DOR (10.8 vs 12.3 mos; P=0.84), or number of metastatic events (55 vs 54). 37E and 36P pts required ≥1 dose reduction. Hematologic toxicities ≥ gr 3 were higher with E (40 vs 22%). PN events were similar: 56 vs 58 total, 4 vs 7 motor, 52 vs 51 sensory. Median duration of PN and median time to 1st PN event were 74 vs 140 and 56 vs 41 days. Worsened numbness/tingling severity and other pt-reported AE rates were similar, but worsened numbness/tingling interference (63% vs 78%, P=0.04) and vomiting frequency (35% vs 57%, P=0.005) were lower with E. **Conclusions:** Clinical outcomes were equivalent with E vs P as 1st/2nd line tx for HER2- advanced BC. The nature and severity of PN were similar between arms, but time of onset, duration, and interference with daily living favor E. E may be a suitable treatment option in this setting. Clinical trial information: NCT02037529. Research Sponsor: Eisai.

1017 Poster Discussion Session; Displayed in Poster Session (Board #102), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II trial of bicalutamide in combination with palbociclib for the treatment of androgen receptor (+) metastatic breast cancer. *First Author: Ayca Gucalp, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Genome-wide transcriptional analysis has identified a unique subset of androgen receptor (AR) +, estrogen receptor (ER)/progesterone receptor (PR)-breast cancer (BC). The functional role of AR was confirmed initially in preclinical models demonstrating that androgen-driven growth could be abrogated by anti-androgen therapy. TBCRC011 established the safety and efficacy of inhibiting AR with bicalutamide (B) in patients (pts) with AR+/ER/PR- metastatic BC (MBC) with a median progression free survival (PFS) of 12 weeks (wks) (95% CI, 11–22 wks). In preclinical data, palbociclib (P) has been shown to reduce growth of AR+/ER/PR- MDA-MB-453 BC cells. It has been shown that AR+ triple negative BC (TNBC) expresses a luminal profile and has intact Rb protein, the target of P activity. We conducted this Phase I/II trial of the AR inhibitor B in combination with the CDK4/6 inhibitor P in pts with AR+/ER/PR/HER2- BC (NCT02605486) to test the hypothesis that androgen blockade, paired with CDK4/6 inhibition would have increased efficacy in pts with androgen-dependent BC. **Methods:** Postmenopausal pts with AR+ TN MBC defined as IHC ≥ 1% nuclear staining (DAKO, Clone AR441 (5/2016-11/2016) then Ventana AR SP107 (11/2016-6/2018), ECOG ≤2, measurable/non-measurable disease were eligible for enrollment. Any number of prior regimens was permitted. Pts received B 150 mg daily and P 125 mg daily 3 wks on 1 wk off. Pts were evaluated for toxicity every 2-4 wks and for response every 8-12 wks. Primary endpoint: 6 month (mo) PFS. Secondary endpoints: clinical benefit rate, toxicity, correlative studies to better characterize AR+ TNBC. A Simon 2-stage minimax design that discriminates between 6 mo PFS rates of 20% and 40% was used. If ≥ 11/33 pts were PF at 6 mo then B+P would warrant further study. **Results:** As of 1.1.20 33 pts were enrolled on study with median (med) age 67 (42-79), performance status 0 (0-1). Number of pts with visceral metastases: 20, measurable disease: 22. AR% 1-9: 3, 10-50: 6; 51-100: 24. Med prior lines for MBC: 3 (0-9). Best response: (31 evaluable pts): 11 pts PF at 6mo: 10 SD > 6mo, 1 PR. Med wks on study: 14 (2-101). Toxicity > 10% grade >3 related: Number of pts with leukopenia: 21, neutropenia: 21, lymphocytopenia: 6, thrombocytopenia: 3. One pt with febrile neutropenia. One death due to disease progression within 30 days off study. **Conclusions:** In this selected subset of pts with AR+ TN MBC, this study met its prespecified endpoint with 11 pts PF at 6 mo on B 150 mg + P 125 mg. B+P has been well tolerated with no unexpected toxicity observed. Clinical trial information: NCT02605486. Research Sponsor: Pfizer.

1018 Poster Discussion Session; Displayed in Poster Session (Board #103), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Exploring impact of mutations in non-*BRCA* DNA damage response (DDR) and non-DDR genes on efficacy in phase III EMBRACA study of talazoparib (TALA) in patients (pts) with germline *BRCA1/2* mutated (g*BRCA*m) HER2-negative (HER2-) advanced breast cancer (ABC). *First Author: Jennifer Keating Litton, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Loss-of-function mutations in genes encoding components of the homologous recombination DNA damage response (DDR) machinery, notably *BRCA1/2*, are associated with tumor sensitivity to poly(ADP-ribose) polymerase inhibitors (PARPi). In EMBRACA, the PARPi TALA showed an improvement in progression-free survival (PFS) (HR [95% CI] 0.54 [0.41-0.71], $P < 0.001$) vs physician's choice of chemotherapy (PCT) in g*BRCA*m HER2− ABC. **Methods:** Baseline tumor tissue from 308 pts (71%; intent-to-treat) was sequenced using the FoundationOne CDx panel. Mutations summarized below were known/likely pathogenic single-nucleotide variants, insertions, deletions, or rearrangements. Best tumor response (BOR) was using RECIST 1.1 by Investigator (confirmation of CR or PR not required). **Results:** 296/308 (96%) of evaluable pts exhibited ≥1 tumor *BRCA* mutation, with 7 of the remaining 12 exhibiting *BRCA* copy number alterations deemed pathogenic. Mutations in other genes implicated in DDR and/or potential sensitization to PARPi were rare, with mutations detected in *BARD1, CDK12, FANCG, STAG2* (each 0.3%), *ATR, BRD4, FANCC, PALB2, RAD51B* (0.6%), *ATM, BRIP1* (1.0%), *NBN* (1.3%), *CHEK2, FANCA* (1.6%), and *ARID1A* (2.3%). No association was observed between total number of DDR mutations, including *BRCA1/2*, and best tumor response (BOR) [odds ratio of 1 vs ≥2 DDR mutations (95% CI): TALA, 0.76 (0.31-1.87), $P = 0.55$; PCT, 0.98 (0.27-3.51), $P = 0.97$]. *TP53* and *PIK3CA* were the most commonly mutated non-*BRCA* genes in *BRCA*m tumors (52.0 and 10.8%, respectively). *TP53* mutations were more prevalent in *BRCA1*m vs *BRCA2*m tumors (85.2 vs 24.8%). *PIK3CA* mutations were more prevalent in *BRCA2*m vs *BRCA1*m tumors (15.9 vs 5.2%). With TALA, PFS was significantly shorter in pts with *TP53* mutations than without [HR (95% CI) 1.693 (1.186-2.418), $P = 0.0033$]. A similar, non-significant, trend was evident with PCT [HR (95% CI) 1.439 (0.859-2.411), $P = 0.1614$]. *PIK3CA* mutational status had no impact on PFS in either arm. **Conclusions:** Selection based on g*BRCA* mutational status is appropriate to identify HER2− ABC pts with potential for clinical benefit from TALA, with the total number of tumor mutations in *BRCA1/2* and other DDR genes not impacting response (within the g*BRCA*m subset). *TP53* mutations were associated with shorter PFS, likely reflecting the worse outcomes observed in g*BRCA1*m patients. Additional correlative analyses are ongoing. Clinical trial information: NCT01945775. Research Sponsor: Pfizer Inc.

1019 Poster Discussion Session; Displayed in Poster Session (Board #104), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Clinical efficacy and molecular effects of lenvatinib (Len) and letrozole (Let) in hormone receptor-positive (HR+) metastatic breast cancer (MBC). *First Author: Joline Si Jing Lim, National University Cancer Institute, Singapore, Singapore*

Background: Preclinical studies show cross talk between RET and estrogen receptor, with at least additive treatment (Tx) effect of Len, a RET inhibitor, with Let. Our previous work concluded a recommended phase 2 dose (RP2D) of Len 14mg daily and Let 2.5mg daily (Lim, ASCO 2019). We present efficacy data from dose escalation and expansion cohorts. **Methods:** Safety, tolerability and efficacy data of MBC patients in both dose escalation (Len dose level 1 [DL]:20mg, DL -1:16mg and DL -2:14mg) and expansion (Len 14mg) cohort of this phase Ib/II study of combination Len+Let study was analysed. Patients were treated with single-agent Len for 2 weeks, followed by Len+Let until disease progression (PD). Serial tumor biopsies at baseline, after Len alone, 4 weeks post Len+Let, and upon PD, were sequenced for 440 genes with the ACTOnco+ platform. **Results:** A total of 33 pts (DL1 6pts, DL-1 6pts, DL-2 + expansion 21pts) with median 5 lines of prior Tx (range 0-11) were enrolled; 87.9%, 75.8%, and 75.8% had prior endocrine therapy (ET), ET+CDK4/6 inhibitor (i), and chemotherapy (CT) respectively. Objective response rate (ORR), disease control rate (DCR) ≥6 months (m), median duration of response (DOR), and percentage progression-free (PPF) at 12m were 33.3%, 45.5%, 11.5m (range 6.3-22.4), and 27.2% respectively. Among patients who previously progressed on CDK4/6i (n = 25), ORR, DCR ≥6m, median DOR, and PPF at 12m were 24.0%, 40.0%, 13.7m (range 6.3-18.2), and 12.0% respectively. Of note, 3/25 (12%) patients had durable response to Len+Let lasting ≥12m, despite having only modest PFS on ET+CDK4/6i (3, 7, and 12 months respectively). Most frequent all-grade toxicities (tox) were HTN (n = 15, G3:15), hypothyroidism (n = 20, G3:0) and fatigue (n = 13, G3:2), with no G4/5 tox. No new toxicity signals were observed compared to dose escalation phase. Pre-treatment tumor molecular profiling showed responders to be more likely to harbor NEFH, USH2A and PTCH1 mutations, while non-responders were more likely to carry PIK3R1, APC and PALB2 mutations. Sequencing of serial biopsies showed downregulation of BRD4, PTCH1, KIT, NTRK1 and CREBBP after Len treatment. **Conclusions:** Len+Let showed significant anti-tumor activity with meaningful duration of response, even in pts who failed prior CT or ET+CDK4/6i. The results support further investigation in randomized studies. Tumor profiling identified mutations associated with response and insights on molecular effects of lenvatinib. Clinical trial information: NCT02562118. Research Sponsor: National Medical Research Council, Singapore, Pharmaceutical/Biotech Company.

1020 Poster Discussion Session; Displayed in Poster Session (Board #105), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Comparison of StemPrintER, a novel biology-based genomic predictor of distant recurrence in breast cancer, with Oncotype DX in the TransATAC cohort. *First Author: Salvatore Pece, European Institute of Oncology, Milan, Italy*

Background: Accurate prediction of distant metastasis (DM) in early stage ER+/HER2- breast cancer (BC) patients is vital to avoid over/under-treatment with adjuvant chemotherapy (CT). The OncotypeDX Recurrence Score (RS) is a widely used tool to assist clinical decision-making for CT. The StemPrintER Risk Score (SPRS) is an alternative genomic predictor based on the biology of cancer stem cells that predicts recurrence risk in ER+/HER2- BCs (Pece S. *et al.*, EBioMedicine 2019). Here, we analyze the prognostic value of SPRS in the TransATAC cohort of post-menopausal ER+/HER2- BC patients, and compare the prognostic information provided by SPRS and RS for 10-year risk of DM. **Methods:** The likelihood χ^2 ($LR\chi^2$) and Kaplan-Meier survival analyses were used to assess prognostic information provided by SPRS, RS and the clinical treatment score (CTS) in 818 TransATAC patients treated with anastrozole or tamoxifen for 5 years. Comparative analyses were made for DM risk over the 10-year follow-up, as well as in the early (0-5 years) or late (5-10 years) interval, according to nodal status. **Results:** Used as a continuous variable, SPRS was an independent predictor of DM in years 0-10 among all patients when adjusted for clinical parameters as expressed by the CTS [HR=1.43 (1.18-1.73), $P<0.0001$], as well as in node-negative [HR=1.51 (1.17-1.94), $P=0.001$] but not node-positive (N1-3) patients [HR=1.29 (0.95-1.75), $P=0.11$]. A predefined SPRS cut-off was used to stratify patients into low *vs.* high risk groups [LOW: N=454, 10-year DM rate=5.8%; HIGH: N=364, 10-year DM rate=21.9%; $HR_{HIGH\ vs.\ LOW}$=2.96 (1.85-4.73); $P<0.0001$]. SPRS outperformed RS in providing prognostic information for 10-year DM risk (SPRS: HR=1.79, $P<0.0001$, $LR\chi^2$=33.4; RS: HR=1.52, $P<0.0001$, $LR\chi^2$=22.1), with even greater differences in late DM prediction in N0 patients. SPRS also provided more prognostic information than RS to CTS ($\Delta LR\chi^2$: SPRS+CTS *vs.* CTS= 14.9; RS+CTS *vs.* CTS= 9.7). **Conclusions:** In ER+/HER2- TransATAC BC patients, SPRS was highly prognostic for DM and was superior to RS in providing additional prognostic information to conventional clinicopathological parameters. Research Sponsor: Italian Association for Cancer Research (AIRC), Cancer Research UK (CRUK).

1022 Poster Discussion Session; Displayed in Poster Session (Board #107), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Prognostic and predictive value of ESR1 mutations in postmenopausal metastatic breast cancer (MBC) patients (pts) resistant to aromatase inhibitors (AI), treated with palbociclib (PAL) in combination with endocrine therapy (ET) or capecitabine (CAP) in the PEARL study. *First Author: Miguel Martin, Instituto de Investigación Sanitaria Gregorio Marañón, Universidad Complutense, CIBERONC, Madrid, Spain*

Background: Prior retrospective data has shown *ESR1* mutation is an acquired resistant mechanism to AI. However, little is known about ist prognostic and predictive value to endocrine-based therapy and chemotherapy. PEARL study compared PAL+ET vs CAP in AI resistant patients. Here we wxplored prospectively the *ESR1* mutational status based on updated PFS and OS. **Methods:** PEARL is a phase 3 study with 2 subsequent cohorts: cohort 1 with 296 pts randomized to PAL+Exemestane (EXE) vs CAP and cohort 2 with 305 pts randomized to PAL+ Fulvestran (FUL) vs CAP. *ESR1* hotspot mutations were analyzed in circulating free DNA at baseline by digital PCR. Cox regresion analysis for PFS and OS were performed. Adjusted hazard ratios (aHR) and interaction test between treatment and *ESR1* status were calculated. **Results:** *ESR1* mutational status was assessed in 557 pts, 91% and 94% treated with CAP and PAL+ET, respectively; 164 (29%) had *ESR1* mutations. Characteristics between *ESR1* wild-type (WT) and mutated pts were balanced except for ECOG, prior sensitivity to ET, treatment line, prior AI for metastatic disease and time from first metastatic diagnosis to randomization. Median follow-up was 22.5 months (m). Median PFS was 9.6 vs. 7.5 m (HR: 1.06 [0.88 - 1.28], p = 0.522) and median OS was 30.2 vs 30.3 (HR: 0.99 [0.78 - 1.26] p = 0.934), for CAP vs. PAL+ET, respectively. No interaction was seen between treatment arm and ESR1 status either for PFS (p = 0.538) or OS (p = 0.957). **Conclusions:** In luminal MBC, *ESR1*-mutated pts had poorer OS than *ESR1*-WT pts regardless of treatment received. Clinical trial information: NCT02028507. Research Sponsor: Pfizer and AstraZeneca.

	Median PFS (m) aHR* (95% CI) p-value	Median OS (m) aHR* (95% CI) p-value
COHORT 1 + COHORT 2		
***ESR1*-WT (N = 393)**	9.3 vs. 7.2	34.2 vs. 25.4
vs	0.83 (0.67 - 1.02)	0.54 (0.42 - 0.70)
***ESR1*-Mutated (N = 164)**	0.071	**< 0.0001**
CAP		
***ESR1*-WT (N = 187)**	10.6 vs. 9.4	34.8 vs. 24.9
vs	0.85 (0.63 - 1.15)	0.50 (0.35 - 0.73)
***ESR1*-Mutated (N = 85)**	0.289	**< 0.0001**
PAL+EXE		
***ESR1*-WT (N = 104)**	9.3 vs. 5.7	37.2 vs. 28.2
vs	0.67 (0.45 - 1.01)	0.65 (0.40 - 1.05)
***ESR1*-Mutated (N = 41)**	0.058	0.081
PAL+FUL		
***ESR1*-WT (N = 102)**	7.5 vs. 7.6	29.6 vs. 26.5
vs	1.03 (0.66 - 1.61)	0.42 (0.24 - 0.76)
***ESR1*-Mutated (N = 38)**	0.882	**0.004**

* adjusted by age, treatment arm (for the global population), disease site (visceral yes/no), prior sensitivity to ET, prior chemotherapy for MBC, prior AI for MBC, number of involved sites and time from first metastatic diagnosis to randomization.

1023 Poster Discussion Session; Displayed in Poster Session (Board #108), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase Ib study to evaluate the oral selective estrogen receptor degrader GDC-9545 alone or combined with palbociclib in metastatic ER-positive HER2-negative breast cancer. *First Author: Elgene Lim, St. Vincent's Hospital, University of New South Wales, Darlinghurst, Australia*

Background: GDC-9545 is a potent, orally available, selective estrogen receptor degrader developed for the treatment of ER-positive (ER+) breast cancer alone or combined with CDK4/6 inhibitors. A first-in-human study evaluated 10-250 mg GDC-9545; tolerability, pharmacokinetic (PK), pharmacodynamic (PD), and clinical results support expansion cohorts at ≥30 mg (Jhaveri et al., 2019). **Methods:** This study evaluated PK, PD, and efficacy of GDC-9545 alone and combined with palbociclib, ± LHRH agonist. Eligible patients (pts) had ER+ (HER2-) metastatic breast cancer (MBC) with ≤ 2 prior therapies in the advanced or metastatic setting. No prior treatment with CDK4/6 inhibitor was allowed in pts receiving palbociclib. **Results:** Eight-five pts were enrolled in 2 cohorts: GDC-9545 100 mg given once daily ± LHRH agonist (Cohort A), and GDC-9545 100 mg +125 mg palbociclib on a 21 day on/7 day off schedule ± LHRH agonist (Cohort B). Of the 39 pts in Cohort A, adverse events (AE) occurring in ≥10% of pts were fatigue, cough, back pain, pain in extremity, and arthralgia. Related AEs were generally Grade (G) 1-2; there were 3 related G3 AEs of fatigue, transaminase increased, and diarrhea. Two pts had GDC-9545 reduced, one due to G3 diarrhea and another due to G3 transaminitis. Of the 46 pts in Cohort B, AEs in ≥10% of pts were neutropenia, fatigue, bradycardia, diarrhea, constipation, dizziness, nausea, anemia, asthenia, thrombocytopenia, pruritus, and visual impairment. Twenty-six (57%) pts had G≥3 AEs. G≥3 neutropenia was reported in 23 (50%) pts. One pt had palbociclib reduced due to G3 febrile neutropenia. Eleven (13%) of 85 pts had G1 asymptomatic bradycardia considered related to GDC-9545. No pts in either cohort discontinued study treatment due to AEs. PK analysis and clinical data demonstrate no clinically relevant drug-drug interactions between GDC-9545 and palbociclib. Reduced ER, PR, and Ki67 levels, and an ER activity signature, were observed in paired pre- and on-treatment biopsies (n = 12). Eighteen of 33 pts in Cohort A had either confirmed partial responses or were on study 24 weeks (clinical benefit rate 55%). Clinical benefit was observed in pts with prior fulvestrant treatment and with detectable ESR1 mutations at enrollment. Clinical benefit data for both cohorts are anticipated to be mature in April 2020. **Conclusions:** GDC-9545 was well-tolerated as a single agent and in combination with palbociclib with encouraging PK, PD, and anti-tumor activity in ER+ MBC to support Phase III development. Clinical trial information: NCT03332797. Research Sponsor: Genentech, Inc.

1024 Poster Discussion Session; Displayed in Poster Session (Board #109), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase I dose escalation and expansion study of the next generation oral SERD AZD9833 in women with ER-positive, HER2-negative advanced breast cancer. *First Author: Erika Paige Hamilton, Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN*

Background: AZD9833 is an oral selective estrogen receptor (ER) antagonist and degrader (SERD) that has shown antitumor efficacy in a range of preclinical models of breast cancer. **Methods:** SERENA-1 (NCT03616587) is an ongoing Phase 1, open-label study in pre- and post-menopausal women, after ≥1 endocrine therapy and ≤2 prior chemotherapies for ER+ HER2- advanced breast cancer (ABC). The primary objective is to determine the safety and tolerability of AZD9833 once daily (QD), with dose-limiting toxicities (DLTs) in 28d defining the maximum tolerated dose. Secondary objectives include pharmacokinetics and anti-tumor response. Pharmacodynamic (PD) analysis includes ER modulation in paired tumor biopsies and ctDNA dynamic changes. **Results:** At 20 January 2020: 60 patients were treated (median prior therapies 5 (1–9); prior fulvestrant (Fv) 82%; prior CDK4/6i 68%) across five doses; 25 mg QD n=12, 75 mg QD n=12, 150 mg QD n=13, 300 mg QD n=13, 450 mg QD n=10. AZD9833 exposure was dose proportional after multiple doses, with a median terminal t1/2 of 12h. Treatment-related AEs experienced by ≥10% of patients were visual disturbances (53%; 91% G1, 6% G2, 3% G3), bradycardia/sinus bradycardia (45%; 93% G1, 7% G2), nausea (18%; 46% G1, 55% G2), fatigue (13%; 38% G1, 63% G2), dizziness (10%; 83% G1, 17% G3) vomiting (10%; 50% G1, 33% G2, 17% G3), and asthenia (10%; 67% G1, 33% G2). Three patients experienced DLTs: G3 QTcF prolongation (300 mg); G3 vomiting (450 mg); and a combination of G2 visual disturbance, G2 headache and G2 gait disturbance (450 mg). DLTs resolved with dose reduction. No G4 or 5 AEs were reported. Efficacy data are presented in the table below; objective response rate (ORR) and clinical benefit rate (CBR) at 24 weeks. Clinical trial information: NCT03616587. ER signalling pathway modulation was observed in all dose cohorts. In patients where clinical responses occurred and paired biopsies obtained, 98% reduction in Ki67 was measured. Updated data will be presented. **Conclusions:** AZD9833 has an encouraging efficacy and dose-dependent safety profile. Evidence of clinical benefit and target engagement was observed at all dose levels in women with ER+ ABC, including patients pre-treated with CDK4/6i and Fv, and those with *ESR1* mutations. A Phase 2 study comparing efficacy and safety of three doses AZD9833 vs Fv is planned (NCT04214288). Research Sponsor: AstraZeneca.

	25mg (n=12)	75mg (n=12)	150mg (n=13)	300mg (n=13)	450mg (n=10)	Total (n=60)
ORR (%)	1/9 (11.1)	1/7 (14.3)	2/11 (18.2)	2/10 (20.0)	1/6 (16.7)	7/43 (16.3)
CBR (%)	4/12 (33.3)	8/12 (66.7)	4/13 (30.8)	3/11 (27.3)	3/4 (75.0)	22/52 (42.3)

1025 Poster Session (Board #110), Fri, 8:00 AM-11:00 AM

International retrospective cohort study of locoregional and systemic therapy in oligometastatic breast cancer (OLIGO-BC1). *First Author: Takayuki Ueno, Breast Oncology Center, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan*

Background: Systemic therapy is the standard care in metastatic breast cancer (BC). However, retrospective studies demonstrated survival benefits of locoregional and systemic (combination) therapy in oligometastatic BC. To clarify it, the Federation of Asian Clinical Oncology conducted an international retrospective cohort study (OLIGO-BC1) (UMIN No.000030047). **Methods:** Oligometastatic BC patients diagnosed from 2007 to 2012 were registered. "Oligometastases" is defined as low volume metastatic disease with limited number and size of metastatic lesions up to five and not necessarily in the same organ by the ABC guidelines. Overall survival (OS) from the diagnosis of oligometastases was the primary endpoint and compared between combination and systemic therapy using a log-rank test. Assuming the 5-year OS of 50% and 40%, respectively, 698 patients were required to achieve 80% power to detect the superiority of combination therapy, at a two-sided significance level. A multivariable Cox regression model with stratification by country was performed to estimate hazard ratio (HR) for therapy and other risk factors. **Results:** While 1,262 cases had been registered from February 2018 to May 2019, 1,200 remained for analysis after exclusion of unavailable cases. Among them, 573, 529 and 98 cases were registered from China, Japan and Korea, respectively. Luminal BC was recorded in 526 cases (44%), luminal-HER2 BC in 189 (16%), HER2 BC in 154 (13%), triple-negative BC in 166 (14%) and others in 165 (13%). One oligometastatic BC was found in 578 cases, 2 in 289, 3 in 154, 4 in 102 and 5 in 77. Bone metastases were recorded in 301 cases, visceral metastases in 387, locoregional recurrence in 25, local recurrence in 83 and multiple metastatic sites in 404. Combination therapy was performed in 595 cases and systemic therapy in 404. At median follow-up of 4.9 years, 5-year OS was 59.6% and 41.9%, respectively ($p < 0.01$). An adjusted HR was 0.61 (95% CI: 0.51, 0.74). Type of systemic therapy, younger age, ECOG performance status 0, stage I BC, non-triple negative subtype, fewer metastatic sites, local recurrence and longer disease-free interval were significantly favorable prognostic factors. Discussions: Oligometastatic BC under some conditions seems to be curable. Taken together with recent molecular targeted therapy, locoregional therapy will be advantageous to conquer it. **Conclusions:** Combination therapy is a promising strategy for patients with oligometastatic BC. Research Sponsor: Federation of Asian Clinical Oncology.

1027 Poster Session (Board #112), Fri, 8:00 AM-11:00 AM

Genomic mapping to identify mutations in RYR2 and AHNAK in basal-like breast tumors expressing PD-L1. *First Author: Francisco J Cimas, Translational Oncology Laboratory, CRIB-UCLM, Albacete, Spain*

Background: Basal-like breast cancer is a specific subtype of breast tumors with limited therapeutic options. Although treatment with the anti-PD-L1 antibody atezolizumab has recently shown clinical activity in this setting, not all patients do respond even expressing high levels of PD-L1. In the present article we explored the presence of mutations in breast cancer tumors with high expression of PD1 and PD-L1 with the aim to identify molecular correlates associated with outcome. **Methods:** We used RNA-seq and mutational data from 971 breast cancer patients using the TCGA dataset, to identify mutations in patients with high levels of PD1 and PD-L1. Data analysis was performed using DESeq R and MAFTools Bioconductor packages. Transcriptomic signatures from the identified mutations were associated with outcome using the Kapplan-Meyer Plotter tool. We correlated the identified transcripts with immune populations using TIMER online tool and correlation between genes with Cancertool online platform. **Results:** We identified co-occurrent mutations in RYR2 and AHNAK in 8% and 5% of basal like tumors, respectively, in patients with high levels of PD1 and PD-1. The transcriptomic signature of these mutations conferred good prognosis for relapse free survival (RFS) and overall survival (OS). CXCL9 for RYR2 and GBP5, C1QA, IL2RG, CSF2RB and IDO1 for AHNAK were the most relevant genes identified in these signatures. Expression of CXCL9, GBP5, IL2RG and IDO1 correlated with the presence of immune cell populations mainly dendritic cells. This signature, including CXCL9, GBP5, C1QA, IL2RG, CSF2RB and IDO1 classified patients with favorable RFS (HR 0.27 CI 0.2-0.30; p = 1.1e-16) and OS (HR 0.18 CI 0.09-0.34; p = 6.8e-9). This signature showed a stronger prediction capacity compared with already described immunologic signatures. Finally we identify that LAG3 was the only gene commonly present in both signatures and correlated positively with the expression of PD1 and PD-L1. **Conclusions:** We describe two novel mutations which transcriptomic signatures associated with favorable outcome in basal-like tumors that express elevated levels of PD1 and PD-L1. Future studies should be performed to confirm the role of these mutations and signatures in relation with clinical activity of PD1/PD-L1 inhibitors. Research Sponsor: CRIS Foundation, AECC Foundation.

1028 Poster Session (Board #113), Fri, 8:00 AM-11:00 AM

Circulating tumor DNA (ctDNA) to evaluate stage III and stage IV metastatic breast cancer (MBC), describe tumor heterogeneity, and outcome. *First Author: Qiang Zhang, Northwestern University, Department of Medicine, Division of Hematology/Oncology, Lurie Cancer Center, Chicago, IL*

Background: MBC is a challenging clinical condition treated with palliative intent due to tumor heterogeneity. We reported in 2019 ASCO that the correlation of HER2 and ESR1 mutations of ctDNA with CTCs results in worse prognosis in MBC. Here we reported that ctDNA mutations is a key point which is different between Stage III and Stage IV, and it would be helpful to evaluate the MBC metastasis and outcome. **Methods:** This study included 33 Stage III and 204 Stage IV MBC patients who received systemic treatments at NMH (2016-2019). Plasma ctDNA before treatment was isolated from patients and then was analyzed by Guardant 360 Health NGS-based assay for a 73 genes panel for genomic alterations including single nucleotide variants, insertions/deletions, gene fusions/rearrangements and copy number variations. Causal Inference with Ensembel Learning was used for statistical analyses. **Results:** Among stage III patients, 40% are luminal, 44% are $HER2^+$ and 16% are TNBC, while in stage IV 50% patients are luminal, 20% are $HER2^+$ and 30% are TNBC. The major differences in ctDNA between two stages lie in several genes including *PIK3CA, ERBB2* and *KRAS*. On the top of the list is PIK3CA, which is detected in 2 out of 33 stage III patients (1 luminal, 1 $HER2^+$) (6.06%) in baseline, each of them carries 1 mutation on PIK3CA (E542K, E545G). In 43 out of 204 stage IV patients (21.57%) who carry this gene, 15 show 1 amplification, 34 have 1 mutation (mainly H1047R, E542K, E545K and H1047L), 11 have 2 mutations (E542K/E726K, D454N/D1029N, E545K/D1017H, E545K/L287L, H1047R/E453K, H1047R/N426S and P539R/H1047R), and 1 has 3 mutations (E542Q/D454N/D1029N and E545K/E726K/R93Q). On treatment effects, PIK3CA is found to be very detrimental on prognosis and on its effects on the treatment outcome. Patients without any mutation in PIK3CA live 2.65 times longer than those with more than one mutations on PIK3CA (p-value = 4.47e-06, CI = [1.731, 3.926]). PIK3CA, ESR1, TP53 and ARID1A are found to significantly affect liver metastasis when RET, FBXW7, ERBB2, CCND2, BRAF and MET are found to be associated with lung metastasis for both stages. EGFR, KIT and ARID1A are associated with CNS metastasis. **Conclusions:** We elucidated that ctDNA mutations on PIK3CA and other genes dramatically increased in Stage IV patients compared to Stage III patients which provides a new insight on the Stage III and Stage IV MBC determination. New set of genes especially PIK3CA are identified to correlate with metastasis and affect the outcome which may also be reliably used to monitor the response to therapy. Research Sponsor: Lynn Sage Breast Cancer Research OncoSET Program, Robert H Lurie Cancer Center.

1029 Poster Session (Board #114), Fri, 8:00 AM-11:00 AM

Prognostic and predictive effects of circulating and disseminated tumor cells in breast cancer: A National Cancer Database (NCDB) analysis. *First Author: Nadeem Bilani, Cleveland Clinic Florida, Weston, FL*

Background: Alongside other biomarkers, circulating tumor cells (CTCs) and disseminated tumor cells (DTCs) could contribute to our growing understanding of the breast cancer (BC) "liquid biopsy". This study evaluated 1) clinicopathologic factors associated with CTCs and DTCs, 2) the prognostic value of CTCs and DTCs by disease stage, 3), the efficacy of chemotherapy by CTC and DTC status. **Methods:** We conducted a retrospective analysis of BC using the 2004-2016 National Cancer Database (NCDB). The NCDB defines CTCs as isolated tumor cells (ITCs) found in the blood (using assays such as reverse transcriptase polymerase chain reaction or immunohistochemistry) distant from the breast. DTCs are ITCs found in the bone marrow or other non-regional tissues. To evaluate variables associated with CTCs or DTCs, we used chi-squared and Wilcoxon rank-sum tests (univariate), followed by multivariate logistic regression. Consequently, we included CTC or DTC status in a multivariate, stage-by-stage Cox regression analysis for overall survival (OS). After adjusting for receptor status and staging, we used the Kaplan-Meier method to explore chemotherapy efficacy in CTC- or DTC-positive vs. CTC- or DTC-negative subsets. **Results:** 4,846 cases reported CTC-status, 1,454 (21.1%) of which were positive. 4,993 cases reported DTC-status, 1,400 (20.3%) of which were positive. Factors associated with positive CTC status were HER2-positivity, progesterone receptor-positivity, lobular histology and N-staging. Factors associated with positive DTC status were being White, HER2-positivity, lobular histology and N-staging. Positive CTC-status was associated with poor OS overall in late-stage (III and IV) (HR 1.477, 95% CI: 1.129-1.931, p = 0.004) but not early-stage BC (0, I, II) (p = 0.110) disease. DTC-status was not associated with OS in early-stage or late-stage subsets. In hormone receptor (HR)-positive disease, chemotherapy was associated with better OS when CTC-status was also positive both in early-stage (p = 0.003) and late-stage (p = 0.023) disease. In a subset of the same BC subtype with negative CTC-status, however, chemotherapy conferred no survival benefit (p = 0.638 for early-stage, p = 0.501 for late-stage). DTC status was not a significant predictor of chemotherapy efficacy in early or late-stage, HR+ disease. **Conclusions:** This study suggests that CTC-status is a stronger prognostic factor at later stages of BC; yet it can also help guide management of early-stage disease as it appears predictive for chemotherapy benefit. Research Sponsor: None.

1030 Poster Session (Board #115), Fri, 8:00 AM-11:00 AM

The contribution of clinical subtype to survival differences among patients with de novo and recurrent metastatic breast cancer (dMBC). *First Author: Danielle Marie File, University of North Carolina, Chapel Hill, NC*

Background: Patients with de novo metastatic breast cancer (dMBC) have superior median overall survival (mOS) compared to recurrent metastatic breast cancer (rMBC). Whether patient characteristics, prior treatment, tumor stage and innate biological differences contribute to this observation is unknown. **Methods:** Clinical and pathological data from patients diagnosed with MBC from 2011 to 2017 at the University of North Carolina (UNC) was obtained from the prospective UNC Metastatic Breast Cancer Clinical Database (223 dMBC, 607 rMBC). Only patients with known survival status were included. Subtype was determined by hormone receptor (HR) and HER2 staining of the primary tumor. Pathologic staging results were used when available, otherwise clinical staging was used. Patient and tumor characteristics were compared using chi-square testing, and survival outcomes by Cox proportional hazards modeling. **Results:** 26.9% of patients with MBC presented with dMBC, with significant variation in the ratio of dMBC to rMBC across subtypes. In particular, there were more cases of HER2+ dMBC than rMBC (26.9% vs 14.0%) and fewer cases of triple negative dMBC (20.6% vs 35.3%)(p-value < 0.001). Nearly half of all cases of HR-/HER2+ MBC were de novo (48.2%). dMBC was significantly associated with older age ($p = 0.002$), lower grade ($p = 0.027$), higher T and N stage ($p < 0.001$) and African American race (30% vs 22%, $p = 0.022$). There was no significant difference in proportion of patients with visceral metastatic disease or in number of metastatic sites at diagnosis. Median follow up was 39 months in both cohorts. mOS was 12 months greater in dMBC than rMBC (34m vs 22m, $p < 0.001$). These differences were significant across all subtypes except HR+/HER2+. The difference in mOS between dMBC and rMBC was greatest in the HR-/HER2+ subgroup (45m vs 15m, $p = 0.006$). In multivariable analysis, dMBC remained associated with improved survival (adjusted hazard ratio 0.59, $p < 0.001$) independent of variables including age, race, subtype, grade and number of metastatic sites at diagnosis. **Conclusions:** Patients with dMBC have significantly better prognosis than those with rMBC. This improved outcome is in part due to subtype variation, with more triple negative and fewer HER2+ tumors in rMBC, however these differences largely remained when stratified by subtype. In multivariable analysis, de novo presentation of MBC remained an independently significant contributor to longer survival. Further investigation should focus on biologic differences between dMBC and rMBC. Research Sponsor: John William Pope Foundation.

1031 Poster Session (Board #116), Fri, 8:00 AM-11:00 AM

Identification of pathogenic *ROS1* alterations in cell-free DNA (cfDNA) from patients with breast cancer. *First Author: Jeremy Meyer Force, Duke University Medical Center, Durham, NC*

Background: ROS1 is an important proto-oncogene involved in the development of various cancers for which we have FDA approved therapies. While activation of the *ROS1* tyrosine kinase receptor has been reported in 1-2% of lung cancers, the frequency and type of *ROS1* alterations in breast cancer have not been fully explored. We previously described the incidence of *ROS1* alterations from breast cancer tissue. The purpose of this study was to identify the incidence of *ROS1* genomic alterations occurring in cfDNA from patients with breast cancer. **Methods:** We queried 16,053 breast cancer samples from the Guardant Health breast cancer database between June 2015 - October 2019 to identify the incidence of *ROS1* alterations detected in cfDNA in breast cancer. We identified fusion partner genes and classified each alteration type into the following categories: fusion, single nucleotide variants (SNVs), and indels. Radical amino acid changes occurring at conserved regions across the *ROS1* gene were identified. *In vitro* analyses were used to investigate the effect of *ROS1* nonsynonymous mutations on the ROS1 protein. We made associations with *ROS1* alterations and co-occurring mutated genes. **Results:** Nonsynonymous *ROS1* alterations from the Guardant Health breast cancer database were found in 162 samples from 142 patients in the 16,053-patient cohort (1%). Alterations found included: 1 (0.6%) *ROS1-SLC35F1* fusion, 155 (95.7%) SNVs, and 6 (3.7%) indels. Of the 155 SNVs, we identified 23 (14.8%) mutations occurring in the *ROS1* kinase, of which, 20 (12.9%) occurred at highly conserved regions and 15 (9.6%) harbored radical amino acid changes. The top 5 co-occurring mutations in samples with *ROS1* alterations were *TP53* (50%), *PIK3CA* (44%), *ESR1* (27%), *EGFR* (21%), and *FGFR1* (18%). **Conclusions:** A modest incidence of *ROS1* genomic alterations occurs in cfDNA from patients with breast cancer. New somatic alterations in the *ROS1* gene were identified from Guardant Health that were not detected in publicly available databases. A portion of mutations occurred at highly conserved regions across the *ROS1* gene suggesting these may be more actionable than currently recognized. *In vitro* analyses of *ROS1* gene activation from these newly discovered somatic alterations are being investigated with results to be reported. Co-occurring mutations reveal a unique genotype associated with *ROS1* alterations that may play a biologic role in ROS1-mediated pathogenesis. Research Sponsor: METAvivor Early Career Investigator Award: Triangle Metsquerade Presented In Memory of Kristie Godwin Rolan.

1032 Poster Session (Board #117), Fri, 8:00 AM-11:00 AM

Organ specificity dictates tumor immune infiltration and composition in metastatic breast cancer; lessons from a rapid autopsy tissue collection study. *First Author: Colt Egelston, City of Hope, Duarte, CA*

Background: Immune composition in the tumor microenvironment (TME) of patient tumors has proven to play a central role in the propensity of tumors to metastasize and respond to therapy. Evidence has suggested that the metastatic TME is immune aberrant, however limited sample size and numbers has made assessment of the immune TME in the development of multi-organ metastases difficult. Here we utilize a rapid autopsy tissue collection protocol to assess the infiltration and composition of the immune TME in numerous metastatic tissue sites, paired disease-free tissue sites, and the associated tissue draining lymph nodes. **Methods:** Post-mortem tissues were collected from six metastatic breast cancer patients shortly after death through City of Hope's "Legacy Project for Rapid Tissue Donation" Program. The average post mortem interval (PMI) for tissue collection was 6 hours. Collected specimens include metastatic lesions and paired non-cancer samples from every cancer-involved organ, disease-free specimens from non-involved major organs, distant and tumor-draining lymph nodes (both cancer-infiltrated and disease free), as well as blood. Immediately following collection, specimens were processed into single cell suspension for flow cytometry. Over 80 immune cell phenotypes were assessed, including CD8+ and CD4+ T cell subsets, B cell subsets, natural killer (NK) cells, tumor associated macrophages (TAMs), dendritic cell subsets, and other cells. **Results:** Tumor infiltrated tissues were found to have comparable immune cell densities and composition compared to paired disease-free tissues of the same organ type. However, immune cell densities in metastatic tissues and disease-free tissues were significantly different between organ types, with lung immune infiltration consistently being greater than liver tissues. Differences in immune composition between tissue sites were also observed. Notably, liver tissues favored the presence of central memory CD8+ T cells, while lung tissues favored the presence of CD8+ tissue resident memory T cells. Relative to disease-free lung tissues, tumor infiltrated lungs contained diminished frequencies of CD8+ tissue resident memory T cells and altered B cell phenotypes. **Conclusions:** These data suggest that immune monitoring and trafficking of metastatic tissues site is dictated by organ type, which can be altered in composition by tumor infiltration. Further studies such as these may reveal organ-specific mechanisms of response to therapeutic interventions. Research Sponsor: Waisman Foundation.

1033 Poster Session (Board #118), Fri, 8:00 AM-11:00 AM

Predictor of trastuzumab-induced cardiotoxicity in breast cancer (BC) patients: HER2/neu 655 polymorphisms, biochemical and clinical features. *First Author: Isabel Blancas, Oncology Department, San Cecilio University Hospital, Granada, Spain*

Background: The introduction of trastuzumab in the treatment scheme of the HER2 BC patients has improved the evolution of the disease. Nevertheless, some of this patients develop cardiotoxicity. We studied some of our population of HER2 positive BC patients treated with trastuzumab trying to find predictors for developing cardiotoxicity, specifically the association of the HER2 Ile655Val A>G polymorphism with trastuzumab-induced cardiotoxicity and with survival and some biochemical and clinical features. **Methods:** For the study breast cancer patients were recruited from San Cecilio University Hospital in Granada (Spain) who were treated with trastuzumab. HER2 Ile655Val A>G polimorphism was performed in 93 patients using Taqman SNP technology. We analyzed the relation of polymorphisms with disease free survival (DFS) and overall survival (OS). We also could asses 66 patients who had biochemical measurement of NTpro BNP during the treatment with trastuzumab and cardiovascular risk factors including diabetes, hypertension, smoking, hypercholesterolemia and body mass index (BMI). Cardiotoxicity was defined as a $\geq$ 10% decrease of the left ventricular ejection fraction (LVEF) from baseline, a LVEF below 40% or any clinical manifestation of heart insufficiency. NT-proBNP cut-off points were considered to stablish normal or abnormal values adjusted by patient age. **Results:** Genotype frequencies of HER2/neu 655 met Hardy-Weinberg equilibrium ($p = 0.363$). Logistic regression analysis adjusted by hormonal status and anthracycline treatment showed higher cardiotoxicity risk for AG vs AA Her2-Ile655 polimorphism (OR = 3.00, CI95% 1.07-8.41, $p = 0.037$) or for AG vs AA+GG Her2-Ile655 polimorphism (OR = 3.21, CI95% 1.15-8.96, $p = 0.026$). We did not find association between HER2neu Ile655Val polymorphism and DFS or OS. NT-proBNP baseline higher than the range (OR 5.9, 95% CI 1.2 - 28.5, $p = 0.028$) and diabetes mellitus (OR 22.0, 95% CI 5.7 - 85.4, $p = 0.000$) were found to be related with the development of cardiotoxicity. **Conclusions:** HER2-Ile655 A>G polymorphism is significantly associated with higher risk of trastuzumab-induced cardiotoxicity but it is not correlated with DFS neither OS. Diabetes or baseline high NT-proBNP levels are predictors for the development of trastuzumab-induced cardiotoxicity. These parameters should be considered for a closer follow up and for preventive actions as accurate glycaemic control for patients who will receive trastuzumab. Research Sponsor: Fundación Ramón Areces, Madrid, Spain.

1035 Poster Session (Board #120), Fri, 8:00 AM-11:00 AM

Detection of actionable gene mutations in breast cancer by amplicon-based next-generation sequencing liquid biopsy. *First Author: Jing Shan Lim, Lucence Diagnostics, Singapore, Singapore*

Background: The PI3K-inhibitor, alpelisib, was approved for the treatment of hormone receptor (HR)-positive, HER2-negative breast cancers with *PIK3CA* mutations based on findings from the SOLAR-1 trial. *PIK3CA*-positivity in tumor tissue was 29% (341/1172), but was only 15% (177/1172) in plasma cell-free DNA (cfDNA). The lower mutation detection rate observed in cfDNA may limit the clinical application of liquid biopsy in breast cancer. Amplicon-based next-generation sequencing (NGS) approach may confer improved sensitivity, allowing more effective profiling. We conducted a study to evaluate the use of this technology. **Methods:** Plasma cfDNA from 113 breast cancer patients (82.3% metastatic) underwent real-world testing in a CAP and ISO15189 accredited central laboratory. We analysed genetic alterations in cfDNA using an amplicon-based NGS technology. The presence of *PIK3CA* and other mutations relevant to breast cancer were correlated to molecular subtypes and treatment histories. **Results:** At least one mutation was detected in 70.8% of cases. Mutations were more frequent in metastatic cases (77.4%) compared to non-metastatic cases (27.3%). Across all patients, mutations in *PIK3CA* (33.6%), *TP53* (32.7%), *ESR1* (22.1%), *GATA3* (7.1%) and *ERBB2* (7.1%) were most frequently detected, in accordance with tumor tissue genotyping studies. *PIK3CA* mutations were more common in HR+ HER2- patients (44.4% vs 28.6% of other patients). Among *PIK3CA*-mutant cases, multiple *PIK3CA* mutations were present in 18.4% of cases, and hotspot mutations H1047R (34.2%), E542K (26.3%) and E545K (15.8%) were most frequent. An association was seen between *PIK3CA* mutation and prior treatment with CDK4/6 inhibitors (palbociclib, ribociclib) or mTOR inhibitor (everolimus), with 58% of *PIK3CA*-mutant cases having received these treatment previously compared to only 20% of *PIK3CA*-wild type (wt) cases. In addition, 75% of previously treated *ESR1*-mutant cases had specifically received hormonal treatment, compared to 60 % of *ESR1*-wt cases that received any treatment. **Conclusions:** We report similar *PIK3CA* mutation frequencies (~30%) with amplicon-based NGS on cfDNA compared to tumor tissue testing in breast cancer. Importantly, other driver mutations were also observed at similar frequencies as external tissue studies, implying high sensitivity as the primary reason for performance. This supports the clinical utility of an amplicon-based NGS-based approach to liquid biopsy for the sensitive detection of actionable mutations in breast cancer. Research Sponsor: Lucence Diagnostics.

1036 Poster Session (Board #121), Fri, 8:00 AM-11:00 AM

Trastumab deruxtecan for HER2-positive metastatic breast cancer: DESTINY-Breast01 subgroup analysis. *First Author: Shanu Modi, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Trastuzumab deruxtecan (T-DXd; DS-8201) is an antibody-drug conjugate composed of an anti-HER2 antibody, a cleavable linker, and a cytotoxic topoisomerase I inhibitor. In the pivotal DESTINY-Breast01 trial, efficacy of T-DXd in HER2-positive metastatic breast cancer (mBC) was demonstrated, with an objective response rate (ORR) of 60.9% and median progression-free survival (mPFS) of 16.4 months. **Methods:** DESTINY-Breast01 was a single-group, open-label, multicenter, phase II trial of 184 patients with HER2-positive mBC previously treated with trastuzumab emtansine (T-DM1) who received T-DXd at 5.4 mg/kg. Multivariate analysis using logistic regression models (ORR) and Cox proportional hazards models (duration of response [DOR], mPFS) explored 15 relevant clinical predictor variables. Circulating tumor DNA (ctDNA) was collected prior to the first dose, every 3 cycles of treatment, and at the end of treatment. Sequencing was done via GuardantOMNI (Guardant Health) for single-nucleotide variation/insertion and deletion, amplification, and fusion of ≈ 500 genes. **Results:** Efficacy in all evaluated clinical subgroups was similar to the overall ORR 60.9% and mPFS 16.4 months with ranges from ORR 46.4%-74.5% and mPFS 12.3-18.1 months. Variables associated with improved ORR, DOR, or mPFS included hormone receptor positive status, fewer prior treatment regimens (continuous variable), pertuzumab given in the first or second line, and normal renal and hepatic function. Variables that did not impact efficacy outcomes compared to the overall population include age, race, region, ECOG PS, HER2 IHC 3+ status, progesterone receptor status, best response to T-DM1, time since diagnosis, and history of brain metastases. In 48 subjects with progression as of data cut date, metastases were most commonly observed in the liver, lung, and lymph nodes. Only 8% (4 of 48) had progression involvement in the brain upon disease progression. Decrease of ERBB2 copy number in ctDNA was seen on treatment and correlated with clinical response. Additional changes in molecular markers on treatment and following progression will be described. **Conclusions:** T-DXd demonstrated strong efficacy in all clinical subgroups analyzed. Further exploration of both clinical and molecular variables to determine biomarkers of efficacy may be warranted. Clinical trial information: NCT03248492. Research Sponsor: Daiichi Sankyo, Inc.

1037 Poster Session (Board #122), Fri, 8:00 AM-11:00 AM

Clinical activity of MCLA-128 (zenocutuzumab) in combination with endocrine therapy (ET) in ER+/HER2-low, non-amplified metastatic breast cancer (MBC) patients (pts) with ET-resistant disease who had progressed on a CDK4/6 inhibitor (CDK4/6i). *First Author: Barbara Pistilli, Gustave Roussy, Villejuif, France*

Background: MCLA-128 (zenocutuzumab) is an ADCC-enhanced humanized bispecific antibody targeting HER2 and HER3 and potently blocking HER3-ligand induced receptor dimerization. Upregulation of Her2:Her 3 pathway is a means of resistance to ET in HR+ breast cancer, indicating a potential role for MCLA-128. In preclinical studies, the combination of MCLA-128 with ET in breast cancer xenografts outperformed single drug treatments. The current study explores the use of MCLA-128 to rescue pts with ET-resistant MBC who have progressed on a CDK4/6i. **Methods:** This phase II, open-label trial planned for up to 40 evaluable women with HR+, HER2 low (IHC 1+/IHC 2+ with negative FISH) MBC, who had progressed on a CDK4/6i and up to 3 lines of ET, who had received ≤ 2 chemotherapy regimens in the metastatic setting. Pts received MCLA-128 (750 mg, 2h IV, flat dose) q3w combined with last ET on which the pt had previously progressed immediately prior to study entry. Disease control rate (DCR; RECIST 1.1, per investigator), best overall response (BOR), overall response rate (ORR), safety, and PK, are evaluated. Data cut off was 14Nov2019. **Results:** 48 pts were treated, all of whom had progressed on a CDK4/6i. Pts had received a median 2 prior ET lines (range 1-5) and 1 line (range 1-3) of chemotherapy. Pts had a median number of 3 metastatic sites (range 1-6) and 42 (88%) had visceral involvement. Among 42 pts evaluable for efficacy, DCR was 45% (90% CI 32-59) with 2 pts having unconfirmed PR and 19 pts SD as BOR. Common related AEs (all grades; G3-4) were asthenia/fatigue (27%; 2%), diarrhea (25%; 0), nausea (21%; 0). No clinically significant LVEF decline was seen. At the end of cycle 1, mean trough level of MCLA-128 was 15.5 μg/mL, and mean terminal half-live was 102 h (n = 19-21). Data on the primary endpoint, clinical benefit rate at 24 weeks, and biomarkers will be provided. **Conclusions:** The addition of MCLA-128 to the last line of ET showed clinical activity after ET+CDK4/6i failure and a favorable safety profile. Clinical trial information: NCT03321981. Research Sponsor: Merus NV.

1038 Poster Session (Board #123), Fri, 8:00 AM-11:00 AM

Addition of endocrine therapy to dual anti-HER2 targeted therapy in initial treatment of HER2+/HR+ metastatic breast cancer. *First Author: Matthew Loft, The Walter and Eliza Hall Institute of Medical Research, Melbourne, VIC, Australia*

Background: The combination of dual anti-HER2 targeted therapy and chemotherapy is the current first line standard of care for HER2+ metastatic breast cancer. Endocrine therapy (ET) is the backbone of treatment in hormone receptor positive (HR+) disease, but the role of the addition of endocrine therapy following chemotherapy in HER2+/HR+ disease remains unclear as pivotal first line clinical trials excluded endocrine therapy use. **Methods:** Data from a multi-site community cohort of consecutive HER2+ metastatic breast cancer patients diagnosed between 1 January 2012 and 31 August 2019 was examined. Patients were treated at clinician discretion. The subset of patients eligible for this analysis were those that were HR+ and had received first line dual anti-HER2 targeted therapy. **Results:** Of 132 eligible patients included in the analysis, 78 (59.1%) received endocrine therapy and 54 (40.9%) did not. Median follow up was 25.9 months. There were no significant differences between the two groups based on age, performance status, previous therapy or de novo disease (Table), however, patients with bone metastases were more likely to receive ET in conjunction with first line dual anti-HER2 therapy (71% vs 52%, $p = .043$). The addition of ET was associated with improved progression free (HR 2.1, 95% CI 1.2-3.5, $p = 0.007$) and overall survival (HR 2.7, 95% CI 1.2-5.5, $p = 0.007$) in multivariate analysis. No increase in serious adverse events was noted although endocrine therapy related toxicities were not specifically collected. **Conclusions:** In this real-world series, the addition of ET to first line dual anti-HER2 therapy in HER2+/HR+ metastatic breast cancer was associated with improved progression free and overall survival. Further research is required to validate these findings and examine the role of CDK4/6 inhibitors in this disease, but may provide reassurance to clinicians considering ET in this clinical context. Research Sponsor: None.

Characteristic	With endocrine n = 78 (59%)	Without endocrine n = 54 (41%)	*p* value
Age			
Median (IQR)	56 (45 – 67)	59 (48 – 69)	0.355
Metastatic at diagnosis			
Yes	31 (39.7%)	31 (57.4%)	0.053
No	47 (60.3%)	23 (42.6%)	
Adjuvant HER2 therapy	n = 47	n = 23	
Yes	33 (70.2%)	13 (56.5%)	0.292
No	14 (29.8%)	10 (43.5%)	
ECOG			
0-1	75 (96.2%)	50 (92.6%)	0.685
>2	3 (3.8%)	3 (5.6%)	
Unknown	0 (0%)	1 (1.8%)	
Hormone receptor status			
ER+, PR+	48 (61.5%)	24 (44.4%)	0.051
ER+, PR-	28 (35.9%)	24 (44.4%)	
ER-, PR+	2 (2.6%)	6 (11.1%)	
Median progression free survival	28.8 months	17.2 months	**0.004**
Median overall survival	63.2 months	34.3 months	**0.005**

1039 Poster Session (Board #124), Fri, 8:00 AM-11:00 AM

A phase I dose escalation study evaluating the safety and tolerability of a novel anti-HER2 antibody-drug conjugate (PF-06804103) in patients with HER2-positive solid tumors. *First Author: Funda Meric-Bernstam, MD Anderson Cancer Center, Houston, TX*

Background: PF-06804103 is an anti-HER2 immunoglobulin G1 antibody-drug conjugate (ADC), comprising an anti-HER2 monoclonal antibody conjugated with a cleavable linker to the cytotoxic agent Aur0101. PF-06804103 demonstrated strong activity in low to high HER2-expressing preclinical tumor models. In this study, the safety and tolerability of PF-06804103 was assessed in patients with advanced breast cancer (BC) or gastric cancer (GC). **Methods:** This multi-center, open-label, first-in-patient, phase I study (NCT03284723) has two parts: dose escalation (Part 1) and dose expansion (Part 2). In Part 1, groups of adult patients (pts) with HER2+ BC or HER2+ GC, who are resistant or intolerant to standard therapy or for which no standard therapy is available, received PF-06804103 intravenously once every 21 days (Q3W); dosage was escalated per cohort. Primary objectives were to evaluate the safety and tolerability of PF-06804103, characterize its dose-limiting toxicities (DLTs), and determine the recommended phase 2 dose. Response was assessed using RECIST v1.1. Objective response rate (ORR) was calculated for response-evaluable pts with target lesions at baseline and ≥1 post-baseline assessment (including unconfirmed responses). **Results:** A total of 35 pts (BC: n = 20; GC: n = 15) received PF-06804103 at escalating dose levels (0.15 mg/kg: n = 2; 0.5 mg/kg: n = 2; 1.2 mg/kg: n = 2; 2 mg/kg: n = 4; 3 mg/kg: n = 10; 4 mg/kg: n = 9; 5 mg/kg: n = 6). The median (range) number of prior therapies was 6 (3–18) and 3 (1–6) for BC and GC groups, respectively (all pts had prior HER2-targeted therapy). The 3 most common, drug-related adverse events (any grade) were alopecia (n = 17, 48.6%), fatigue (n = 15, 42.9%), and neuropathy (n = 9, 25.7%). DLTs (mostly grade 3) occurred in 3 pts and included arthralgia, neuropathy, myalgia, fatigue, and osteomuscular pain. Preliminary ORR in the patients treated with doses ≥3mg/kg was 52.4% (11/21). **Conclusions:** The PF-06804103 ADC demonstrated manageable toxicity and promising anti-tumor activity in this small, heavily pretreated study population. Clinical trial information: NCT03284723. Research Sponsor: Pfizer.

1040 Poster Session (Board #125), Fri, 8:00 AM-11:00 AM

SOPHIA analysis by chemotherapy (Ctx) choice: A phase III (P3) study of margetuximab (M) + Ctx versus trastuzumab (T) + Ctx in patients (pts) with pretreated HER2+ metastatic (met) breast cancer (MBC). *First Author: Santiago Escrivá, Medical Oncology Department, Vall d'Hebron University Hospital. Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain*

Background: Despite advances, pretreated HER2+ MBC remains incurable with ongoing need for new therapies. Investigational M has similar HER2 binding and antiproliferative effects as T. Relative to T, M Fc engineering increases binding affinity for both variants of activating Fc receptor (FcR) CD16A and decreases affinity for inhibitory FcR CD32B, coordinately activating innate and adaptive immunity. In a Phase 3 (P3) trial, M prolonged PFS over T (Table). Second interim OS results from Sept 2019 also favor M (hazard ratio [HR], 0.89; 95% CI 0.69–1.13; nominal *P*=0.326). **Methods:** SOPHIA (NCT02492711), an open-label P3 trial, enrolled pts with HER2+ MBC after pertuzumab and 1–3 lines of prior treatment (Tx) for MBC. Randomization was 1:1 to M (15 mg/kg IV q3w + Ctx) or T (6 [8 for loading dose] mg/kg IV q3w + Ctx), stratified by met sites (≤2, >2), lines of Tx for met disease (≤2, >2), and Ctx choice, including capecitabine (Cap), eribulin (Eri), gemcitabine (Gem), or vinorelbine (Vin). Primary endpoints were central blinded PFS and OS, assessed sequentially using the stratified log-rank test. **Results:** Investigator chemotherapy choices and results by chemotherapy are shown in the table. Subjects receiving Eri and Gem had the lowest PFS hazards ratios (HRs), favoring M over T, although no statistical significance of individual chemotherapy subgroups was seen. There was variable toxicity among Ctx subgroups, and fewer subjects receiving Cap had Ctx related Grade 3 or higher (>=Gr 3) AEs. In this unblinded study, more subjects on M than T in all subgroups discontinued Ctx while continuing study antibody. **Conclusions:** In combination with chemotherapy in pretreated HER2+ MBC, M improved PFS over T. Safety was manageable in all Ctx subgroups. Differences among HRs for chemotherapy subgroups may be driven by selection bias and/or sensitivity differences. Clinical trial information: NCT02492711. Research Sponsor: MacroGenics.

SOPHIA results by chemotherapy.

	PFS, 265 events HR (95% CI)*	>= Gr 3 Ctx Related AEs**	AEs leading to Ctx Discontinuation**
Intent-To-Treat (N=536)	0.76 (0.59-0.98)	41.7% M vs 40.6% T	11% M vs 6.4% T
Capecitabine (n=143)	0.77 (0.47-1.26)	25% M vs 28% T	11.8% M vs 8.5% T
Eribulin (n=136)	0.66 (0.42-1.05)	45.5% M vs 48.5% T	13.6% M vs 5.9% T
Gemcitabine (n=66)	0.58 (0.29-1.18)	40% M vs 53.1% T	17.1% M vs 15.6% T
Vinorelbine (n=191)	0.90 (0.60-1.35)	51.6% M vs 40% T	6.3% M vs 2.1% T

* Primary PFS data cutoff 10 October 2018: 536 Intent-To-Treat subjects ** Safety data cutoff 10 April 2019: 530 subjects receiving any study therapy

1041 Poster Session (Board #126), Fri, 8:00 AM-11:00 AM

Preliminary safety, efficacy and pharmacokinetics (PK) results of KN026, a HER2 bispecific antibody in patients (pts) with HER2-positive metastatic breast cancer. *First Author: Dongmei Ji, Fudan University Shanghai Cancer Center, Shanghai, China*

Background: KN026 is a novel bispecific antibody that simultaneously binds to two distinct HER2 epitopes, the same domains as trastuzumab (ECD4) and pertuzumab (ECD2). It blocks ligand-dependent and independent tumor growth and enhances HER2 receptor internalization. In preclinical studies, KN026 showed activity in trastuzumab plus pertuzumab resistant tumor cell lines. This first-in-human study evaluated the safety/tolerability, pharmacokinetics (PK), and preliminary efficacy of KN026 monotherapy. **Methods:** This dose-escalation and expansion study enrolled Chinese patients (pts) with metastatic breast cancer who have failed prior anti-HER2 therapy. All pts intravenously received KN026 monotherapy at ascending dose of 5 mg/kg (QW), 10 mg/kg (QW), 20 mg/kg (Q2W) or 30 mg/kg (Q3W). Dose limiting toxicity (DLT) evaluation period was 28 days for QW and Q2W, and 21 days for Q3W. Efficacy evaluation was performed by RECIST 1.1 every 6 weeks and safety assessment according to CTCAE v 4.03. **Results:** As of the Jan, 22, 2020, 63 pts [median age: 54 years (31~69)] enrolled and 62 pts were included in the efficacy analysis. 41 pts remained on treatment and 22 pts discontinued treatment due to disease progression (n = 21) and adverse events (n = 1). The median treatment duration was 12 weeks (range: 4~62 weeks). Median prior lines of therapies are 3 (range: 1~15), and median prior lines of HER2 target therapies are 2 (range: 1~12). No DLTs were observed. Treatment-related AEs (TRAEs) occurred in 49 pts and 4 pts experienced 4 grade 3 TRAE (hypertension, infusion related reaction, transaminases increased and ventricular arrhythmia). The common (≥ 10%) TRAE were pyrexia (23.8%), diarrhea (19.0%), aspartate aminotransferase increased (15.9%), neutrophil count decreased (11.1%) and white blood cell count decreased (11.1%). The objective response rate at recommended Phase 2 dose levels (n = 56) was 32.1% (95% CI 20.3, 46.0) and disease control rate 76.8% (95% CI 63.6, 87.0). Pharmacokinetic analysis showed exposure (C_{max} and $AUC_{0\text{-}t}$) of KN026 increased by dose. The recommended Phase 2 dose (RP2D) were 20 mg/kg Q2W and 30 mg/kg Q3W. **Conclusions:** KN026 is well tolerated and has demonstrated encouraging anti-tumor activity in HER2-positive breast cancer patients who have failed standard anti-HER2 therapies. The recommended Phase 2 dose (RP2D) of KN026 were 20 mg/kg Q2W and 30 mg/kg Q3W. Phase II trials in various HER2-positive and HER2-low/intermediate solid tumors are currently ongoing. Clinical trial information: NCT03619681. Research Sponsor: Alphamab (Australia) Co Pty Ltd.

1043 Poster Session (Board #128), Fri, 8:00 AM-11:00 AM

Management of adverse events in patients with HER2+ metastatic breast cancer treated with tucatinib, trastuzumab, and capecitabine (HER2CLIMB). *First Author: Alicia Frances Clare Okines, The Royal Marsden NHS Foundation Trust, London, United Kingdom*

Background: Tucatinib (TUC) is an investigational TKI, highly selective for HER2 without significant inhibition of EGFR. HER2CLIMB is a randomized trial of TUC vs placebo in combination with trastuzumab and capecitabine in patients (pts) with HER2+ breast cancer (NCT02614794, Murthy NEJM 2019). The most common G ≥3 adverse events (AEs) with higher incidence on the TUC arm (diarrhea, palmar-plantar erythrodysesthesia syndrome [PPE], and elevated liver enzymes) are described herein. **Methods:** Given that pts on the TUC arm had a longer duration of tx than those on the control arm, time-at-risk exposure-adjusted incidence rates of diarrhea, AST, ALT, and PPE were calculated as the number of pts with an event divided by the total exposure time-at-risk of an initial occurrence of the event among pts in the tx group. Time-to-event analyses were conducted for AST/ALT/bilirubin (in aggregate), diarrhea, and PPE. **Results:** Diarrhea and elevated AST/ALT/bilirubin on both the TUC and control arms were primarily G1/2 and manageable with dose modifications, and in some cases of diarrhea, with antidiarrheal tx. Median time to diarrhea onset was shorter on the TUC arm compared to control. For AST/ALT/bilirubin and PPE, median time to first onset was Cycles 1 and 2. On the TUC arm, antidiarrheals were used in 49.7% of cycles in which diarrhea was reported (39.8% on the control arm), and when used, the median duration of use on each arm was 3 days per cycle. Prophylactic antidiarrheals were not required per protocol. When adjusted for exposure (time-at-risk exposure-adjusted incidence rate per 100 person-years), the difference in G ≥3 events between tx arms becomes similar for diarrhea and PPE (21 vs 17 and 21 vs 19). The difference in G ≥3 events between arms is reduced for AST and ALT (7 vs 1 and 8 vs 1). **Conclusions:** TUC with trastuzumab and capecitabine was well-tolerated. Rates of G ≥3 diarrhea and PPE were similar between tx arms. Elevated liver enzymes were higher on the TUC arm, but were transient and reversible. Discontinuation of TUC due to AEs was rare. Clinical trial information: NCT02614794. Research Sponsor: Seattle Genetics, Inc.

	Diarrhea		Elevated AST/ALT/bilirubin		PPE	
	TUC	C	TUC	C	TUC	C
Pts with any event, %	80.9	53.3	21.3 / 20 / 18.6	11.2 / 6.6 / 10.2	63.4	52.8
G ≥3 events	12.9	8.6	4.5 / 5.4 / 0.7	0.5 / 0.5 / 2.5	13.1	9.1
Median days to onset	12	22	36	32	33	34.5
Events resolved, %	79.6	84.1	83.7	68.8	54.2	58.3
Median days to resolution	8	6	22	26.5	62.5	51
Dose holds, %	13.9	8.6	5.4 / 6.4 / 8.2	1.0 / 0.5 / 7.1	6.4	2
Dose reductions, %	5.7	4.6	4.2 / 4.7 / 2.2	1.0 / 0.5 / 1.0	1.2	0.5
Dose discontinuations, %	1.0	0.5	0.7 / 1.0 / 0.7	0.5 / 0.5 / 0.5	0	0

TUC = TUC arm; C = control arm

1044 Poster Session (Board #129), Fri, 8:00 AM-11:00 AM

Peripheral endothelial function changes during HER2-directed therapy differ based on whether or not a patient receives anthracycline. *First Author: Antonious Ziad Hazim, Mayo Clinic, Rochester, MN*

Background: Trastuzumab is well-demonstrated to be associated with cardiotoxicity (typically reduced ejection fraction), most commonly in patients who also receive anthracycline. The vascular effects of trastuzumab and anthracycline are understudied; we aimed to compare change in endothelial function during and after trastuzumab and to assess how anthracycline receipt affects this. **Methods:** This is an observational prospective study of women with newly diagnosed HER2-positive breast cancer. All participants underwent baseline evaluation of endothelial function testing by use of the EndoPAT2000 device approximately every three months over the subsequent 18 months after the initiation of HER2-directed therapy +/- anthracycline. The primary endpoint was change in endothelial function over time using the reactive hyperemia index (RHI). Framingham Risk Score (FRS) and lower RHI are both known to be independent predictors of future cardiovascular events in the general population. RHI deterioration was defined as a 20% reduction from baseline RHI to any available follow-up RHI assessment. Univariate analyses assessed if age, FRS, baseline RHI, and RHI deterioration differed between recipients and non-recipients of anthracycline using the Wilcoxon test. A multivariate logistic model evaluated FRS, age, and anthracycline receipt as possible independent predictors of RHI deterioration. **Results:** Among 38 eligible patients who consented and completed baseline assessments in addition to at least one follow-up assessment, 17 (45%) subsequently received anthracycline. 145 total follow-up RHI assessments were available overall (5 per patient on average). There were no differences between recipients and non-recipients of anthracyclines with regard to age [mean 49 years (SD 12) vs 53 years (SD 11); p=0.25], baseline FRS [mean 1.0 (SD 1.0) vs 1.5 (SD 1.4); p= 0.28] or baseline RHI [mean 2.4 (SD 0.6) vs 2.1 (SD 0.7); p=0.09]. RHI deterioration was more common for anthracycline recipients (mean 43% vs 21%; p=0.004), and in the multivariate model, anthracycline use was the only independent predictor of RHI deterioration (odds ratio: 2.8; 95% confidence interval: 1.35-6.07; p=0.006). **Conclusions:** This study suggests that endothelial dysfunction is more common after combined anthracycline and HER2-directed therapy than after HER2-directed therapy alone. RHI should be further studied as a possible early biomarker of cardiovascular toxicity in patients receiving treatment for breast cancer. Research Sponsor: Breast Cancer Research Foundation (CLL), Other Foundation.

1045 Poster Session (Board #130), Fri, 8:00 AM-11:00 AM

Interstitial lung disease in Japanese patients with HER2-expressing metastatic breast cancer receiving trastuzumab deruxtecan. *First Author: Masaya Hattori, Department of Breast Oncology, Aichi Cancer Center, Nagoya, Japan*

Background: Trastuzumab deruxtecan (T-DXd) is a new potent HER2-targeting antibody-drug conjugate in patients with HER2-expressing breast cancer. Interstitial lung disease (ILD), including fatal cases, have been reported in patients receiving T-DXd, which have indicated high incidence in Japanese patients. In this study, we aimed to characterize the severity, management, and the time course of ILD in Japanese patients receiving T-DXd. **Methods:** Patients with HER2-expressing metastatic breast cancer who developed ILD during treatment with T-DXd in our hospital were included in this study. We reviewed clinical charts and assessed CT images. ILD was graded according to the Common Terminology Criteria for Adverse Events (version 4.0). **Results:** A total of 10 patients (38.5%) of 26 metastatic breast cancer patients who received T-DXd in our hospital developed ILD during their treatment with T-DXd. Of the 10 patients with a median age of 55 years, 8 were with HER2-positive tumors and 2 were with low HER2-expressing tumors. All HER2-positive patients were previously treated with trastuzumab, pertuzumab and T-DM1. Four patients received the dose with 5.4 mg/kg, 3 with 6.4 mg/kg, 2 with 4.4 mg/kg, and 1 with 7.4 mg/kg. Median time to ILD onset was 7.6 months (range, 1.7-19.8). Severity of ILD was grade 1 in 7 patients, grade 2 in one patient, grade 3 in one patient and grade 5 in one patient. All patients with grade $\geq$2 ILD received corticosteroids. T-DXd was interrupted in all cases after the diagnosis of ILD and was re-administered in one case after recovery. In the fatal case, T-DXd was continued after the appearance of small reticular opacities without symptoms. In some cases, sustained off-treatment responses for more than 6 months after interruption was observed. **Conclusions:** T-DXd-induced ILD in Japanese breast cancer patients mostly occurred asymptomatically and improved by T-DXd interruption and/or steroid administration. Careful radiographic monitoring and, in case with ILD is suspected, prompt ILD management with interruption of T-DXd should be considered. Research Sponsor: None.

1046 Poster Session (Board #131), Fri, 8:00 AM-11:00 AM

A phase Ib study of pembrolizumab (pembro) plus trastuzumab emtansine (T-DM1) for metastatic HER2+ breast cancer (MBC). *First Author: Adrienne Gropper Waks, Dana-Farber Cancer Institute, Boston, MA*

Background: Preclinical evidence suggests treatment (tx) with T-DM1 plus an anti-PD1 antibody triggers antitumor immunity. We conducted a phase 1 trial to determine the safety and explore the efficacy of T-DM1 plus pembro. **Methods:** Eligible patients (pts) had MBC previously treated with trastuzumab (H) and taxane (T), were T-DM1-naïve, and received >1 prior line of tx for MBC or developed recurrence within 6 months (mo) of adjuvant tx. A dose de-escalation (esc) design was used with 6 pts in the dose-finding cohort, followed by an expansion (exp) cohort at the recommended phase 2 dose (RP2D), with mandatory baseline biopsies (bx). The primary endpoint was safety and tolerability. Secondary endpoints included objective response rate (ORR), progression-free survival (PFS), and clinical benefit rate (CBR: complete response + partial response + stable disease >24 weeks). Associations between immune biomarkers and tx response were explored. **Results:** 20 pts started protocol tx (6 in dose de-esc cohort; 14 in exp cohort). Median follow-up was 23.5 mo. Pts had median age 54 yrs and median 1 line of prior MBC tx (range 0-2); 100% had received prior T, H, and pertuzumab. There were no dose-limiting toxicities in the dose de-esc cohort; thus full doses of T-DM1 (3.6 mg/kg q21 days) and pembro (200 mg q21 days) were the RP2D. 85% of pts experienced tx-related adverse events (AEs) > grade (gr) 1; 20% of pts experienced gr3 AEs. There were no gr>4 AEs. Gr3 AEs were fatigue; AST increase; ALT increase; pneumonia; pneumonitis; oral mucositis; and vomiting, each in 1 pt. 17 pts had baseline bx; 6 pts had repeat bx after 1 tx cycle. Efficacy results, overall and by PD-L1 Combined Positive Score (CPS; 22C3 staining) and tumor-infiltrating lymphocyte (TIL) status, are shown in the table. Tumors' antigen presentation will be explored through HLA/dendritic cell marker staining and immune signatures by RNA sequencing. **Conclusions:** T-DM1 plus pembro was safe and tolerable. The regimen demonstrated clinical activity. Further exploration of immune-related predictive biomarkers is warranted. Clinical trial information: NCT03032107. Research Sponsor: Merck.

		PD-L1 (evaluable in N = 13)		TILs (evaluable in N = 13)	
	Overall	(CPS ≥1) N = 7	(CPS < 1) N = 6	> 10% N = 2	0-10% N = 11
ORR	20% (8.1-41.6)	29% (8.2-64.1)	33% (9.7-70)	0% (0-65.8)	36% (15.2-64.6)
CBR	50% (29.9-70.1)	43% (15.8-75)	67% (30-90.3)	50% (2.6-97.4)	55% (28-78.7)
PFS, median	9.6 mo (2.9 – NA)	2.9 mo (2.6 – NA)	8.7 mo (2.8 – NA)	2.7 mo (2.7 – NA)	6.1 mo (2.8 – NA)
Duration of response, median	10.1 mos (3.1 – NA)	10.1 mos (8.4 – 11.7)	NA (3.1 – NA)	NA	10.1 mos (3.1 – NA)

Values are listed as estimate (95% confidence interval)

1047 Poster Session (Board #132), Fri, 8:00 AM-11:00 AM

Targeted next generation sequencing to expand *HER2* status detection: Implication for newer *HER2*-directed agents. *First Author: Ning Liao, Guangdong Provincial People's Hospital, Guangzhou, China*

Background: Establishment of *ERBB2* (*HER2*) amplification status in breast carcinoma (BC) and gastric carcinoma (GC) is essential for treatment selection, but no anti-*HER2* therapies have been approved for tumors with low level of *HER2* expression. The clinical trial (NCT02564900) was initiated to evaluate the safety and efficacy of trastuzumab deruxtecan (DS-8201a) in BC patients with lower *HER2* expression by current methods. This study aims to validate NGS-based detection for *HER2* low expression. **Methods:** 275 BC and 425 GC were collected and subjected to NGS for genomic alteration detection. The testing was carried out by a College of American Pathologists (CAP) accredited and Clinical Laboratory Improvement Amendments (CLIA) certified laboratory, Shanghai, China. Protein expression was analyzed by using IHC. FISH was carried out on 108 samples, including 63 BC and 45 GC. To set up NGS cutoff, FISH was performed on additional 34 samples. Sensitivity, specificity and accuracy were evaluated based on FISH as a gold-standard reference. **Results:** In BC, the expression level of *HER2* protein detected by IHC was overall IHC 0 in 28.7%, 1+ in 18.9%, 2+ in 27.3% and 3+ in 25.1%, respectively, while in GC, the expression level was 60.7%, 18.6%, 14.8% and 5.9%, respectively. Log2ratio was used to assess *ERBB2* amplification status detected by NGS. According to the FISH results of 34 other samples with high sensitivity (98%) and specificity (100%), the threshold was determined as 0.5. 8 and 10 samples of IHC 1+/2+ met the cutoff in BC and GC, respectively. In 63 BC, there were 17 positive and 46 negative by FISH. According to the threshold, the sensitivity and specificity of NGS detection was 94.1% and 97.8%, respectively. The proportion of samples with IHC 2+ that couldn't determine NGS *ERBB2* status was 49.2%. However, except for false positive and false negative, the NGS results were concordant with FISH. In 45 GC, there were 5 positive and 40 negative by FISH. The specificity and sensitivity was 97.5% and 40%, respectively. In 4 samples with IHC 2+, 2 of them were discordant with the results of NGS and FISH. All IHC 1+ didn't meet the cutoff of NGS and was FISH negative in 108 samples. The accuracy of NGS in *ERBB2* detection was 96.8% and 91.1% for BC and GC, respectively. **Conclusions:** Our data indicated that the NGS-based detection of *ERBB2* amplification had high sensitivity, specificity and accuracy. In samples with IHC 1+/2+, the results of NGS detection were high concordant with FISH detection. Research Sponsor: None.

1048 Poster Session (Board #133), Fri, 8:00 AM-11:00 AM

Pyrotinib plus capecitabine for HER2-positive, trastuzumab-resistant metastatic breast cancer: A pooled analysis of three randomized controlled trials. *First Author: Zefei Jiang, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China*

Background: Trastuzumab is the most widely used anti-HER2 agent in patients (pts) with HER2-positive breast cancer, both in (neo)adjuvant and metastatic settings; however, drug resistance is inevitable. This pooled study aimed to investigate the efficacy of pyrotinib plus capecitabine in pts with HER2-positive, trastuzumab-resistant relapsed or metastatic breast cancer. **Methods:** Data were derived from three randomized controlled trials, including a phase II (NCT02422199) and the PHOEBE phase III (NCT03080805) study comparing pyrotinib plus capecitabine vs lapatinib plus capecitabine and the PHENIX phase III (NCT02973737) study comparing pyrotinib plus capecitabine vs placebo plus capecitabine. Pts with trastuzumab-resistant disease were included in the analyses, including 39 pts who had relapsed within six months after adjuvant trastuzumab and 57 pts who had progressed within three months of trastuzumab treatment for metastatic disease. The pooled tumor response data (per blinded independent central review) were reported herein. **Results:** In the pooled analysis of all three studies, 63 pts received pyrotinib plus capecitabine. Among them, 28 (44.4%) pts had disease progression or died. The median progression free survival (PFS) was 12.4 months (95% CI, 6.9 to not reached). In total, 40 pts (63.5% [95% CI, 50.4% to 75.3%]) achieved objective response, and the estimated median duration of response (DoR) was 11.1 months (95% CI, 6.9 to not reached). In the pooled analysis involving the phase II and PHOEBE phase III, 43 pts were treated with pyrotinib plus capecitabine and 33 pts with lapatinib plus capecitabine. In total, 18 (41.9%) pts with pyrotinib plus capecitabine and 17 (51.5%) pts with lapatinib plus capecitabine had disease progression or died. The PFS tended to be prolonged with pyrotinib plus capecitabine vs lapatinib plus capecitabine (median, 12.4 months [95% CI, 6.9 to not reached] vs 6.9 months [95% CI, 5.5 to not reached]; hazard ratio, 0.62 [95% CI, 0.31 to 1.24]; p=0.0864). The objective response rate was 67.4% (95% CI, 51.5% to 80.9%) with pyrotinib plus capecitabine compared with 54.5% (95% CI, 36.4% to 71.9%) with lapatinib plus capecitabine. The estimated median DoR was 11.1 months [95% CI, 6.9 to not reached] vs not reached [95% CI, 4.2 months to not reached], respectively. **Conclusions:** Pyrotinib plus capecitabine showed favorable efficacy in pts with HER2-positive, trastuzumab-resistant relapsed or metastatic breast cancer. This combination could be a treatment option for this population. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

1049 Poster Session (Board #134), Fri, 8:00 AM-11:00 AM

A first in-human study of A166 in patients with locally advanced/metastatic solid tumors which are HER2-positive or HER2-amplified who did not respond or stopped responding to approved therapies. *First Author: Yongheng Liu, Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China*

Background: HER2 is an effective therapeutic target for breast and gastric cancer. A166 is an antibody-drug conjugate composed of a novel cytotoxic drug site-specifically conjugated to transtuzumab sequence via a stable protease-cleavable valine citrulline linker. **Methods:** This was a single arm, open-label, multicenter, dose escalating Phase 1 first-in-human study of A166 as monotherapy in solid tumor patients. Dose escalation and MTD identification was directed using a Bayesian logistic regression model with overdose control. The following dose levels were evaluated in this study: 0.3, 1.2, 3.6, 4.8 mg/kg. (ClinicalTrials.gov NCT03602079) **Results:** As of November 1, 2019 35 pts have completed the DLT evaluation period across 4 dose levels. Overall, A166 had an acceptable toxicity profile with no unexpected toxicities related to the study drug. No adverse events recorded met the protocol specified definition of a dose limiting toxicity at any studied dose level. Most frequently (≥10%) occurring TEAEs include were Keratitis, Decreased appetite, Dry eye, Vision blurred etc. Overall incidence of ophthalmic toxicities in the 3.6 mg/kg cohort was 80% and in the 4.8 mg/kg cohort it was 83%. Among the 27 patients evaluable for efficacy, best response was progression of disease in 11 patients (41%), stable disease in 9 patients (33%) and partial response in 7 patients (26%), for the total disease control rate of 59%.Responses were seen only at the dose levels of 3.6 mg/kg and 4.8 mg/kg. **Conclusions:** A166 demonstrated clinically meaningful efficacy in heavily pretreated patients with relapsed or refractory advanced solid cancers. The achievement of an ORR of 36% at efficacious dose levels and up to 100% in HER2 positive patients regardless of histology (2 CRC, 1 BC and 1 NSCLC) at the highest studied dose level exceed Clinical trial information: NCT03602079. Research Sponsor: KLUS Pharm Inc.

1050 Poster Session (Board #135), Fri, 8:00 AM-11:00 AM

Patient-matched tissue and liquid biopsies identify shared and acquired genomic alterations in breast cancer. *First Author: Ethan Sokol, Foundation Medicine, Inc., Cambridge, MA*

Background: Liquid biopsy-based comprehensive genomic profiling (CGP) is a minimally invasive approach to potentially identify truncal driver alterations and mechanisms of acquired resistance. However, there are limited data comparing solid tissue and plasma biopsies from the same patient in breast cancer. **Methods:** CGP was performed on matched tumor tissue and plasma samples from 444 patients with breast cancer (Foundation Medicine, Inc.) to identify short variant mutations and rearrangements in at least 62 genes. ER/PR/HER2 status was abstracted for a subset of patients (n = 273). Patients were primarily ER+/HER2- (58%) with fewer HER2+ (16%) and TNBC (25%). **Results:** Samples were temporally heterogeneous with a median time between matched tissue-plasma collection of 276 days (interquartile range 45 - 650). Positive percent agreement (PPA) to tissue biopsy was 81.5% with higher PPA for collection interval ≤1y v > 1y (82.5% v 76.5%). PPA was highest in known truncal driver genes (*AKT1*, *PTEN*, *BRCA2*, *BRCA1*, *TP53*, *PIK3CA*: 85-89% PPA). PPA of tissue to liquid biopsy was 50.5% with strong time dependence (62.4% ≤1y, 37.9% > 1y), presumably due to intervening therapies. Acquired alterations in liquid biopsy were primarily known resistance mechanisms (*ESR1*, *NF1*, *ERBB2*, *PIK3CA*, *PTEN*, *TP53*, *BRCA1*, and *BRCA2*), were often polyclonal, associated with longer collection intervals, and exhibited higher prevalence in the ER+/HER2- subtype (62% ER+/HER2-, 33% HER2+, 42% TNBC). Acquired alterations significantly enriched in ER+ cases included *ESR1, NF1, ERBB2* and *TP53*. For *PIK3CA*, a PPA of 84.6% was observed with solid as baseline and 79.1% with liquid as baseline; prevalence was similar (36.5% solid, 35.6% liquid). Alpelisib companion diagnostic alterations (CDx) had a similar PPA (84.0% solid, 83.3% liquid). Overall percent agreement (OPA) for PIK3CA CDx in paired samples was 91.4% (406/444). When acquired *PIK3CA* alterations are observed they tend to be subclonal, co-occur with shared *PIK3CA* alterations, and consist of rare alterations (E726K, E453K, M1043I). **Conclusions:** While high PPA to tissue was observed for alterations in truncal driver genes, acquired alterations observed in plasma were frequently polyclonal, often identify potential mechanisms of therapeutic resistance and are, in part, a function of time and intervening treatments relative to tissue CGP. These results demonstrate high PPA to tissue suggesting that liquid biopsy has clinical validity in identifying truncal alterations and can also identify acquired alterations in breast cancer. Research Sponsor: None.

1051 Poster Session (Board #136), Fri, 8:00 AM-11:00 AM

A phase Ib study of abemaciclib in combination with pembrolizumab for patients with hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) locally advanced or metastatic breast cancer (MBC) (NCT02779751): Interim results. *First Author: Hope S. Rugo, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

Background: Abemaciclib is an orally administered, selective small molecule cyclin-dependent kinase (CDK)4 and 6 inhibitor, approved to treat HR+, HER2- MBC patients (pts) on a continuous twice daily dosing schedule as monotherapy or in combination with an aromatase inhibitor as initial endocrine based therapy or in combination with fulvestrant. Abemaciclib monotherapy increased tumor immunogenicity and synergized with anti-PD-1 to boost antitumor efficacy in murine models. Here we report safety and antitumor activity of abemaciclib plus pembrolizumab in HR+, HER2- MBC pts. **Methods:** This multicenter, nonrandomized, open-label, multi-cohort phase Ib study of abemaciclib plus pembrolizumab enrolled a cohort of endocrine resistant HR+, HER2- MBC pts who had received 1 or 2 prior chemotherapy regimens for MBC. No prior CDK4/6 inhibitor was allowed. Patients received 150mg abemaciclib orally every 12 hours plus pembrolizumab 200mg IV on day 1 every 21 days. Primary objective was to characterize safety of the abemaciclib plus pembrolizumab combination. Secondary objectives included objective response rate (ORR), progression-free survival (PFS), and overall survival (OS). **Results:** Of 28 pts enrolled, 15 (54%) received 1 line and 10 (36%) 2 lines of prior systemic chemotherapy in the locally advanced/metastatic setting. Safety of the combination was generally consistent with known side effects of abemaciclib and pembrolizumab and was generally manageable. Grade 3/4 adverse events in >2 pts included neutropenia (8 pts/29%), AST increase (5 pts/18%), diarrhea, and ALT increase (3 pts/11% each). Eight pts had confirmed partial response (29% ORR), and disease control rate (complete response [CR]+partial response [PR]+stable disease [SD]) was 82%. Clinical benefit rate (CR+PR+SD persisting for ≥6 months) was 46%. Median PFS and OS were 8.9 months (95% CI 3.9, 11.1) and 26.3 months (95% CI 20.0, 31.0), respectively. **Conclusions:** Combination of abemaciclib plus pembrolizumab demonstrated a generally tolerable safety profile with numerically higher rate of transaminase elevations than reported for the individual treatments. Compared to historical data for abemaciclib monotherapy in a similar pt population, a numerically higher but not obviously different ORR, PFS, and OS was observed. Clinical trial information: NCT02779751. Research Sponsor: Eli Lilly and Company.

1052 Poster Session (Board #137), Fri, 8:00 AM-11:00 AM

Biomarker analysis from a phase I study using gedatolisib+palbociclib+hormone therapy in ER+/HER2- metastatic breast cancer (mBC). *First Author: Robert Wesolowski, The Ohio State University Comprehensive Cancer Center, Columbus, OH*

Background: Endocrine therapy with a CDK4/6 inhibitor (CDKi) is standard of care (SOC) for patients (pts) with estrogen-receptor-positive (ER+) metastatic breast cancer (mBC). Resistance to therapy may arise from mutations in ESR1, PIK3CA, and activation of receptor tyrosine kinase signaling pathways. In this study, gedatolisib (G), a PI3KCA/mTOR inhibitor, was added to a CDKi (palbociclib, P) + letrozole (L) or fulvestrant (F) for treatment of pts with ER+/HER2- mBC. **Methods:** This phase 1b study (NCT02684032) comprises a dose escalation phase evaluating the dose-limiting toxicity and maximum tolerated dose of G+P+L/F and a dose expansion phase assessing the objective response rate of G+P+L/F, compared with historical data for P+L or P+F. Response was assessed using RECIST v1.1. Genomic and transcriptomic analyses were performed on archival pt tumor biopsies. Longitudinal plasma ctDNA analysis was performed on samples taken at baseline, on-treatment, and end-of-treatment. Unsupervised data analysis was conducted. **Results:** Genomic information was available for 25 of 35 pts with measurable disease (G+P+L: 11; G+P+F: 14). No relationship was observed between responses (1 complete response [CR] and 11 partial responses [PR]) and baseline PIK3CA pathway alterations. Pt tumor tissue analysis (n = 25) confirmed pts with FGF3/4/19 amplification (n = 4) had larger changes in tumor size in response to G+P+L/F (p = 0.029). Of the 6 pts with an ESR1 mutation, 1 pt with an ESR1 Y537S mutation exhibited a partial response (PR) to G+P+L. Longitudinal plasma ctDNA analysis (73-gene panel) revealed that decreases in PIK3CA and PTEN were most associated with clinical response. Plasma sample analysis (n = 21) showed that pts with somatic alterations in EGFR (n = 4) had a greater response to therapy (p = 0.066), compared with pts without somatic EGFR alterations. Transcriptomic profiling also revealed responsive patients had higher levels of EGFR expression. Pts exhibiting CR/PR had a lower somatic tumor mutation burden at Cycle 5 Day 1 compared with baseline (p = 0.0013). **Conclusions:** The addition of G to SOC endocrine + CDKi therapy may help overcome resistance due to activation of FGFR or EGFR signaling pathways and the ESR1 Y537S mutation. Somatic frequency changes of PI3K pathway alterations were most correlated with clinical response. Genomic data analysis from dose expansion samples is currently ongoing. Clinical trial information: NCT02684032. Research Sponsor: Pfizer.

1053 Poster Session (Board #138), Fri, 8:00 AM-11:00 AM

Acquired RB1 mutations in estrogen receptor-positive (ER+) clinically advanced and metastatic breast cancer (MBC). *First Author: Kimberly McGregor, Foundation Medicine, Cambridge, MA*

Background: Prior to use of cell cycle inhibitor drugs such as palbociclib, mutations in the retinoblastoma cell cycle inhibitory gene (*RB1*) were extremely uncommon. To assess recent descriptions of *RB1* mutations in MBC as treatment related, we compared primary untreated ER+ breast cancer samples from patients who developed MBC with ER+ MBC metastasis biopsies in post-primary treatment patients. **Methods:** Extracted DNA from 15 untreated primary breast tumors (PBx) and 36 treated metastatic MBC tumors (MBx) were sequenced by hybrid capture genomic profiling to evaluate all classes of genomic alterations (GA). Tumor mutational burden (TMB) was determined on up to 1.1 Mbp of sequenced DNA. PD-L1 expression was determined by IHC (Dako 22C3). **Results:** The age distribution, GA per tumor, *CDH1* and *ERBB2* GA frequencies were similar in PBx and MBx. GA in *ESR1* ($P < 0.0008$), classically associated with acquired hormonal therapy resistance, and *PIK3CA* ($p < 0.11$) were increased in the MBx vs the PBx samples. *RB1* GA were more frequent in the MBx samples (11%) than the pre-treatment PBx samples (0%, $P < 0.31$). GA not associated with targeted therapy programs were similar in both groups. In addition to low frequencies of *ERBB2* amplification in the ER+ tumors, the most frequent potentially targetable GA identified in both PBx and MBx included GA in *FGFR1* and *NF1*. *BRCA1* GA were identified in the MBx group only. Biomarkers of potential immunotherapy benefit including MSI status, TMB levels and PD-L1 IHC staining were at similarly low levels in both groups. Additional cases are being identified to expand the cohort sizes for final presentation. **Conclusions:** In addition to the well-known acquisition of hormonal therapy resistance mutations in *ESR1* and *PIK3CA* in ER+ MBC, this study also supports the acquisition of *RB1* mutations when post-treatment metastasis biopsies are sequenced rather than pre-treatment primary tumors. This increase in *RB1* mutation identification is associated with exposure of the tumors to anti-cell cycle drugs such as palbociclib in the treated but not the untreated cohort. Research Sponsor: Foundation Medicine Inc.

	PBx		MBx	
Cases	15		36	
Median Age/Range (years)	55 (39-83)		60 (33-76)	
GA/tumor	5.8		5.8	
***RB1* GA**	0%		11%	
***ESR1* GA**	0%		47%	
PIK3CA	20%		47%	
***CDH1* GA**	20%		25%	
Most Frequent	*CCND1*	40%	*TP53*	36%
Currently	*GATA3*	27%%	*MYC*	19%
Untargetable GA	*TP53*	20%	*GATA3*	19%
	MYC	13%	*CDKN2A*	6%
Potential	*NF1*	13%	*FGFR1*	11%
Targeted	*ERBB2*	7%	*PTEN*	8%
Therapy	*FGFR1*	7%	*ERBB2*	8%
Impacting GA			*BRCA1*	6%
			NF1	11%
MSI High Status	0%		0%	
TMB Median (mut/Mb)	3.8		3.8	
TMB > 10 mut/Mb	0%		8%	
TMB > 20 mut/Mb	0%		0%	
PD-L1 IHC Low	14%		0%	
PD-L1 IHC High	0%		0%	

1054 Poster Session (Board #139), Fri, 8:00 AM-11:00 AM

Overall survival (OS) in patients (pts) with advanced breast cancer (ABC) with visceral metastases (mets), including those with liver mets, treated with ribociclib (RIB) plus endocrine therapy (ET) in the MONALEESA (ML) -3 and -7 trials. *First Author: Denise A. Yardley, Sarah Cannon Research Institute and Tennessee Oncology PLLC, Nashville, TN*

Background: In the Phase III ML-3 (NCT02422615) and ML-7 (NCT02278120) trials, RIB + ET demonstrated a significant OS benefit (ML-3: HR, 0.72, P = 0.00455; ML-7: HR, 0.71, P = 0.00973) over placebo (PBO) + ET in pts with HR+/HER2- ABC (Im et al. *N Engl J Med.* 2019; Slamon et al. *N Engl J Med.* 2019). The presence of visceral mets generally portends a poor prognosis, which is especially poor in pts with liver mets (He et al. *Ann Oncol.* 2019). Here we report OS in pts with visceral mets with a focus on those with liver mets in ML-3 and ML-7. **Methods:** In ML-3, postmenopausal pts were randomized 2:1 to receive RIB + fulvestrant (FUL) or PBO + FUL as first- (1L) or second-line (2L) treatment. In ML-7, premenopausal pts were randomized 1:1 to receive RIB + ET or PBO + ET (this analysis included only pts who received an NSAI as ET partner to match approved indication). **Results:** Visceral mets were identified in 293 pts (60.5%) in the RIB arm and 147 (60.7%) in the PBO arm in ML-3 and 150 (44.8%) and 142 pts (42.1%), respectively, in ML-7. In ML-3, the median age of pts with visceral mets was 63 and 65 years in the RIB and PBO arms, and in ML-7 it was 42.5 and 45.0 years, respectively. In ML-3, 214 pts with visceral mets received 1L therapy (RIB, n = 137; PBO, n = 77), while 219 pts received 2L therapy or had early relapse (RIB, n = 151; PBO, n = 68). Lung and liver were the most common sites of visceral mets for pts in ML-3 (49.8% and 44.8%, respectively) and ML-7 (51.4% and 58.2%, respectively). OS HRs in pts with visceral mets were consistent with the benefit in the overall pt populations and suggested a particularly substantial OS benefit in pts with liver mets (HR for liver mets group in ML-3, 0.629 [95% CI, 0.421-0.942]; HR in ML-7, 0.531 [95% CI, 0.321-0.877]; Table). No new safety signals were observed. **Conclusions:** Approximately half of the pts in ML-3 and ML-7 had visceral mets. The OS data in these pts are consistent with the benefit observed with RIB in the overall populations of each trial. In pts with liver mets, a group with an especially poor prognosis, RIB + ET demonstrated a substantial OS benefit compared with PBO + ET. Clinical trial information: NCT02422615; NCT02278120. Research Sponsor: Novartis Pharmaceuticals Corporation.

	ML-3 RIB + FUL	ML-3 PBO + FUL	ML-7 RIB + ET	ML-7 PBO + ET
Visceral mets, n	293	147	150	142
OS, median mo (95% CI)	41.0 (38.5-NE)	39.4 (30.6-42.2)	NE	39.9 (37.0-NE)
HR (95% CI)	0.804 (0.596-1.083)		0.698 (0.462-1.054)	
Liver mets, n	134	63	83	87
OS, median mo (95% CI)	36.1 (29.1-NE)	24.1 (17.8-39.4)	NE	33.6 (25.7-NE)
HR (95% CI)	0.629 (0.421-0.942)		0.531 (0.321-0.877)	

NE, not evaluable.

1055 Poster Session (Board #140), Fri, 8:00 AM-11:00 AM

Updated results from the phase IIIb complement-1 study of ribociclib (RIB) plus letrozole (LET) in the treatment of HR+, HER2-advanced breast cancer (ABC). *First Author: Michelino De Laurentiis, Istituto Nazionale Tumori "Fondazione G.Pascale-IRCCS, Naples, Italy*

Background: Real-world evidence is important as it complements data from randomized controlled trialse report updated results from CompLEEment-1, a Phase IIIb trial evaluating RIB+LET in an expanded population, the largest CDK4/6i trial in ABC to date. **Methods:** Patients (pts) with HR+, HER2– ABC, ≤ 1 line of prior CT and no prior ET for ABC received RIB+LET. Study design has been reported previously (De Laurentiis, et al. ASCO 2019). Primary endpoints were safety and tolerability. **Results:** 3,246 pts received ≥ 1 dose of study treatment. Median duration of follow-up was 25.4 months (mos) (15 additional mos since interim analysis [De Laurentiis, et al. ABC5 2019]). Median treatment exposure was 17.8 mos. Baseline characteristics indicated a diverse population, including men (1.2%), premenopausal women (22.2%), and pts aged ≥ 70 years (19.5%); 112 (3.5%) pts had an ECOG PS of 2, 194 (6.0%) pts received prior CT for ABC, and 51 (1.6%) pts had stable CNS lesions. The most common adverse events (AEs) were neutropenia (61.1%), nausea (35.9%), and fatigue (23.4%). Grade 3/4 hematologic abnormalities (> 5.0 %) were decreased neutrophils (54.8%), leukocytes (25.9%), and lymphocytes (12.6%). Grade 3/4 biochemical abnormalities (> 5.0 %) were increased ALT (9.1%) and AST (6.7%). An increase of > 60 ms in QTcF interval from baseline occurred in 189 (5.9%) pts, while post-baseline QTcF of > 480 to ≤ 500 ms and > 500 ms occurred in 59 (1.8%) and 42 (1.3%) pts, respectively. Treatment-related AEs led to treatment discontinuation in 418 (12.9%) pts. Of 74 (2.3%) on treatment deaths, 38 (1.2%) were due to breast cancer. Median time to progression was 27.1 mos (95% CI, 25.7-NE), overall response rate was 43.6% (95% CI, 41.5-45.8%), and clinical benefit rate was 69.1% (95% CI, 67.1-71.1%) for pts with measurable disease at baseline. **Conclusions:** This analysis confirms the safety and efficacy of RIB+LET in a large, diverse cohort of pts with HR+, HER2– ABC (with no previous ET for ABC), closely resembling real-world clinical practice. Safety and efficacy data were consistent with those observed in the MONALEESA trials, supporting the use of RIB+LET in the first-line setting. NCT02941926. Clinical trial information: NCT02941926. Research Sponsor: Novartis Pharmaceuticals Corporation.

1056 Poster Session (Board #141), Fri, 8:00 AM-11:00 AM

The efficacy of first-line chemotherapy in endocrine-resistant hormone receptor-positive (HR+), human epidermal growth factor receptor 2- negative (HER2-) metastatic breast cancer (MBC). *First Author: Sudpreeda Chainitikun, Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Combinations of endocrine therapy (ET) and targeted therapy (CDK4/6 or mTOR inhibitors) are standard of care for HR+/HER2- MBC. When ET is not effective, chemotherapy is commonly used. However, clinical outcomes of chemotherapy in the endocrine-resistant setting are limited. We hypothesized that clinicopathological baseline and prior ET factors determine chemotherapy's efficacy. We sought to identify predictive factors and the compare efficacies of chemotherapy agents in endocrine-resistant MBC. **Methods:** We conducted a retrospective study of patients with HR+/HER2- MBC who received chemotherapy after progression on ET with or without targeted therapy at MD Anderson Cancer Center from 1999-2017. We collected baseline clinicopathological and all treatment data. The primary endpoint was time to treatment failure (TTF) of first-line chemotherapy for MBC. We performed univariate and multivariate analyses using the Cox proportional hazard model. Kaplan-Meier methods were used to analyze TTF. **Results:** In the 1,258 patients analyzed, the mean age was 55.3 years (range 21-91). Forty-five patients (3.6%) had inflammatory breast cancer (IBC). Three hundred ninety patients (31%) received previous targeted therapy: 264 with CDK4/6 inhibitor, 205 with mTOR inhibitor, and 79 with both. The most frequent chemotherapy agents were capecitabine (48.9%) and taxanes (paclitaxel, nab-paclitaxel, or docetaxel; 28.6%). After adjustment for all factors in a multivariate model, IBC and prior exposure to a CDK4/6 inhibitor were significantly associated with shorter TTF. Previous treatment with a CDK4/6 inhibitor had the strongest negative effect on chemotherapy TTF regardless of ET duration (adjusted hazard ratio [HR] 1.84; 95%CI 1.49-2.27; $p < 0.001$). Capecitabine had significantly longer median TTF than taxanes regardless of whether patients had prior exposure to taxanes in (neo) adjuvant setting (6.1 vs 4.9 months; HR 0.64; 95%CI 0.55-0.75; $p < 0.001$). Conversely, the median TTF for taxanes was shorter in patients who received prior (neo)adjuvant taxanes than in those who did not (4.5 vs 5.1 months). **Conclusions:** Previous exposure to CDK4/6 inhibitor had a negative predictive effect for the efficacy of chemotherapy. Capecitabine had the best efficacy against endocrine-resistant breast cancer. Research Sponsor: Morgan Welch Inflammatory Breast Cancer Research Program.

1057 Poster Session (Board #142), Fri, 8:00 AM-11:00 AM

Integration of the stem cell biology-based genomic tool, StemPrintER, with clinicopathological parameters for the prediction of distant recurrence in ER+/HER2- breast cancer (BC) patients. *First Author: Salvatore Pece, European Institute of Oncology, Milan, Italy*

Background: The StemPrintER risk score (SPRS) is a 20 gene-based predictor that estimates the "degree of stemness" of the primary tumor and provides additional prognostic information regarding distant metastasis (DM) risk in early stage ER+/HER2- breast cancer (BC) patients beyond that obtained from standard clinicopathological parameters. Here we describe a further refined model, that combines prognostic information from SPRS with tumor size (pT) and nodal status (pN), termed SPARE (SPRS for Personalized Adjuvant therapy in Receptor-Expressing patients). SPARE was compared to the clinical treatment score (CTS) for 10-year risk of DM in a consecutive-retrospective ER+/HER2- BC patient cohort (n=1,827) with 15-year complete follow-up from the European Institute of Oncology (IEO) in Milan. **Methods:** The SPARE model was developed in patients randomly assigned to a training set (n=609), using the ridge-penalized Cox regression, and tested in an independent validation set (n=1,218). Likelihood χ^2 ($LR\chi^2$) and Kaplan-Meier survival analysis were used to compare the prognostic information from SPARE and CTS (based on age, pN, pT, endocrine treatment). Comparative analyses were made for the DM risk over the 10-year follow-up, as well as in the early (0-5 years) or late (5-10 years) interval, according to nodal status. **Results:** SPARE outperformed CTS in providing prognostic information for 10-year DM risk ($LR\chi^2$: SPARE = 141.2, $P<0.0001$; CTS=118.1, $P<0.0001$), with even greater differences in node-negative patients ($LR\chi^2$: SPARE=47.6, $P<0.0001$; CTS=27.5, $P<0.0001$) and in 1-3 node-positive patients ($LR\chi^2$: SPARE=30.6, $P<0.0001$; CTS=15.1, $P<0.0001$). When reciprocally adjusted for each other, SPARE added prognostic information to CTS ($\Delta LR\chi^2$: CTS+SPARE *vs.* CTS = 25.2; $P<0.0001$), while CTS did not provide any statistically significant information to SPARE (SPARE+CTS *vs.* SPARE = 2.1, $P=0.14$). Using predefined cut-offs to stratify chemo-naïve patients clinically estimated at low recurrence risk, SPARE identified low, intermediate and high risk patients based on their annual rate of DM in the early (low, 0.2%, intermediate, 0.8%, high, 3.3%) and late (low, 0.3%, intermediate, 0.9%, high, 1.6%) interval. **Conclusions:** SPARE represents a more refined clinical tool, compared to standard clinicopathological parameters, that could be used for personalized therapeutic decision making in ER+/HER2- BC patients. Research Sponsor: Italian Association for Cancer Research (AIRC).

1059 Poster Session (Board #144), Fri, 8:00 AM-11:00 AM

Cell-free DNA comparative analysis of hormone receptor-positive, first-line metastatic breast cancer genomic landscape in the United States and China. *First Author: Huiping Li, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Breast Oncology, Peking University Cancer Hospital & Institute, Beijing, China*

Background: Metastatic breast cancer (MBC) is a heterogeneous disease associated with known somatic mutations of variable biological value in different subtypes. Furthermore, the clinical evolution of the disease demonstrates clonal evolution resulting in disease resistance more accurately detected using blood-based sequencing. Few studies have explored differences in genomic features of tumors across populations. Here, we performed circulating tumor DNA (ctDNA) sequencing to compare the genomic landscape of patients with hormone-receptor positive MBC at time of first recurrence or *de-novo* metastatic diagnosis in the United States (US) and China. **Methods:** Twenty-three US patients from Northwestern University and 65 Chinese patients from Peking University had ctDNA sequencing from plasma performed using the harmonized CLIA-certified, 152-gene PredicineCARE assay in laboratories in the US and China, respectively. The data analysis was conducted in China. Institutional Review Boards at each site approved the study. Fisher's exact test was performed to compare mutational frequencies across populations. **Results:** Median age of patients at MBC diagnosis was 51 in the US cohort and 55 in the Chinese cohort. 87% of US patients and 82% of Chinese patients had received prior therapy for primary breast cancer, including endocrine therapy. Mutations were detected in 17 of 23 (74%) US patients and 59 of 65 (91%) Chinese patients. CNAs were observed in 57% of US patients and 58% of Chinese patients. The most common mutations detected in US patients were *TP53* (26%), *PIK3CA* (22%), *AKT1* (22%), *CDH1* (17%), *PTEN* (13%), and *ESR1* (9%) vs. *PIK3CA* (46%), *TP53* (35%), *ESR1* (12%), and *BRCA2* (11%) in Chinese patients. Frequency of *AKT1* and *CDH1* mutations were significantly higher in the US population ($P < 0.05$), while *PIK3CA* mutations were higher in the Chinese population ($P < 0.05$). CNA gains in CCND3 and CDK4 were significantly higher in the US cohort, and FGFR1 was significantly more common in the Chinese cohort (all $P < 0.05$). **Conclusions:** To our knowledge, this is a first cross-regional comparison study in HR+ MBC patients in the US and China using a harmonized cfDNA NGS platform. At a population level, there were notable differences observed in somatic variants in two cohorts. Future sequencing efforts and clinical trials should include patients of diverse ethnic backgrounds to explore the impact of differences in genomic landscape on probability of benefit from treatments. A larger validation cohort is required to confirm these findings. Research Sponsor: National Natural Science Foundation of China.

1060 Poster Session (Board #145), Fri, 8:00 AM-11:00 AM

Meta-analysis of cyclin-dependent kinase (CDK) 4/6 inhibitors with endocrine therapy versus endocrine therapy alone on progression-free survival (PFS) and overall survival (OS) for metastatic breast cancer (MBC). *First Author: Ranju Kunwor, Thomas Jefferson University Hospital, Philadelphia, PA*

Background: CDK 4/6 inhibitors with Endocrine therapy (ET) are the preferred first line treatment for Hormone Receptor positive and Human Epidermal Growth factor receptor 2 negative (HR+/HER2-) MBC. Over the last few years multiple trials have shown benefit in PFS. Only two studies evaluating Ribociclib and Abemaciclib showed an OS benefit while no statistically significant OS benefit has been reported in any of the studies evaluating Palbociclib raising the possibility that this benefit may be drug specific rather than applicable to all CDK 4/6 Inhibitors. This updated meta-analysis of randomized controlled trials (RCTs) aims to assess the PFS and OS of all three CDK 4/6 inhibitors in HR+/HER2- MBC. **Methods:** We performed a systematic search for RCTs using Cochrane Library, PubMed, Embase, and Web of Science. Only the phase II and III RCTs comparing CKD 4/6 inhibitors plus ET with ET alone were eligible for this meta-analysis. The pooled analysis of Hazard Ratio (HR) was performed with Review Manager 5.3 using random effect model. **Results:** A total of 8 RCTs including 4338 patients with HR+/HER2- MBC were included in this meta-analysis (table). The pooled HR for PFS was 0.55 (95% confidence interval (CI), 0.50-0.59; $P < .00001$) and the pooled HR for OS was 0.75 (95% CI, 0.68-0.84; $P < .00001$). **Conclusions:** The result of our meta-analysis confirms the previously reported PFS benefit from CDK 4/6 inhibitors plus ET and shows an OS benefit when including RCTs of all 3 CDK 4/6 inhibitors for the treatment of HR+/HER2- MBC. Research Sponsor: None.

List of included RCTs.

Study	Sample size	Experimental group	Control group	Study participants	PFS Hazard ratio (CI)	OS Hazard Ratio (CI)
PALOMA 1	165	Palbo + Let	Let	Postmenopausal	0.49 (0.32-0.75)	0.81 (0.49-1.34)
PALOMA 2	666	Palbo + Let	Let	Postmenopausal	0.58 (0.46-0.73)	
PALOMA 3	521	Palbo + Ful	P + Ful	Pre and Postmenopausal	0.46 (0.36-0.59)	0.81 (0.64-1.03)
MONARCH 2	669	Abem + Ful	P + Ful	Postmenopausal	0.55 (0.45-0.67)	0.76 (0.61-0.95)
MONARCH 3	493	Abem + NSAI	P + NSAI	Postmenopausal	0.54 (0.41-0.71)	
MONALEESA 2	668	Ribo + Let	P + Let	Postmenopausal	0.56 (0.43-0.73)	0.75 (0.52-1.08)
MONALEESA 3	726	Ribo + Ful	Ful	Postmenopausal	0.59 (0.48-0.73)	0.72 (0.57-0.91)
MONALEESA 7	672	Ribo + Tamoxifen/ NSAI + Goserelin	P + Tamoxifen/NSAI + Goserelin	Pre or Perimenopausal	0.55 (0.44-0.69)	0.71 (0.57-0.91)

(NSAI: Non steroidal aromatase inhibitor; Palbo: Palbociclib; Let: Letrozole; Ful:Fulvestrant; Ribo: Ribociclib; Abem: Abemaciclib; P: Placebo)

1061 Poster Session (Board #146), Fri, 8:00 AM-11:00 AM

MONARCH 2: Subgroup analysis of patients receiving abemaciclib + fulvestrant as first- and second-line therapy for HR+, HER2- advanced breast cancer. *First Author: Patrick Neven, Hospital Gasthuisberg, Leuven, Belgium*

Background: In MONARCH 2 (M2), abemaciclib (A), an oral selective cyclin dependent kinase 4 & 6 inhibitor, + fulvestrant (F) demonstrated statistically significant improvements in progression-free survival (PFS) and overall survival (OS) compared to placebo (P) + F in hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer (ABC). Numerically more pronounced PFS & OS improvement was noted in subgroups (Sub) with visceral (V) disease and primary endocrine resistance. Here we report efficacy data for M2 with respect to 1L and 2L Sub (last line of endocrine therapy [ET] in (neo)adjuvant and metastatic setting, respectively). **Methods:** M2 (NCT02107703) was a global, randomized, double-blind Phase 3 trial of A+ F (N = 446) or P + F (N = 223) in women with ET resistant (ETR) HR+, HER2- ABC regardless of menopausal status. Patients (pts) were stratified by site of metastasis (V, bone-only, or other) and resistance to prior ET (primary vs secondary). Exploratory Sub analyses of PFS and OS were conducted among pts in the ITT population with 1L vs 2L. Hazard ratios (HR) were estimated using Cox models with a test of interactions of Sub with treatment performed. **Results:** At data cut-off (June 20th, 2019), the effect of A + F vs P + F was consistent across 1L (N = 265/133) and 2L (N = 170/86) Sub, with no statistically significant interaction for PFS (p = 0.341) or OS (p = 0.265). For 1L pts, improvements in PFS (HR: 0.57; 95% CI:0.45, 0.73) and OS (HR: 0.85; 95% CI:0.64, 1.14) were observed. Similar efficacy results were observed for 2L pts (PFS: HR: 0.48; [95% CI: 0.36, 0.64]; OS HR: 0.66 [95% CI: 0.46, 0.94]). The numerically largest effects in the 1L population were noted in pts with less favorable prognostic factors such as primary ETR (PFS: HR 0.40 [95% CI: 0.26, 0.63]; OS: HR 0.58 [95% CI:0.35, 0.97]) and V disease (PFS: HR 0.54 [95% CI: 0.39, 0.73]; OS: HR 0.82 [95% CI: 0.57, 1.17]). **Conclusions:** The statistically significant benefit observed in the M2 study was observed across 1L and 2L patients. In 1L patients (A+F Arm), improvements were observed for PFS and OS with the most pronounced effects noted in patients with less favorable prognostic factors. Clinical trial information: NCT02107703. Research Sponsor: Eli Lilly and Company.

1062 Poster Session (Board #147), Fri, 8:00 AM-11:00 AM

A phase II trial of cabozantinib in hormone receptor-positive breast cancer with bone metastases. *First Author: Jing Xu, Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA*

Background: We assessed the antitumor activity of cabozantinib, a potent multireceptor oral tyrosine kinase inhibitor with activity against MET, RET, VEGFR2, and AXL, in patients with hormone-receptor positive (HR+) breast cancer with bone metastases. **Methods:** In this single-arm multicenter phase II study, patients with HR+, HER2- metastatic breast cancer and ≥ 1 prior line of therapy received an initial starting dose of 100 mg cabozantinib, later reduced to 60 mg per day. The primary endpoint was bone scan response rate determined by independent central review and defined as percent change of bone scan area from baseline. The target bone scan response rate was 30% compared to a null response rate of 10%. Secondary endpoints included objective response rate (ORR) by RECIST v1.1, progression free (PFS) and overall survival (OS). Bone scan and CT were obtained every 12 weeks. **Results:** Among 52 enrolled patients, median age was 55, and 54% and 42% had > 2 lines prior endocrine and chemotherapy, respectively and 18 (35%) had bone-only disease. 20 (38%) experienced a partial bone scan response and 6 (12%) had stable disease (SD). 16 (31%) patients discontinued study prior to week 12 assessment for early clinical progression or toxicity, and three (6%) had missing follow-up scans. Best extra-osseous overall response revealed SD in 26 (50%), but no objective responses. In 25 patients with bone scan disease control at 12 weeks, only 3 (12%) developed extra-osseous progression. Median PFS was 4.3 months (90% CI 2.8 - 5.5) and OS was 19.6 months (90% CI 18.0 – 26.8). In a landmark analysis, patients with bone scan disease control at 12 weeks had longer OS (median 24.2 months, 90% CI 16.4 – 31.7) than those without (median OS 13.3 months, 90% CI 9.5 – 18.2), with a hazard ratio of 0.37 (90% CI 0.21 – 0.65). Most common grade 3 or 4 toxicities were hypertension (10%), anorexia (6%), diarrhea (6%), fatigue (4%) and hypophosphatemia (4%). Dose reduction or delay occurred in 42 (81%) patients. **Conclusions:** This study met its primary endpoint with bone scans improved in 38% of patients with metastatic HR+ breast cancer and remained stable in an additional 12% with cabozantinib treatment. Bone scan response correlated with improved OS. This is the first reported study in breast cancer to use bone scan response as a primary endpoint. Further studies with cabozantinib in HR+ breast cancer and additional validation of bone scan response as a surrogate for clinical benefit in breast cancer are warranted. Clinical trial information: NCT01441947. Research Sponsor: Exelixis, Inc, Conquer Cancer Foundation of the American Society of Clinical Oncology.

1063 Poster Session (Board #148), Fri, 8:00 AM-11:00 AM

Prevalence and characterization of dermatologic adverse events related to alpelisib (BYL719) in breast cancer patients. *First Author: Dulce M. Barrios M.S, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Rash develops in approximately 50% of breast cancer patients receiving alpelisib, often requiring dose modifications. Herein, we describe the characteristics of alpelisib-related dermatologic adverse events (dAEs). **Methods:** A single center retrospective analysis was conducted via review of electronic medical records. We collected clinical, laboratory and management data relevant to patients treated with alpelisib for advanced breast cancer under four different randomized clinical trials or post approval by regulatory agencies from 6/1/2013 to 7/31/2019. Type and severity of dAEs was recorded using the Common Terminology Criteria for Adverse Events version 5.0 (CTCAE v5.0). **Results:** A total of 102 patients (mean age 56 years, range 27-83) receiving alpelisib from 200 to 350 mg daily, most frequently in combination with endocrine therapy (79, 77.5%) were included. We identified 41 (40.2%) patients with all-grade rash [CTCAE grade 1/2 = 22 (21.6%); CTCAE grade 3 = 19, (18.6%)] distributed primarily along the trunk (18, 78%) and developing, on average, within 12.8 +/- 1.5 days of treatment initiation (n = 38). Mean duration of rash was 7.1 +/- 3.8 days; and no grade 4 dAEs were observed. Of 29 patients with documented morphology of alpelisib-related dAEs, the majority (26, 89.7%) had maculopapular rash. Thirteen (68%) of 19 patients with any-grade rash and report of any associated symptoms had pruritus (7, 36%) or burning pain (6, 32%). All-grade dAEs correlated with an increase in serum eosinophils from 2.7% to 4.4% ($p < 0.05$), and prophylaxis with non-sedating antihistamines (n = 43) was correlated with a reduction of grade 1/2 rash onset (OR 0.39, p = 0.09). Sixteen (84.2%) of 19 patients with grade 3 dAEs had interruption of alpelisib, followed by management with antihistamines, topical and/or systemic corticosteroids. We did not observe rash recurrence in 12 (75%) of these 16 patients who re-initiated therapy; and the majority (9, 56.3%) were re-challenged *without* a dose reduction. **Conclusions:** Pruritus and increased blood eosinophils occur with maculopapular rash within the first two weeks of initiating alpelisib and persists for approximately seven days. To reduce onset of grade 1/2 rash, non-sedating antihistamines (i.e. cetirizine) are recommended during the first eight weeks. While grade 3 rash leads to interruption of alpelisib, dermatologic improvement is evident with systemic corticosteroids; and most patients can resume therapy at a maintained or reduced dose upon re-challenge. Research Sponsor: U.S. National Institutes of Health.

1064 Poster Session (Board #149), Fri, 8:00 AM-11:00 AM

The effect of neutropenia on patient-reported functioning and quality of life (QOL) among palbociclib participants of the MADELINE study. *First Author: David Richardson, RTI Health Solutions, Research Triangle Park, NC*

Background: MADELINE is an observational, multicenter study of women with HR+/HER2- advanced or metastatic breast cancer who were followed for 6 months to evaluate patient reported QOL after initiating palbociclib combination therapy or other approved treatment in the US. A novel mobile application was developed to capture PROs for QOL at daily, weekly, monthly/cycle-based intervals for up to 6 months. QOL measures were evaluated to determine if palbociclib-treated patients experiencing episodes of neutropenia had associated decreases in QOL compared to patients without episodes of neutropenia. **Methods:** Patients completed the SF-12 and CES-D-10 at baseline and each cycle. Change from baseline was assessed using mean scores and mixed-effects models. Daily pain and fatigue severity were measured on an 11-point scale (0-10, 10 being worst possible pain/fatigue) and averaged to create weekly scores. Patients indicated weekly how breast cancer or its treatment interfered with family/social life, productivity, physical activity and energy on a 5-point scales (from not at all to a great deal). Demographic and clinical data including adverse events were recorded in an eCRF. **Results:** 25 sites contributed 139 patients (median [range] age 60 [34, 82]; white: 83%; ECOG 0-1: 87%). During the 6-month follow up period, 45% of patients experienced ≥1 neutropenia event (grade 1-4: 17%, 27%, 24%, 2%) and 11% had an event resulting in a dose change. Least-square (LS) mean change from baseline to end of study for the SF-12 Physical/Mental Component summaries (PCS/MCS) and the CES-D-10 showed no association between neutropenia and decreased QOL. Daily pain/fatigue was relatively stable for those with neutropenia (cycle 1, week 1: 2.8 [1.95] and 1.8 [0.95]; cycle 6, week 1: 2.4 [1.95] and 2.3 [1.59]) and those without (cycle 1, week 1: 2.2 [2.46] and 2.8 [2.39]; cycle 6, week 1: 1.6 [2.29] and 2.4 [2.22]). There was no significant change for impact of breast cancer or treatment across cycles. **Conclusions:** Patients with neutropenia did not experience decreased QOL compared to patients without neutropenia nor did patients as a whole experience numerically or clinically meaningful decrease in QOL throughout the follow up period. Daily PROs collected suggest a low level of pain/fatigue that did not change substantially over time. Research Sponsor: Pfizer, Inc.

Scale	No Neutropenia Change from baseline (LS Mean, 95% CI)	Neutropenia Change from baseline (LS Mean, 95% CI)
SF-12		
PCS	−0.6 (−2.1, 1.0)	−0.3 (−2.1, 1.6)
MCS	0.9 (−0.6, 2.3)	−0.3 (−2.1, 1.6)
CES-D-10	−0.3 (−1.1, 0.4)	0.8 (−0.1, 1.8)

1065 Poster Session (Board #150), Fri, 8:00 AM-11:00 AM

Combination of fulvestrant and chemotherapy in ESR1 Y537S mutant breast cancer cells and potential synergy mechanism related to p53 wildtype. *First Author: Wen Ma, Dana-Farber Cancer Institute, Boston, MA*

Background: The acquisition of ligand-independent ESR1 mutations during endocrine therapy in metastatic ER+ breast cancer is a common mechanism of resistance to endocrine treatment, particularly aromatase inhibitors, and found in more than 30% of patients with metastatic ER+ breast cancer. Our recent work showed that the ER mutations confer resistance to currently available endocrine treatments while promoting an aberrant ER transcriptional activity that drives metastases. These results underscore the importance of targeting the ESR1 mutations even after the development of endocrine resistance. We hypothesized that during chemotherapy treatment, the ESR1 mutations remain an important driver of tumor growth and metastases and therefore drugs targeting the ESR1 mutation could enhance the efficacy of chemotherapy. In this study we investigated the combination of chemotherapy with the selective estrogen receptor degrader in the presence of WT and mutant ER. **Methods:** We performed synergy studies testing the combination of fulvestrant with chemotherapy treatments commonly used in ER+ metastatic breast cancer including 5FU (representing capecitabine), adriamycin and paclitaxel using MCF7 and T47D breast cancer cell lines engineered to express doxycycline inducible Y537S-ESR1 mutation. **Results:** We found that in MCF7 cells the combination of chemotherapy and fulvestrant was synergistic and the synergy was augmented with the induction of the Y537S mutation. In contrast, there was no synergy in T47D cells that harbor a P53 mutation. We confirmed that the synergistic activity of fulvestrant with chemotherapy is dependent on P53 by generating P53 knock-out MCF7 cells using CRISPR-cas9. Additionally, cell cycle and apoptosis analyses showed that the synergistic activity was mainly due to increased effects on G1 arrest rather than apoptosis. **Conclusions:** Our study indicates that chemotherapy and fulvestrant are synergistic in ER+ breast cancer and the synergy is increased in the presence of the Y537S ESR1 mutation and is dependent on P53 activity. These results support a clinical trial testing the addition of fulvestrant or other novel selective estrogen receptor degraders in patients with metastatic ER+ breast cancer who are starting chemotherapy treatment. Research Sponsor: U.S. National Institutes of Health.

1066 Poster Session (Board #151), Fri, 8:00 AM-11:00 AM

Phase Ib trial to evaluate safety and anti-tumor activity of the AKT inhibitor, ipatasertib, in combination with endocrine therapy and a CDK4/6 inhibitor for patients with hormone receptor positive (HR+)/HER2 negative metastatic breast cancer (MBC) (TAKTIC). *First Author: Seth Andrew Wander, Massachusetts General Hospital Cancer Center, Boston, MA*

Background: The cyclin-dependent kinase 4/6 inhibitors (CDK4/6i), with an anti-estrogen, are the standard of care for HR+/HER2- MBC. Insights from patient biopsies and preclinical analysis suggest that AKT1 activation can provoke CDK4/6i resistance. We hypothesized that targeting AKT1 following CDK4/6i progression may provide clinical benefit. **Methods:** TAKTIC is an open-label phase Ib trial exploring the combination of the AKT1 inhibitor, ipatasertib (ipat), with an aromatase inhibitor (Arm A), fulvestrant (Arm B), or the triplet combination (Arm C) of fulvestrant + ipat + palbociclib (palbo). The primary objective is to evaluate the safety and tolerability of ipat in combination with endocrine therapy +/- CDK4/6i. Key inclusion criteria include unresectable HR+/HER2- MBC; at least 1 prior therapy for MBC including any CDK4/6i; up to 2 prior lines of chemotherapy for MBC (no limit on prior endocrine therapy). Here, we present an interim analysis from the triplet combination (Arm C). **Results:** As of 1/31/2020, 25 pts have enrolled, including 12 on Arm C, all of whom received prior CDK4/6i (median no of prior lines = 5.5, range 2-7). Along with fulvestrant, 3 pts received ipat at 200mg + 125mg palbo, 7 pts received 300mg + 125mg palbo, and 2 pts received 400mg + 100mg palbo. To date, 8/12 pts remain on treatment including 2 with partial response, 3 with stable disease, 3 with restaging studies pending and 4 with progressive disease. The triplet combination was well tolerated. Grade 3 toxicities included reduced WBC (8/12), reduced neutrophil count (11/12), reduced lymphocyte count (2/12) and single instances of transaminitis, rash, and reduced platelet count. The only grade 4 toxicity was reduced neutrophil count (4/12). There were no DLTs observed and no discontinuations due to toxicity. Mean steady state pharmacokinetic parameters for ipat were similar to historical data from single agent trials suggesting that combined treatment with palbo + fulvestrant did not affect the pharmacokinetics of ipat. Updated analysis will be presented at the meeting. **Conclusions:** The triplet combination of endocrine therapy with CDK 4/6i and AKTi appears to be well tolerated in heavily pre-treated pts, with a subset demonstrating signs of clinical benefit. The trial demonstrates how insights into the molecular mechanisms of CDK4/6i resistance could be leveraged into actionable therapeutic regimens for HR+/HER2- MBC. Clinical trial information: NCT03959891. Research Sponsor: Genentech, Inc.

1067 Poster Session (Board #152), Fri, 8:00 AM-11:00 AM

Serum biomarkers of inflammation (ferritin, IL-8, TNFR1) and outcomes in BOLERO-2, a phase III trial of HR+/HER2- metastatic breast cancer treated with everolimus (mTOR inhibitor). *First Author: Suhail M. Ali, Lebanon VAMC, Lebanon, PA*

Background: Everolimus (EVE) plus exemestane (EXE) doubled PFS while maintaining quality of life versus EXE alone in postmenopausal hormone receptor-positive (HR^+), HER2-negative metastatic breast cancer (MBC) (BOLERO-2 phase 3; NCT00863655). Here we investigated several serum biomarkers of inflammation: ferritin, interleukin-8 (IL-8), and tumor necrosis factor receptor 1 (TNFR1). Both higher IL-8 (ASCO 2018, #3025) and TNF (Nature 569:428-32, 2019) have been reported to be associated with worsened outcome to immune checkpoint inhibitors (ICI), and IL-8- and TNF-targeted therapies combined with ICIs are in phase I trials. We evaluated the prognostic/predictive ability of serum ferritin, IL-8, and TNFR1 to everolimus in BOLERO-2. **Methods:** Serum biomarkers were determined on pretreatment serum samples using the ELLA immunoassay platform (ProteinSimple, San Jose, CA). Cox-proportional hazards model was used to assess the efficacy of EVE, and the prognostic and predictive effect on PFS and OS. **Results:** Pretreatment serum biomarker levels were determined in 510 patients (70 %) of 725 BOLERO-2 patients randomized 2:1 to EVE+EXE or EXE). Serum levels (25%, 50%, 75%) were: ferritin (68.9, 125.5, 253.1 ng/ml); IL-8 (14.5, 19.4, 27.7 pg/ml); and TNFR1 (1205, 1470, 1868 pg/ml). Ferritin correlated significantly with TNFR1 ($r=0.45$, $p<0.0001$), while IL-8 correlated weakly with TNFR1 ($r=0.10$, $p=0.023$). Higher levels of all 3 biomarkers were prognostic for significantly shorter PFS and OS (table). But no biomarkers were predictive: everolimus was efficacious regardless of the 3 biomarker levels ($p>0.05$). **Conclusions:** High levels of serum ferritin, IL-8, and TNFR1 were significantly associated with shorter PFS and OS in HR+/HER2- MBC patients. Everolimus had superior outcomes compared to placebo, regardless of serum biomarker level. These 3 significant prognostic biomarkers are all associated with increased inflammatory processes through different pathways. Anti-inflammatory therapy targeted against these biomarkers should be evaluated based on serum level as potential combination therapy with everolimus or CDK 4/6 inhibitors in HR+ MBC. Research Sponsor: Novartis.

Biomarker	Level	# patients	Median PFS (mo)	HR (PFS)	95% CI (PFS)	Median OS (mo)	HR (OS)	95% CI (OS)
IL-8								
	low	128	6.8			39.2		
	middle	256	6.8	1.11	0.87 - 1.42	30.7	1.34	1.00 - 1.80
	high	127	2.9	1.84	1.39 - 1.84	17.5	2.47	1.80 - 3.40
TNFR1								
	low	128	6.8			36.5		
	middle	255	6.8	1.15	0.90 - 1.47	33.6	1.25	0.93 - 1.69
	high	127	4	1.85	1.40 - 2.44	17.5	2.72	1.98 - 3.73

1068 Poster Session (Board #153), Fri, 8:00 AM-11:00 AM

Pazopanib (PZ) plus endocrine therapy as treatment for hormone resistant advanced breast cancer (ABC). *First Author: Ozge Gumusay, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, CA*

Background: A major limitation of endocrine therapy in hormone receptor positive (HR+) ABC is the development of resistance. Preclinical data suggests that higher levels of vascular endothelial growth factor (VEGF) are associated with endocrine therapy resistance. We conducted a phase II trial to evaluate the clinical benefit (CB) of PZ, a VEGF receptor tyrosine kinase inhibitor (TKI) combined with nonsteroidal aromatase inhibitors (NSAIs) in pts with ABC resistant to NSAIs. **Methods:** Eligibility included postmenopausal women with HR+ ABC and progressive disease (PD) after at least one month of NSAIs. Treatment was PZ 800 mg/day plus either letrozole or anastrozole. The primary endpoint was clinical benefit rate at 12 weeks (CBR12, wks). Secondary endpoints were PFS and safety. A CBR of 20% was considered a clinically meaningful comparison to the expected CBR of $< 5\%$ with continued NSAIs after PD. Using a 2-stage design, stable disease in at least 1 of the first 13 pts allowed continued enrollment to a planned 28. **Results:** 32 pts were enrolled; 28 are evaluable for study endpoints and all patients completed the study. The median age was 58 years (range: 41-77). Pts were heavily pre-treated, with a median of 2 prior hormone therapies (range 1-6) and 1 prior chemotherapy (range 0-8). 8 pts (28.6%) stopped treatment due to adverse events (AE) including hypertension (HTN), fever, transaminitis, nausea, vomiting, rash, hand foot syndrome and pulmonary embolism (PE); 6 pts progressed before wk 12. CBR12 was 46.4% (12 SD, 1 PR); CBR24 was 25% (5 SD, 2 PR). Median PFS was 20 wks (95% CI 11-48, and median PFS for pts with CBR12 was 24 wks. 7 pts had PFS $>$ 6 months (24, 32, 36, 36, 48, 184 and 274 wks); 2 pts had PFS $>$ 3 years (184 and 274 weeks). The most common grade 1/2 AE were nausea (48.2%), fatigue (33.3%), diarrhea (29.6%), back pain (22.2%), and arthralgias (22.2%). Grade 3/4 AEs included HTN (3/28; 11.1), transaminitis (3/28; 11.1%), headache (2/28; 7.4), heart failure, vertigo, nausea, oral pain, vomiting, fever, fatigue, and hypokalemia (one patient each: 3.7%). **Conclusions:** The addition of PZ to NSAIs resulted in a CBR12 of 46.4%, and a CBR24 of 25% in pts with heavily pre-treated ABC resistant to NSAIs. These results support clinical efficacy of antiangiogenic TKI in HR+ ABC, and suggest benefit in hormone resistant disease. Expected toxicities resulted in early discontinuation in 28.6%, which limited drug exposure. Clinical trial information: NCT 01466972. Research Sponsor: GSK/Novartis.

1069 Poster Session (Board #154), Fri, 8:00 AM-11:00 AM

***PIK3CA* mutation status and progression-free survival in advanced hormone receptor positive (HR+)/ human endocrine receptor negative (HER2–) metastatic breast cancer (mBC): A meta-analysis of published clinical trials.** *First Author: James Signorovitch, Analysis Group, Inc., Boston, MA*

Background: Approximately 40% of HR+/HER2- mBC patients harbor *PIK3CA* mutation. Associations between *PIK3CA* mutation status and clinical outcomes among patients with HR+/HER2- mBC have been heterogeneous across clinical trials. We synthesized available evidence from clinical trials to estimate the association between *PIK3CA* status and progression-free survival (PFS) using a meta-analysis adjusting for study design differences. **Methods:** Randomized clinical trials reporting PFS stratified by *PIK3CA* status in HR+/HER2- mBC were identified via a systematic literature review. Trial arms receiving *PIK3CA* targeted therapies were excluded. Median PFS, 6-, 12- and 18-month PFS rates, and data on trial design features were extracted. Associations between *PIK3CA* status and PFS were estimated adjusting for study follow-up duration, *PIK3CA* testing method (ctDNA vs tissue) and study treatment using multi-level random effects meta-regression. **Results:** The analyzed data included 3,238 patients from 33 study arms across 11 trials (*PIK3CA* mutated (MT): 1,386, wild type (WT): 1,852). *PIK3CA* mutation was overall associated with shorter median PFS (difference [95% CI] (months): -2.15 [-4.14, -0.15]) with substantial heterogeneity across studies ($I^2 = 98.34\%$). The direction of this association was robust to adjustment for study treatment (-1.27 [-2.22, -0.32]). The association was stronger for ctDNA testing (-2.16 [-3.65, -0.66]; N (total patients): 1,876) than for tissue testing (-0.65 [-2.2, 0.91]; N: 998). Findings were similar for 6-month PFS rates (absolute rate difference -9.17% [-14.22, -4.12], N: 3,179; MT: 1,366, WT: 1,813). Associations were directionally consistent but not statistically significant at 12 months (N = 2,487; MT: 1,056, WT: 1,431) and 18 months (N = 1,745; MT: 811, WT: 934), potentially due to the decreasing precision towards the tails of the PFS curves and significant heterogeneity across studies. **Conclusions:** Pooling evidence across multiple studies, *PIK3CA* mutation was associated with shorter PFS, especially when ctDNA testing was used. These findings suggest a negative prognostic value of *PIK3CA* mutation in patients with HR+/HER2- mBC. Research Sponsor: Novartis.

1070 Poster Session (Board #155), Fri, 8:00 AM-11:00 AM

Phase I/II study of SAR439859, an oral selective estrogen receptor degrader (SERD), in estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer (mBC). *First Author: Mario Campone, Institut de Cancérologie de l'Ouest, René Gauducheau, St Herblain, France*

Background: SERDs competitively antagonize and degrade the ER and can block signaling in ER-dependent tumors resistant to standard endocrine therapy (ET). This study (NCT03284957) investigates SAR439859, a potent oral SERD, in ER+/HER2- mBC. We present pooled dose escalation/expansion (Part A/B) data for SAR439859. **Methods:** Postmenopausal patients (pts) with ER+/HER2- mBC treated for ≥ 6 mos with prior ET received SAR439859 ≥ 150 mg QD (Part A) or 400 mg QD (Part B). Chemotherapy and targeted therapy in the advanced setting were allowed. Objective response rate (ORR; RECIST v1.1), clinical benefit rate (CBR; complete or partial response [PR] or stable disease [SD] ≥ 24 weeks), safety, and pharmacokinetics (PK) were assessed. **Results:** Pts (n = 62; Part A, 13; Part B, 49) had a median age of 63 yrs (range 37–88) and ECOG PS 0 (59.7%) or 1 (40.3%); 93.5% had visceral disease. All had prior ET, 74.2% had prior targeted therapy and 48.4% had ≥ 3 prior lines in the advanced setting. 61.3% of pts had treatment-related adverse events (TRAEs), all grade 1–2. Most frequent: hot flush (16.1%), constipation, arthralgia (both 9.7%), decreased appetite, vomiting, diarrhea, nausea (all 8.1%), fatigue (6.5%). No pts discontinued due to AEs. CBR was 35.6% overall, with antitumor activity irrespective of *ESR1* mutation status (Table). In pts with no prior SERD, CDK4/6 or mTOR inhibitors (n = 14), ORR was 21.4% and CBR 64.3%. PK data for Part B and *ESR1* mutation data will be provided. **Conclusions:** SAR439859 had a favorable safety profile with limited TRAEs. In these heavily pre-treated pts (prior targeted therapy in 74.2%), ORR and CBR were similar to historical fulvestrant performance in pts with no prior targeted therapy. Encouraging ORR and CBR in pts with no prior SERD, CDK4/6 or mTOR inhibitors (n = 14; ORR 21.4%; CBR 64.3%) supports SAR439859 development in earlier lines of therapy. Clinical trial information: NCT03284957. Research Sponsor: Sanofi.

Pts, n (%)	All n = 59	*ESR1* wildtype n = 30[a]	*ESR1* mutant n = 28[a]
Best response			
PR	4 (6.8)	3 (10.0)	1 (3.6)
SD	25 (42.4)	12 (40.0)	13 (46.4)
Progressive disease	30 (50.8)	15 (50.0)	14 (50.0)
ORR	4 (6.8)	3 (10.0)	1 (3.6)
CBR	21 (35.6)	12 (40.0)	9 (32.1)

[a]*ESR1* status available for n = 58

1071 Poster Session (Board #156), Fri, 8:00 AM-11:00 AM

A phase II study of rh-endostatin in combination with chemotherapy in human epidermal growth factor receptor 2 (HER-2) negative advanced breast cancer (ABC). *First Author: Yuan Huang, Institute of Cancer and Basic Medicine (ICBM), Chinese Academy of Sciences, Department of Breast Medical Oncology, Cancer Hospital of the University of Chinese Academy of Sciences, Department of Breast Medical Oncology, Zhejiang Cancer Hospital, Hangzhou, China*

Background: There is an urgent need to improve the efficacy of chemotherapy for HER-2 negative patients (pts) who lack anti-HER-2 therapies. Rh-Endostatin (endostar), a recombinant human endostatin, is a potent inhibitor of angiogenesis. This single-arm multicenter phase 2 study was designed to assess the efficacy and safety of endostar combined with chemotherapy in HER-2 negative ABC. **Methods:** Eligible pts had HER-2 negative inoperable locoregionally recurrent or metastatic breast cancer and an ECOG PS of 0 or 1. Pts with either measurable or nonmeasurable disease were eligible. Endostar (15 mg/m^2, continuous infusion, day 1-7) plus chemotherapy were administered every 21 days until disease progression, intolerable toxicity or other reasons. Chemotherapy regimens were selected by investigators based on clinical decision. Primary endpoint was progression-free survival (PFS). Secondary endpoints included objective response rate (ORR), disease control rate (DCR) and adverse events (AEs). **Results:** From August 2016 to December 2019, 40 female pts were enrolled in 3 centers. The median age was 52. Ten pts were previously untreated and 30 pts had at least 1 line of chemotherapy for advanced disease. 31 pts were triple negative BC (TNBC) and 9 pts were hormonal receptor positive (HR+). Platinum combined with paclitaxel or gemcitabine were administered with endostar in 55% of pts. Others received paclitaxel or gemcitabine combined with endostar. 12 pts achieved a best response of partial response (PR) and 13 pts had stable disease (SD). Among 30 pts with measurable disease, ORR was 40% and DCR was 83%. The ORR for patients treated as the first-line therapy was 75% while as the second line or beyond was 27%. For TNBC and HR+ BC pts, the ORR was 46% and 17% respectively. Median PFS was not reached after a median follow-up of 7.6 months. The most common Grade 3/4 AEs observed during this study were neutropenia (10%), leukopenia (10%) and thrombocytopenia (5%). **Conclusions:** Endostar combined with chemotherapy was effective and well tolerated for the treatment of HER-2 negative ABC, especially TNBC. Its efficacy and safety could be further studied in randomized trials. Clinical trial information: NCT03907098. Research Sponsor: Simcere.

1072 Poster Session (Board #157), Fri, 8:00 AM-11:00 AM

Preliminary safety and efficacy of GX-I7, a long-acting interleukin-7, in combination with pembrolizumab in patients with refractory or recurrent metastatic triple negative breast cancer (mTNBC): Dose escalation period of Phase Ib/II study (KEYNOTE-899). *First Author: Joohyuk Sohn, Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea*

Background: Pembrolizumab monotherapy did not significantly improve OS as 2nd and 3rd-lines treatment for mTNBC compared to standard chemotherapy in phase III study (KEYNOTE-119) leading to high unmet needs of effective treatment. Recent studies showed that higher lymphocyte count is an independent factor which correlates with better response to checkpoint blockade in cancer patients. GX-I7, a long-acting interleukin-7, could potentially provide synergistic anti-tumor efficacy with pembrolizumab by increasing number of T cells both in tumor microenvironment (TME) and peripheral blood (PB). **Methods:** This is an open-label, phase Ib/II study in patients with refractory or recurrent TNBC who failed from standard chemotherapy in the metastatic setting, with ≤3rd-lines of previous chemotherapy. The dose escalation phase adopted the 3+3 design. The GX-I7 doses were administered IM q9w or q12w, with or without cyclophosphamide pre-conditioning depending on the allocation, and in combination with pembrolizumab 200 mg IV q3w. The objectives were dose limiting toxicities (DLTs), safety, pharmacodynamic markers including lymphocyte increase and RP2D. **Results:** As of January 30, 2020, GX-I7 and pembrolizumab were exposed to 24 patients (median age 46.0 years [29-75], ECOG PS 1 [58.3%], median cycle no. 3 [1-9]). Treatment was discontinued in 13 (54.2%), majority due to PD and 11 patients are ongoing. No DLTs were reported in all dose groups. Treatment related AEs occurred in 91.7% of patients with grade 1-2 and 9.1% with grade 3 (no grade 4). Common AEs were injection site reaction (39.0%) and fever (13.0%), which were easily managed. Grade 3 toxicity were AST/ALT elevation and infusion related reaction, reported from 1 patient each (4.2%). GX-I7 induced dose-dependent lymphocyte proliferation in PB, with approximately 4-folds increase in high doses. 17 patients were evaluable; confirmed objective responses from ongoing patients included one partial response (5.9%), 2 stable disease (11.8%) and 1 durable unconfirmed PD (5.9%). **Conclusions:** GX-I7 in combination with pembrolizumab was well tolerated, with no DLTs reported. There was no apparent increase of immune-related AEs with the addition of GX-I7. Pharmacodynamics data support proof of mechanism and it warrants further clinical studies. Clinical trial information: NCT03752723. Research Sponsor: Korea Drug Development Fund, Pharmaceutical/Biotech Company.

1073 Poster Session (Board #158), Fri, 8:00 AM-11:00 AM

Dual anti-CTLA-4 and anti-PD-1 blockade in metaplastic carcinoma of the breast: Dart (SWOG S1609, Cohort 36). *First Author: Sylvia Adams, New York University Cancer Institute, New York, NY*

Background: Immune checkpoint blockade, specifically anti-CTLA-4 and anti-PD-1-directed approaches, has improved outcomes in various tumors and is being tested in SWOG S1609 in rare solid tumors (DART=Dual Anti-CTLA-4 & Anti-PD-1 blockade in Rare Tumors). Metaplastic breast cancer (MpBC) is a rare subtype of breast cancer with poor response to cytotoxics and median survival of < 1 year for metastatic disease. A MpBC stratum was added based on promising activity of immunotherapy in a patient with MpBC (Adams, npj Breast Cancer 2017). Here, we report the MpBC cohort of S1609 DART. **Methods:** In this prospective, open-label, multicenter phase II trial patients received ipilimumab (1mg/kg q6 weeks) plus nivolumab (240mg intravenously every 2 weeks). Eligibility for cohort 36 required histologically confirmed MpBC, measurable disease, and ECOG PS 0-2. Prior anti-CTLA4 or anti-PD-1/PD-L1 treatment (but not both) was permitted as well as treated brain metastases. The primary endpoint was overall response rate (ORR, confirmed CR, PR) by RECIST v1.1; 2 or more responses in 16 patients was considered a success. Secondary endpoints: toxicity (CTCAE v4.0), PFS and ORR by immune-related RECIST (iRECIST), overall survival (OS). Biomarker analyses are ongoing. **Results:** Nineteen patients were registered to the cohort and seventeen eligible patients received therapy. The median age was 60 (range 26-85), most tumors were high grade, triple negative and had a high ki67 (median 87%), median prior therapy = 2 lines. The ORR was 12% (RECIST 1.1) and 18% (iRECIST), with ongoing responses at 23, 18 and 11 months, respectively; SD was seen in 24%, none $>$ 6 months (Table). Median OS was 12 months. AEs were observed in 11 patients (65%), with 3 patients (18%) having Grade 3/4 AEs and 1 patient with a fatal AE (myocarditis). The most common toxicities were LFT abnormalities and fatigue. **Conclusions:** Cohort 36 met its primary endpoint: ipilimumab plus nivolumab was clinically active in advanced MpBC, with durable responses observed in 3/17 patients. Further investigation of this combination is warranted. Clinical trial information: NCT02834013. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

Metaplastic breast cancer (n=17)	RECIST 1.1	iRECIST
CR	0 (0%)	1 (6%)
PR	2 (12%)	2 (12%)
Unconfirmed PR	1 (6%)	0 (0%)
SD	4 (24%)	4 (24%)
PD or not assessed*	10 (59%)	10 (59%)
ORR (CR + PR)	2 (12%)	3 (18%)
Duration of response	23 and 18 months, both ongoing	23, 18, and 11 months, all ongoing
PFS at 6 months	12% (3%, 43%)	18% (6%, 49%)
Median PFS and OS	2 and 12 months	2 and 12 months

*1 death and 1 consent withdrawal (after first cycle) before assessment

1074 Poster Session (Board #159), Fri, 8:00 AM-11:00 AM

Evaluation of DNA repair biology signatures to predict specific carboplatin (C) versus docetaxel (D) benefit in advanced triple-negative breast cancer (aTNBC). *First Author: Holly Tovey, Clinical Trials and Statistics Unit, The Institute of Cancer Research, London, United Kingdom*

Background: In the Triple Negative Trial we observed no improved response rate (RR) to C over D in aTNBC [Tutt et al, Nat Med 2018], but we did in *BRCA1/2* mutated (mut) patients (pts). We hypothesise tumors with other aberrant DNA damage response (DDR) characteristics having higher RR to DNA damage inducing C than D. **Methods:** We tested the predictive value of DDR process related gene expression signatures (PARPi7, chromosomal instability CIN70, TP53 & DDR Deficiency (DDRD)) on 192 treatment naïve primary tumours (PT) by total RNA-sequencing. Odds ratio (OR) for RR are reported. Paired PT & recurrent (REC) signature scores were compared. **Results:** Unexpectedly, high DDRD and PARPi7 were associated with higher RR to D than C (p =0.01 & 0.06). No effect was observed for CIN70 or *TP53* signature. To assess whether the unexpected results were due to biological changes 12 PT-REC pairs were available from pts who received chemotherapy (CT) between PT & REC. CIN70 increased from PT to REC, DDRD (non-significantly) & PARPi7 decreased. 4/5 *TP53* wildtype classified PT samples classified as mut in REC. The *BRCA1/2* & DDRD-treatment interactions only held in pts who received CT before trial entry (table). The PARPi7-treatment interaction only held in CT naïve pts. In CT naïve pts, high CIN70 tumors suggested higher C RR as hypothesized. Restricted to the 149 PAM50 basal-like pts, results were non-significant but similar trends seen. **Conclusions:** In this trial of aTNBC, DDRD high pts with prior CT had better RR to D than C. A possible explanation for this unexpected result is selective pressure of adjuvant DNA damaging CT and selection for relative taxane sensitivity in those who recur despite a high DDRD score. The hypothesised CIN70 treatment interaction was observed in CT naïve pts. Our results suggest care is required in application of signatures to initial diagnostic material when predicting response to DNA damaging agents at REC particularly in pts with prior CT. Research Sponsor: Cancer Research UK and Breakthrough Breast Cancer.

Odds ratios (OR) within treatment by CT status.

	CT Status (n)	C: OR (95%CI)	D: OR (95%CI)	Interaction *p*
BRCA1/2*	Naïve (78)	1.48 (0.21 – 10.46)	0.98 (0.19 – 5.03)	0.75
	Treated (236)	8.00 (2.65 – 24.14)	0.92 (0.22 – 3.78)	0.02
DDRD	Naïve (36)	0.08 (0.00 - 4.58)	2.10 (0.06 - 69.05)	0.23
	Treated (156)	1.44 (0.35 - 5.84)	24.83 (3.41 - 180.95)	0.02
PARPi7	Naïve (36)	0.07 (0.00 - 1.62)	5.26 (0.77 - 35.93)	0.02
	Treated (156)	0.75 (0.37 - 1.54)	1.35 (0.61 - 2.99)	0.29
CIN70	Naïve (36)	56.38 (0.82 - 3874.77)	0.94 (0.31 - 2.81)	0.07
	Treated (156)	0.76 (0.37 - 1.57)	0.58 (0.25 - 1.32)	0.62

*Mut vs. wildtype

1075 Poster Session (Board #160), Fri, 8:00 AM-11:00 AM

RNA sequencing analysis and T-cell receptor repertoire in triple-negative breast cancer (TNBC). *First Author: Ju Won Kim, Korea University Anam Hospital, Seoul, South Korea*

Background: Triple negative breast cancer (TNBC) is defined by the lack of two hormone receptors (HR) and human epidermal growth factor receptor 2 (HER2), and well known to have poor prognosis. In this study, we conducted a RNA sequencing including T-cell receptor (TCR) repertoire analysis to develop prognostic biomarker in patients with TNBC. In addition, genes and signaling pathways that correlated with selected biomarker were also investigated. **Methods:** Total of 78 tumor tissues from TNBC patients were participated for RNA-seq (IIlumina Hiseq) analysis. Groups of significant genes were selected by differentially expressed genes (DEGs) analysis, whose expression levels differed more than 1.5 times between patients and normal, or early stage and advanced stage TNBC. Transcript expression levels for prognostic biomarker were analyzed based on R v3.4.3. Using CBS ProbePINGS, a genomic big data analytics platform, we evaluated druggable pathways and protein-protein interaction (PPI). The Interaction Frequency Ratio Score (IFRS) was calculated by investigating highly interactive pathways, and the drugs were matched to patients. TCR repertoire analysis was performed by MiXCR. **Results:** Ten candidate gene signatures were selected based on RNA sequencing data of each sample. Cross-validation through machine learning showed that the accuracy of the first-ranked signature was 92.3%, the second was 92.0%, and the third was 90.3%. The accuracy of 4^{th} to 6^{th} was 88.7%, and the accuracy of 7^{th} to 10^{th} was over 88.0%. Cross-validated gene signature, age, and TNM staging showed significant discriminant power under univariate Cox regression analysis ($p < 0.05$). In the CBS ProbePINGS, human papillomavirus infection, MAPK pathway, and tumorigenesis pathway were correlated with cell signaling. CDK2, FN1, and JUN genes were highly interactive each other. In addition, the drug matching result according to IFRS value suggested imatinib and regorafenib could be possible candidates. TCR repertoire analysis presented that number of clonecount was lower in recurrent or metastatic TNBC than early stage cancer. **Conclusions:** This study revealed a specific gene signatures that can accurately determine recurrence and metastasis in patients with TNBC based on RNA sequencing analysis. TCR repertoire analysis and CBS ProbePINGS could be valuable method in treatment selection Research Sponsor: None.

1076 Poster Session (Board #161), Fri, 8:00 AM-11:00 AM

A phase Ib trial of the cyclin-dependent kinase inhibitor dinaciclib (dina) in combination with pembrolizumab (P) in patients with advanced triple-negative breast cancer (TNBC) and response correlation with MYC-overexpression. *First Author: Amy Jo Chien, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

Background: Increased expression of the MYC transcriptional oncogene is found in about 70% of TNBC and is associated with poor prognosis. In MYC-overexpressing TN xenografts, CDK1 inhibition with dina results in synthetic lethality, and attenuates distant metastasis. In syngeneic models, the combination of dina with anti-PD1 therapy is synergistic and increases immune cell tumor infiltration and activation. **Methods:** Patients (pts) with advanced TNBC received dina IV day 1 and 8 in combination with fixed dose P 200 mg once every 21 days. Dina was dose escalated using a toxicity probability interval design targeting a dose limiting toxicity (DLT) rate of 25%. Evaluable disease and pre-treatment metastatic biopsies were required. After 17 pts were enrolled, eligibility was amended to require $\leq$2 lines of prior chemotherapy, and LDH $\leq$1.5x normal. MYC IHC was performed on baseline tumor biopsies and correlated with clinical response using Welch's unequal variances t-test. **Results:** 32 pts were enrolled (median age 53, median 2 prior lines of therapy, 13 pts (41%) had disease which was previously ER+). 18 pts were enrolled in the dose escalation phase with no observed DLTs; 33 mg/m2 was determined to be the recommended phase 2 dose (RP2D). 14 additional patients were enrolled in dose expansion at 33 mg/m2, completing trial accrual. Grade $\geq$3 adverse events (AEs) in all pts included neutropenia (ntp) (37.5%), febrile ntp (12.5%), fatigue (12.5%), transaminitis (3.2%), and neuromuscular weakness (3.2%). Most common all grade AEs included fatigue (63%), diarrhea (63%), nausea (63%), and ntp (53%). Possible immune-related AEs included sinusitis (4 pts), hemolytic anemia (1 pt), pneumonitis (1 pt), rash (2 pts), neuromuscular weakness (1 pt), and transaminitis (1 pt). Of the 29 patients evaluable for response, 1 pt (3.4%) had a CR, 4 pts (13.8%) had a PR, and 6 pts (20.6%) had SD. MYC IHC staining on baseline metastatic tumor biopsies in 19 pts correlated significantly with clinical response. Additional biomarker testing will be reported. **Conclusions:** The RP2D of dina given in combination with standard dose P is 33 mg/m2 on D1, 8 of a 21-day cycle. Toxicities were generally manageable and non-overlapping. In exploratory analysis, greater MYC IHC staining correlated significantly with response to study therapy. Clinical trial information: NCT01676753. Research Sponsor: Merck, U.S. National Institutes of Health.

1077 Poster Session (Board #162), Fri, 8:00 AM-11:00 AM

Preliminary efficacy data of triple-negative breast cancer cohort of NCI 9881 study: A phase II study of cediranib in combination with olaparib in advanced solid tumors. *First Author: Navid Hafez, Yale University School of Medicine, New Haven, CT*

Background: Cediranib, a pan-vascular endothelial growth factor receptor tyrosine kinase inhibitor, suppresses expression of *BRCA1, BRCA2*, and *RAD51* and increases sensitivity of tumors to poly-(ADP-ribose) polymerase (PARP) inhibitors *in vitro*. Olaparib, a PARP inhibitor, demonstrates clinical efficacy in patients with germline *BRCA1/2* mutations and HER2-negative metastatic breast cancer. We therefore tested the anti-tumor activity of the combination of cediranib and olaparib in patients (pts) with metastatic triple-negative breast cancer (TNBC). **Methods:** This multi-institutional, two-stage, phase II study enrolled patients with metastatic TNBC previously treated with a minimum of one prior line of systemic therapy in the advanced setting. Patients were treated with cediranib 30mg po daily plus olaparib 200mg po BID until disease progression or unacceptable toxicity. The primary endpoint was objective response rate by RECIST v1.1. Baseline tumor biopsies were obtained for biomarker analyses. **Results:** Baseline characteristics of the 37pts enrolled are summarized below. The overall objective response rate was 14% (95% CI: 0.025, 0.2453). Median duration of response was 2.0 months (mos) with a range of 1.8 to 6.3 mos. Disease control rate ((# of pts with CR, PR or SD)/(# of evaluable pts)) was 81% (95% CI: 0.6846, 0.937). Median PFS was 3.7 mos (95% CI: 2.1, 4.3). Grade 3/4 adverse events (G3/4 AEs), irrespective of attribution, occurred in 25 of 38 (66%).G3/4 AEs occurring in $>$ 5% of pts were hypertension (24%) and dyspnea (11%), diarrhea (8%) vomiting (8%). **Conclusions:** The cediranib/olaparib combination resulted in promising objective responses in 14% of biomarker-unselected patients with heavily pre-treated, metastatic TNBC. The regimen required prompt initiation of antihypertensives, but AEs were overall manageable. Analyses of mutation status in homologous recombination DNA repair genes are ongoing and will be correlated with clinical outcome. Clinical trial information: NCT02498613. Research Sponsor: U.S. National Institutes of Health.

	Total N = 37, Median (range)
Age	49 (32-68)
ECOG PS	1 (0-1)
# of prior therapies	4 (2-11)
Prior platinum-based chemotherapy	92%
Platinum-sensitive (> 90 days interval to start subsequent therapy)	19%
Prior immunotherapy	41%

1078 Poster Session (Board #163), Fri, 8:00 AM-11:00 AM

Translational relevance of androgen receptor immunohistochemistry scoring systems for data harmonization in triple negative breast cancer (TNBC). *First Author: Suhail Sayeed Mufti, HealthCare Global Enterprises Ltd, Bangalore, India*

Background: Androgen receptor (AR) expressing triple negative breast cancer (TNBC) is a sub-set of TNBC with an evolving prognostic and predictive behaviour. AR immunohistochemical threshold for positivity has not been standardized and a wide range of cut-offs have been used across studies ($>$ 0% to 75%). In this study we explored AR immunohistochemistry thresholds in relation to disease free survival (DFS) and clinical outcomes in non-metastatic TNBC using the Allred and H-Score systems. Increasing interest in AR as a therapeutic target for TNBC and the use of digital tissue image analysis makes it important to standardize AR immunohistochemistry reporting. **Methods:** 100 FFPE (formalin-fixed paraffin-embedded) tumour blocks were retrieved for non-metastatic TNBCs diagnosed between January 2015 and May 2017 and immunostained using AR441 (IgG1) mouse monoclonal antibody. Clinical follow-up ranged from 59 to 31 months and DFS was calculated. Cut-off scores were explored using *Evaluate Cutpoints* (*R maxstat* package) and *X-tile* software. The score with maximum split in DFS (based on log-rank statistics and lowest p-value) was chosen as the cut-off. Descriptive and survival statistics was performed. **Results:** The median age was 51 (SD 11.262; range 28 to 82) years. Using *Evaluate Cutpoints* $\geq$3 was found as the threshold for AR by Allred Score. 36% cases were AR positive using Allred score (HR 0.508; CI 0.234 - 1.11; p-value 0.08). Using *Evaluate Cutpoints* $\geq$30 was found as the threshold for AR by H-Score (HR 0.624, CI 0.306 - 1.27; p-value 0.19). 35% cases were AR positive using H-Score. *X-tile* analysis also found the cut-offs as $\geq$3 and $\geq$30 for Allred and H-Score respectively ($p < 0.05$). A significant correlation was seen between the two scoring systems (Pearson Correlation 0.935; $p < 0.01$). A significantly higher number of grade III TNBCs were AR negative (n = 55/76) compared to grade II (n = 9/24) (p = 0.002). Cut-off for Ki67 was 75 (HR 1.61, CI 0.85-3.04, p-value 0.141) with a significantly higher number of AR negatives in the Ki67$\geq$75 group (21/26; $p < 0.05$). The overall median DFS was 51.9 months. There was no significant difference in DFS for the AR negative (median: 47.4 months; mean: 39.39 months) and AR positive (Median survival not reached; mean: 41.3 months) groups(p = 0.23). **Conclusions:** AR immunohistochemistry cut-offs using the Allred ($\geq$3) and H-Score ($\geq$30) are close to the ones used for ER/PR immunohistochemistry as per ASCO/CAP guidelines, making a strong case for universal application of these systems for harmonization of AR data. Research Sponsor: Astellas Pharma India Pvt. Ltd.

1079 Poster Session (Board #164), Fri, 8:00 AM-11:00 AM

Frequency of brain metastases in patients with locally advanced triple negative breast cancer after neoadjuvant platinum-based chemotherapy: Impact of *BRCA1/2* mutations. *First Author: Elena Glazkova, N.N. Blokhin National Medical Research Center of Oncology, St. Petersburg, Russian Federation*

Background: patients with triple negative breast cancer has poor survival outcomes. Achievement of pathological complete response (pCR) after neoadjuvant chemotherapy can significantly improve survival of these patients, however some patients will relapse even after pCR. **Methods:** we reviewed prospectively-maintained outcomes database of N.N. Blokhin NMRCO. We extracted information about patients with locally advanced non-metastatic (stage IIIA-IIIC) triple negative breast cancer who were treated with neoadjuvant platinum based chemotherapy in 2014-2018 years. All included patients were tested for the presence of *BRCA1/2* mutation with whole-exome next-generation sequencing or for "founder" hot-spot mutations. **Results:** we identified 80 patients who received neoadjuvant treatment with various platinum-based regimens. Pathological complete response rate was 62.5%. *BRCA*-mutations was found at 22 (27.5%) patients. Median follow-up time was 35.6 months (17.0 – 61.3). 2-year DFS was 77.3%, and 3-year DFS was 70.0%, there was significant differences in DFS in patients, who achieved and patients with residual tumor – 85,2% vs 64,3% (p=0,028). 2-year OS was 91%, 3-year OS was 78,5%. 18 patient had disease progression, the most common sites of disease progression were brain (9 [50.0%]), lungs (5 [27.8%]), 3 (16.7%) patients had locoregional relapses and 1 (5,6%) liver metastases. We separately analysed characteristics of patients with brain metastases (table). There were no significant differences in tumour pathologic response and patient age. All patients, who relapced after pCR, had brain metastases. We also found, that 7 of 9 patients with brain metastases had different *BRCA* mutations. Brain metastases developed in 40,9% (9/22) of patients with *BRCA1* mutations and 3,4% (2/58) of patients with wild type *BRCA1* (p<0,00001). **Conclusions:** *BRCA1* mutation is significant prognostic factor for brain metastases development in locally advanced triple negative breast cancer. Research Sponsor: None.

Patient, age	pCR/no pCR	*BRCA1*	DFS, months
1; 25 y.o.	pCR	wtBRCA	28,1
2, 56 y.o.	no pCR	wtBRCA	13,9
3, 35 y.o.	pCR	mutBRCA	15,83
4, 40 y.o.	no pCR	mutBRCA	9,9
5, 47 y.o.	pCR	mutBRCA	25,23
6, 30 y.o.	no pCR	mutBRCA	16,17
7, 46 y.o.	no pCR	mutBRCA	15,47
8, 38 y.o.	no pCR	mutBRCA	20,8
9, 35 y.o.	pCR	mutBRCA	10,0

1080 Poster Session (Board #165), Fri, 8:00 AM-11:00 AM

Disparities in the receipt of National Comprehensive Cancer Network (NCCN) guideline adherent care in triple-negative breast cancer (TNBC) by race/ethnicity, socioeconomic status, and insurance type. *First Author: Chimezie Ubbaonu, University of California, Irvine, CA*

Background: Breast cancer is the most commonly diagnosed cancer in women in the United States and the second leading cause of cancer mortality in women.TNBC is more likely to present at an earlier age with more advanced and aggressive disease. The overarching goal of treatment recommendations listed in the National Comprehensive Cancer Network (NCCN) guidelines are to improve patient outcomes. Here we examine factors which may contribute to NCCN guideline adherence. **Methods:** This was a retrospective cohort study of women with triple negative breast cancer using data from the California Cancer Registry (CCR) between 2004-2016 (with follow-up through 11/2018). Indicators for concordance with NCCN guidelines for TNBC was used as the dependent variable in the analysis. A multivariable logistic regression was used to determine the effects of independent variables on adherence to NCCN guidelines. Odds ratios and 95% Confidence Intervals (CI) were calculated. Non-Hispanic Whites, having medical insurance and highest socioeconomic status (SES) were set as references values in the regression models. Disease specific survival was calculated using the Cox regression analysis. **Results:** A total of 16,858 women were included in this study, 32.5% (n = 5,472) received NCCN adherent care ($p < 0.0001$). Non-Hispanic Blacks (NHB) and Hispanic patients were less likely to receive guideline adherent care (respectively, OR 0.87, 95%CI 0.79-0.95 and OR 0.87, 95%CI 0.79-0.95). Patients of lowest and lower-middle socioeconomic status (SES) were less likely to receive NCCN guideline adherent care (respectively, OR 0.77, 95%CI 0.68-0.87 and OR 0.88, 95%CI 0.79-0.98). Overall, non-adherent care was associated with an increased disease-specific mortality (HR 1.21, 95%CI 1.11-1.31, $p < 0.0001$). Hazard ratios were calculated after adjusting for adherent care and NHB patients had an increased disease-specific mortality (HR 1.28, 95%CI 1.16-1.42, $p < 0.0001$) in addition to patients with Medicare or Medicaid payer status (respectively, HR 1.20, 95%CI 1.08-1.34, $p < 0.001$ and HR 1.29, 95%CI 1.15-1.43, $p < 0.0001$). **Conclusions:** A significant portion of TNBC patients in California continue to receive non-guideline adherent care. Non-Hispanic black patients and lower SES quintile groups were less likely to receive guideline adherent care. Patients with non-adherent care had worse disease specific survival compared to recipients of NCCN-adherent care. Research Sponsor: None.

1082 Poster Session (Board #167), Fri, 8:00 AM-11:00 AM

Induction bevacizumab, etoposide and cisplatin followed by whole brain radiotherapy (WBRT) versus WBRT alone in breast cancer with untreated brain metastases: Results of a randomized phase II A-PLUS trial. *First Author: Yen-Shen Lu, National Taiwan University Hospital, Taipei, Taiwan*

Background: Our previous study (*Clin Cancer Res.* 2015;21(8):1851) demonstrated that bevacizumab preconditioning followed by etoposide and cisplatin (BEEP) is a highly effective treatment for breast cancer (BC) patients (pts) with brain metastases (BM) progressing from WBRT. We conducted a randomized phase II study A-PLUS (NCT02185352) to test whether using BEEP as an induction therapy could enhance the efficacy of WBRT and provide systemic control. **Methods:** BC pts with measurable BM not suitable for surgery/radiosurgery and had not received WBRT were randomized (2:1) to experimental arm: induction BEEP for 3 cycles (~2 months [ms]) followed by WBRT or control arm: upfront WBRT. The BEEP regimen consists of bevacizumab 15 mg/kg on day 1, and etoposide 70 mg/m^2/day on days 2-4, cisplatin 70 mg/m^2 on day 2, followed by prophylaxis GCSF, every 21 days. After WBRT in both arms, pts received treatment of physician's choice except BEEP until BM progression. Stratification was based on the Graded Prognostic Assessment score. Primary endpoint was brain-specific progression free survival (BS-PFS) based on RECIST 1.1, with a total of 108 pts, power of 0.8 at the 2-sided α level of 0.2. **Results:** Of 112 enrolled pts, 74 were in experimental arm and 38 in control arm. Baseline patient characteristics were generally balanced between arms. With median follow up of 28.7 ms, median BS-PFS was 8.1 vs. 6.5 ms (p= 0.146; HR 0.71 [95% CI 0.44-1.13]), which met the primary endpoint (pre-defined α level of 0.2). Results of preplanned analysis included: 2-month brain-specific objective response rate of BEEP alone vs. WBRT was 41.9% vs. 52.6% (p= 0.613); 8-month BS-PFS rate was 48.7% vs. 26.3% (p= 0.027); median PFS was 6.4 vs. 4.7 ms (p= 0.071; HR 0.67 [95% CI 0.43-1.04]), and extra-BM PFS was 7.9 vs. 5.0 ms (p= 0.141; HR 0.71 [95% CI 0.46-1.12]). Median overall survival was 15.6 vs. 13.6 ms (p= 0.855; HR 0.96 [95% CI 0.59-1.55]), with 31.6% of pts in control arm received BEEP regimen treatment after BM progression. The most common all-grade adverse events (AEs) in experimental arm were neutropenia (30.2%), nausea (27.9%), anemia (27.4%), and leukopenia (24.2%). Most AEs were mild to moderate in severity. Two pts discontinued BEEP treatment due to grade 4 nephrotoxicity and grade 3 infection, respectively. **Conclusions:** BEEP as induction treatment followed by WBRT for BC pts with BM may improve control of both BM and systemic disease. Further validation by a phase III study is necessary. Clinical trial information: NCT02185352. Research Sponsor: Roche Products Ltd., Other Foundation, Other Government Agency, Pharmaceutical/Biotech Company.

1084 Poster Session (Board #169), Fri, 8:00 AM-11:00 AM

The landscape of genomic alterations detected in serial circulating tumor DNA (ctDNA) in clinical progressive metastatic breast cancer. *First Author: Saya Jacob, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL*

Background: Metastatic breast cancer (MBC) is associated with genomic evolution, representing a challenge at clinical progression. While tissue and blood next-generation sequencing (NGS) allows for the baseline detection of alterations, non-invasive longitudinal assessment of ctDNA can provide a tool for monitoring tumor evolution. We characterized genomic changes using serial ctDNA testing in patients with clinical progression. **Methods:** Patient data was obtained under an IRB-approved protocol and ctDNA was collected at Northwestern University between 2015-2019. All ctDNA samples were analyzed using the Guardant360 NGS assay. Of 255 patients with MBC, 86 had at least two serial ctDNA collections with the second collection drawn at first progression (P1) by imaging and clinical assessment. Participants were followed until second clinical progression (P2). We analyzed type of alterations, mutant allele frequency (MAF), number of alterations (NOA), and sites of disease on imaging in close proximity to ctDNA evaluation. Matched pairs variations in MAF and NOA at P1 and P2 were tested through Wilcoxon test. **Results:** We identified 44 HR+, 20 HER2+ and 22 TNBC cases. Median lines of therapy were 3 (interquartile range (IQR): 1-6) for HR+, 3 (IQR: 1-5) for HER2+, and 2 (IQR: 1-4) for TNBC. The most likely alterations between baseline to P1 were *TP53* ($p < 0.0075$), *PIK3CA* ($p < 0.0126$), *AR* ($p < 0.0126$), *FGFR1* ($p < 0.0455$) and *ESR1* ($p < 0.0143$). In the HR+ subset, *ESR1* was statistically more likely at P1. *ESR1* at P1 was also associated with development of new liver lesions ($p < 0.0320$). *ERBB2* mutation at P1 was associated with new lung ($p < 0.0050$) or bone lesions ($p < 0.0030$). Increase in NOA was observed between baseline and P1 ($p < 0.0001$), P1 and P2 ($p < 0.0001$), and baseline to P2 ($p < 0.0004$). MAF was increased between baseline and P2 ($p < 0.0480$). **Conclusions:** Serial ctDNA testing identified resistance alterations (*TP53, PIK3CA, AR, ESR1, FGFR1),* with some mutations indicating new sites of disease (*ESR1, ERBB2*). Heterogeneity of ctDNA was significantly associated with progressive disease. Prospective evaluation of the impact of serial ctDNA testing on treatment decisions is needed to expand the role of precision medicine in MBC. Research Sponsor: None.

	Baseline	P1	P2
NOA	4 (IQR: 1-6)	5 (3-8)	6 (4-10)
MAF	3.3 (IQR:0.3-11.4)	3.6 (0.8-15.4)	5.0 (0.5-14)
Cases with NOA Increase from Baseline		**58% ($p < 0.0001$)**	**81% ($p < 0.0004$)**
Cases with MAF Increase from Baseline		55% ($p < 0.2390$)	**65% ($p < 0.0480$)**
New Alterations		***TP53, PIK3CA, AR, FGFR1, ESR1***	
New Metastases		***ESR1*: Liver** ***ERBB2*: Lung, Bone**	

1085 Poster Session (Board #170), Fri, 8:00 AM-11:00 AM

Metastatic behavior of mixed invasive ductal lobular carcinoma (mIDC/ILC). *First Author: Azadeh Nasrazadani, UPMC Hillman Cancer Center, Pittsburgh, PA*

Background: Mixed invasive ductal lobular carcinoma (mIDC/ILC) is a poorly described subtype of invasive breast cancer, characterized by its composition of both ductal and lobular histopathology. It is unclear if individual or both components drive metastasis. Literature is sparse regarding sites of metastatic spread of this elusive subtype of invasive breast cancer. **Methods:** Cohorts of patients with mIDC/ILC, invasive ductal carcinoma (IDC), and invasive lobular carcinoma (ILC) were identified from the UPMC Network Cancer Registry. Among these, 46 patients with mIDC/ILC, 1,131 patients with IDC, and 145 patients with ILC seen at UPMC Magee Women's Hospital from 1990 – 2017 were found to have developed distant metastasis during the course of their disease. The metastatic pattern of spread was compared between the cohorts. Formalin-fixed, paraffin-embedded patient samples from the metastatic sites of a portion of the mIDC/ILC cases (n = 19) was acquired and evaluated by H&E staining. **Results:** Patients with IDC were more likely than patients with ILC to have metastasis to the liver ($p = 0.001$) and lung ($p < 0.001$), and less likely to have metastasis to the peritoneum ($p < 0.001$). Patients with mIDC/ILC were more likely than patients with IDC to have peritoneal metastasis ($p = 0.01$), similar to patients with ILC. Compared to patients with ILC, patients with mIDC/ILC were more likely to have liver metastasis ($p = 0.001$), similar to patients with IDC. Evaluation of the metastatic lesions originating from mIDC/ILC displayed a spectrum of histopathology including mixed histology (n = 3), pure IDC (n = 3), pure ILC (n = 5), and indeterminate lesions with features of both IDC and ILC (n = 6). Two cases were uninterpretable due to significant crush artifact. Metastatic mIDC/ILC lesions with retained mIDC/ILC histology were found in vertebral, pleural, and skin tissues. Metastatic mIDC/ILC lesions with IDC histology were found in a cerebellar, liver, and chest wall lesion; whereas, those with ILC histology were found in bowel, omental fat, ovary, bone, and sacrum. Indeterminate histology metastatic lesions were found at liver, chest wall, cerebellar, and bone sites. **Conclusions:** mIDC/ILC metastasizes to a range of distant sites with a higher preference to the liver and peritoneum as compared to ILC and IDC, respectively. Metastatic lesions arising from mIDC/ILC tumors showed a spectrum of histologies, including mIDC/ILC, IDC, ILC and indeterminate lesions with features of both IDC and ILC. Ongoing genomics studies will provide further insight into development of metastases from mIDC/ILC tumors. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

1086 Poster Session (Board #171), Fri, 8:00 AM-11:00 AM

Outcomes for black versus white women with stage IV breast cancer enrolled on investigator-initiated clinical trials at Emory. *First Author: Princess Ekpo, Emory University, Atlanta, GA*

Background: Black women are 40% more likely to die from their breast cancer compared to White women. Inadequate representation of Blacks in clinical trials may contribute to health care inequity. Emory's Winship Cancer Institute (WCI) in Atlanta serves a significant Black population and has a unique opportunity to engage these underrepresented patients in clinical trials. We aimed to assess clinical outcomes in Black versus White women with metastatic breast cancer (MBC) enrolled on investigator-initiated clinical trials (IITs) at Emory. **Methods:** Black and White women with MBC enrolled on IITs conducted at WCI between 1/2009 and 1/2019 were retrospectively evaluated. Descriptive statistics were generated for all patient characteristics. Univariate analyses and a multiple logistic regression model were used to assess the effect of age and race on clinical response, length of time on trial, number of therapy lines prior to trial enrollment, and toxicity on trial. Overall survival was assessed using Kaplan Meier analysis. **Results:** Sixty-two women with MBC were included [White, n = 41 (66%), and Black, n = 21 (34%), p = 0.55]. Over 90% of women were enrolled on phase II clinical trials and received targeted therapy. Mean age at clinical trial consent was 53.2 and 55.9 years in Black and White women, respectively (p = 0.36). While the majority of women had hormone-receptor positive disease, a higher percentage of Blacks had triple negative breast cancer (29% vs. 17% in Whites, p = 0.39). Black women had fewer lines of systemic therapy prior to trial enrollment (2.86 vs. 4.3, respectively, p = 0.017) and were enrolled on trial for less time than White women (5.67 mo vs. 7.83 mo, respectively, p = 0.22). There were no differences in toxicity rates among patients enrolled on IITs based on race. Black women were more likely to have progressive disease (PD) on trial (45% in Blacks vs. 20% in Whites, p = 0.05). While there was no significant difference in overall survival (p = 0.482), there was a trend towards shorter survival in Black women (51.3 mos vs. 64 mos, respectively). **Conclusions:** Black women with MBC who enrolled on IIT trials at Emory had worse treatment response and a trend towards poorer survival compared to White women. More research is needed to determine whether this is due to adverse biology. These results reinforce the need for exploration of biomarkers of response by race and ethnicity and improved representation of Blacks in clinical trials to inform real world efficacy. Research Sponsor: None.

1087 Poster Session (Board #172), Fri, 8:00 AM-11:00 AM

Real-world clinical effectiveness and safety of olaparib monotherapy in HER2-negative gBRCA-mutated metastatic breast cancer: Phase IIIb LUCY interim analysis. *First Author: Karen A. Gelmon, Department of Medical Oncology, BC Cancer, Vancouver, BC, Canada*

Background: OlympiAD (NCT02000622) demonstrated the benefit of olaparib over standard of care in patients (pts) with HER2-negative (HER2-) metastatic breast cancer (MBC) and germline *BRCA* mutations (gBRCAm). LUCY (NCT03286842) aimed to provide additional data on the real-world effectiveness and safety of olaparib monotherapy in this setting. **Methods:** This Phase IIIb, open-label, single-arm study of olaparib 300 mg twice-daily, enrolled pts with HER2- gBRCAm MBC who had received a taxane and/or anthracycline in the (neo)adjuvant/metastatic setting, and ≤2 lines of chemotherapy for MBC. Hormone receptor-positive (HR+) pts had progressed on prior endocrine therapy (ET), and further ET was considered unsuitable. Primary endpoint: investigator-defined progression-free survival (PFS). Secondary endpoints: overall survival, time to first subsequent therapy or death (TFST), and investigator-assessed clinical response rate (CRR). The interim analysis was planned after 160 PFS events. **Results:** From Oct 2018-Sept 2019, 252 pts were enrolled (160 sites, 15 countries; mean age 46.2 [range 22-75] years; 73.4% ECOG PS 0). Median total treatment duration: 7.9 months (mo; range 0.2-20.0). Median PFS: 8.1 mo (95% confidence interval [CI] 6.9, 8.7; 166 events [65.9%]). Clinical trial information: NCT03286842. Median TFST: 9.7 mo (95% CI 8.7, 11.1). CRR: 48.6% (95% CI 42.2, 55.0). Adverse events (AEs) in >20% of pts (all grades): nausea, anemia, asthenia, vomiting, and fatigue. 24.6% of pts reported a grade ≥3 AE, including anemia (n=33 [13.1%]). 4.4% of pts had an AE leading to treatment discontinuation. **Conclusions:** Interim results in this real-world population of pts with HER2- gBRCAm MBC were consistent with the OlympiAD study, and support olaparib as a chemotherapy-free alternative treatment for pts with gBRCAm advanced BC. Research Sponsor: This study was sponsored by AstraZeneca and is part of an alliance between AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA (MSD).

	Subgroup (%)	Events, n (%)	Median PFS, mo	95% CI
HR status	HR+ (52.0)	84 (64.1)	8.3	7.6, 9.8
	Triple -ve BC (48.0)	82 (67.8)	6.8	5.5, 9.0
Prior platinum therapy	Yes (32.1)	57 (70.4)	6.5	4.9, 8.1
	No (67.9)	109 (63.7)	8.5	7.6, 9.7
Line of therapy	1st (54.4)	87 (63.5)	8.3	7.0, 9.7
	2nd+ (45.6)	79 (68.7)	7.4	5.6, 8.8
gBRCAm	*BRCA1* only (54.0)	95 (69.9)	6.8	5.9, 8.3
	BRCA2 only (41.3)	63 (60.6)	8.5	7.6, 11.0

1088 Poster Session (Board #173), Fri, 8:00 AM-11:00 AM

Clinical predictors of long-term response to capecitabine in metastatic breast cancer (MBC). *First Author: Deirdre Kelly, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Select patients (pts) with metastatic breast cancer (MBC) treated with capecitabine (cape) experience long-term disease control. We aimed to evaluate the clinical and biological predictors of long-term response. **Methods:** Pts receiving cape monotherapy for breast cancer from 01/2006 to 01/2016 at Princess Margaret Cancer Centre in Toronto, Canada (N = 352) or Alberta, Canada (N = 798) were identified through central pharmacy records. A median time-to-progression (MTTP) 3-fold higher (19.3 months) than those seen in published studies for patients treated with cape monotherapy at 1000mg/m2 was applied to select for pts with long-term response. MBC pts meeting these criteria were identified through chart review, with collection of clinical, pathological, and survival outcomes in addition to oncologist assessed (o) best response (eg: oCR, oPR, oSD) by radiology report review. Descriptive statistics, Kaplan-Meier and Cox-regressions were applied. **Results:** Overall, 41 (4%) pts met long-term response criteria. Median age of the study cohort was 62 (range 40-80), with 39% metastatic at diagnosis and 76% post-menopausal. At initiation of cape, a majority of pts were HR positive (85%), with an LDH < ULN (56%), and had bone (83%) or visceral (63%) metastases. Only 1 (2%) patient was HER2+. In the metastatic setting, most patients were chemotherapy-naive (83%) and had received 0-1 lines of hormonal therapy (61%). Median treatment duration with cape was 2.2 years (range 1.7-5.7) with 37% of pts having ≥40 cycles (range 22-94). Visceral (49%), bone (34%), and lymph nodes (24%) were the most common sites of progression, with 41% requiring 1 dose reduction and 27% requiring 2 dose reductions of cape. Overall response rate was 56% (oCR = 2%, oPR = 54%) with 44% having oSD as best response. Median follow-up was 6.8 years (95% CI: 5.5-8.2). Median PFS was 2.3 years (2.0-2.6), with a median OS of 3.8 years (2.9-4.6). 5 patients (12%) remained alive at data-cutoff, and 1 (2%) remained on treatment after 94 cycles of cape. **Conclusions:** Clinical features associated with long-term response on cape include HR positive, HER2 negative postmenopausal patients with bone predominant metastasis who have received 0-2 lines of prior hormone therapy and 0-1 lines of chemotherapy in the metastatic setting. This is the largest reported analysis of MBC patients with prolonged responses to cape. In the absence of randomized controlled trials; real-world evidence could aid clinicians in the optimal patient selection for treatment with cape. Research Sponsor: None.

1089 Poster Session (Board #174), Fri, 8:00 AM-11:00 AM

Mutation profile differences in younger and older patients with advanced breast cancer using circulating tumor DNA (ctDNA). *First Author: Katherine Clifton, Washington University School of Medicine, St. Louis, MO*

Background: Although the noninvasive nature of ctDNA testing is attractive in an older adult population, less is known regarding the mutation profiles of ctDNA in the older adult breast cancer population as this population is often excluded from studies. Previous tissue testing has shown differences in mutation profiles between older and younger adults with breast cancer. The objective of this study is to assess differences in mutation profiles in the older and younger adult breast cancer population using a ctDNA assay. **Methods:** Patients (pts) with advanced breast cancer underwent molecular profiling using a plasma-based ctDNA NGS assay (Guardant360) between 5/2015-10/2019 at Siteman Cancer Center. Clinicopathological histories were obtained from the medical record. The results of a multicenter database of pts with advanced breast cancer who had undergone molecular profiling using Guardant360 were obtained. Associations between mutations and age were measured using a Fisher's exact test. **Results:** In the single institution cohort, of the 214 patients who underwent testing, 148 (69.16%) were < 65 and 66 (30.84%) ≥ 65 years-old. The most frequently mutated genes in age < 65 pts were *TP53* (48.65%), *PIK3CA* (35.81%), and *ESR1* (30.41%) while the most frequently mutated genes in age≥65 pts were *PIK3CA* (56.06%), *TP53* (51.52%), *ESR1* (25.76%), and *ATM* (21.21%). *ATM, BRAF* and *PIK3CA* mutations were found more frequently in age≥ 65 pts with ER+ HER2- breast tumors ($p < 0.01$). *MYC* and *ESR1* mutations were not significantly associated with age, overall or within subtype. Overall ctDNA resulted in change in management in 19.8% pts (40/202). In the larger multicenter cohort, of the 8803 pts who underwent testing, 5367 (61.0%) were < 65 and 3417 (38.8%) ≥ 65 years-old. *ATM, ESR1* and *PIK3CA* mutations were more common in age≥65 pts ($p < 0.0001$) and *MYC* mutations were less common in age≥65 pts ($p < 0.0001$). **Conclusions:** This study found that ctDNA is a feasible, attractive alternative to traditional biopsies and may identify actionable mutations in older adults with breast cancer. When controlling for subtype, results from a single institution were similar to the larger multicenter cohort showing *ATM* and *PIK3CA* were more common in the older adult population. This data suggests there may be additional molecular differences between breast cancer in older compared to younger adults that warrants further investigation. Research Sponsor: St. Louis Men's Group Against Cancer.

1090 Poster Session (Board #175), Fri, 8:00 AM-11:00 AM

Systemic therapy for patients with breast cancer and one to three brain metastases (BM). *First Author: Zaid A Soomro, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Despite advances in systemic therapies and improved overall survival of metastatic breast cancer (MBC) patients, the development of brain metastases (BMs) remains a challenging complication that affects quality of life and increases morbidity and mortality. Current clinical practice guidelines recommend local treatment of BMs without changing systemic therapy (CST) in patients with stable systemic disease. **Methods:** We retrospectively investigated the impact of CST (when applicable as per treating physician's discretion) after diagnosis of the initial 1-3 BMs on the patient's progression-free survival time (PFS), defined as time to death, to a second BMs or to extracranial metastases. All MBC patients with 1 to 3 BMs only (without extracranial disease) treated at our institution between 2002 and 2017 were identified. For each patient, full information on follow-up and administered therapies were mandatory for inclusion. Hazard ratios (HR) were calculated using the Cox proportional hazard model. We also computed the restricted mean survival time (RMST) up to 5 years of follow-up. **Results:** Among the 2645 patient with BM treated at our institution, 80 were included for analysis. In regards to primary BMs management in patients, 46 of 80 (57%) were treated by radiation therapy, 6 of 80 (7.5%) underwent surgical resection, and 28 of 80 (35%) were managed by a combination of surgery and radiation therapy. All patients had staging imaging documenting lack of extracranial metastases at the time of local therapy of BMs. Following the primary management of BM, we observed that providers changed systemic therapy in 32 of 80 (40%), defined as the CST group. CST included both initiation of therapy in 16 of 80 (20%) and switching of adjuvant therapy in 16 of 80 (20%). Median PFS among CST was 7.7 months vs. 7.2 months among no CST (HR = 0.855, 95% confidence interval (CI) 0.53-1.38, p = 0.52). 5-year RMST for the CST group was 16.6 months vs. 12.8 months in no CST group. The difference of 3.8 months (95% CI 4.3-11.8) was not statistically significant. **Conclusions:** Patients with 1-3 BMs without extracranial disease had a median PFS close to 7.5 months after local therapy. Consistent with current standard of care of maintaining the same systemic therapy approach upon developing isolated BMs, our findings did not demonstrate a significant difference in PFS between patients who experienced a change in systemic therapy compared to those who did not. Research Sponsor: None.

1091 Poster Session (Board #176), Fri, 8:00 AM-11:00 AM

Veliparib (V) monotherapy (monoTx) following combination therapy with V + carboplatin/paclitaxel (CP) in patients with g*BRCA*-associated advanced breast cancer: Exploratory results from BROCADE3. *First Author: Hyo S. Han, Moffitt Cancer Center, Tampa, FL*

Background: In BROCADE3 (NCT02163694), addition of PARP inhibitor V to CP resulted in improved progression-free survival (PFS) (HR 0.71 [95% CI 0.57−0.88], p=0.002) in patients (pts) with advanced HER2-negative breast cancer and g*BRCA1/2* mutation. A subset of pts transitioned to V/placebo (PL) monoTx at an intensified dose/schedule after CP discontinuation prior to progression (investigator discretion). Here, we evaluate the impact of this transition on efficacy and safety. **Methods:** Pts were randomized 2:1 to CP with V (n=337) or PL (n=172). V (120 mg po BID) or PL was given on Days (D) −2 to 5, C (AUC 6) on D1, and P (80 mg/m^2) on D1, 8, and 15 (21-day cycles). Pts who transitioned to monoTx received V/PL 300-400mg BID daily until progression. A Cox model with a time varying covariate indicating transition from V/PL with CP to V/PL monoTx was fit to estimate treatment effect during combination and monoTx phases. PFS by cycles of CP prior to monoTx and AEs during monoTx are summarized. **Results:** A subgroup of 136 (40%) and 58 (34%) pts on the V and PL arms, respectively, received monoTx. When a Cox model with a time-varying covariate was fit for PFS (per investigator), the nominal P-value for treatment by covariate interaction was 0.038. The HRs (95% CI) for V vs PL during combination therapy and monoTx were 0.81 (0.62–1.06) and 0.49 (0.33–0.73). The Table summarizes PFS by cycles of C and/or P prior to monoTx. Common AEs (>20% of pts) during V or PL monoTx were nausea (52%/10%), fatigue (23%/12%), headache (21%/17%), and diarrhea (21%/9%). Seizures (2.2%/0%) were reported during monoTx. Rates of cytopenias for V or PL monoTx were: anemia 12%/14%; neutropenia 13%/12%; and thrombocytopenia 10%/5%. **Conclusions:** These analyses suggest that pts treated with V + CP derive benefit from both combination therapy as well as V monoTx after CP discontinuation. Pts receiving V monoTx after ≤ 6 cycles of VCP experienced a similar benefit to those who transitioned to monoTx after 7–12 cycles of VCP, suggesting that V maintenance therapy may be suitable following a limited duration of combination therapy. Clinical trial information: NCT02163694. Research Sponsor: AbbVie.

Median PFS (investigator-assessed) in pts who received V/PL monoTx.

Cycles of C and/or P before monoTx	V + CP Events, n/N at risk (%)	PL + CP	V + CP Median PFS, mo (95% CI)	PL + CP	HR (95% CI)
≤6	15 / 27 (56)	12 / 13 (92)	18.4 (12.5, -)	12.8 (6.2, 14.7)	0.38 (0.16, 0.88)
7–12	39 / 62 (63)	21 / 27 (78)	18.9 (15.1, 22.3)	13.3 (10.6, 19.7)	0.54 (0.31, 0.95)
Any	70 / 136 (52)	45 / 58 (78)	25.7 (20.5, -)	14.6 (12.8, 19.7)	0.49 (0.34, 0.73)

1092 Poster Session (Board #177), Fri, 8:00 AM-11:00 AM

Diagnostic yield and clinical utility of germline genetic testing following somatic testing in breast cancer patients. *First Author: Stephen E Lincoln, Invitae, San Francisco, CA*

Background: Germline genetic testing is recommended for breast cancer patients with specific presentations or family histories. Separately, tumor DNA sequencing is increasingly used to inform therapy, most often in patients with advanced disease. Recent NCCN and ESMO guidelines recommend germline testing following somatic testing, under specific circumstances and for specific genes. We examined the utility of germline findings in patients referred for both test modalities. **Methods:** We reviewed somatic and germline mutations in a consecutive series of patients who: (a) had a current or previous breast cancer diagnosis, (b) were referred for germline testing, and (c) previously received tumor sequencing. Diverse reasons for germline testing included: a tumor finding of potential germline origin, treatment or surgical planning, personal or family history, and patient concern. **Results:** 227 patients met study criteria of whom 88 (39%) harbored a pathogenic germline variant (PGV) in a high or moderate risk cancer predisposition gene. Mutations in certain genes were most likely to be of germline origin, and most PGVs were potentially actionable (Table). 13% of PGVs were not reported by tumor tests as either germline or somatic findings, usually a result of tumor test limitations. Of note, 27 of the patients with PGVs (31%) had these variants uncovered only after presenting with a second, possibly preventable, malignancy. **Conclusions:** Germline testing following tumor sequencing often yielded findings that may impact care. Indeed, the 39% PGV rate we observed suggests that such testing may be underutilized. We observed actionable PGVs missed by somatic tests, PGVs uncovered in patients' second malignancies, and PGVs not within germline reflex testing criteria. These results reinforce the utility of germline testing separate from somatic testing in appropriate patients. Research Sponsor: None.

Somatic and germline findings by gene. Genes with no germline findings are not shown.

Gene	Total Findings	#Germline (%Total)	ESMO Criteria	Potential Utility
BRCA1/2	119	53 (45)	Yes	MG,PT,CT
TP53	53	4 (8)	No *	MG,CT
ATM	18	9 (50)	No	MG,CT
PTEN	15	1 (7)	No	MG,CT
CHEK2	12	8 (67)	No	MG,CT
PALB2	11	9 (82)	Yes	MG,CT
Other	15	4 (26)	No *	MG

*ESMO criteria for TP53 and RB1 require age < 30 -- our *TP53/RB1* PGV-positive patients were older. Abbreviations: ESMO: Germline test recommended (PMID 31050713). Utility: PGVs associated with management guidelines (MG), approved precision therapies (PT) or clinical trial eligibilities (CT). Other genes: *RB1, CDKN2A, BRIP1*.

1093 Poster Session (Board #178), Fri, 8:00 AM-11:00 AM

Efficacy and safety of liposomal mitoxantrone (Lipo-MIT) in advanced breast cancer (ABC): A randomized, open label, active-controlled, single-center, phase II clinical trial. *First Author: Leiping Wang, Fudan University Shanghai Cancer Center, Shanghai, China*

Background: Anthracyclines are associated with cardiotoxicity and myelosuppression in breast cancer (BC) patients. A new drug delivery system, liposomal preparation has shown higher anti-cancer effect and lower toxicity due to modified drug release and particle shape. This trial aimed to evaluate the efficacy and safety of Lipo-MIT in ABC. **Methods:** This is a randomized, open label, active-controlled, single-center, phase II clinical trial. Eligible patients were randomized in a ratio of 1:1 to receive Lipo-MIT or mitoxantrone hydrochloride injection (MIT) intravenously. The dosage was 20 mg/m^2 for Lipo-MIT and 14 mg/m^2 for MIT, once every four weeks (i.e., one treatment cycle). The primary endpoint was objective response rate(ORR). The secondary endpoints were progression free survival (PFS) and safety. **Results:** From Oct 2015 through Jul 2017, 60 patients were randomized to Lipo-MIT group (n = 30) or MIT group (n = 30). The Median (Q1,Q3) age was 56.0 (41.0,62.0) years in Lipo-MIT group and 54.5 (44.0,62.0) years in MIT group. Nineteen patients in Lipo-MIT group and 23 in MIT group received < 4 cycles of treatment, 11 patients in Lipo-MIT group and 7 in MIT group were treated for 4 or more cycles. When Lipo-MIT group was compared with MIT group, ORR was 13.3% (4/30) and 6.7% (2/30), disease control rate (PR+SD) was 50% (15/30) and 30% (9/30), median PFS was 2.30 (95% CI: 1.74-3.91) and 1.86 (95% CI: 1.74-2.40) months (P> 0.05). Lipo-MIT showed significantly lower incidence of all-grade white blood cell decreased (86.7% vs 96.7%), neutrophil count decreased (80.0% vs 96.7%), conjugated bilirubin increased (53.3% vs 56.7%), aspartate aminotransferase increased (40.0% vs 53.3%), and troponin T increased (3.3% vs 36.7%) than MIT, but higher incidence of anemia (76.7% vs 46.7%), skin hyperpigmentation (66.7% vs 3.3%), and platelet count decreased (56.7% vs 53.3%) than MIT. **Conclusions:** Lipo-MIT provided numerically better ORR, DCR, and PFS than MIT in ABC. Lower incidence of troponin T increased might suggest lower cardiotoxicity of Lipo-MIT. It is worthwhile to further explore the clinical utility of Lipo-MIT in ABC. Clinical trial information: NCT02596373. Research Sponsor: CSPC ZhongQi Pharmaceutical Technology Co., Ltd., shijiazhuang, China.

1094 Poster Session (Board #179), Fri, 8:00 AM-11:00 AM

Comparison of the cell-free DNA genomics in patients with metastatic breast cancer (MBC) who develop brain metastases versus those without brain metastases. *First Author: Neelima Vidula, Massachusetts General Hospital, San Francisco, CA*

Background: The genomics of patients with metastatic breast cancer (MBC) who develop brain metastases (BM) is not well understood given the difficulty in obtaining brain tumor for genotyping. We compared tumor genotyping results via cell-free DNA (cfDNA) collected at MBC diagnosis in patients who developed BM after MBC diagnosis with those who did not develop BM (non-BM). **Methods:** Patients at an academic institution who had cfDNA testing (Guardant 360/Next generation sequencing, 73 gene assay) at MBC diagnosis between 1/2016-12/2017, with ≥ 6 months of follow-up post testing, were identified. A chart review was done to identify tumor subtype, demographics, cfDNA results, and development of BM at or after MBC diagnosis. Pearson's chi-squared and Wilcoxon rank sum tests were used to determine differences in clinical and cfDNA characteristics in BM vs. non-BM ($p<0.05$ for statistical significance). **Results:** CfDNA results were available for 49 patients, of whom 13 (27%) developed BM (4 with BM at MBC diagnosis). The median time to BM development was 11 months. While patients with BM were younger at MBC diagnosis than non-BM (median age BM 53 vs. non-BM 61, p=0.05), they had similar subtype (BM vs. non-BM: HR+/HER2- 62% vs. 69%, HER2+ 8% vs. 14%, TNBC 23% vs. 17%, unknown 8% vs. 0%, p=0.3), de-novo vs. recurrent disease (BM vs. non-BM: de-novo 8% vs. 14%, recurrent 92% vs. 86%, p=0.6), and visceral disease (BM vs. non-BM: 77% vs. 56%, p=0.2) distributions. All patients with BM had ≥1 detectable cfDNA mutation vs. 88% of non-BM. While the median mutant allele frequency of the most common mutation was similar in BM vs. non-BM (2.4% vs. 3.7%, p=0.5), the mutation pattern varied. Patients with BM more often had mutations in *BRCA1* (15% vs. 3%, p=0.1), *APC* (15% vs. 0%, p=0.02), and *CDKN2A* (15% vs. 0%, p=0.02), compared to non-BM. In 4 patients with BM at MBC diagnosis, mutations in *APC* (50%), *CDKN2A* (50%), and *BRCA 1/2* (25%) were noted; 1 had coexisting *APC* and *BRCA1/2* mutations and another had coexisting *APC* and *CDKN2A* mutations. **Conclusions:** Patients with MBC who develop BM may have different cfDNA genomics, particularly *BRCA1*, *APC*, and *CDKN2A* mutations. Further research is needed to determine the predictive value of cfDNA at MBC diagnosis in the identification of patients at higher risk of developing BM. Research Sponsor: None.

CfDNA mutations.

Mutation	BM (n=13)	Non-BM (n=36)	p-value
TP53	54%	39%	0.4
PI3KCA	31%	39%	0.6
BRCA1	15%	3%	0.1
BRCA2	15%	6%	0.3
APC	15%	0%	0.02
CDKN2A	15%	0%	0.02
NF1	15%	22%	0.6
ERBB2	15%	14%	0.9
EGFR	8%	8%	0.9
FGFR2	0%	8%	0.3
NOTCH1	0%	8%	0.3
KRAS	0%	8%	0.3

1095 Poster Session (Board #180), Fri, 8:00 AM-11:00 AM

A phase I study of SHR6390, a cyclin-dependent kinase 4/6 inhibitor in patients with advanced breast cancer (ABC). *First Author: Pin Zhang, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: SHR6390 is a novel inhibitor of cyclin-dependent kinase 4/6 (CDK 4/6). This study was conducted to evaluate the tolerability, pharmacokinetics, safety, and preliminary antitumor activity of SHR6390 in patients (pts) with advanced breast cancer (ABC). **Methods:** In this open-label, single-arm phase I study, pts who had failed standard therapy were enrolled to receive oral SHR6390 in 3 + 3 dose-escalation pattern at doses of 25−175 mg. Eligible pts were given a single-dose of SHR6390 in week 1, followed by once daily continuous doses for three weeks, and one week off in 28-day cycle. Based on the tolerability, pharmacokinetics, and activity data revealed from the dose-escalation phase, three dose cohorts were selected to expand to 8−10 pts. The primary endpoints were maximum tolerated dose (MTD) and pharmacokinetics. **Results:** Between Apr 15, 2016 and Dec 21, 2018, 40 pts were enrolled. All pts were diagnosed of hormone receptor positive and HER2-negative ABC. 45.0% of pts had at least three prior chemotherapies and 55.0% had at least two prior endocrine therapies. SHR6390 100 mg, 125 mg, and 150 mg cohorts were expanded to 10 pts, respectively. No dose limiting toxicity was observed and the MTD was not reached. Adverse events (AEs) of grade ≥3 were observed in 22 (55.0%) of 40 pts, being neutropenia (52.5%), leukopenia (35.0%), thrombocytopenia (5.0%), and hypertension (2.5%). No serious AEs were reported. At the doses of 50−175 mg, median time to peak concentration was 2.5−4.0 h, and mean terminal half-life was 40.3−51.4 h with single-dose SHR6390. Following multiple dosing, steady state SHR6390 was observed on day 8. The steady state areas under the concentration and peak concentration increased slightly greater than the increase rate of dose, with steady state C_{max} at day 21 of 41.1, 53.4, 87.0, 115.0, 126.0, and 155.0 ng/mL in 50, 75, 100, 125, 150, and 175 mg cohorts, respectively. The disease control rate was 62.5% (25/40, 95% CI 45.8% to 77.3%). Two pts (5%, one in 125 mg, one in 150 mg cohort) achieved partial response, with responses lasting 169 and 356+ days, respectively. **Conclusions:** SHR6390 showed acceptable safety profile and dose-dependent plasma exposure in pts with ABC. The recommended phase II dose was 150 mg. Preliminary evidence of clinical activity was observed, warranted further study. Clinical trial information: NCT02684266. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

1096 Poster Session (Board #181), Fri, 8:00 AM-11:00 AM

The incidence and impact of brain metastasis in patients with hereditary *BRCA1/2* mutated invasive breast cancer in a prospectively followed cohort. *First Author: Haven Garber, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Previous reports suggest the incidence of brain metastasis is higher in patients with hereditary *BRCA1* mutations compared to *BRCA1* noncarriers among breast cancer patients who develop recurrent disease. PARP inhibitors are now standard therapies for metastatic breast cancer patients with germline *BRCA1* or *BRCA2* mutations (*gBRCA1/2*) based on their efficacy in treating systemic disease. However, as management of systemic disease improves, a concern is that patients with hereditary *BRCA* mutations may experience higher rates of disease progression in the CNS. We aimed to estimate the incidence of brain metastasis in breast cancer patients with *gBRCA1/2* using a prospectively maintained *gBRCA* database and to assess the impact of brain metastasis on survival. **Methods:** To determine incidence, we queried a prospectively maintained electronic database that included patients referred to the MDACC genetics department and who underwent *gBRCA1/2* testing. We identified patients with stage I-III invasive breast cancer who were treated between 2000-2017 and assessed for disease recurrence and brain metastasis. To expand our cohort for descriptive characteristics (separate from the incidence analysis), we queried the Breast Medical Oncology database for patients with brain metastasis who had undergone *BRCA1/2* testing outside the genetics department or at outside institutions. **Results:** Of 474 patients with Stage I-III breast cancer and *gBRCA1*, 77 (16.2%) developed distant metastasis (median f/u: 9.1 years). Of these patients, 34/77 (44.2%) developed brain metastasis. In comparison, 42 of 318 (13.2%) of *gBRCA2* patients with Stage I-III breast cancer developed distant recurrence (median f/u: 8.4 years), and 7/42 (16.7%) experienced brain metastasis. In *gBRCA1* patients with brain metastasis, 45/48 (83.8%) had triple negative disease, and the median time from diagnosis to brain metastasis was 2.45 years. The brain was among the initial sites of disease recurrence in 24/48 (50%) of *gBRCA1* patients. For *gBRCA1* patients with distantly recurrent disease, median OS from diagnosis was 3.19 years for patients with brain metastasis vs. 5.37 years for patients without brain mets (HR 0.54; 95% CI 0.34 to 0.85; $P = 0.0082$). **Conclusions:** Brain metastasis is frequent among breast cancer patients with recurrent disease and hereditary *BRCA1* mutations. Development and testing of agents with intracranial activity is critical for improving long-term outcomes in *gBRCA1* patients with metastatic breast cancer. Research Sponsor: UT MD Anderson Cancer Center.

1097 Poster Session (Board #182), Fri, 8:00 AM-11:00 AM

Veliparib (V) monotherapy after progression on placebo (PL) + carboplatin/paclitaxel (CP) in patients with advanced HER2-negative g*BRCA*-associated breast cancer: Crossover outcomes and exploratory biomarker analyses in BROCADE3. *First Author: Shannon L Puhalla, University of Pittsburgh Medical Center Cancer Centers, Pittsburgh, PA*

Background: In BROCADE3 (NCT02163694), addition of the PARP inhibitor (PARPi) V to CP improved PFS in patients (pts) with g*BRCA*-associated advanced breast cancer (hazard ratio 0.71 [95% CI 0.57–0.88], p = 0.002). Reversion mutations may account for resistance to platinum-based CT and PARPi. Efficacy, safety, and exploratory biomarker analyses for pts randomized to PL + CP who received crossover (Cx) V monotherapy after progression are reported. **Methods:** 513 total pts were randomized 2:1 to V + CP or PL + CP. V/PL, C, and P could be discontinued independently prior to progression, leading to varying platinum-free intervals at the time of progression. After progression, pts in the PL + CP arm could receive open-label Cx V monotherapy (300–400 mg BID continuous), beginning within 60 d of progression and continuing to second progression. Adverse events (AEs) and activity during Cx V were assessed. Exploratory analysis of *BRCA* reversion mutations restoring *BRCA1/2* protein function that emerged during PL + CP treatment was performed on plasma circulating tumor DNA using targeted-amplicon next generation sequencing. **Results:** At data cutoff, 75 pts initially randomized to PL + CP had ≥1 dose of Cx V. Mean (range) duration of Cx V was 154 d (2–966). Activity during Cx V is in the Table. Mean (range) platinum-free interval at time of first dose of Cx V was 3.1 mos (0.4–10.9) vs 8.1 mos (1.0–34.9) in pts who had progressed vs had not progressed by 24 wks after first dose of Cx V. *BRCA* reversion analysis was completed for 18 Cx pts. Reversion mutations were identified in 1/18 pts (5.6%). This patient had Cx V duration of 19 d and had progressed by 24 wks. *BRCA* reversion analysis on additional Cx pts will be presented. Most common AEs during Cx V were nausea (61%), vomiting (29%), fatigue (24%), and diarrhea (21%). Any grade anemia, neutropenia, and thrombocytopenia occurred in 7%, 15%, and 7% of pts. Three pts (4%) experienced a convulsion event. **Conclusions:** Platinum-free interval may influence efficacy of subsequent PARPi. Impact of *BRCA* reversion mutations warrants further evaluation. Cross-resistance may limit PARPi efficacy after platinum failure. Clinical trial information: NCT02163694. Research Sponsor: AbbVie.

Activity of Cx V after progression on PL+ CP.

	N = 75
Best response[a], n/N (%)	
Complete response	0 / 50
Partial response	8 / 50 (16)
Clinical Benefit Rate at 24 wk, % (95% CI)[b]	30.5 (21.9 – 39.5)
Median PFS, mo (95% CI)	2.1 (2.1 – 4.4)

[a] Includes pts with at least 1 measurable lesion at baseline
[b] From Kaplan-Meier estimates

1098 Poster Session (Board #183), Fri, 8:00 AM-11:00 AM

Trends of skeletal related events in patients with breast cancer metastasized to bone. *First Author: Prasanth Lingamaneni, John H. Stroger, Jr. Hospital of Cook County, Chicago, IL*

Background: Up to three-quarters of women with advanced breast cancer develop bone metastases, predisposing to Skeletal Related Events (SRE), which are associated with a significant health care burden, poor prognosis, loss of functional independence and a decrease in quality of life. We performed a retrospective analysis on predictors of SRE in this population. We also evaluated temporal trends of outcomes and resource utilization in those with SRE. **Methods:** Adult breast cancer patients with metastases to bone, admitted from January 2012 to September 2015 were identified from the Nationwide Inpatient Sample database. Based on previous studies, SRE was defined by using ICD-9 codes for pathologic fracture, spinal cord compression, necessity for radiation to bone or surgery to bone. Multivariable analysis of predictors of SRE in patients with breast cancer metastatic to bone, as well as mortality in the SRE group were performed. Temporal trends of resource utilization across the years were evaluated. **Results:** A total of 143,455 patients with breast cancer with metastases to bone were identified, of which 17.2% had SRE. Patients with SRE had a mean age of 66 years and were predominantly white (70.2%). After adjusting for confounders, African Americans and Hispanics were less likely than Whites to develop SRE. On multivariable analysis, only comorbidity burden (in the form of high Charlson comorbidity index) predicted inpatient mortality. Rates of SRE in breast cancer patients with bone metastases did not change over the years (17.2% to 17.1%). Inpatient mortality of patients with SRE remained stable (3.76% to 3.79%). There was a statistically significant increase in surgical intervention (43.4% to 47.7%, $p<0.01$) and decrease in radiation to bone (25.7% to 19.7%, $p<0.001$) over time. Length of hospital stay and total hospital charges, after adjusting for inflation, remained largely unchanged. **Conclusions:** Incidence of SRE, inpatient outcomes and health care costs remained stagnant in those with metastatic breast cancer between 2012 and 2015, despite the advent of novel bone-targeted agents. There has been an increased trend towards surgical intervention and less utilization of local radiation over time. Research Sponsor: None.

Predictors of SRE in breast cancer patients with bone metastases.

Predictor	Adjusted OR (95% CI)	P-value
Age (per year increase)	1.008 (1.005-1.011)	**<0.001**
African American	0.86 (0.80-0.94)	**<0.01**
Hispanic	0.88 (0.77-0.99)	**0.04**
Medicaid insurance	1.31 (1.18-1.46)	**<0.001**
Private insurance	1.15 (1.06-1.25)	**<0.01**
Teaching hospital	1.36 (1.27-1.46)	**<0.001**

1099 Poster Session (Board #184), Fri, 8:00 AM-11:00 AM

Surgery at primary and metastatic sites for stage IV breast cancer (BC): A National Cancer Database (NCDB) analysis. *First Author: Nadeem Bilani, Cleveland Clinic Florida, Weston, FL*

Background: There is no clear evidence of a survival benefit of primary tumor resection in patients with stage IV breast cancer (BC). This large study evaluated factors associated with undergoing primary tumor resection, and whether resection at the primary site, or distant site resection (metastasectomy), was associated with better overall survival (OS). **Methods:** This retrospective analysis of stage IV BC cases used the 2004-2016 National Cancer Database (NCDB) population. To evaluate variables associated with primary tumor resection, we used univariate analyses (chi-squared and Wilcoxon rank-sum test), followed by multivariate logistic regression. Consequently, we conducted multivariate Cox regression survival analyses on the following groups: 1) all stage IV BC patients; 2) a subset of those with only 1 site of metastasis; and 3) another subset with metastasis to > 1 distant site. **Results:** A total of 54,871 stage IV BC patients were included in this analysis. From this, we analyzed a subset with only 1 distant site involved (n = 30,480) and another subset with multiple secondary sites (n = 17,344). In total, 15,661 patients underwent surgery at the primary site: 11,451 (73.1%) were non-Hispanic white; 2479 (15.8%) were non-Hispanic black; 981 (6.3%) were Hispanic and 484 (3.1%) were Asian. Variables associated with undergoing resection of the primary tumor were: age, race, Charlson/Deyo score, insurance and facility type, involved breast quadrant, receptor status, N-staging, extent of metastasis and year of diagnosis. Survival analysis of all stage IV patients showed that both lumpectomy (HR 0.59, 95% CI: 0.57-0.62, $p < 0.0001$) and mastectomy (HR 0.62, 95% CI: 0.60-0.64, $p < 0.0001$) were associated with better OS when compared to no surgery. The statistical effect was larger in the subgroup with metastasis to 1 site, but still significant in the subgroup with multiple metastatic sites. Distant site resection also yielded a survival benefit compared to no metastasectomy across all 3 groups. In the subgroup with metastasis to only 1 site, metastasectomy was associated with better OS when the metastatic site was liver (HR 0.60, 95% CI: 0.43-0.82, p = 0.0018), lung (HR 0.47, 95% CI: 0.37-0.61, $p < 0.0001$), and brain (HR 0.70, 95% CI: 0.55-0.88, p = 0.0022). **Conclusions:** Across all 3 patient subgroups, primary tumor resection (lumpectomy or mastectomy) and metastasectomy were associated with improved OS. Additional stratified analysis in the subgroup with only 1 metastatic site showed benefit of metastasectomy when that site was the lung, liver or brain. Research Sponsor: None.

TPS1100 Poster Session (Board #185), Fri, 8:00 AM-11:00 AM

Trastuzumab deruxtecan (T-DXd; DS-8201) in combination with pembrolizumab in patients with advanced/metastatic breast or non-small cell lung cancer (NSCLC): A phase Ib, multicenter, study. *First Author: Hossein Borghaei, Fox Chase Cancer Center, Philadelphia, PA*

Background: T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and potent topoisomerase I inhibitor. In a phase II trial in patients (pts) with heavily pretreated, metastatic HER2+ breast cancer (BC), T-DXd had a confirmed objective response rate (cORR) of 60.9% (112/184) and median progression-free survival (PFS) of 16.4 mo (Modi *N Engl J Med* 2019); these results led to the recent FDA approval for HER2+ unresectable or metastatic BC after $\geq$ 2 prior anti-HER2 based regimens. For HER2-low BC and HER2-expressing/mutated NSCLC, no HER2-directed therapies have been approved. In a phase I trial of T-DXd in pts with HER2-low BC or HER2-expressing/mutated NSCLC, cORR was 44.2% (19/43) (Modi SABCS 2018), and 55.6% (10/18) (Tsurutani *Thorac Oncol* 2018), respectively. In preclinical models, T-DXd combined with an anti–PD-1 antibody was more effective than monotherapy with either agent (Iwata *Mol Cancer Ther* 2018). Here we describe a phase Ib study of T-DXd in combination with pembrolizumab in pts with locally advanced/metastatic HER2-expressing BC or HER2-expressing/mutated NSCLC (DS8201-A-U106; NCT04042701). **Methods:** This is an open-label, multicenter, nonrandomized, multidose, 2-part study in adult (aged $\geq$18 y) pts in the United States and Europe. In part 1 (dose escalation), pts received T-DXd 3.2 or 5.4 mg/kg IV q3w and pembrolizumab 200 mg IV q3w to determine the recommended dose for expansion (RDE). The RDE will be given to 4 cohorts (part 2): 2 cohorts with BC (HER2+ [IHC 3+ or IHC 2+/ISH+] with progression on prior T-DM1; and HER2-low [IHC 1+ or IHC2+/ISH-] with progression on prior standard treatments) and 2 cohorts with NSCLC (anti–PD-1, –PD-L1, and -HER2 treatment naive either HER2-expressing [IHC $\geq$ 1+] or HER2-mutated). Enrollment began in February 2020 with approximately 115 to 133 pts planned to be enrolled at 5 sites for part 1 and expanding to 25 sites for part 2. The primary endpoint in part 1 is dose-limiting toxicities. The part 2 primary efficacy endpoint is cORR by independent central review (ICR) per RECIST 1.1. Additional endpoints include duration of response, disease control rate, and progression-free survival by ICR, overall survival, safety, and pharmacokinetics. Clinical trial information: NCT04042701. Research Sponsor: Daiichi Sankyo, Inc.

TPS1101 Poster Session (Board #186), Fri, 8:00 AM-11:00 AM

First-in-human phase I study of anti-HER2 ADC MRG002 in patients with relapsed/refractory solid tumors. *First Author: Jin Li, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China*

Background: MRG002 is an antibody drug conjugate (ADC) composed of a humanized anti-HER2 IgG1 monoclonal antibody conjugated to a microtubule disrupting agent monomethyl auristatin E (MMAE). MRG002 is presently being investigated in an ongoing phase I study for safety, tolerability, pharmacokinetics (PK), and preliminary antitumor activity in patients (pts) with solid tumors. **Methods:** MRG002 is evaluated as monotherapy for the treatment of pts with confirmed HER2 positive locally advanced or metastatic cancers, including breast cancer (BC), gastric cancer (GC), salivary gland cancer (SGC) and others. The primary objective is to determine the maximum tolerated dose (MTD) and a recommended phase II dose (RP2D). Secondary objectives include evaluation of PK, tumor response, and immunogenicity. In the dose escalation phase with "3+3" design, approximately 24 pts will be enrolled to identify MTD. The starting dose of MRG002 is 0.3 mg/kg, followed by 0.6, 1.2, 1.8, 2.2, 2.6, and 3.0 mg/kg. In the dose expansion phase, about 50 pts with HER2 positive advanced cancers will be enrolled to further evaluate the safety, antitumor activity, and PK at an appropriate confirmed dose. In this phase I study, each pt receives single agent MRG002 once every 3 weeks (Q3W) for a maximum of 8 treatment cycles. Pts with BC and GC should have HER2 positive advanced solid tumors per College of American Pathologists (CAP) guidelines. For other cancers, pts must have IHC status of 2+ or 3+, regardless of FISH results. Pts should have either failed or are ineligible for standard treatments. All pts must have at least 1 measurable lesion per RECIST 1.1. ECOG should be 0-1, and bone marrow, hepatic, renal, cardiac functions should be adequate. Observations include adverse events (AEs), dose-limiting toxicity (DLT), and antitumor activity, which is assessed every two treatment cycles. Further clinical trial details can be found on chinadrugtrials.org.cn (CTR20181778). Enrollment is ongoing since November 2018. Clinical trial information: CTR20181778. Research Sponsor: Shanghai Miracogen Inc.

TPS1102 Poster Session (Board #187), Fri, 8:00 AM-11:00 AM

Trial in progress: A phase II open-label, randomized study of PARP inhibition (olaparib) either alone or in combination with anti-PD-L1 therapy (atezolizumab) in homologous DNA repair (HDR) deficient, locally advanced or metastatic non-HER2-positive breast cancer. *First Author: Patricia LoRusso, Yale University School of Medicine, New Haven, CT*

Background: While immunostimulatory therapies have shown great success, a major challenge remains identification of mechanisms to effectively treat the majority of patients with so-called "non-inflamed" tumors lacking marked lymphocyte infiltration and PD-L1 expression. The DNA repair proficiency of a tumor may impact its potential for immune recognition and sensitivity to immune checkpoint blockade. Preclinically, PARP inhibition in HDR-deficient tumors has been shown to trigger antitumor immunity through a STING-dependent antitumor immune response. Effects of PARP inhibitors were augmented when combined with PD-1 blockade. We hypothesize that enhanced DNA damage and cell death induced by PARP inhibition in tumors with homology directed repair (HDR) deficiency will enhance adaptive anti-tumor immune responses and increase sensitivity to PD-1 axis blockers. **Methods:** This is a randomized, open-label phase II clinical trial exploring the PARP inhibitor olaparib either alone or in combination with the anti-PD-L1 human monoclonal antibody atezolizumab in BRCA1/2 mutated locally advanced or metastatic non-HER2-positive breast cancer. HDR deficiency is defined as the presence of deleterious BRCA 1/2 mutations. Randomization occurs in a 1:1 fashion to two arms: (1) olaparib 300 mg PO bid continuously in 21-day cycles or (2) olaparib 300 mg PO bid continuously in combination with atezolizumab 1200 IV every 3 weeks in 21-day cycles. Patients undergo baseline evaluations and pre-treatment biopsy within 2 weeks of starting therapy. Repeat biopsies are required at the time of first tumor assessment scan (6 weeks from the start of treatment) and in the event of disease progression. Correlative studies, including detailed analysis of the genomic profile and tumor immune contexture, will be performed at each biopsy time point. The primary objective is to compare progression free survival between the study arms. If progression occurs on the olaparib monotherapy arm, cross-over to the combination arm is allowed. This study began enrolling in August 2018; 47 of the planned 72 patients have been registered. Clinical trial information: NCT02849496. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

TPS1103 **Poster Session (Board #188), Fri, 8:00 AM-11:00 AM**

A phase I dose-escalation trial of alpha-tocopheryloxyacetic acid and concurrent trastuzumab in patients with treatment refractory HER2+ metastatic breast cancer. *First Author: William R Gwin, University of Washington, Seattle, WA*

Background: Metastatic HER2+ breast cancer, while initially responsive to trastuzumab, pertuzumab, and TDM-1, eventually progresses. The FDA recently approved trastuzumab deruxtecan, showing benefit in progression free survival but not in overall survival to date. Thus, additional therapies are needed for patients who progress on these HER2 directed agents. In metastatic HER2+ breast cancer, HER2-specific Th1 immune responses and higher CD4+ Th1 and CD8+ TIL levels are associated with a survival benefit. As this Type 1 immunity occurs in a minority of patients, additional immune modulation is needed. Alpha-tocopheryloxyacetic acid (α-TEA) has been reported to augment Type 1 immunity through increasing activated effector memory CD4+ and CD8+ T cells and decreasing immune suppressive CD4+CD25+ regulatory T cells in the tumor microenvironment. When given concurrently with an anti-HER2 antibody (7.16.4) in a pre-clinical tumor model, α-TEA synergized with 7.16.4 to induce tumor regression. We hypothesize that α-TEA and trastuzumab combination therapy in metastatic HER2+ breast cancer will be well tolerated, induce a clinical response, and augment anti-tumor Th1 immunity. **Methods:** *Trial Design*: Phase I dose escalation trial of α-TEA in combination with trastuzumab. Patients with metastatic HER2+ breast cancer will receive one of four doses sequentially of α-TEA: 0.6 mg/kg, 1.2 mg/kg, 2.4 mg/kg, and 4.8 mg/kg. Toxicity is assessed at baseline and through end of study. Blood and tumor tissue will be collected for immunologic monitoring and evaluation. Clinical response will be evaluated according to RECIST 1.1. *Eligibility:* Patients with progressive metastatic HER2+ breast cancer who have previously progressed on trastuzumab/pertuzumab and TDM-1. *Specific Aims*: Determine: (1) safety of four escalating doses of α-TEA with concurrent trastuzumab, (2) clinical response rate of α-TEA with concurrent trastuzumab (3) if concurrent α-TEA and trastuzumab increases activated effector memory CD4+ and CD8+ T cells, and (4) if concurrent α-TEA and trastuzumab increase the number of HER2-specific T cells. *Statistical Methods*: (1) The sample size of 24 and cohort size of 6 are determined by simulation experiments and practical consideration, (2) clinical response will be evaluated; overall PFS and OS will be calculated, (3) activated effector memory CD4+ and CD8+ T-cells will be analyzed (4) HER2-specific IFN-g/IL-10 ratios will be evaluated. *Targeted Accrual:* Twenty-four (24) patients. Clinical trial information: NCT04120246. Research Sponsor: Veana Therapeutics, Inc.

TPS1104 **Poster Session (Board #189), Fri, 8:00 AM-11:00 AM**

SGNLVA-001: A phase I open-label dose escalation and expansion study of SGN-LIV1A administered weekly in breast cancer. *First Author: Heather Christine Beckwith, Univ of Minnesota, Minneapolis, MN*

Background: LIV-1 is a highly prevalent transmembrane protein in breast cancer cells. Ladiratuzumab vedotin (LV), SGN-LIV1A, is an investigational antibody-drug conjugate (ADC) that targets LIV-1 via a humanized IgG1 monoclonal antibody conjugated to monomethyl auristatin E (MMAE) by a protease-cleavable linker. LV is internalized when it binds LIV-1 on cell surfaces and MMAE is released, which binds tubulin and induces apoptosis. LV has been shown to be active and tolerable in metastatic breast cancer (mBC) at a recommended dose of 2.5 mg/kg every 21 days (Modi 2017). More frequent, fractionated dosing has improved the activity and/or safety of other ADCs. Thus, this study is actively accruing subjects with metastatic triple negative breast cancer (mTNBC; estrogen receptor (ER)/progesterone receptor (PR)/human epidermal growth factor receptor 2 (HER2) receptor-negative) and endocrine-resistant ER+ or PR+ (hormone receptor [HR+])/HER2-negative mBC to test weekly dosing of LV (Days 1, 8, and 15 of every 3-week cycle). **Methods:** This study is enrolling up to 82 subjects (42 HR+/HER2-negative and 40 mTNBC) into dose escalation and dose expansion cohorts (NCT01969643). Eligible subjects are females $\geq$18 years old with pathologically and radiologically confirmed metastatic HR+/HER2-negative or mTNBC with at least 1 measurable lesion per RECIST v1.1. Subjects with HR+/HER2-negative disease must have received no more than 1 prior line of cytotoxic chemotherapy in the locally advanced (LA)/mBC setting, either as single agent or combination therapy. Subjects with mTNBC must have received 1 prior line of cytotoxic chemotherapy in the LA/mBC setting. Progression within 6 months of completion of neoadjuvant or adjuvant therapy is considered an LA/mBC regimen. Subjects must have adequate organ function, ECOG status of $\leq$1, and no $\geq$ Grade 2 peripheral neuropathy. Subjects with brain lesions must have received definitive treatment of the lesions. Prior therapy with MMAE-containing agents is not allowed. Dose escalation follows the modified toxicity probability interval method (Ji 2010). Dose expansion cohorts will provide data about activity and tolerability. Tumor assessments will be conducted every 2 cycles per RECIST v1.1 and all subjects will be followed for safety. Pharmacokinetics and markers of pharmacodynamics will be assessed. Primary safety endpoint is the incidence of adverse events and dose-limiting toxicities. Key efficacy endpoints include confirmed overall response rate, duration of response, and progression-free survival. Clinical trial information: NCT01969643. Research Sponsor: Seattle Genetics Inc.

TPS1105 **Poster Session (Board #190), Fri, 8:00 AM-11:00 AM**

A phase II trial of nivolumab (NIVO) + abemaciclib (ABE) or palbociclib (PAL) + anastrozole (ANA) in postmenopausal women and men with estrogen receptor (ER)+/human epidermal growth factor 2 (HER2)- primary breast cancer (BC): CheckMate 7A8. *First Author: Sara M. Tolaney, Dana-Farber Cancer Institute, Boston, MA*

Background: Cyclin-dependent kinase 4/6 (CDK 4/6) inhibition coupled with ER signaling blockade is an efficient treatment approach for patients (pts) with metastatic hormone receptor-positive, HER2− BC. Preclinical data suggest synergistic activity of CDK 4/6 inhibition and PD-1 blockade; in a syngeneic mouse tumor model, improved efficacy and complete tumor regression were observed with phased administration of ABE + PD-L1 therapy. **Methods:** CheckMate 7A8 (NCT04075604) is a randomized, noncomparative, multicenter, phase 2 study evaluating (NIVO) + PAL + ANA in postmenopausal pts with ER+, HER2− primary BC. After determining safe doses for NIVO combination regimens in the safety run-in phase, pts will be randomized in a 4:4:3 ratio to 1 of 3 treatment arms (Table) stratified by PD-L1 expression, node status and tumor size. Following treatment, all pts will undergo surgery and safety follow-up. Eligible pts are postmenopausal women and men with newly diagnosed, untreated, histologically confirmed ER+, HER2− BC with primary tumor $\geq$ 2 cm; suitable for neoadjuvant endocrine monotherapy and surgery; ECOG PS of 0–1; have baseline tumor tissue available; willing to undergo on-treatment research biopsy and tissue collection at surgery. Primary endpoints are number of pts with occurrence of dose-limiting toxicity (safety run-in phase) and residual cancer burden 0–I rate by central assessment at time of definitive surgery (randomized phase). Secondary endpoints include safety and tolerability, pathologic complete response, objective response rate and breast-conserving surgery rate. Key exploratory endpoints include biomarkers indicative of pharmacodynamic changes and potentially predicting treatment sensitivity. Interim analyses are planned. The study is currently enrolling. Clinical trial information: NCT04075604. Research Sponsor: Bristol-Myers Squibb.

Treatment arms in the safety run-in and randomized phases.

Safety run-in phase	NIVO + PAL 3 wks on 1 wk off + ANA × 5 cycles
Randomized phase	
Arm A	NIVO + PAL 3 wks on 1 wk off + ANA × 5 cycles
Arm B	PAL 3 wks on 1 wk off + ANA × 1 cycle then NIVO + PAL 3 wks on 1 wk off + ANA × 4 cycles
Arm C	PAL 3 wks on 1 wk off + ANA × 5 cycles
	ANA, 1 mg orally once daily; NIVO, 480 mg intravenously every 4 wks; PAL, 125 mg orally once daily

TPS1106 **Poster Session (Board #191), Fri, 8:00 AM-11:00 AM**

[OPTIMAL 3] A phase III trial to evaluate the efficacy and safety of DHP107 (Liporaxel, oral paclitaxel) compared to Taxol (IV paclitaxel) as first line therapy in patients with recurrent or metastatic HER2 negative breast cancer (BC) (NCT03315364). *First Author: Sung-Bae Kim, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea*

Background: Paclitaxel is a microtubule-stabilizing drug used for various cancers including breast cancer (BC) and gastric cancer (GC). DHP107 is an oral paclitaxel solution formulated with non-toxic excipients using DH-LASED technology, which doesn't require pre-treatment. DHP107 demonstrated comparable efficacy and safety to IV paclitaxel for patients with advanced GC (Ann Oncol 2018), and was market approved as the first oral paclitaxel in 2016 for GC in Korea. In previous OPTIMAL phase II study, the primary endpoint objective response rate (ORR) was 54.5% in HER2 negative metastatic BC (MBC) patients and 44.4% in triple negative BC (TNBC) patients. Disease control rate (DCR) was 90.9% by the investigators' assessment. Toxicity was manageable (2019 ESMO). OPTIMAL phase III is being conducted in Korea, China and Eastern Europe based on this result and another phase II study (OPERA) is being performed in USA. **Methods:** OPTIMAL 3 study is a multinational, multi-center, randomized and open-label trial enrolling HER2 negative (HR+/HER2- or TNBC) recurrent or metastatic BC patients. Patients are randomized to either study (DHP107) or control group (IV paclitaxel) in a 1:1 ratio and stratified by disease free interval (DFI$\leq$48 weeks vs >48 weeks), visceral metastasis status (visceral vs non-visceral) and country. Patients are administrated with DHP107 (200mg/m^2 p.o. bid) or IV paclitaxel (80mg/m^2 infused) on D1, 8, 15, q4wks. Tumor assessments are performed on every 8 weeks ($\pm$7 days) from C1D1 until disease progression (RECIST V1.1). Key inclusion & exclusion criteria are hormone receptor (ER/PR) positive or negative, HER2 negative, ECOG performance status $\leq$1 and no prior chemotherapy in recurrent or metastatic disease. The primary endpoint is progression free survival (PFS). Secondary endpoints include ORR, overall survival (OS), time to treatment failure (TTF), DCR, quality of life (QoL) and safety. Total target number of patients is 476 with an estimated 10% drop-out rate. The test is based on non-inferiority hypothesis (HR=1.33) with 80% power. The primary endpoint will be analyzed using a one-sided test at a 2.5% significance level, and other endpoints will be analyzed using a two-sided test at a 5% significance level, with 95% confidence interval. The first subject was enrolled in Jan 2019 and recruitment is ongoing and is expected to be completed in Dec 2020. Final results of this study will be announced by the end of 2022. Clinical trial information: NCT03315364. Research Sponsor: DAEHWA Pharmaceutical Co,.Ltd.

TPS1107 **Poster Session (Board #192), Fri, 8:00 AM-11:00 AM**

Phase II trial of SAR439859 vs endocrine monotherapy in pre- and postmenopausal, estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-), locally advanced or metastatic breast cancer (BC) with prior exposure to hormonal therapies. *First Author: Sara M. Tolaney, Dana-Farber Cancer Institute, Boston, MA*

Background: Endocrine therapy (ET) targeting ER signaling is the mainstay of care for ER+ metastatic BC. There remains an unmet need in patients (pts) whose tumors become resistant to currently available ET. Selective ER degraders (SERDs) were developed to overcome resistance to existing ER-directed therapies by both competitively antagonizing and degrading ERs, while exploiting continued dependence of the tumor on ER signaling. SAR439859 is a potent SERD with robust preclinical ER degrading activity. In a Phase I dose escalation trial, SAR439859 demonstrated a favorable safety profile with no dose-limiting toxicities across all doses (20–600 mg QD). ER occupancy generally exceeded $>$ 87% with plasma concentrations $>$ 100 ng/mL. Overall response rate was 6.3% and clinical benefit rate was 50% (Campone. SABCS 2019. P5-11-02). The recommended Phase II monotherapy dose was 400 mg QD. **Methods:** This international, prospective, open-label, randomized Phase II study (NCT04059484; ACT16105) assesses safety and efficacy of SAR439859 in pts with ER+ ($>$ 1%)/HER2- metastatic or locally advanced BC progressing on $\geq$ 6 months of continuous ET (0–2 lines in the metastatic setting). Prior CDK inhibitors are allowed. Exclusion criteria include Eastern Cooperative Oncology Group performance status (ECOG PS) $\geq$ 2, life expectancy $<$ 3 months, $>$ 1 chemotherapy or targeted therapy in the metastatic setting, concomitant illness and factors potentially affecting SAR439859 absorption. Pts are randomized 1:1 to SAR439859 400 mg QD orally or physician's choice of endocrine monotherapy (fulvestrant, tamoxifen, aromatase inhibitor). Pts receive 28-day cycles until unacceptable toxicity, progression, death, investigator decision or pt request. Stratification factors include visceral metastases, prior CDK4/6 inhibitors, and ECOG PS. Primary endpoint is progression-free survival (RECIST v1.1). Secondary endpoints include overall survival, response rate, duration of response, clinical benefit, pharmacokinetics, quality of life and safety. Target enrollment: n = 282; current enrollment: n = 9. Funding: Sanofi Clinical trial information: NCT04059484. Research Sponsor: Sanofi.

TPS1108 **Poster Session (Board #193), Fri, 8:00 AM-11:00 AM**

Phase II preoperative window study of SAR439859 versus letrozole in postmenopausal women with newly diagnosed estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-) breast cancer. *First Author: Mario Campone, Institut de Cancérologie de l'Ouest, René Gauducheau, St Herblain, France*

Background: Endocrine therapy targeting ER signaling is the standard of care for women with ER+ breast cancer. Selective ER degraders (SERDs) block ER signaling through dual competitive antagonism and receptor degradation. SAR439859, a potent, oral SERD, is in clinical development for ER+/HER2- breast cancer. This study is a 14-day preoperative non-therapeutic 'window of opportunity' trial to assess the direct effects of SAR439859 on tumor cell proliferation by evaluating the pharmacodynamic activity of SAR439859 in ER+/HER2- breast cancer. **Methods:** This international, open-label, Phase II randomized study (NCT04191382; ACT16106) evaluates SAR439859 at two dose levels versus the aromatase inhibitor letrozole by assigning 126 preoperative patients 1:1:1 to receive SAR439859 400 mg/day, SAR439859 200 mg/day or letrozole 2.5 mg/day. SAR439859 dosing is based on an ongoing Phase I/II study (NCT03284957; TED14856) in metastatic breast cancer (Campone. SABCS 2019. P5-11-02). Postmenopausal women with ER+/HER2- breast cancer indicated for immediate surgery (Stage I, Stage II or operable Stage III), Eastern Cooperative Oncology Group performance status 0–1 and Ki67 levels of $\geq$ 15% are eligible. Exclusion criteria include disorders potentially affecting absorption of SAR439859 or letrozole, and any prior therapy for breast cancer. Patients receive study treatment for 14 days, with the last dose given on the day before surgery. Paired tumor biopsies for assessment of biomarkers are performed at baseline and during surgery. The primary study endpoint is change in Ki67, a predictor of treatment benefit and long-term survival outcomes, after 14 days of treatment compared with baseline. Secondary endpoints include proportion of patients with $\geq$ 50% decrease in Ki67, ER expression to assess degradation, and safety. Pharmacokinetics of SAR439859, additional tumor markers, genomic mutation profile, Preoperative Endocrine Prognostic Index and pathological Complete Response will also be assessed. The study is currently recruiting; target enrollment: n = 126. Clinical trial information: NCT04191382. Research Sponsor: Sanofi.

TPS1109 **Poster Session (Board #194), Fri, 8:00 AM-11:00 AM**

A phase III trial of capivasertib and paclitaxel in first-line treatment of patients with metastatic triple-negative breast cancer (CAPItello290). *First Author: Peter Schmid, Barts Cancer Institute, Centre for Experimental Cancer Medicine, London, United Kingdom*

Background: Therapeutic options for patients with metastatic triple-negative breast cancer (TNBC) are limited to sequential chemotherapy, although recent advances with novel agents have been made for specific subgroups (PD-L1 inhibitor atezolizumab in combination with nab-paclitaxel in patients with PD-L1-positive tumors and PARP inhibitors in patients with germline BRCA mutations). The PI3K/AKT/PTEN signaling pathway is often activated in TNBC, mainly through activating mutations in *PIK3CA* or *AKT1* and/or inactivating alterations in PTEN. The phase II PAKT study (NCT02423603) demonstrated that addition of the oral AKT inhibitor capivasertib to first-line paclitaxel resulted in significantly longer progression-free survival (PFS) and overall survival (OS) in patients with advanced TNBC, especially in patients with PIK3CA/AKT1/PTEN-altered tumors (Schmid et al, 2019). This phase III trial (NCT03997123) will further evaluate the efficacy and safety of capivasertib in combination with paclitaxel in first-line treatment of patients with metastatic TNBC in an unselected population and will also explore potential predictive markers of sensitivity to the combination of paclitaxel and capivasertib. **Methods:** Eligible patients for this double-blind, randomized, placebo-controlled trial must have metastatic TNBC or locally advanced disease not amenable to resection with curative intent. Patients must be candidates for single-agent taxane therapy and have received no prior systemic therapy for locally advanced inoperable or metastatic disease. Prior chemotherapy in the (neo)adjuvant setting must be completed $\geq$12 months prior to enrollment. Patients will be randomized 1:1 to paclitaxel 80 mg/m^2 (days 1, 8 and 15) with either capivasertib 400 mg twice daily or placebo (days 2–5, 9–12 and 16–19) every 28 days, until objective radiologic disease progression as defined by RECIST 1.1, unacceptable toxicity or death. Stratification factors will be prior adjuvant chemotherapy, visceral versus non-visceral disease, and geographic region. Post-randomization central testing of tumor tissue (collected prior to enrollment) will be carried out to identify predictive markers of sensitivity to treatment. The primary endpoints of this study are PFS and OS. Secondary endpoints include safety and tolerability, time to second progression or death, objective response rate, duration of response, and clinical benefit rate. Enrollment for this study started in May 2019. Clinical trial information: NCT03997123. Research Sponsor: AstraZeneca.

TPS1110 **Poster Session (Board #195), Fri, 8:00 AM-11:00 AM**

First-in-human phase I/Ib multicenter, open-label dose escalation study to assess safety and tolerability of PMD-026 in patients with metastatic breast cancer with expansion in metastatic triple negative breast cancer. *First Author: Muralidhar Beeram, START, San Antonio, TX*

Background: Metastatic triple negative breast cancer (mTNBC) has a poor prognosis with limited durable treatment options. RSK (P90 ribosomal S6 kinase) is a signaling protein at the convergence point of PDK-1 and MAPK signaling pathways. RSK1-3 phosphorylates transcription factors, including Y-box binding protein-1 (YB-1), thereby inducing drug resistance and cancer growth genes. Phosphorylated YB-1 is involved in tumor cell survival, proliferation, and drug resistance. In human breast tumor samples, RSK2 protein is expressed across all breast cancer subtypes (TNBC, ER+ and HER2+) and is associated with poor overall survival. Expression of RSK2 is found in approximately 87% of mTNBC tumors and of those tumors approximately 41% have very high expression of RSK2. PMD-026 is a potent, oral, small molecule RSK inhibitor with high selectivity for RSK2. Preclinical *in vivo* studies have demonstrated activity both as a single agent and in combination with standard of care therapies. Further, a CAP/CLIA certified IHC method has been developed with Roche to determine tumor expression of RSK2. **Methods:** This single-arm, open-label, first-in-human, phase I/Ib study evaluates the safety and efficacy of single agent PMD-026 in patients with metastatic breast cancer for whom standard therapies are no longer effective. During dose escalation, the study utilizes an accelerated titration design with single patient cohorts until the occurrence of DLT or Grade 2+ toxicity; then reverts to 3+3 design to define the maximally tolerated dose (MTD) and recommended phase II dose (RP2D). The dose expansion portion will enroll approximately 20 patients with mTNBC. Patients are dosed orally once daily in 21-day cycles with measures to adapt the dosing schedule based on the pharmacokinetic (PK) data, as needed. Tumor tissue is required for all enrolled patients; RSK2 expression will be retrospectively correlated with clinical outcomes. The primary objectives are to determine safety and tolerability of PMD-026, determine the MTD, define a RP2D, and assess anti-tumor activity of PMD-026 in patients with TNBC. Secondary objectives are to evaluate PK, time to response, mTNBC subtyping using NanoString, and duration of response of PMD-026. To date, cohorts 1 and 2 have been completed without DLT. Enrollment to cohort 3 began in January 2020. Clinical trial information: NCT04115306. Research Sponsor: Phoenix Molecular Designs.

TPS1111 Poster Session (Board #196), Fri, 8:00 AM-11:00 AM

CONTESSA TRIO: A multinational, multicenter, phase (P) II study of tesetaxel (T) plus three different PD-(L)1 inhibitors in patients (Pts) with metastatic triple-negative breast cancer (TNBC) and tesetaxel monotherapy in elderly pts with HER2-metastatic breast cancer (MBC). *First Author: Sara M. Tolaney, Dana-Farber Cancer Institute, Boston, MA*

Background: Chemotherapy treatments with robust efficacy that preserve quality of life are needed. T is a novel, oral taxane that has potential advantages over currently available taxanes, including: oral administration with a low pill burden and once every 3 week (Q3W) dosing; no observed hypersensitivity reactions; preclinical evidence of central nervous system (CNS) penetration; and improved activity against chemotherapy-resistant tumors. More than 600 pts have been treated with T in clinical studies. T had robust monotherapy activity in a P2 study in 38 pts with HER2-, HR+ MBC, with a confirmed objective response rate (ORR) per RECIST 1.1 of 45%. **Methods:** CONTESSA TRIO is a 2-cohort, multinational, multicenter, P2 study. In Cohort 1, 90 pts (potential expansion to up to 150 pts) with metastatic TNBC who have not received prior chemotherapy for advanced disease will be randomized 1:1:1 to receive T at 27 mg/m^2 Q3W plus either: (1) nivolumab at 360 mg Q3W; (2) pembrolizumab at 200 mg Q3W; or (3) atezolizumab at 1,200 mg Q3W. Nivolumab and pembrolizumab (PD-1 inhibitors) and atezolizumab (a PD-L1 inhibitor) are approved for the treatment of multiple types of cancer; atezolizumab, in combination with nab-paclitaxel, was recently approved in the US for the treatment of metastatic TNBC. The dual primary endpoints for Cohort 1 are ORR and progression-free survival (PFS). A sample size of 30 pts in each PD-(L)1 inhibitor treatment group has approximately 70% power to detect an ORR difference of $\geq$ 35% between the treatment group with the highest ORR and the treatment group with the lowest ORR. Secondary endpoints include duration of response (DoR) and overall survival (OS). Efficacy results for each of the 3 PD-(L)1 inhibitor combinations will be assessed for correlation with the results of each of the 3 approved PD-L1 diagnostic assays. CONTESSA TRIO is the first randomized clinical study to compare 3 approved PD-(L)1 inhibitors. In Cohort 2, 40 elderly pts (potential expansion to up to 60 pts) with HER2- MBC who have not received prior chemotherapy for advanced disease will receive T monotherapy at 27 mg/m^2 Q3W. The primary endpoint for Cohort 2 is ORR. A sample size of 40 will allow the ORR to be estimated with a maximum standard error of $<$ 8%. Secondary endpoints include PFS, DoR and OS. Pts with CNS metastases are eligible for both cohorts. The study was initiated in March 2019. Clinical trial information: NCT03952325. Research Sponsor: Odonate Therapeutics, Inc.

TPS1112 Poster Session (Board #197), Fri, 8:00 AM-11:00 AM

A phase II trial of atezolizumab (anti-PD-L1) with carboplatin in patients with metastatic triple-negative breast cancer (mTNBC). *First Author: Eric Michael Lander, Vanderbilt University Medical Center, Nashville, TN*

Background: Patients with metastatic triple negative breast cancer (mTNBC) have limited treatment options. Recent studies with a PD-L1 inhibitor and taxane based chemotherapy have demonstrated an increase in median progression free survival (PFS) in mTNBC. While taxanes target microtubules, platinum agents directly alkylate DNA and may generate additional neoantigens to enhance anti-tumor immunity via immune checkpoint inhibition. In this study, we are evaluating the combination of carboplatin with and without atezolizumab in patients with mTNBC. Serial biopsies are poised to help elucidate biological differences in responders and nonresponders. As optimal timing of adding checkpoint inhibition to chemotherapy is debatable, the randomized, crossover design will give insight into whether priming mTNBCs with DNA damaging chemotherapy results in cellular and immune changes that lead to a greater likelihood of response. **Methods:** This is a randomized phase II multicenter study at seven sites within the Translational Breast Cancer Research Consortium (TBCRC). Patients with mTNBC, ECOG 0-1, and 0-1 prior regimens for mTNBC are eligible. 106 patients will be randomized 1:1 to receive atezolizumab 1200 mg plus carboplatin AUC 6 (n = 53; Arm A) or carboplatin AUC 6 alone (n = 53; Arm B) every 3 weeks until intolerable toxicity or disease progression occurs. Patients receiving carboplatin alone have the option to cross over to atezolizumab upon progression (Arm Bx). Patients will undergo clinical assessment every cycle, and tumor assessment every 3 cycles with CT scan of the chest, abdomen, and pelvis and bone scan. Core biopsies of a metastatic lesion are performed at baseline and at progression. The primary endpoint is median progression free survival (PFS) with 95% confidence intervals based on RECIST 1.1. The sample size of 106 with 1:1 randomization is powered to detect a 1.5-month difference in PFS between arms (α = 0.10, β = 0.20). Secondary endpoints include overall response rate (ORR), duration of response (DOR), clinical benefit rate, and overall survival. The PFS, ORR, and DOR will also be measured by irRECIST to account for delayed effects of atezolizumab on tumor burden. The quantification of tumor infiltrating lymphocytes (TILs) will study the prognostic effects of TILs on PFS in patients receiving atezolizumab. Biopsy-derived PD-L1 expression by IHC and RNA-seq will assess treatment-induced changes, define triple-negative subtypes, and evaluate for resistance mechanisms. To date, 89 of 106 patients are enrolled. Clinical trial information: NCT03206203. Research Sponsor: Genentech, Conquer Cancer Foundation of the American Society of Clinical Oncology, Translational Breast Cancer Research Consortium; SPORE.

TPS1113 Poster Session (Board #198), Fri, 8:00 AM-11:00 AM

Phase II trial of a PARP inhibitor in somatic *BRCA* mutant metastatic breast cancer. *First Author: Neelima Vidula, Massachusetts General Hospital, San Francisco, CA*

Background: Poly(ADP-ribose) polymerase (PARP) inhibitors are now approved for patients with germline *BRCA1/2* mutated HER2 negative metastatic breast cancer (MBC). However, germline *BRCA1/2* mutations only account for 5-10% of breast cancer. We previously demonstrated that a subset of MBC may harbor somatic *BRCA1/2* mutations detectable by cell-free DNA (cfDNA) (Vidula, SABCS, 2017). We hypothesize that somatic *BRCA1/2* mutant MBC may also respond to PARP inhibition, similar to ovarian cancer, where PARP inhibition is efficacious in both somatic and germline tumors (Oza, 2017). **Methods:** This single arm, open label, phase II clinical trial is evaluating the efficacy of talazoparib, a PARP inhibitor, in 30 patients with somatic pathogenic *BRCA1/2* mutant MBC identified by cfDNA. Patients may have triple-negative disease with receipt of at least 1 prior chemotherapy regimen, or hormone receptor positive, HER2 negative disease with at least 1 prior hormone therapy for MBC. Patients may have received a prior platinum, in the absence of progression on platinum chemotherapy. Patients must not have a known germline *BRCA1/2* mutation. Patients will be treated with talazoparib 1 mg daily until progression, unacceptable toxicity, or withdrawal of consent, with clinical exams monthly, scans (CT chest, abdomen, and pelvis, and bone scan as appropriate) every 3 months, and serial cfDNA collected monthly. The primary endpoint is progression-free survival, as defined by RECIST 1.1. Subjects are enrolled in a 2-stage design, which provides 80% power to demonstrate that treatment is associated with "success" (PFS $>$ 12 weeks) in ^{3} 53% patients (4% alpha). Additional endpoints include objective response rate and toxicity (per NCI CTCAE version 5.0). Correlative endpoints include determining changes in *BRCA1/2* mutant allele fraction, genomic evolution including emergence of *BRCA* reversion mutations, and the impact of biomarker changes on outcomes. This trial is currently enrolling patients at the Massachusetts General Hospital. Successful completion of this study may help expand the patient population that is able to benefit from PARP inhibition. Clinical trial information: NCT03990896. Research Sponsor: Pfizer Aspire Award.

TPS1114 Poster Session (Board #199), Fri, 8:00 AM-11:00 AM

Immunotherapy and chemotherapy combination for chest wall disease: TBCRC 044 trial. *First Author: Neelima Vidula, Massachusetts General Hospital, San Francisco, CA*

Background: Immunotherapy combined with chemotherapy is being studied in metastatic breast cancer, and may have durable outcomes. Chest wall recurrence represents a difficult to treat subtype of breast cancer with a poor prognosis, with lymphovascular invasion in the primary tumor a significant risk factor. Given the inflammatory nature of this disease and the association of programmed cell death 1 (PD-1) expression with lymphovascular invasion, we hypothesized that the combination of pembrolizumab, an anti-PD-1 antibody, with carboplatin may be effective as treatment for breast cancer chest wall recurrences. **Methods:** This randomized phase II study is enrolling 84 patients with breast cancer involving the chest wall, who may also have distant metastases. Patients receive treatment with pembrolizumab 200 mg and carboplatin AUC 5 every 3 weeks for 6 cycles (Arm A, n = 56) followed by maintenance pembrolizumab +/- carboplatin (Arm Ax), or carboplatin AUC 5 every 3 weeks for 6 cycles (Arm B, n = 28) with an option to cross-over to pembrolizumab +/- carboplatin on progression (Arm Bx). Patients with all disease subtypes, triple-negative, hormone receptor positive/HER2- after 2 prior lines of hormone therapy, and HER2+ disease (with the option to continue trastuzumab) are eligible, with no limit on the number of prior therapies. Prior platinum chemotherapy is allowed in the absence of overt disease progression. Patients undergo clinical assessment with every cycle of treatment including chest wall photography, scans (CT chest, abdomen, and pelvis) every 2 cycles, and have peripheral blood and chest wall biopsies collected at baseline and the start of cycle 3 for correlative studies. The primary endpoint is the disease control rate in the chest wall and distant sites at 18 weeks of treatment based on RECIST 1.1. The study is powered to determine a 20% difference in disease control between arms (hazard ratio 0.52, α = 0.10, β = 0.20). Additional endpoints include response by tumor programmed death ligand 1 (PD-L1) status and irRECIST, progression-free survival, and toxicity. Chest wall tumor samples will be analyzed for changes in tumor immune composition, and PD-L1 and MYC oncogene expression, based on preclinical data to suggest that PD-L1 may be upregulated by MYC. Peripheral blood samples will be evaluated for changes in PD-L1 expression, cell-free DNA, and circulating tumor cells with treatment. The study is enrolling patients at 7 sites within the Translational Breast Cancer Research Consortium (TBCRC), with current enrollment of 38/84 patients. Clinical trial information: NCT03095352. Research Sponsor: Grants from Merck, UCSF Breast Oncology Development Grant.

TPS1115 Poster Session (Board #200), Fri, 8:00 AM-11:00 AM

B-TREUH: A single-arm phase II pilot study of euthyroid hypothyroxinemia in metastatic breast carcinoma. *First Author: Shruti Trehan, Aultman Hosp Cancer Ctr, Canton, OH*

Background: It is estimated that there are approximately 155,000 people living with metastatic breast cancer in the US. Studies exploring the connection between hypothyroidism or hyperthyroidism and breast cancer have yielded varying results with up to 33% prevalence of thyroid disease in these patients. L-thyroxine (T4) is the most commonly prescribed agent in the US to manage hypothyroidism. However, there are data suggesting that T4 is a pro-oncogenic agent with proposed mechanisms such as stimulation of mitogenesis, angiogenesis, resistance to apoptosis. In addition, T4 May counter anti-PDL-1 and radiation effects. Triiodothyronine (T3), which is deiodinated form of T4 and also commercially available, is felt to be less oncogenic and less mitogenic. Therefore, exogenous supplementation of T3 would decrease the T4 levels creating the desired state of EUTHYROID HYPOTHYROXINEMIA. The study hypothesizes that replacing L-thyroxine (T4) with Triiodothyronine (T3) in hypothyroid patients with metastatic breast carcinoma, while they simultaneously continue to receive standard systemic therapy, with titrating T3 dose to achieve a state of Euthyroid Hypothyroxinemia would result in improved disease outcomes. **Methods:** Eligible participants are adults with metastatic breast carcinoma with estimated life expectancy of $>$ 3months, hypothyroidism, and with normal TSH on L-thyroxine (T4). Following consent, participants will discontinue L-thyroixne (T4) and initiate Triiodothyronine (T3) dose based on current T4 dose after an appropriate washout period. Drug titration will be in accordance with thyroid function testing to maintain levels of free T4 at $<$ 50% normal range. The treatment period will continue for 9 months with periodic assessment of disease status, quality of life (FACT-B) and laboratory measures. The primary endpoint is the progression free survival at 12 months while the secondary endpoints are prevalence of hypothyroidism in the cohort, overall survival, quality of life, and duration of time to achieve the Euthyroid Hypothyroxinemia state. Given many uncertainties to calculate power precisely, the sample size is estimated to be approximately 30 patients. Clinical trial information: NCT03787303. Research Sponsor: None.

1500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Targeted therapy based on germline analysis of tumor-normal sequencing (MSK-IMPACT) in a pan-cancer population. *First Author: Zsofia Kinga Stadler, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Tumor mutational profiling for identification of somatic alterations for targeted treatment is increasingly being performed in advanced cancer patients (pts). We sought to assess the clinical utility of germline mutation profiling for targeted therapeutic interventions in a pan-cancer patient population. **Methods:** All pts who had germline genetic testing through a prospective protocol via a next-generation sequencing panel (MSK-IMPACT) were identified (N=11,975) from 2015-5/2019. The medical record of pts with likely pathogenic/pathogenic germline (LP/P) alterations in genes with known therapeutic targets were reviewed to identify germline-targeted treatment either in a clinical or research setting. **Results:** We identified 2,043 (17.1%) pts who harbored LP/P variants in a cancer predisposition genes including 777 (6.5%) in genes with potentially targetable therapeutic implications: 416 *BRCA1/2,* 149 DNA mismatch repair genes (Lynch syndrome, LS), 122 *ATM*, 45 *PALB2*, 26 *RAD51C/D*, 7 *RET*, 4 *TSC*, 3 *PTCH1*, 2 *ALK*, 1 *EGFR*, 1 *MET* and 1 *KIT*. Of those with advanced disease (n=554), 45.3% received targeted therapeutic treatment (Table) including 50.9% BRCA1/2, 58.3% LS (67.4% of microsatellite-high LS cases), 41.7% *PALB2*, 36.8% RAD51C/D and 19.3% *ATM* carriers. Of patients receiving a poly (ADP-ribose) polymerase inhibitor (PARP-I) in the setting of a *BRCA1/2* mutation, 55.1% had breast or ovarian cancer; however, 44.8% had other tumors, including pancreas, prostate, bile duct, gastric, wherein the drug was given in a research setting. Among *PALB2* pts receiving PARP-Is, 53.3% (8/15) had breast or pancreas cancer; 46.7% had cancer of the prostate, ovary or unknown primary. **Conclusions:** In our pan-cancer analysis, 6.5% of pts harbored a targetable germline variant highlighting the importance of germline analysis in advanced cancer pts for selection of both FDA-approved treatments and clinical trial participation with germline-targeted therapeutics. Research Sponsor: Internal MSK Funding.

Gene(s) with potential targetable therapy	Drug Class	% of advanced cancer patients receiving targeted therapy
BRCA1, BRCA2	PARP-I	50.9% (165/324)
Lynch syndrome (*MLH1, MSH2, MSH6, PMS2, EPCAM*)	Checkpoint-inhibitors	58.3% (42/72) (irrespective of MSI) 67.4% (29/43) (MSI-High)
ATM	PARP-I	19.3% (17/88)
PALB2	PARP-I	41.7% (15/36)
RAD51C, RAD51D	PARP-I	36.8% (7/19)
RET	Tyrosine kinase inhibitor	60% (3/5)
TSC	mTOR inhibitor	0% (0/3)
PTCH1	Hedgehog-signaling inhibitor	33.3% (1/3)
ALK	ALK kinase inhibitor	0% (0/2)
EGFR	EGFR inhibitor	100% (1/1)
MET	MET kinase inhibitor	0% (0/1)

1501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Tumor/normal genomic profiling in patients with metastatic solid tumors identifies pathogenic germline variants of therapeutic importance. *First Author: Erin Frances Cobain, University of Michigan, Ann Arbor, MI*

Background: Tumor molecular profiling via next-generation sequencing (NGS) is routinely utilized to direct patients toward clinical trials of targeted therapeutics. NGS testing of paired tumor/normal samples identifies incidental pathogenic germline variants (PGVs), having potential implications for patients and their families. **Methods:** From 2011-2018, 1,015 patients with metastatic, refractory solid tumors underwent targeted (1700 genes) exome and transcriptome sequencing of matched tumor/normal samples through the Michigan Oncology Sequencing program. Identified PGVs that conferred increased cancer risk or were associated with certain autosomal recessive conditions were reported to the treating oncologist. Chart reviews were conducted every 3 months to assess whether PGV identification impacted treatment decision making. **Results:** 169 PGVs were identified in 160 unique patients (15.8% of cohort). 69 PGVs (41%) harbored a clear somatic second hit event in the tumor. PGVs associated with defects in double-strand DNA repair (*BRCA1, BRCA2, ATM, PALB2, BRIP1)* or DNA mismatch repair (*MLH1, MSH2 and PMS2*) were identified in 49 patients (5% of cohort, 31% of patients with PGVs), 37 of which had not previously been identified. 14 PGVs in DNA double-strand repair and 7 PGVs in DNA mismatch repair were identified in cancer types not commonly associated with hereditary breast ovarian cancer or Lynch syndromes, including cancers of unknown primary origin and sarcomas. 7 patients received a PARP inhibitor (PARPi), 3 patients received an immune checkpoint inhibitor (ICI) and 1 patient received both PARPi and ICI therapy on the basis of a PGV in DNA repair. 6 patients achieved clinical benefit, defined as time on treatment $\geq$ 6 months. A patient with cancer of unknown primary origin and PGV in MSH2 achieved exceptional response to ICI therapy, with complete response ongoing and lasting 23 months. **Conclusions:** Targeted NGS of matched tumor/normal samples identified PGVs in about 1 in every 6 patients with metastatic solid tumors. Approximately 40% of PGVs are associated with a somatic second hit in the tumor, supporting their role in tumor pathogenesis. Unexpected PGVs with therapeutic implications are identified in patients with diverse cancer types, providing opportunities to use targeted therapies with potential for significant clinical benefit. Given this finding, testing for PGVs in DNA repair genes should be considered in all patients with metastatic solid tumor malignancies. Research Sponsor: U.S. National Institutes of Health, Other Foundation, University of Michigan Rogel Cancer Center.

1502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Characterization of patients with multiple primary tumors. *First Author: Karen Anne Cadoo, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: 17% of patients (pts) with a cancer diagnosis in the U.S. have a prior malignancy. We sought to characterize pts with multiple (≥2) primary cancers (MPC) & identify potential drivers of cancer risk to guide management. **Methods:** Pts prospectively consented (1/2013-2/2019) to tumor-normal sequencing via custom targeted NGS panel. A subset consented to testing of >76 germline cancer predisposition genes. IARC 2004 rules for defining MPC were applied.Age adjusted gender specific standardized incidence ratios (SIR) for cancer event combinations occurring in at least 5pt were calculated using R statistical package. **Results:** Of 24417 pts sequenced, 4341 had MPC (18%). (Table) 3465 (80%) had 2, 4% had >4 cancers. Cancer pairs where SIR of 2nd cancer was higher than expected included: colon-colon, prostate-pancreas, bladder-prostate in men & lung-lung, breast-pancreas, thyroid-pancreas in women. 1580 (36%) pts had germline testing; 324 (21%) had 361 pathogenic/likely pathogenic (P/LP) variants (vts). Of these, 157 (48%), 66(20%), pts had high, moderate penetrance vts. The remainder had low penetrance, recessive or vts of uncertain utility. Of pts with high penetrance vt, 132 (84%) had at least one tumor type concordant with germline findings. **Conclusions:** 18% of pts in this cohort had MPC. There was a significant excess over expected incidence in some cancer combinations. Of pts with germline testing, 21% had a P/LP vt, with most (69%) being high or moderate penetrance. Assessment for loss of heterozygosity in tumor & germline sequencing of the full MPC cohort is ongoing. Research Sponsor: Robert and Kate Niehaus Center for Inherited Cancer Genomics.

N=4341		N (%)	
Male (M)		1917 (44)	
Female (F)		2424 (56)	
Ever smoker		2230 (51)	
Caucasian		3697 (91)	
Ashkenazi Jewish		919 (21)	
# primary cancers:			
2		3465 (80)	
3		684 (16)	
>4		192 (4)	
Median age at first diagnosis (range)		58 (0-89)	
<18 yrs		11 (2%)	
BMI median (range)			
M		27(16-47)	
F		25 (15-54)	
M	SIR Confidence Interval	F	SIR CI
Cancer 1-Cancer 2	(CI)	Cancer 1-Cancer 2	
Colon-colon	**8 3.9-12.5**	Lung-lung	**13 10.8-15.4**
Prostate-pancreas	**7 5.7-9.4**	Breast-pancreas	**10 7.7-12.6**
Bladder-prostate	**7 5.4-8.4**	Thyroid-pancreas	**9 1.9-18.1**
Lung-Lung	**6 4.5-7.7**	Colon-colon	**7 3.2-12.2**
Colon-pancreas	6 1.2-11.3	Colon-lung	**7 4.3-9.8**
Bladder-lung	**5 3.7-7.2**	Thyroid-lung	**6 3.2-9.3**
Colon-bladder	4 1.1-6.6	Colon-thyroid	5 1.1-10.6
Prostate-bladder	**4 2.7-4.4**	Breast-breast	**5 4.8-5.8**
Prostate-thyroid	3 1.4-5.5	Breast-lung	**5 4.2-5.7**
Colon-Lung	**3 1.6-5.0**	Thyroid-breast	**5 3.1-6.6**
Colon-prostate	**3 1.9-4.3**	Bladder-lung	**5 2.0-7.7**
Prostate-lung	2 2.4-3.5	Breast-thyroid	**3 1.7-3.6**
Thyroid-prostate	2 1.1-3.4	Breast-colon	**2 1.5-3.1**

Bold=second tumor SIR observed>expected

1503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Performance of the IBIS/Tyrer-Cuzick (TC) Model by race/ethnicity in the Women's Health Initiative. *First Author: Allison W. Kurian, Stanford School of Medicine, Stanford, CA*

Background: The TC model, a breast cancer (BC) risk assessment tool based on family cancer history, reproductive and lifestyle factors is used to guide BC screening and prevention. TC was developed and validated largely in non-Hispanic White (NHW) women. We evaluated the calibration and discrimination of TC version 7.02 among racially/ethnically diverse post-menopausal women enrolled in the Women's Health Initiative (WHI) clinical trials or observational study. **Methods:** WHI enrolled post-menopausal women from 1993-1998 and followed them prospectively for BC incidence. We included women aged ≤80 years at enrollment with no prior BC or mastectomy and with data required for TC, including weight, height, ages at menarche, first birth and menopause, menopausal hormone therapy use and family history of breast or ovarian cancer in first or second-degree relatives. Calibration was assessed by the ratio of observed BC cases to the number expected by TC (O/E), with expected cases calculated as the sum of cumulative hazards. We tested for differential discrimination by race/ethnicity (NHW, African American, Hispanic, Asian/Pacific Islander, Native American, other) using Cox regression. Time to BC was modeled using age, race/ethnicity, TC estimate (transformed by log of relative lifetime risk), and a term for interaction between race/ethnicity and TC estimate. **Results:** During the follow-up period (median 18.9 years, maximum 23.4 years), 6,836 new BC cases were diagnosed among 91,893 women. TC was well-calibrated overall (O/E 0.95) in NHW and African Americans, but over-estimated risk for Hispanics (O/E 0.75, Table). Results suggested good calibration for Asian/Pacific Islanders and Native Americans, but sample sizes were small. Discrimination did not differ significantly by race/ethnicity (two-sided p-value for interaction = 0.33). **Conclusions:** TC provided similar risk discrimination among post-menopausal women of different racial/ethnic groups over nearly 20 years of follow-up; however, it overestimated risk for Hispanics. Future studies in diverse populations are warranted, with need for a more accurate breast cancer risk assessment tool for Hispanics. Research Sponsor: Myriad Genetics, U.S. National Institutes of Health.

Race/Ethnicity	N	Observed (O) BC cases	Expected (E) BC cases	Calibration (O/E Ratio) (95% CI)
NHW	80,260	6133	6408.6	0.96 (0.93-0.98)
African American	5903	373	411.0	0.91 (0.82-1.00)
Hispanic	2368	115	153.2	0.75 (0.62-0.90)
Asian/Pacific Islander	2131	140	139.2	1.01 (0.85-1.19)
Native American	305	22	20.9	1.05 (0.66-1.59)
Other	926	53	66.5	0.80 (0.60-1.04)
TOTAL	91,893	6836	7199.5	0.95 (0.93-0.97)

1504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Comprehensive breast cancer (BC) risk assessment for CHEK2 carriers incorporating a polygenic risk score (PRS) and the Tyrer-Cuzick (TC) model. *First Author: Shannon Gallagher, Myriad Genetics, Inc., Salt Lake City, UT*

Background: Women with pathogenic variants in the moderate penetrance *CHEK2* gene have on average an estimated > 20% lifetime risk for breast cancer, thereby meeting an established threshold for more aggressive screening, including consideration of breast magnetic resonance imaging (MRI). However, we previously showed that *CHEK2* penetrance is modified by an 86-SNP PRS. *CHEK2* risk is further modified by family history (FH) and other TC model variables. Here, we describe development of a comprehensive risk prediction model for women of European ancestry to more precisely estimate risk by incorporating *CHEK2*, PRS and TC V7.02. The number of *CHEK2* carriers with low (< 20%), moderate (20%-50%) and high (> 50%) remaining lifetime risk based on the combined model was examined in an independent study cohort. **Methods:** This IRB-approved study included de-identified clinical records from 358,471 women of European ancestry who were tested clinically for hereditary cancer risk with a multi-gene panel. Model development was based on analysis of *CHEK2* PV carriers (*N*= 4,331) and women negative for BC gene PV (*N* =353,681) who were tested between September 2013 and July 2019. Risk estimates incorporating *CHEK2*, PRS and TC were calculated using a fixed-stratified (FS) method that accounts for correlations between risk factors in a manner equivalent to multivariable co-estimation. Risk stratification was assessed in an independent cohort of *CHEK2* carriers (*N*= 459) who were tested after July 2019 and not included in model development. **Results:** We detected significant correlation of *CHEK2* status with FH ($p = 4.1 \times 10^{-17}$) and of PRS with FH among *CHEK2* carriers ($p = 1.7 \times 10^{-5}$). For these factors, joint effects were co-estimated using the FS method. In an independent cohort, 24.0% of *CHEK2* carriers were categorized as low risk (< 20%), and 62.6% were categorized as moderate risk (20-50%). For 13.4% of *CHEK2* carriers, risk estimation incorporating PRS and TC generated BC risks of greater than 50%, consistent with genes recognized as highly penetrant. **Conclusions:** In *CHEK2* PV carriers, comprehensive risk assessment could inform individualized decision-making and may lead to improved targeting of screening and prevention strategies. Research Sponsor: Myriad Genetics.

1505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

BARCODE 1: A pilot study investigating the use of genetic profiling to identify men in the general population with the highest risk of prostate cancer to invite for targeted screening. *First Author: Ros A. Eeles, Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom*

Background: Genetic profiling could be used to target population screening for prostate cancer (PrCa). Approximately 170 single nucleotide polymorphisms (SNPs) have been identified that associate with PrCa development. Although these confer a low to moderate risk of PrCa, the risk is cumulative with increasing number of risk alleles. BARCODE1 is the first study to prospectively investigate the use of a genetic profile in PrCa screening in the UK general population. **Methods:** A custom Eurek Genomics (EG) SNP assay was developed. Healthy males aged 55-69 were invited to participate via their General Practitioners (GPs). Saliva samples were collected via mailed collection kits. After DNA extraction, genotyping was conducted using the EG assay and a polygenic risk score (PRS) was calculated for each participant. The PRS was calculated using the sum of the weighted alleles for 130 risk loci. Men in the top 10% of the genetic risk profile were invited for prostate MRI and biopsy at the Royal Marsden Hospital (RMH) in London. **Results:** Invitation letters were sent to 1434 men; overall uptake was 26% (range 13%-47%). 87% of responders were eligible for study entry. DNA was extracted from 303 samples and genotyped. Data were available for 285 men following QC. Mean PRS was 10.33 with a standard deviation of 0.64; twenty-five participants with a PRS above the 90^{th} centile were identified for screening with MRI and prostate biopsy. Of these men (after exclusions due to medical comorbidity/invitations declined) 9 out of 20 had an abnormal MRI (45%) and 18 men underwent biopsy with 7 diagnoses of PrCa (38.8%). All cancers were low-risk with a mean PSA of 1.8 and were managed with Active Surveillance (AS). There were two adverse events following biopsy, both simple lower urinary tract infections managed with oral antibiotics. Average duration of follow-up is 4.5 months (range 1-11). **Conclusions:** Successful completion of recruitment has shown this community study to be feasible, with an average uptake of 26%. Approximately 70 GP sites have been identified to allow a transition to the full BARCODE-1 study which will recruit 5000 men. The use of genetic profiles to guide PrCa screening is attractive; it requires a one-off test utilising germline DNA which can be assessed for risk loci which are constant, unlike PSA which fluctuates. The results of the BARCODE1 study will be important in defining the role of genetic profiling in targeted PrCa population screening. Research Sponsor: European research council.

1506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Results from MAGENTA: A national randomized four-arm noninferiority trial evaluating pre- and post-test genetic counseling during online testing for breast and ovarian cancer genetic risk. *First Author: Elizabeth M. Swisher, University of Washington School of Medicine, Seattle, WA*

Background: Hereditary breast and ovarian cancer (HBOC) is preventable when genetic risk is identified. We aimed to test whether pre and/or post-test genetic counseling is needed to optimally deliver online accessible genetic testing. **Methods:** MAGENTA (Making GENetic Testing Accessible) is a four-arm non-inferiority trial evaluating electronic genetic education and results delivery alone or combined with pre-test only, or post-test only telephone genetic counseling compared to mandatory pre- and post-test counseling (control arm) in women at risk of HBOC (NCT02993068). Regardless of assigned arm, all subjects with a pathogenic mutation received post-test telephone counseling. All subjects were enrolled electronically as part of either a family history cohort (FHC) or a cascade cohort (CC, known familial mutation). The primary outcome was cancer risk distress at 3 months and the trial was powered for the FHC. Secondary outcomes included completion of testing (i.e., received results), anxiety, depression, quality of life, and decisional regret, all measured by standardized scales. **Results:** Enrollment is complete and a total of 3,822 participants were randomized, 3,111 in FHC and 711 in CC. Participants were enrolled from all 50 states, but most were white/non-Hispanic (88%). Among participants that completed genetic testing, 173 (7.2%) had a mutation in a breast or ovarian cancer gene, with 114 (5.7%) of FHC and 59 (14.2%) of CC. In the primary intention-to-treat analysis of FHC, each of the three experimental arms was non-inferior to the control arm for distress at 3 months ($p < 0.025/3 = 0.0083$). In the CC, no and pre-test only counseling were also non-inferior ($p < 0.025/3 = 0.0083$). Distress was lowest in the arm with neither pre nor post-test counseling. Overall, 318 (18%) participants had very high distress at three month follow-up, and this rate was not significantly different across arms. Anxiety, depression and decisional regret did not have statistically significant differences across arms at follow-up. Test completion was highest in the no counseling arm (86.4%) and lowest in the control arm (60.6%). **Conclusions:** Electronic genetic education and results release without genetic counseling was non-inferior with regard to patient distress and was associated with higher test completion and lower distress. These results support use of a genetic testing paradigm providing individualized genetic counseling only for patients with positive test results. Clinical trial information: NCT02993068. Research Sponsor: Stand up to Cancer.

1507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A randomized controlled trial of video-education or in-person genetic counseling for men with prostate cancer (ProGen). *First Author: Huma Q. Rana, Medical Oncology, Dana-Farber Cancer Institute, Boston, MA*

Background: Approximately 10% of men with advanced prostate cancer (PC) have pathogenic/likely pathogenic variants (PV) in cancer susceptibility genes and their identification may lead to targeted therapy. Genetic testing (GT) can also guide cancer surveillance and prevention for family members. While GT is recommended for men with potentially lethal PC, traditional testing models are strained, and access limited. The ProGen study examined a novel pretest model aimed at providing access to GT while promoting informed consent. **Methods:** Inclusion criteria were: potentially lethal PC (metastatic, localized with Gleason score ≥8, rising/persistent PSA after local therapy), diagnosis age ≤ 55 years, prior malignancy, family history suggestive of a PV and/or at oncologist's discretion. Consented subjects from 3 sites were randomized 3:1 to video education (VE) or in-person genetic counseling (GC). Subjects who consented to GT had 67 genes analyzed (Ambry, USA) with results disclosed by telephone by a genetic counselor. Outcomes included GT uptake, PV prevalence, and survey measures of satisfaction, distress, genetics knowledge, family communication, and impact on cancer care (obtained at the time of intervention, and at 1, 4, and 12 months after result disclosure). Two-sided Fischer exact tests were used for between-arm comparisons. **Results:** Over a 2-year period: 662 subjects were randomized, VE or GC were completed by 604 subjects (VE: 93.1%, GC: 88.8%) of whom 596 subjects (VE:98.9%, GC:97.9%) consented to GT. To date, 591 subjects have completed GT (VE: 99.3%, GC: 98.6%). At the time of intervention, most subjects agreed or strongly agreed that their assigned arm was useful (VE: 95%, GC: 88%). Differences were not statistically significant. Notably, 84 PV were identified in 78 subjects (13.2%), with *BRCA1/2* PV accounting for 32% of subjects with a positive result (*BRCA2*:21, *BRCA1*:4). **Conclusions:** In this randomized trial, both novel VE and traditional GC yielded high GT uptake without significant differences in outcome measures of acceptability and satisfaction. VE enabled access to critical GT results while maintaining the core tenants of informed consent. PV were found in 13.2% of subjects, 32% of whom had *BRCA1/2* PV. Analysis of collected survey data to inform strengths and limitations of VE as compared with pretest GC will be presented. Clinical trial information: NCT03328091. Research Sponsor: 2018 Medical Oncology Department Award.

1508 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Uptake of oophorectomy in women with findings on multigene panel testing: Results from the Prospective Registry of Multiplex Testing (PROMPT). *First Author: Susan M. Domchek, University of Pennsylvania, Philadelphia, PA*

Background: With the expansion of multigene panel testing for cancer susceptibility, increasing numbers of patients are identified with pathogenic/likely pathogenic variants (P/LP V) in genes which do not have a clearly actionable increased risk of ovarian cancer (OC) (lifetime risk of OC >5%). However, there is concern that patients and/or providers may ascribe OC risk to such genetic findings with the potential for unnecessary oophorectomy (ooph). **Methods:** The Prospective Registry of Multiplex Testing (PROMPT) is an online registry for individuals with a genetic alteration detected on multiplex panel testing for cancer susceptibility. Participants self-enroll and complete baseline and annual follow-up questionnaires. PROMPT has enrolled 7388 participants (6936; 93.9% women) since September 2014. **Results:** 1566 women in the PROMPT registry reported ooph, the indications for which were reported as either cancer treatment (n=481, 30.7%) or benign disease (n=432, 27.6%). An additional 186 (12.8%) reported PV in genes associated with lifetime OC risk >5% (*BRCA1, BRCA2, RAD51C, RAD51D, BRIP*, or Lynch syndrome genes). The remaining 467 did not have guideline based indications for ooph due to OC risk and are described further here. 92 (19.7%) had a variant of uncertain significance (VUS) in genes associated with OC, 241 (51.6%) had a personal history of breast cancer (BC) and no VUS in OC genes, and 119 (25.5%) had no personal history of BC and no VUS in OC genes. The majority of women had no family history (FH) of OC in first or second degree relatives (Table). Most ooph occurred prior to age 50. Of the 405 women with *CHEK2* P/LP, 11.4% reported ooph (59% under age 50 when age known), as did 13.2% (of 228) with *CHEK2* VUS, 8.8% (of 261) with *ATM* P/LP (66.7% under age 50), and 8.3% (of 387) with *ATM* VUS. In addition, of the 184 women with *PALB2* P/LP, 14.1% reported ooph (35.3% under age 50) as did 11.6% (of 198) with *PALB2* VUS. Of those who reported provider discussions, 47.2% stated "my provider recommended this" (including >60% in the OC gene VUS group) and an additional 25.2% stated "my provider presented this as an option, but not a requirement". In those with no FH of OC, 45.8% stated that their provider recommended ooph. **Conclusions:** 10-15% of women with PV/VUS in genes not associated with a high risk of OC reported ooph without a clear indication. Research Sponsor: Komen, Breast Cancer Research Foundation.

Underwent ooph	No reported FH OC	Ooph <50
VUS in gene associated with OC N=92	68.1%	51.5%
Personal history BC (no OC VUS) N=241	85.0%	58.7%
No BC, no OC VUS N=119	56.2%	73.0%

1510 Poster Discussion Session; Displayed in Poster Session (Board #2), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Vitamin D supplements and marine omega-3 fatty acids and development of advanced cancer. *First Author: Paulette Chandler, Brigham and Women's Hospital/Harvard Medical School, Boston, MA*

Background: Epidemiologic data suggest that vitamin D supplementation may reduce cancer mortality. We tested whether vitamin D and/or omega-3 supplementation reduces the incidence of advanced stage cancer at diagnosis or lethal cancer, and whether body mass index (BMI) modifies these associations. **Methods:** The VITamin D and OmegA-3 TriaL (VITAL) is a randomized, placebo-controlled, 2x2 factorial trial of vitamin D3 (cholecalciferol, 2000 IU/day) and marine omega-3 fatty acids (1 g/day) that enrolled men aged ≥50 years and women aged ≥55 years free of cancer and cardiovascular disease at baseline. For this particular analysis, the primary outcome is a composite of metastatic and fatal invasive total cancer. Secondary analyses included examination of BMI (<25, 25-<30, and >= 30 kg/m^2) as effect modifiers of the observed associations. **Results:** VITAL randomized 25,871 participants, among whom 1,617 were diagnosed with invasive cancer over a median 5.3 year intervention period. No significant differences by treatment arm (vitamin D vs placebo: hazard ratio [HR]=0.96; 95% confidence interval, 0.88-1.06; p=0.47; omega-3 vs placebo; HR 1.03 [0.93-1.13]; p=0.56) were observed. However, a significant reduction in advanced cancers (metastatic or fatal) was found for those randomized to vitamin D, compared to placebo (226 assigned to vitamin D and 274 to placebo; HR 0.83 [0.69-0.99]; p=0.036). There was no difference by omega-3 assignment (246 assigned to omega-3 and 254 to placebo: HR 0.97 [0.81-1.15], p=0.72). When stratified by BMI, there was a significant reduction for the vitamin D arm in incident metastatic or fatal cancer among those with normal BMI (BMI<25: HR 0.62 [0.45-0.86], but not among those who were overweight or obese (BMI 25-<30: HR 0.89 [0.68-1.17]; BMI >=30: HR 1.05 [0.74-1.49]); p for interaction by BMI =0.03. There was no effect modification by BMI noted for the omega 3 arm. **Conclusions:** In a randomized clinical trial, supplementation with vitamin D, but not omega-3s, reduced incidence of advanced (metastatic or fatal) cancer in the overall cohort, with strongest risk reduction in normal weight individuals. Further research is needed to understand these findings. Clinical trial information: NCT01169259. Research Sponsor: U.S. National Institutes of Health.

1511 Poster Discussion Session; Displayed in Poster Session (Board #3), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Complete human papillomavirus vaccination coverage over a 13-year period in a large population of privately insured U.S. patients. *First Author: Yull Edwin Arriaga, University of Texas Southwestern Medical Center, Dallas, TX*

Background: In the US, Human Papillomavirus (HPV) vaccination coverage is low, particularly in adolescents aged 13-15 years with respect to the Healthy People 2020 goal of 80%. There has been variability in the definition of measuring vaccination coverage in published studies. We examined complete HPV vaccination coverage in a population of privately insured individuals in the US. **Methods:** This retrospective study used IBM MarketScan Commercial Database, years 2006 to 2018. Inclusion criteria were ages 9 to 45 years and continuous enrollment from age 9 years or from 2006. Complete HPV vaccination coverage was defined as receipt of 2 doses (age 9-15 years) or 3 doses (age 16-45 years) within 12 months and stratified by year, demographics, and US region. Mean vaccination costs per dose were summarized by vaccine brand and health plan type. **Results:** The table summarizes complete HPV vaccination coverage by selected age groups for 2006 (n=12,221,938), 2010 (n=4,692,633), 2014 (n=2,808,132), and 2018 (n=1,662,148). From 2017 to 2018, the percentage of members who received HPV vaccine increased; for females ages 13-15 by 1% and 16-17 by 5% while for males ages 13-15 by 6% and 16-17 by 15%. In 2018, by region, the highest coverage was in females aged 18-26 at 53% and males aged 16-17 at 43% in the Northeast, and mean cost for each brand was $120 (-6% from 2017), $165 (-3%) and $220 (+5%) for Cervarix (n=151), Gardasil (n=8,201) and Gardasil 9 (n=139,356), respectively. The rate of utilization of Gardasil 9 increased from 33% (2015) to 94% (2018) of all vaccines. The lowest mean HPV vaccine cost by health plan type and brand was with Point-of-Service (POS) and Cervarix at $106, and the highest was with POS with Capitation and Gardasil 9 at $243. **Conclusions:** In a commercially insured US population, complete HPV vaccination coverage was lower than the Healthy People 2020 goal, but increased over time. Coverage varied according to health plan type and by region. In 2018, Gardasil 9 had the highest mean cost but was the most utilized vaccine, which may be related to broader coverage of HPV types. This study was limited by the transient nature of member enrollment and complexity of measuring complete vaccination coverage. These results should inform policy makers and practicing clinicians about the gap in vaccination coverage. Research Sponsor: IBM Watson Health.

Complete HPV vaccination coverage by year, sex, and age.

		Vaccination Coverage (%) by Year			
Sex	**Age (years)**	**2006**	**2010**	**2014**	**2018**
Female	11-12	0	13	20	19
	13-15	0	26	32	37
	16-17	0	27	37	43
	18-26	0	19	34	41
Male	11-12	0	0	14	16
	13-15	0	0	20	32
	16-17	0	0	13	33
	18-26	0	0	4	18

1512 Poster Discussion Session; Displayed in Poster Session (Board #4), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Smoking cessation (SC) and lung cancer (LC) outcomes: A survival benefit for recent-quitters? A pooled analysis of 34,649 International Lung Cancer Consortium (ILCCO) patients. *First Author: Aline Fusco Fares, Princess Margaret Hospital, Toronto, ON, Canada*

Background: Tobacco smoking profoundly impacts LC risk; however, data are limited as to what extent SC prior to diagnosis impacts LC overall survival (OS) and lung cancer specific survival (LCSS). LC screening offers a possible teachable moment, but there is uncertainty of SC benefits after a lifetime of smoking. We use the ILCCO database to answer if SC prior to LC dx is associated with better OS and LCSS, considering time since smoking cessation (TSSC). **Methods:** Using individual data, analysis was performed on 17 ILCCO studies with available TSSC to estimate survival using univariable analysis and models of stage-adjusted and cumulative smoking-adjusted multivariable analysis. Adjusted Hazard Ratios (aHR) from Cox models, cubic spline smooth curves and Kaplan-Meier curves were created. Sensitivity analysis was performed for TSSC and LCSS on 13 studies. **Results:** Of 34649 patients, 14322 (41%) were current smokers 14273 (41%) ex-smokers and 6054 (18%) never smokers at diagnosis. We confirmed that ex-smokers (aHR 0.88 CI 0.86-0.91) and never smokers (aHR 0.76 CI 0.73-0.8) improved OS compared to current smokers. Amongst ex-smokers, < 2y TSSC (aHR 0.88 CI 0.82-0.94), 2-5y TSSC (aHR 0.83 CI 0.77-0.90) and > 5y TSSC (aHR 0.8 CI 0.76-0.84) had improved OS compared to CS. Sensitivity analysis showed a trend towards improved LCSS survival for < 2y TSSC (aHR 0.95 CI 0.86-1.05) and 2-5y TSSC (aHR 0.93 CI 0.83-1.04), whereas > 5y TSSC significantly improved LCSS by 15% (aHR 0.85 CI 0.78-0.92). To mimic the LC screening participants, in analysis of > 30 pack-years individuals, associations were strikingly strong: < 2y TSSC had improved OS by 14% (aHR 0.86 CI 0.80-0.93); 2-5y TSSC by 17% (aHR 0.83 CI 0.76-0.90); and > 5 TSSC by 22% (aHR 0.78 CI 0.74-0.83), compared to current smokers; for < 30 packs-years, a trend towards better OS was observed for < 2y TSSC (aHR 0.95 CI 0.92-1.02) and 2-5y TSSC (aHR 0.86 CI 0.74-1.01), whereas > 5y TSSC improved OS by 23% (aHR 0.77 CI 0.72-0.82). **Conclusions:** Among ex-smokers, the risk of overall death was reduced by 12% on < 2y TSSC, 17% on 2-5y TSSC and 20% > 5y TSSC, whereas for LCSS, the benefit was significant only for > 5y TSCC, compared to current smokers at time of diagnosis. Here we demonstrate that convincing screening participants to quit smoking at any point of their trajectory, even just prior to dx such as < 2y TSSC, improved OS, and LCSS benefit was present beyond 5y of quitting. These relationships are independent of pack-years, age, across all stages and other prognostic variables. Research Sponsor: ILCCO studies: including multiple supporters (Alan Brown Chair in Molecular Genomics, NCI grants, the Intramural Research Program of the Center for Cancer Research, Mayo Foundation, etc).

1513 Poster Discussion Session; Displayed in Poster Session (Board #5), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The impact of poly ADP ribose polymerase (PARP) inhibitors on clonal hematopoiesis. *First Author: Kelly L Bolton, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Poly (ADP-ribose) polymerase (PARP) inhibitors are an important new class of anti-cancer therapies. Therapy-related myeloid neoplasia (tMN) has been reported following PARPi therapy, and is associated with adverse outcomes. Further insight is required into the risk of tMN conferred by PARPi therapy, independent of germline genetic background and prior therapy. We have shown that oncologic therapy selects for acquired mutations in the blood (clonal hematopoiesis; CH) particularly those in the DNA damage response pathway (DDR) including *PPM1D*, *TP53* and *CHEK2* and that CH confers an increased risk of tMN. We hypothesized that characterization of the relationship between CH and PARPi therapy provides insight into its potential for leukemogenesis and may offer opportunities for tMN prevention. **Methods:** We assessed for CH in the blood of 10,156 cancer patients, including 54 who received PARPi therapy, 5942 who received another systematic therapy or radiation therapy and 4160 untreated prior to blood draw. **Results:** Patients exposed to PARPi therapy were more likely to have CH (33%) compared to those exposed to other systemic therapies or radiation (18%) or untreated patients (16%). This was particularly pronounced for DDR CH; 25% of PARPi treated patients had DDR CH compared to 2% of untreated patients. In a multivariable model accounting for demographics, exposure to chemotherapeutic agents, radiation therapy and germline *BRCA* mutation status, exposure to PARPi conferred an increased risk of DDR CH (OR = 3.6, 95% CI 1.5-8.5, p = 0.004). This effect was attenuated after accounting for cumulative exposure to therapy (OR = 2.8, 95% CI 0.97-8.2, p = 0.06) suggesting a multifactorial contribution to the enrichment of CH following PARPi therapy. To characterize this further we performed a prospective collection of patients with CH over a median follow-up time of 58 months. During the follow-up period, 17 patients received PARPi, 360 received cytotoxic therapies or radiation and 232 were untreated or received targeted therapies. The growth rate of DDR CH was significantly higher among those who were exposed to PARPi (median, +2.8% increase in VAF per year) compared to untreated patients (+0.08% per year, p = 0.02) and those exposed to other cytotoxic therapies (+1% per year, p = 0.04). **Conclusions:** Taken together our data suggests that PARPi therapy promotes the expansion of DDR CH. Future studies should examine the potential of CH to identify individuals at high risk of tMN following PARPi therapy and to develop therapies aimed to prevent tMN in patients with CH. Research Sponsor: Internal Funds.

1514 Poster Discussion Session; Displayed in Poster Session (Board #6), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Clinical conundrums: Developing a strategy for discerning TP53-associated chip and coherent clinical care. *First Author: Jeffrey N. Weitzel, City of Hope, Duarte, CA*

Background: Germline *TP53* mutations are associated with Li-Fraumeni syndrome (LFS). However, approximately 20% of commercial laboratory multigene panel test (MGPT)-detected pathogenic *TP53* variants represent aberrant clonal expansion (ACE), rather than a germline finding, and are often detected in individuals that lack classic features of LFS. Clonal hematopoiesis (CH) is a form of ACE, and in the absence of an abnormal hemogram is termed Clonal hematopoiesis of indeterminate potential (CHIP). CHIP is often associated with a pathogenic variant (PV) in hematopoietic pathway gene(s) at a variant allele frequency (VAF) less than expected for a heterozygous germline finding. The prevalence increases with age and exposure to chemotherapy. The presence of a skewed VAF is usually noted in a comment on a genetic test result, however, clinicians without genetic training often lack understanding of the comment and need strategies to discern the difference between germline findings, CHIP, and post-zygotic mosaicism. Our studies illuminate possible strategies for discernment for clinicians. **Methods:** Among 113 cases with MGPT-detected *TP53* PVs, enrolled in the Clinical Cancer Genomics Community Research Network registry, we obtained additional tissues, family history and complete blood count (CBC) reports on 42 cases. DNA extracted from formalin fixed paraffin embedded (FFPE) tumor/normal tissues, blood, saliva, eyebrow plucks, was analyzed using a previously validated custom myeloid and CH gene (n = 79) amplicon-based QIAseq panel. PVs with VAF $>$ 2% were included in analyses. **Results:** Germline status was confirmed for 6 cases (one with a CH PV), post-zygotic mosaicism was supported for 5 cases and 2 were indeterminant. 12 had results supporting ACE/CH, with additional CH-associated PV(s) identified in 5/12 (41%); n = 2 of each *TET2*, *ATM*, *TP53*; and increasing VAF over time for the driver *TP53* PV was noted in 2. Of these 2 one was identified to have a hematopoietic malignancy identified through analysis of the CBCs and bone marrow biopsy in parallel with the increasing VAF. Additional results are pending for 7 cases. **Conclusions:** With the use of our multi-tissue NGS strategy, serial sampling of suspected ACE/CH cases, family history and CBC analyses we were able to discern the status of most *TP53* genetic findings. This work has direct translational impact, refining risk estimation and improving the clinical care of patients with *TP53* PVs, while avoiding unnecessary LFS-related care and enabling appropriate care for those with ACE. Research Sponsor: U.S. National Institutes of Health.

1515 Poster Discussion Session; Displayed in Poster Session (Board #7), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Genetic counseling referrals after next generation sequencing testing. *First Author: Rafael Gonzalez, Duke University Health System, Durham, NC*

Background: Next generation sequencing (NGS) testing of tumor tissue or blood is performed to identify 'actionable' mutations that might guide patient care. NGS testing might incidentally identify germline mutations associated with cancer syndromes. No distinction is made between germline and somatic alterations on NGS reports, thus confirmatory germline testing is required. In this quality improvement (QI) initiative, we evaluated the frequency of referrals to genetic counseling (GC) for patients with potentially heritable germline mutations identified through NGS testing. **Methods:** We generated a list of high-risk mutations (HRMs) which merit GC referral based on NCCN guidelines. NGS test results for 3,400 consecutive patients with solid tumor malignancies were reviewed by the molecular tumor board from 1/2014-9/2019 and were screened for pathogenic HRMs. Basic demographic, oncologic, and GC data were retrospectively abstracted for each patient. The outcomes of interest were the frequency of HRMs identified through NGS testing, the proportion of patients subsequently referred to GC, and the proportion of patients ultimately diagnosed with a hereditary cancer syndrome. **Results:** 472 individual patients (14%) had NGS testing with one or more HRM identified; 465 patients were evaluable which corresponded to 519 HRMs that were included in the analysis (Table). Malignancies included were gastrointestinal 199 (42.8%), lung 83 (17.8%), genitourinary/renal 56 (12.0%), breast 49 (10.5%), gynecologic 35 (7.5%), and other 43 (9.2%). 75 (16.1%) patients had germline testing prior to NGS testing. Of those patients without prior germline genetic testing, 62 (15.9%) were referred to GC, and 19 (4.9%) patients were diagnosed with a hereditary cancer syndrome. **Conclusions:** Tumor NGS testing identifies HRMs that may represent an undiagnosed heritable germline mutation. Providers ordering NGS tests should review results for HRMs, refer to GC when appropriate, and offer confirmatory germline testing for patients and their families. Research Sponsor: None.

HRM	Frequency, N	Referred to GC, n (%)	+ Hereditary germline mutation, n (%)
MLH1	10	2 (20.0)	1 (10.0)
MSH2	18	1 (5.6)	4 (22.2)
MSH6	18	6 (33.3)	3 (16.7)
PMS2	12	3 (25.0)	4 (33.3)
SMAD4	149	12 (8.1)	3 (2.0)
BMPR1A	1	1 (100)	0 (0)
BARD1	5	0 (0)	0 (0)
BRCA1	54	9 (16.7)	15 (27.8)
BRCA2	75	27 (36.0)	19 (25.3)
BRIP1	12	3 (25.0)	3 (25.0)
PALB2	18	3 (16.7)	1 (5.6)
RAD51C	4	0 (0)	0 (0)
NBN	8	1 (12.5)	0 (0)
ATM	108	13 (12.0)	4 (3.7)
CHEK2	27	4 (14.8)	4 (14.8)

1516 Poster Discussion Session; Displayed in Poster Session (Board #8), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The prevalence of germline mutations among patients with solid tumors with genomic alterations identified on tumor testing: Results from a tertiary care academic center molecular tumor board. *First Author: Catherine Watson, Duke University, Durham, NC*

Background: The proportion of germline versus somatic mutations identified on genomic tumor testing of solid malignancies is not well characterized. We compared somatic and germline testing results in patients with breast, ovarian, pancreatic or prostate cancer with a genomic alteration identified on tumor testing. **Methods:** Retrospective chart review was performed using a tertiary care academic center's database of somatic tumor testing results obtained via FoundationOne and Guardant testing. Patients with breast, ovarian, pancreatic or prostate cancer who had a genomic alteration identified on tumor testing, including pathogenic and VUS variants, in *BRCA1*or *BRCA2*,*CHEK2*, *ATM*, *BRIP1*, *RAD51-C*,*RAD51D*, *PALB2*and *CDH1*and who had also received germline testing were identified. Analysis was performed to assess prevalence of germline results. The association between mutant allele fraction (MAF) and germline mutation status was also assessed. **Results:** Results: 124 patients with breast, ovarian, pancreatic or prostate cancer were identified who had a genomic alteration of interest also tested for via germline testing. 54 (32.5%) of tumor mutations were also identified on germline testing. Proportion of genomic results that were germline was wide, ranging from 0-85.7% depending on the gene and variant classification (Table). Germline mutations were present in 36.4% of breast, 25% of ovarian, 53.3% of pancreatic, and 20.9% of prostate cancer patients who had a tumor alteration present. Alterations that were found to be concordant in both somatic and germline testing had an average MAF of 0.54, and alterations identified on somatic testing only had an average MAF of 0.30. **Conclusions:** Our findings suggest that approximately one-third of genomic alterations on tumor testing will be of germline origin. However, concordance rates may be gene and variant dependent. Higher MAF may be associated with germline alteration status, but further evaluation is needed. Thus, while information provided by genomic tumor testing may be suggestive of a correlating germline mutation, no single alteration type or MAF value is reliably predictive. Research Sponsor: None.

Concordance between somatic and germline alterations.

Gene	Total N	Somatic and Germline (%)
BRCA1	29	10 (34.5)
BRCA2	62	20 (32.3)
RAD51C	2	0 (0)
BRIP1	6	2 (33.3)
PALB2	9	7 (77.8)
BARD1	8	2 (25)
ATM	32	6 (18.8)
CHEK2	7	6 (85.7)
CDH1	11	1 (9.1)

1517 Poster Discussion Session; Displayed in Poster Session (Board #9), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The impact of tumor NGS testing on hereditary cancer risk assessment and population management in an integrated community health care system. *First Author: Sachdev P. Thomas, Kaiser Permanente, Dept of Medical Oncology, Vallejo, CA*

Background: Next-generation sequencing (NGS) for tumor molecular profiling is used in Oncology to identify 'actionable alterations' for clinical trials or on/ off-label therapy. Tumor NGS can also reveal potentially heritable germline mutations. The frequency of such incidental germline mutations has been estimated to be 4-15%. The 2015 ASCO Statement supports communication of medically relevant incidental germline findings from somatic mutation profiling to patients (PTS). The impact of tumor NGS testing on hereditary cancer risk assessment programs in the context of a wider population management strategy is unknown. We sought to evaluate this within our Kaiser Permanente Northern California (KPNC) population with ready access to tumor NGS and an ongoing hereditary cancer risk assessment program. **Methods:** Kaiser Permanente Northern California (KPNC) is part of a large, integrated health care system. NGS at KPNC is performed in collaboration with STRATA Oncology, a precision oncology partnership. All NGS results are reviewed by a multidisciplinary KPNC Genomic Oncology Committee (GOC)which also includes genetic counselors and pathologists. We examined all NGS reports between November 2017 through December 2019 to determine the types of cancers tested, number with a possible germline mutation and number referred for genetic counseling and testing (GCT). **Results:** 4,825 PTS with advanced cancer underwent STRATA NGS testing. A total of 207 PTS (4.3%) were identified as potential germline mutation carriers, all 207 were recommended for GCT referral. Of these, 92 (45.0%) separately met 2020 NCCN Criteria for Genetic/Familial High-Risk Assessment (2020NG/FA), prior to tumor NGS; 115 (53.6%) did not and 3 (1.4%) had insufficient information. The cancers most frequently meeting NCCN criteria were pancreatic, breast and colon. Of the 92 PTS who met 2020NG/FA, 60 (65%) underwent GCT and 34 (57%) were confirmed to have a germline mutation. Of the 115 PTS that did not meet 2020NG/FA, 47 (41%) underwent GCT and 19 (40%) were confirmed to have a germline mutation. Overall germline mutations were confirmed in 16.5% of patients who did not meet 2020NG/FA and 37% who did. **Conclusions:** In our community-based integrated healthcare system, systematic review of next-generation sequencing results by an expert GOC led to more robust identification of germline mutation carriers and navigated them to appropriate GCT. Ongoing work will clarify data on cascade testing. We are currently developing automated workflows for GCT. Research Sponsor: None.

1518 Poster Discussion Session; Displayed in Poster Session (Board #10), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Expanding the diagnostic yield of germline genetic testing in cancer patients using deep learning. *First Author: Saud H Aldubayan, Dana-Farber Cancer Institute/Harvard Medical School, Boston, MA*

Background: Germline genetic analysis is an essential tool for implementing precision cancer prevention and treatment. However, only a small fraction of cancer patients, even those with features suggestive of a cancer-predisposition syndrome, have detectable pathogenic germline events, which may in part reflect incomplete pathogenic variant detection by current gold-standard methods. Here, we leveraged deep learning approaches to expand the diagnostic utility of genetic analysis in cancer patients. **Methods:** Systematic analysis of the detection rate of pathogenic cancer-predisposition variants using the standard clinical variant detection method and a deep learning approach in germline whole-exome sequencing data of 2367 cancer patients (n = 1072 prostate cancer, 1295 melanoma). **Results:** Of 1072 prostate cancer patients, deep learning variant detection identified 16 additional prostate cancer patients with clinically actionable pathogenic cancer-predisposition variants that went undetected by the gold-standard method (198 vs. 182), yielding higher sensitivity (94.7% vs. 87.1%), specificity (64.0% vs. 36.0%), positive predictive value (95.7% vs. 91.9%), and negative predictive value (59.3% vs. 25.0%). Similarly, germline genetic analysis of 1295 melanoma patients showed that, compared with the standard method, deep learning detected 19 additional patients with validated pathogenic variants (93 vs. 74) with fewer false-positive calls (78 vs. 135) leading to a higher diagnostic yield. Collectively, deep learning identified one additional patient with a pathogenic cancer-risk variant, that went undetected by the standard method, for every 52 to 67 cancer patients undergoing germline analysis. Superior performance of deep learning, for detecting putative loss-of-function variants, was also seen across 5197 clinically relevant Mendelian genes in these cohorts. **Conclusions:** The gold-standard germline variant detection method, universally used in clinical and research settings, has significant limitations for identifying clinically relevant pathogenic disease-causing variants. We determined that deep learning approaches have a clinically significant increase in the diagnostic yield across commonly examined Mendelian gene sets. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology, Other Foundation.

1519 Poster Discussion Session; Displayed in Poster Session (Board #11), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Deep learning to identify high-risk smokers for lung cancer screening from chest radiographs. *First Author: Vineet Raghu, Cardiovascular Imaging Research Center (CIRC), Department of Radiology, Massachusetts General Hospital & Harvard Medical School, Boston, MA*

Background: Appearance on chest radiography may inform selection of high-risk smokers for lung cancer screening CT, beyond Centers for Medicare & Medicaid Services (CMS) eligibility criteria. **Methods:** A convolutional neural network (CXR-LC) predicting 12-year incident lung cancer from the chest radiograph image, age, sex, and smoking status (current/former) was developed in 41,856 persons aged 55-74 from the Prostate, Lung, Colorectal & Ovarian trial (PLCO). The final model was tested in held-out smokers from PLCO (n=5,615, 37.9% CMS eligible, 12-year follow-up), and externally in the National Lung Screening Trial (NLST, n=5,493, all CMS eligible, 6-year follow-up). Sensitivity was compared at a fixed screening population size defined by CMS eligibility. Ordinal CXR-LC risk score (low/indeterminate/high/very high) was based on development dataset 12-year probability thresholds (<2%/2-<3.3%/3.3-<8%/≥8%). Results are provided in test datasets only. **Results:** In the PLCO test dataset, CXR-LC was more sensitive than CMS eligibility at a fixed screening population size (74.9% vs. 63.8%, p=0.01) and missed 30.8% fewer lung cancers. CXR-LC risk groups were associated with incident lung cancer in PLCO test dataset smokers (very high vs. low CXR-LC risk: 12.4 vs 1.1 lung cancers/1,000 person-years) with external testing in NLST (all CMS eligible: 12.7 vs 2.3) (Table). This association was robust to adjustment for radiologist findings and the PLCOm2012 risk score. **Conclusions:** CXR-LC identified smokers at high risk of incident lung cancer, beyond CMS eligibility. Research Sponsor: U.S. National Institutes of Health.

Incident lung cancer within CXR-LC risk strata by test dataset.

	PLCO (N = 5,615)				NLST (N = 5,493)			
CXR-LC risk score	12-year lung cancer incidence (%)	per 1,000 person-years (95% CI)	Adj HR* (95% CI)	p	6-year lung cancer incidence (%)	per 1,000 person-years (95% CI)	Adj HR* (95% CI)	p
Low	30 / 2541 (1.2%)	1.1 (0.8,1.6)	Ref		17/1279 (1.3%)	2.3 (1.4,3.7)	Ref	
Indeterminate	22 / 948 (2.3 %)	2.2 (1.4,3.3)	1.8 (1.0,3.1)	0.04	17/871 (2.0%)	3.4 (2.1,5.5)	1.3 (0.7,2.6)	0.41
High	82 / 1497 (5.5%)	5.3 (4.3,6.6)	4.0 (2.6,6.1)	<0.001	115/2509 (4.6%)	8.1 (6.8,9.8)	3.0 (1.8,5.1)	<0.001
Very High	73 / 629 (11.6%)	12.4 (9.8,15.6)	7.5 (4.8,11.9)	<0.001	57/834 (6.8%)	12.7 (9.8,16.4)	3.9 (2.2,6.9)	<0.001
Total	207 / 5615 (3.7%)	3.5 (3.1,4.0)			206/5493 (3.8%)	6.6 (5.8,7.6)		

*adjusted for PLCOm2012 score and radiologist findings Abbreviations: Adj HR, Adjusted Hazard Ratio; CI, confidence interval

1520 Poster Discussion Session; Displayed in Poster Session (Board #12), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Comparing and assessing the reported penetrance of cancer susceptibility genes for breast cancer. *First Author: Kanhua Yin, Massachusetts General Hospital, Boston, MA*

Background: It is critical for oncologists to be aware of unbiased and interpretable cancer risks (i.e., penetrance) in carriers with germline pathogenic variants in cancer susceptibility genes. However, relevant literature is large and varies significantly in study design, patient ascertainment, and types of risk estimates reported. This heterogeneity can cause inconsistent conclusions between studies and create barriers for clinicians to understand and apply them in practice. To further understand the current literature, we assessed penetrance studies associated with non-BRCA breast cancer susceptibility genes based on study design and ascertainment adjustment. **Methods:** We used a validated natural language processing-based abstract classifier to identify all penetrance studies regarding eleven genes: ATM, BARD1, CDH1, CHEK2, NBN, NF1, PALB2, PTEN, RECQL, STK11, and TP53. Relevant studies were then manually annotated as "with ascertainment adjustment" if a study was based on: (1) a general population; (2) a pedigree analysis or a family-based study with appropriate ascertainment adjustment; or (3) a hospital-based study or a panel testing analysis with well-matched cases and controls. **Results:** A total of 49 penetrance studies were identified, with a median of nine studies for each gene (range: 4-16). The case-control study was the dominant study type, accounting for over 80% in five genes, 50% in two genes, and 18% to 43% in the other four genes. The proportion of studies with ascertainment adjustment was generally low (mean: 33%) and varied widely between different genes (7% to 80%). Contradictory breast cancer risks (no increased risk vs. significantly increased risk) were found in eight genes (73%) (Table). The most common ascertainment bias identified was a case-control study with cases (patients) who had a strong family history but using general population controls. **Conclusions:** Ascertainment bias is common in penetrance studies, but few studies adjust for it appropriately. Clinicians should be aware of this issue, and new methods are warranted to select unbiased risk estimates, synthesize them, and provide the accurate general-population penetrance. Research Sponsor: None.

As an example: Reported penetrance of NF1 for breast cancer.

First author	Study design	Risk type	Risk estimates (95%CI)	Statistical significance
Wang X	Cohort	SIR	5.2 (2.4-9.8)	Yes
Sharif S	Cohort	SIR	3.5 (1.9-5.9)	Yes
Uusitalo E	Cohort	SIR	3.04 (2.06-4.31)	Yes
Walker L	Cohort	SIR	1.87 (0.61-4.37)	No
Madanikia SA	Cohort	SIR	1.71 (0.54-4.12)	No
Couch FJ	Case-control	OR	0.94 (0.55-1.62)	No

1521 Poster Session (Board #13), Fri, 8:00 AM-11:00 AM

Evaluation of a mainstream model of genetic testing for men with prostate cancer. *First Author: Tahlia Scheinberg, Chris O'Brien Lifehouse, Camperdown, Australia*

Background: In order to identify the ~12% with inherited cancer predisposition, it is recommended that all men with metastatic prostate cancer (mPC) be offered testing. This has implications for treatment choices and cancer prevention in family. Limited geneticists/genetic counsellors globally present a major barrier to testing. We tested a potential solution, mainstreaming, where testing is performed by the patient's oncologist. **Methods:** Men with mPC at three Australian sites were offered germline genetic testing at their medical oncology appointment. Panel testing (*ATM*, *BRCA1*, *BRCA2*, *BRIP1*, *CHEK2*, *EPCAM*, *FANCA*, *HOXB13*, *MLH1*, *MSH2*, *MSH6*, *NBN*, *PALB2*, *PMS2*, *RAD51D* and *TP53*) was performed on saliva/blood (Invitae). Primary outcomes were clinician and patient acceptability (modified Royal Marsden Satisfaction Questionnaires). Secondary outcomes included mutation rates and cost-effectiveness. A sample size of 44 provided 90% power, with a one-sided alpha of 5%, to distinguish a proportion of men happy with mainstreaming of 80% vs. 60% or less. Allowing for 25% drop-out, we aimed to recruit 60 men. **Results:** Of 66 men offered testing from April to November 2019, 63 (95%) accepted. Four pathogenic variants were identified (2 *BRCA2*, 1 *NBN*, 1 *MSH6*). 48 patients and eight clinicians completed questionnaires. Acceptability was high. All (48/48) patients were happy to have been tested, and 45/48 (94%) were happy to have been tested at their oncology appointment. All were happy to receive their results from their oncologist. All clinicians were satisfied mainstreaming and 88% (7/8) felt confident doing so. Mainstreaming was cost-effective, requiring 87% fewer genetic consultations than traditional genetic counselling. **Conclusions:** This study shows that mainstreaming of men with mPC is feasible, resource efficient and acceptable to both clinicians and patients. Widespread implementation as a new standard of care would facilitate timely access to genetic testing for men with mPC. Research Sponsor: Cancer Institute NSW, Sydney Catalyst, University of Sydney, Australian Prostate Cancer Research Centre, NSW.

1522 Poster Session (Board #14), Fri, 8:00 AM-11:00 AM

Discovery of a core-panel of markers for a blood-assay for cancer detection utilizing cfDNA methylation changes. *First Author: Lasika Seneviratne, SCORA/LA Cancer Network, Los Angeles, CA*

Background: Cancer screening is limited to several cancers despite improved outcome A screening test should be acceptable, safe, and relatively inexpensive[1] Tumors shed cfDNA to the blood where abundant tumor-specific methylation changes can be detected [1]https://www.who.int/cancer/detection/variouscancer/en/. **Methods:** This is a prospective, multicenter, observational study under two protocols NCT04264767, NCT04264754. Plasma was collected from 1,255 subjects: 586 treatment-naïve cancer patients and 639 controls, in 21 sites and biobanks. Training set I (211 cases/99 controls) was used to select the 6 final markers for the core panel, training set II (200 controls) was used to lock the algorithm, and set the threshold to a score yielding specificity of 95%. The validation set (342 cases/310 controls) was performed utilizing the pre-specified algorithm and threshold. Plasma was separated from a single EDTA tube within 4 hours of blood draw. EpiCheck's reagents and methylation-sensitive enzymes (Nucleix, Israel) were used for DNA extraction, digestion, and amplification in real-time PCR (ABI 7500 Fast Dx, Applied Biosystems). **Results:** Age was comparable but sex and smoking history were different (more women in cases, more smokers in controls). In the validation cohort twelve cancer types were included, with prominent representation of major cancer types (19% Breast, 14% colorectal and 21% lung) and stages I&II (56%). Specificity and sensitivity were maintained high at 94% and 62%. Highest sensitivity was demonstrated in GI cancers (77% colorectal, 83% esophageal, 100% gastric) and non-solid malignancies (83%). Sensitivity in early stage cancers (stages I, II & IIIA) was 51%, led by Sarcoma (83%) esophageal (76%) and colorectal (61%). **Conclusions:** This 6-marker blood-based methylation assay is a promising initial component in a future cancer screening test, generating significant signal in early cancers and utilizing simple and inexpensive PCR technology. Clinical trial information: NCT04264767, NCT04264754. Research Sponsor: Nucleix.

	Training I (cases)	Training I (controls)	Training II (controls)	Validation (cases)	Validation (Controls)
N	211	99	200	342	310
Sex, M/F	91/118	84/15	149/51	134/208	217/93
Age, median (range)	64 (25-93)	54 (45-81)	60 (45-84)	63 (25-91)	61 (43-83)
Smoking history (current /former/never/ unk)	25/11/68/107	27/72/0/0	62/134/4/0	69/48/70/155	85/207/17/1
Specificity %		96	95		94
Sensitivity %	60			62	
Sensitivity by stage – solid tumors % (I/II/III/IV)	27/ 57/ 74/ 77			41/ 60/ 67/ 86	
Sensitivity early stages (I, II, IIIa)/ late stages (IIIB, IIIC, IV) %	51/ 79			52/82	
Sensitivity non-solid tumors %	69			82	

1523 Poster Session (Board #15), Fri, 8:00 AM-11:00 AM

Comprehensive molecular assessment of mismatch repair deficiency in Lynch-associated ovarian cancers using next-generation sequencing (NGS) panel. *First Author: Rachel Soyoun Kim, University of Toronto, Toronto, ON, Canada*

Background: Abnormalities in mismatch repair (MMR) gene may be the result of pathogenic germline (Lynch syndrome) and somatic mutations as well as epigenetic events. Abnormalities in MMR have been described in non-serous/non-mucinous ovarian cancer (OC) but few studies have examined the causes of these MMR defects (MMRd). To address this, we have completed targeted mutational and methylation sequencing on MMRd OC cases. **Methods:** Women with newly diagnosed non-serous/mucinous OC (N = 215) were prospectively recruited from three cancer centers in Ontario, Canada between 2015-18. Tumors were reflexively assessed for MMR protein expression by immunohistochemistry. Tumor DNA was extracted from macrodissected MMRd cases and MMR-intact (MMRi) controls following pathology review. Matched tumor-normal samples were run on a custom NGS panel to identify germline and somatic mutations, copy number variants, rearrangements and promoter methylation in MMR and associated genes. **Results:** Of the 215 women enrolled in our study, 185 (86%) had OC alone and 30 (14%) had synchronous OC and endometrial cancer. Twenty-eight (13%) cases were MMRd, 11 of which were synchronous. The MMRd cohort had median age of 52.5 years, with mostly stage I (N = 14; 50%), grade 1 or 2 disease (N = 18; 64%) with endometrioid histotype (N = 18; 64%). One patient had recurrence after median follow-up of 33.6 months (13.2-93.6). There was no significant difference in overall/progression-free survival between the MMRd and MMRi patients. Using the NGS panel, Lynch syndrome (LS) was detected in 39% of MMRd cases (11/28; 7 OC and 4 synchronous): 7 *MSH6*, 2 *MLH1*, 1 *PMS2*, and 1 *MSH2*. Clinical germline sequencing was performed on all cases and verified panel findings. An explanation for the observed MMR phenotype was available for 18/20 deficient cases, including 9/10 $MLH1^{-}/PMS2^{-}$ (7 somatic methylation, 1 bi-allelic somatic deletion, 1 germline mutation), 0/1 $PMS2^{-}$, 6/7 $MSH6^{-}$ (6 germline mutations) and 2/2 $MSH2^{-}/MSH6^{-}$ (1 germline mutation, 1 bi-allelic somatic mutation). Concordance between clinical and research panel sequencing results was 90%. None of the germline mutations were missed by the panel. **Conclusions:** Use of our custom NGS panel allows for the streamlined assessment of hereditary and somatic causes of MMR deficiency in OC and may be an attractive screening strategy for LS in this population. Research Sponsor: Canadian Cancer Society Research Institute Prevention Grant.

1524 Poster Session (Board #16), Fri, 8:00 AM-11:00 AM

Genotype and phenotype correlation of common cancer predisposition syndromes in sarcoma cases. *First Author: Milita Zaheed, Garvan Institute of Medical Research, Darlinghurst, NSW, Australia*

Background: Sarcomas are rare heterogenous cancers affecting a predominantly younger population. The most recognised autosomal dominant contributor being pathogenic *TP53* variants associated with Li Fraumeni Syndrome (LFS). When referred, patient eligibility for germline *TP53* testing is assessed using classic or Chompret LFS criteria. Other heritable cancer syndromes which can be associated with sarcoma (breast/ovarian, colorectal) are more commonly considered in clinical practice. In some centres germline testing is offered to only those who meet established clinical criteria. Heritable cancer predisposition has several implications including therapy and clinical risk management. Here we report the concordance between clinical criteria and genotypes in sarcoma families. **Methods:** We included 1,664 sarcoma probands from the International Sarcoma Kindred Study. Eligibility for genetic testing was assessed using internationally accepted clinical criteria for recognised cancer syndromes. Whole genome sequencing was performed on peripheral blood DNA and variants in the ACMG cancer gene list were classified as pathogenic or likely pathogenic using established bioinformatics pipelines. **Results:** The median age of sarcoma diagnosis in 1664 probands (798 males, 866 Females) was 48 years (range 1-93). The median age of first cancer diagnosis was 46.5 years (0-93) with 291 probands having multiple primary cancers. Of 1504 informative pedigrees, 243 (16%) met criteria for testing; 207 (14%) *TP53*; 19 (1%) *BRCA1/2*; 2 (<1%) colorectal cancer (CRC) genes and 15 (1%) familial melanoma. Of 12 *TP53* PVs identified, 9 met *TP53* testing criteria. Of 13 PVs identified in HR genes (7 *BRCA2*, 4 *PALB2* and 2 *BRCA1*) only 1 (*PALB2*) met *BRCA1/2* testing criteria and 2 met Chompret criteria. Both *BRCA1* cases were male with a 1st degree relative with ovarian cancer. In CRC genes (1 *APC*, 2 *MSH2*, 4 *MSH6*, 1 *PMS2*), none met CRC testing criteria but 4 met Chompret criteria. No *CDKN2A* PVs were identified in melanoma families. **Conclusions:** In probands with sarcoma, clinical criteria for eligibility for testing for common non-LFS heritable syndromes perform poorly. This should be considered when making decisions regarding germline testing. Research Sponsor: Rainbows for Kate Foundation, Australian National Health and Medical Research Council.

1525 Poster Session (Board #17), Fri, 8:00 AM-11:00 AM

Characterization of clonal hematopoiesis of indeterminate potential mutations from germline whole exome sequencing data. *First Author: Hsin-Ta Wu, Natera, Inc., San Carlos, CA*

Background: Clonal hematopoiesis of Indeterminate Potential (CHIP) is an age-related phenomenon where somatic mutations accumulate in cells of the blood or bone marrow. It is a source of biological noise that causes false-positives in ctDNA analysis and is present in up to 20% of individuals over the age of 70. The presence of CHIP has been linked to an increased risk of hematologic cancers and cardiovascular disease. The Signatera assay filters CHIP mutations through tumor tissue and germline sequencing thereby reducing false-positive results and focuses on tumor-specific mutations for each patient. **Methods:** Whole exome sequencing data (average depth ~250x) analyzed from patients' buffy coat (n = 159) was used to characterize CHIP mutations. Variant calling was performed using Freebayes variant caller with allele frequency threshold between 1% and 10%. Following which variant annotation and selection was performed based on the top 54 genes that are most implicated in myeloid disorders. The selected variants were further screened based on the reported variants in the literature and/or the Catalog of Somatic Mutations in Cancer (COSMIC). **Results:** The analysis revealed an average of 0.14 (0-2) CHIP mutations per patient with an average variant allele frequency of 3.49% (1%-8.5%). The most common CHIP mutations were observed in *DNMT3A*, (n = 17), *TET2* (n = 7) and *TP53* (n = 7) genes. The percentage of patients with at least 1 mutation found in *DNMT3A, TET2,* and *TP53* were 4.2%, 1.94%, and 1.38%, respectively. Other genes containing CHIP mutation included *CEBPA, ETV6, HRAS, PDGFRA, NRAS, KMT2A, EZH2, GATA2, GNAS* at a frequency below 1%. CHIP mutations were not observed in patients younger than 40 years, but they increased in frequency with every decade of life thereafter. The incidence of CHIP increased from 0.04 for the 40-50 yrs age group to 0.18 for individuals older than 60. Further analysis of associations between incidence of CHIP and cancer type, prior exposure to chemotherapy as well as longitudinal evolution of CHIP mutations during cytotoxic treatment are underway and will be presented. **Conclusions:** CHIP, a common finding in the elderly population is an important factor to consider in ctDNA analysis and most frequently involves *DNMT3A, TET2,* and *TP53* genes. The frequency of CHIP can be impacted by a number of other factors such as cytotoxic chemo- or radiotherapy. Research Sponsor: Natera, Inc.

1526 Poster Session (Board #18), Fri, 8:00 AM-11:00 AM

BRCA testing concordance with national guidelines for patients with breast cancer in community cancer programs. *First Author: Leigh Boehmer, Association of Community Cancer Centers, Rockville, MD*

Background: Current National Comprehensive Cancer Network guidelines for genetic/familial high-risk assessment state that testing for highly penetrant breast/ovarian cancer genes is clinically indicated for women with early onset ($\leq$ 45 years) or metastatic HER-2 negative breast cancer. A recent Association of Community Cancer Centers (ACCC) survey (N = 95) showed that $>$ 80% of respondents reported $\leq$ 50% testing rate of patients with breast cancer who met guidelines. Given this disconnect, ACCC partnered with 15 community cancer programs to assess practice gaps and support interventions to improve access to genetic counseling (GC)/testing. **Methods:** Pre-intervention data from 9/15 partner programs for women diagnosed with stages 0-III breast cancer between 01/01/2017 and 06/30/2019 was collected. De-identified variables included: family history documentation, GC appointment/test results, and timing of results relative to treatment decisions. **Results:** There were 2691 women with stages 0-III breast cancer. Forty-eight percent (1284/2691) had a documented high-risk family history, 57% (729/1284) of whom had a GC appointment. This was a significantly higher rate of GC compared to the 23% (181/778) of women with no family history and 6% (35/629) of women with no documentation of family history ($p < 0.0001$). Patients $\leq$ 45 years old attended a GC appointment 72% (199/278) of the time and 49% (135/278) had genetic test results, with 84% (113/135) receiving results before surgery. For women with test results available before surgery, 37% (119/322) had breast conserving surgery, compared to 60% (144/240) with test results disclosed post-operatively ($p < 0.0001$). **Conclusions:** Genetic testing is underutilized in a community cohort of women with breast cancer. Further analysis is needed to understand the impact genetic test results have on surgical decisions. Opportunities exist to improve current rates of appropriate GC/testing. ACCC will share results of quality improvement projects to illuminate which strategies hold promise in reducing the hereditary breast cancer GC/testing practice gap. Research Sponsor: Pfizer, Inc.

1527 Poster Session (Board #19), Fri, 8:00 AM-11:00 AM

Prevalence and clinical characterization of MMR-D/MSI extra-colonic cancers among germline PMS2 mutation carriers. *First Author: Alicia Latham, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: *PMS2*-associated Lynch syndrome (LS) may have a more modest phenotype than that associated with other mismatch repair (MMR) genes (*MLH1, MSH2, MSH6, EPCAM*). Recent studies suggest limited extra-colonic cancers, and modified risk-reducing measures can be provided. Understanding the spectrum of risk is of critical importance as some LS-associated cancers do not have effective screening, requiring risk-reducing surgery (endometrial, ovarian). As MMR-deficiency (MMRD)/ microsatellite instability (MSI) is associated with LS pan-cancer, we sought to characterize *PMS2*-associated malignancies according to MMR/MSI status. **Methods:** Review of cancer patients (pts) consented to an IRB-approved protocol of tumor/germline next-generation sequencing (NGS) identified 43 germline heterozygous *PMS2* mutation carriers. Tumors were evaluated for MSI via MSIsensor and/or corresponding MMR protein expression via immunohistochemical staining (IHC). Clinical variables were correlated with MMR/MSI status, comparing via Chi-square or standard T-test. **Results:** There were $>$ 10 tumor types; 69.8% (30/43) were extra-colonic cancers (endometrial (n = 4), ovarian (n = 6), small bowel (n = 3), urothelial (n = 2), pancreas (n = 3), prostate (n = 3), breast (n = 3), brain (n = 3), biliary (n = 1), spindle cell sarcoma (n = 1), and hepatoblastoma (n = 1)). 46.5% (20/43) of tumors were MMRD/MSI. 61.5% (8/13) of colorectal cancers (CRC) were MMRD/MSI, compared to 40% (12/30) of extra-colonic tumors. All endometrial and small bowel cancers were MMRD/MSI. Of 6 ovarian cancers, 3 were clear-cell, 1 endometrioid, and 2 high-grade serous (HGS). The only MMRD/MSI ovary tumor was HGS. 73.9% (17/23) of pts with MMRP/MSS tumors had recurrent/metastatic disease vs 30% (6/20) of pts with MMRD/MSI tumors (p= 0.004). Mean age at diagnosis did not differ significantly between MMRP/MSS and MMRD/MSI groups (49 vs. 57, respectively, p= 0.146). 11.6% (5/43) of pts had a prior cancer, with only one patient having prior CRC. Pts with extra-colonic tumors were less likely to meet clinical pt and family history LS testing criteria than those with CRC (63.3% (19/30) vs. 7.7% (1/13); $p<$ 0.001). **Conclusions:** While *PMS2*-related LS may have a more modest clinical phenotype, in this single-institution study, 60% (12/20) of patients with MMRD/MSI tumors presented with extra-colonic cancers. We caution counseling pts with *PMS2*-associated LS about reduced extra-colonic risk until more complete information about penetrance, spectrum, and age distribution of cancer is available. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

1528 Poster Session (Board #20), Fri, 8:00 AM-11:00 AM

Performance of polygenic risk scores for cancer prediction in an academic biobank. *First Author: Heena Desai, University of Pennsylvania Perelman School of Medicine, Philadelphia*

Background: The discovery of rare genetic variants associated with cancer have a tremendous impact on reducing cancer morbidity and mortality when identified; however, rare variants are found in less than 5% of cancer patients. Genome wide association studies (GWAS) have identified hundreds of common genetic variants significantly associated with a number of cancers, but the clinical utility of individual variants or a polygenic risk score (PRS) derived from multiple variants is still unclear. **Methods:** We tested the ability of polygenic risk score (PRS) models developed from genome-wide significant variants to differentiate cases versus controls in the Penn Medicine Biobank. Cases for 15 different cancers and cancer-free controls were identified using electronic health record billing codes for 11,524 European American and 5,994 African American individuals from the Penn Medicine Biobank. **Results:** The discriminatory ability of the 15 PRS models to distinguish their respective cancer cases versus controls ranged from 0.68-0.79 in European Americans and 0.74-0.93 in African Americans. Seven of the 15 cancer PRS trended towards an association with their cancer at a $p<0.05$ (Table), and PRS for prostate, thyroid and melanoma were significantly associated with their cancers at a bonferroni corrected $p<0.003$ with OR 1.3-1.6 in European Americans. **Conclusions:** Our data demonstrate that common variants with significant associations from GWAS studies can distinguish cancer cases versus controls for some cancers in an unselected biobank population. Given the small effects, future studies are needed to determine how best to incorporate PRS with other risk factors in the precision prediction of cancer risk. Research Sponsor: U.S. National Institutes of Health.

Association of Cancer PRS with associated cancers in an institutional biobank.

Cancer*	EUR Case / Control	AUC-EUR	OR (95% CI) - EUR	p	AFR Case	AUC - AFR	OR (95% CI) - AFR	p
Prostate	396 / 2937	0.757	1.580 (1.405 -1.779)	**2.87E-14**	213 / 943	0.838	1.282 (1.077 - 1.532)	**5.61E-03**
Thyroid	119 / 4699	0.686	1.480 (1.233 - 1.778)	**2.69E-05**	64 / 3125	0.748	1.284 (0.996 - 1.657)	**5.37E-02**
Melanoma	262 / 4699	0.720	1.287 (1.135 - 1.457)	**7.62E-05**	10 / 3125	0.797	0.795 (0.407 - 1.503)	**4.90E-01**
CRC	162 / 4699	0.728	1.246 (1.061 - 1.464)	**7.47E-03**	85 / 3125	0.780	1.244 (0.999 - 1.553)	**5.24E-02**
Lung	199 / 4699	0.681	1.158 (1.011 - 1.317)	**2.93E-02**	115 / 3125	0.841	1.112 (0.927 - 1.307)	**2.23E-01**
Breast	238 / 1762	0.700	1.160 (1.005 - 1.338)	**4.18E-02**	190 / 2182	0.777	1.223 (1.043 - 1.437)	**1.35E-02**
Glioma	38 / 4699	0.716	1.149 (0.830 - 1.592)	**4.03E-01**	16 / 3125	0.762	1.871 (1.777 - 3.002)	**8.51E-03**

1529 Poster Session (Board #21), Fri, 8:00 AM-11:00 AM

ATM mutation carriers and family history of pancreatic cancer. *First Author: Jeannie Klavanian, Beaumont Hospital, Royal Oak, MI*

Background: Multigene panel testing (MGT) is commonly utilized in patients with a personal or family history of cancer. One of the more common gene mutations identified is in the *ATM* gene, associated with a moderately increased risk of breast and other cancers. There are reports of an association with pancreatic cancer, however the exact risks are unclear. The aim of this study is to describe the family history of pancreatic cancer in a cohort of *ATM* mutation carriers, and to evaluate possible genotype/phenotype correlation. **Methods:** Patients who underwent MGT, between '13 and '19, and tested positive for a pathogenic/likely pathogenic *ATM* mutation were included in this study. Family history, with a focus on pancreatic cancer, and genetic testing results were analyzed. **Results:** A total of 114 patients were identified to carry an *ATM* mutation. Twenty-two (19.3%) individuals had a family history of pancreatic cancer in a close relative, and of those, 13 (11.4%) had an affected first degree relative, and 11 (9.6%) had an affected second degree relative. Among the families with pancreatic cancer, 20 close relatives had a personal history of pancreatic cancer, with the youngest diagnosed at age 40, the oldest diagnosed at age 91, and a mean age of diagnosis of 66.5 years. Thirteen unique variants were identified: 4 splice site, 3 missense, 3 frameshift, 1 nonsense, and 1 silent. Two families had the known high-penetrance *ATM* mutation, c.7271T > C (p.V2424G). **Conclusions:** This study describes the association of pancreatic cancer in individuals found to carry pathogenic *ATM* mutations. A significant proportion (19.3%) of patients had a family history of pancreatic cancer in a close relative, diagnosed as young as age 40. The mean age of diagnosis was slightly younger than the average age in the general population (age 70). As pancreatic cancer screening continues to improve, this information will be an important component to help guide cancer risk assessment and future screening recommendations for *ATM* mutation carriers. Additional larger studies are needed to further characterize pancreatic cancer risks in patients with ATM gene mutations. Research Sponsor: None.

1531 Poster Session (Board #23), Fri, 8:00 AM-11:00 AM

Functional analysis of patient-derived PALB2 missense variants of uncertain significance. *First Author: Shijie Wu, Department of Breast Surgery, the Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China*

Background: Inherited *PALB2* pathogenic variants are associated with an increased lifetime risk for breast cancer development. However, the interpretation of numerous *PALB2* missense variants of uncertain significance (VUS) identified in germline genetic testing remains a challenge. Here, we assessed the impact of breast cancer patient-derived VUS on PALB2 function and identified pathogenic *PALB2* missense variants that may increase cancer risk. **Methods:** A total of seven potentially pathogenic *PALB2* VUS identified in 2,279 breast cancer patients were selected for functional analysis. All these selected VUS were assessed by SIFT, Align-GVGD, and PolyPhen2 *in silico* and were predicted to be deleterious by at least two *in silico* algorithms. The p.L35P [c.104T > C] variant was also included, for which pathogenicity has been recently confirmed. The effects of the VUS on the homologous recombination (HR) activity of PALB2 were tested by U2OS/DR-GFP reporting system. Functional characterization was further validated by protein co-immunoprecipitation and RAD51 recruitment assay. **Results:** *PALB2* variants p.L24F [c.72G > C] and p.L35P [c.104T > C] showed the most significant disruption to the HR activity of PALB2 relative to the wild-type condition, retaining only 52.2% ($p = 0.0013$) and 8.5% ($p < 0.0001$) of HR activity respectively. Moderate but statistically significant HR deficiency was observed for four other variants (p.P405A [c.1213C > G], p.T1012I [c.3035C > T], p.E1018D [c.3054G > C], and p.T1099M [c.3296C > T]). We found no statistical differences for the p.K628N [c.1884G > T] and p.R663C [c.1987C > T] in the HR activity compared to wild-type PALB2. The p.L24F and p.L35P variants compromised the BRCA1-PALB2 interaction and reduced RAD51 foci formation in response to DNA damage. **Conclusions:** We have identified a novel patient-derived pathogenic *PALB2* missense variant, p.L24F [c.72G > C], that compromises PALB2-mediated HR activity. We suggest the integration of the identified pathogenic variants into breast cancer genetic counseling and individualized treatment regimens for better clinical outcomes. Research Sponsor: the Key Program of the Natural Science Foundation of Zhejiang Province (LZ16H160002), the Zhejiang Provincial Program for the Cultivation of High-level Innovative Health Talents.

1532 Poster Session (Board #24), Fri, 8:00 AM-11:00 AM

Cancer risk management and family communication of genetic test results among women with inherited breast cancer genes. *First Author: Tuya Pal, Vanderbilt University Med Center, Nashville, TN*

Background: Identification of inherited breast cancer may guide care, with benefits amplified through family testing. **Methods:** Females with a pathogenic/likely pathogenic (P/LP) variant in *BRCA1/2, PALB2, CHEK2,* and/or *ATM* were surveyed about cancer risk management, family communication of genetic test results, and family testing. Comparisons were made across genes. **Results:** The 235 participants with P/LP variants (186 *BRCA1/2*, 28 *PALB2*, 15 *CHEK2*, and 6 *ATM*) had a median age of 54 and 61% had a prior breast cancer diagnosis. For women with P/LP variants in *BRCA1/2*, *PALB2*, and *ATM/CHEK2*, bilateral mastectomy rates were 79%, 61%, and 52%, respectively; and risk-reducing oophorectomy rates were 89%, 30%, and 37%, respectively. All women with *PALB2* and *ATM/CHEK2* P/LP variants with a bilateral mastectomy had a personal or family history of breast cancer; however, only 27% of those with a risk-reducing oophorectomy had a family history of ovarian cancer. Family communication of genetic test results and family testing rates were higher for those with P/LP variants in *BRCA1/2* compared to others. **Conclusions:** Bilateral mastectomy and risk-reducing oophorectomy were relatively common among women with *PALB2* and *ATM/CHEK2* P/LP variants in our study, suggesting overtreatment through risk-reducing surgery. Furthermore, strategies to improve family communication of genetic test results and family testing are needed to amplify testing benefits. Research Sponsor: U.S. National Institutes of Health, Institutional Funding.

1533 Poster Session (Board #25), Fri, 8:00 AM-11:00 AM

Urgent cancer genetic counseling and testing for young, premenopausal women with breast cancer (BC): Impact on surgical decision-making for contralateral risk-reducing mastectomy. *First Author: Phuong L. Mai, UPMC Magee-Womens Hospital, Pittsburgh, PA*

Background: In women newly diagnosed with unilateral breast cancer (BC), contralateral risk-reducing mastectomy (CRRM) to decrease risk for additional primary BC is an appropriate option for some individuals, such as those with significantly increased risk due to a pathogenic variant (PV) in a breast cancer predisposition gene. Genetic testing at the time of BC diagnosis for young women has become more available and could aid in the decision-making process. We evaluated the trends for CRRM in a cohort of women diagnosed with BC at age ≤45 years who were seen in a multidisciplinary clinic where genetic counseling and testing is offered to each patient. **Methods:** A single institution, prospectively maintained database of patients seen in a BC multidisciplinary clinic between November 2014 and June 2019 was reviewed. Patients were included if they had non-metastatic, unilateral BC diagnosed ≤45 years of age, and underwent genetic testing at the time of BC diagnosis. Associations between surgical treatment (lumpectomy, mastectomy, or mastectomy with CRRM) and age at diagnosis, BC stage, family history, and genetic testing results were evaluated. **Results:** 184 patients were included in the analysis. The prevalence of a PV in a breast cancer predisposition gene was 15.8% (29/184; 1 in *ATM*, 12 in *BRCA1*, 8 in *BRCA2*, 5 in CH*EK2*, 2 in *NBN*, and 1 in *NF1*). 69% of the PV were in *BRCA1* and *BRCA2*. 126 (68.4%) tested negative, and 29 (15.8%) had a variant of uncertain significance (VUS) in various genes. Overall, 63 patients (34.2%) elected to have CRRM. Of the 29 patients with a PV, 24 (82.8%) had CRRM. Women who chose CRRM were younger, more likely to test positive for a PV in a breast cancer predisposition gene, and more likely to have a significant family history of breast and/or ovarian cancer. Among the 155 patients who tested negative or had a VUS, there was no statistically significant association between CRRM and age ($p = 0.58$), test result (negative vs. VUS. $p = 0.12$), or family history ($p = 0.32$). **Conclusions:** For young women with BC seen in a multidisciplinary clinic, a younger age, significant family history, and positive genetic testing result were found to be associated with the decision to undergo CRRM. Among those without a genetic predisposition, having a VUS result was not associated with choosing CRRM. Incorporation of genetic services in the initial evaluation of young patients newly diagnosed with BC could add relevant information in surgical decision making and promote risk-appropriate management. Research Sponsor: None.

1534 Poster Session (Board #26), Fri, 8:00 AM-11:00 AM

Five year letrozole versus placebo in *BRCA1/2* germline mutations carriers: Final results of LIBER, a double-blind randomized phase III breast cancer prevention trial. *First Author: Pascal Pujol, Centre Hospitalier Universitaire, Montpellier, Montpellier, France*

Background: Women with germline *BRCA1/2* (gBRCA1/2) mutations have a 70% lifetime risk of breast cancer (BC). Medical prevention by aromatase inhibitors is effective in high-risk patients (pts), including those with familial risk. However, hormone prevention has not been specifically addressed in women (wn) carrying gBRCA1/2 mutations. **Methods:** LIBER is a randomized, double-blind, placebo-controlled phase III trial evaluating 5-year treatment with letrozole 2.5 mg/day (L) versus placebo (P) on decreasing BC incidence in post-menopausal women with gBRCA1/2 mutations (NCT00673335). Eligible wn were aged 40-70 and could have had unilateral BC $>$ 5 years ago. Randomization was stratified on mutation (*BRCA1/BRCA2*), bilateral oophorectomy and history of prior BC. Primary endpoint was 5-year invasive BC-free survival (BC-FS) in wn with or without previous BC. Main secondary endpoints were safety and quality of life (menopause rating scale, SF36). 270 pts were required to observe 37 events to show a gain in 5-year invasive BC-FS from 80% to 92% (HR=0.35) with 1-sided α=0.05 and 90% power. **Results:** 170 wn were randomized from 02/2008 to 02/2013; 86 and 84 were assigned to the P and L arm. Median age was 55 years (range 40-70). Pt characteristics were well balanced; 59% and 41% carried gBRCA1 and gBRCA2 mutations. In P and L arms, 47% and 43% had prior BC, 43% and 42% stopped treatment prematurely, 37 and 23 serious adverse events occurred, and during active treatment, 8 and 10 wn had grade 3/4 toxicity. Median follow-up was 72.7 months. Five-year BC-FS did not significantly differ between the P and L arms (92% vs 91%, HR 0.83; 95%CI: 0.3-2.3, p=0.73) in the overall population, nor in the subgroups of wn with and without previous BC (74% vs 91%; HR 0.43; 95% CI: 0.1-1.3; 90% vs 86%; HR 1.29; 95% CI 0.4-3.9), gBRCA1 versus gBRCA2 or hormone receptor-positive BC. Letrozole had no effect on quality of life. The two groups did not significantly differ in bone density, which decreased over time in the overall population. **Conclusions:** In this prospective preventive trial, BC-FS was not significantly decreased by letrozole versus placebo in women with *BRCA1/2* mutations. However, the study was underpowered (170 of 270 pts expected). Despite no differences in safety and quality of life, drop-out rate was high in both P and L arms. Clinical trial information: NCT00673335. Research Sponsor: institut national du cancer, programme hospitalier de recherche clinique, unicancer, Pharmaceutical/Biotech Company.

1535 Poster Session (Board #27), Fri, 8:00 AM-11:00 AM

Evaluating the association between clonal hematopoiesis and germline pathogenic and likely pathogenic variants in cancer predisposition genes. *First Author: Elizabeth Anne Comen, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Clonal hematopoiesis (CH) is most commonly associated with mutations in genes with a known or putative role in leukemia and with an increased risk for hematologic malignancies. Nearly 50% of primary breast cancers contain leukocytes with CH mutations and CH mutations can be found in breast cancer (BC) tumor infiltrating leukocytes years prior to the development of secondary leukemia. It is currently not known whether CH is more prevalent among BC patients with both germline pathogenic variants and likely pathogenic variants (collectively referred to as PV) in cancer predisposition genes. Here we evaluated the relationship of CH to PV in 546 BC patients (pts). **Methods:** 546 BC pts underwent targeted capture sequencing of tumor and peripheral blood (PB) samples using MSK-IMPACT. Sequencing results from PB were used for identifying PV affecting up to 89 cancer predisposition genes and somatic mutations in 15 genes commonly associated with CH using previously validated methods. All pts consented via an IRB-approved protocol. **Results:** The majority (82.3%) of pts had non-metastatic disease. 59.7% of the 546 pts received chemotherapy and 42.7% received radiation. Of the 546 pts, 90 patients had germline PV in a cancer predisposition gene for a total of 98 germline PV identified (8 patients had 2 germline PV). Mutations in *DNMT3A* followed by *TET2* were the most common CH mutations identified. *CHEK2* PV were statistically significantly associated with CH in a multivariate analysis after controlling for age, prior chemotherapy and radiation therapy (OR: 3.94, CI: 1.51-10.26, p-value $\leq$0.005). Age by decade was significantly associated with the presence of CH in that model (OR: 1.93, CI: 1.53-2.42, p value $\leq$0.001). Of the 8 patients with *CHEK2* germline PV and CH, the most common mutated CH genes were *DNMT3A* (4 pts), followed by *TET2* (2 pts), although our sample size is too small to test for significant enrichment for any specific CH gene, type of CH mutation, or trinucleotide context. Further, CH was not associated with germline PV in other cancer predisposition genes. **Conclusions:** Our findings provide evidence of an association between *CHEK2* germline PV with CH in BC pts, which will be further tested in an expanded cohort. If this association is confirmed, it might have theoretical and practical implications, including cancer prevention strategies. Research Sponsor: None.

1536 Poster Session (Board #28), Fri, 8:00 AM-11:00 AM

Genome Wide Association Study (GWAS) of cognitive impairment after blood or marrow transplantation (BMT) for hematologic malignancy. *First Author: Noha Sharafeldin, University of Alabama at Birmingham, Birmingham, AL*

Background: Cognitive impairment is prevalent in hematologic malignancy patients treated with BMT (autologous: 18.7%; allogeneic: 35.7%; Sharafeldin JCO; 2018). Given the inter-individual variability in risk of cognitive impairment in this population, we investigated the role of genetic susceptibility using a genome-wide single nucleotide polymorphism (SNP) array platform to identify novel genetic associations. **Methods:** *Discovery:* Cognitive function was assessed objectively in 239 adult BMT recipients at pre-specified timepoints: pre-BMT and at 6 mo, 1y, 2y, and 3y post-BMT. A global deficit score (GDS - a summary score of 14 standardized neuropsychological tests) was computed for each patient; a higher score indicated greater cognitive impairment. SNPs passing standard quality control filters ($>$ 1.4M) were used for analysis. Linear mixed effects models used GDS as the outcome, adjusted for age, sex, BMT type, baseline cognitive reserve, and the first four principal components. We used additive, codominant, and genotype models and an adjusted genome-wide significance threshold of 1.25×10^{-8}. Replication: An independent cohort of 544 BMT survivors (192 cases with self-endorsed cognitive problems and 352 controls without) was used for replication. **Results:** *Discovery:* Median age at BMT was 51.3y; primary diagnoses: 47% leukemia, 32% lymphoma, 21% multiple myeloma; 57% males; 69% non-Hispanic whites: 50% allogeneic BMT, median GDS score = 0.22 (range 0-2). Forty-four SNPs were significantly associated with increased GDS (additive model: 3 SNPs; codominant model: 20 SNPs; genotype model: 21 SNPs). Estimates ranged from increase in GDS score by 0.28 points for each additional copy of risk allele, $p = 1.07 \times 10^{-8}$ to increase in GDS score by 1.82 points for two copies of risk allele, $p = 2.3 \times 10^{-11}$. *Replication:* Median age at BMT was 44y; primary diagnoses: 32% leukemia, 49% lymphoma, 19% multiple myeloma; 54% males; 80% non-Hispanic whites: 34% allogeneic BMT. Three SNPs were successfully replicated: rs116334183 resides within *lncRNA-SEMA6D-2*, which facilitates neuronal migration; rs13286152 86kb downstream of *TLE-1*, which promotes neuronal survival; and rs12486041 0.36Mb downstream from *lncRNA-SPTSSB-1*, which regulates sphingolipid production in neuronal axons and 0.36Mb upstream from *TOMM22P6* linked to neural repair. **Conclusions:** In this first GWAS of cognitive impairment post-BMT, we identify 3 SNPs with plausible links to genes implicated in neuronal integrity. Functional studies are currently underway. Research Sponsor: Leukemia and Lymphoma Society (62771-11, Bhatia).

1537 Poster Session (Board #29), Fri, 8:00 AM-11:00 AM

Heterozygous germline ATM mutations in breast cancer: A single academic center experience. *First Author: Anish S Konde, Oakland University William Beaumont Hospital - Rose Cancer Center, Royal Oak, MI*

Background: Heterozygous germline *ATM* mutation carriers have an increased risk of developing breast, pancreas, and other cancers. The clinical and pathologic characteristics of *ATM*-associated breast cancers have not been well defined. **Methods:** Patients who underwent multigene panel testing (MGPT) between 2013-2019 and identified to harbor *ATM* mutations were included in the study. We evaluated demographics, pathology, and surgical management of our *ATM* mutation carriers with breast cancer. **Results:** At total of 319 individuals were identified to have variants in *ATM*, of which 114 were pathogenic/likely pathogenic. The majority of patients were female (82%) and Caucasian (88%). A total of 56 patients (49%) had a personal cancer diagnosis, the most common of which was breast cancer (n = 39). Nine individuals had more than one primary malignancy. The mean age at breast cancer diagnosis was 52, with a range of 25-82. The majority of patients had invasive ductal carcinoma (74%), grade 2 or 3 (90%), and ER and /or PR positive (87%). Of those with known HER2 status, 24% were positive. Thirty-nine percent of patients were lymph node positive, and 42% had lymphovascular invasion. The most common stage at diagnosis was 2 (53%). Of the 39 mutation carriers with breast cancer, 16 (42%) received radiation therapy, and 16 underwent bilateral mastectomy. Of 114 *ATM* positive patients, there were 55 distinct variants. Sixteen (14%) individuals had a mutation in additional cancer predisposition genes. One variant, c.5015delG, was identified in ten patients in a large, consanguineous Iraqi family with an extensive history of pancreatic and other cancers. Eight individuals were identified to have the known high-penetrance variant, c.7271T $>$ G. **Conclusions:** Our study describes the clinical and pathological characteristics of *ATM* mutations carriers with breast cancer. The majority of patients had intermediate to high grade disease, hormone receptor positive, with a suggestion of a higher rate of HER2 positivity and lymph node involvement. Additional studies are needed to elucidate the unique characteristics of *ATM*-associated breast cancer, which may have implications for personalized management. Research Sponsor: None.

1538 Poster Session (Board #30), Fri, 8:00 AM-11:00 AM

A single-institution and commercial laboratory database analysis of BRIP1-associated cancer risks. *First Author: Kristen Danielle Whitaker, Fox Chase Cancer Center, Philadelphia, PA*

Background: *BRIP1/FANCJ* participates in DNA replication and repair via interactions with *BRCA1* and possibly *MLH1*. Previous studies have reported that pathogenic variants (PV) in *BRIP1* are associated with an ~2-fold increase in risk for ovarian cancer (OC) and triple-negative breast cancer (TNBC). Although multigene panel testing for hereditary cancer (CA) has identified *BRIP1* PV and uncertain variants (VUS) in patients with diverse CAs including breast (BC), colorectal (CRC) and melanoma (Mel), association with these CA types has not been established. **Methods:** We examined *BRIP1* risks in two independent populations: Fox Chase Cancer Center (FCCC) and Myriad Genetics (MGL). At FCCC, pedigrees of *BRIP1* PV (*N*= 10) and VUS families (*N*= 47) were reviewed. The MGL population included patients referred for testing by multigene panel (9/2013-12/2019) (*N*= 586,740). Multivariable logistic regression analysis estimated *BRIP1* CA risks as odds ratios (ORs) and 95% confidence intervals (CIs). Models were adjusted for age, sex, ancestry, personal CA history (PHX), and family CA history. **Results:** In the FCCC cohort, *BRIP1* PV carriers (*N*= 12) reported PHX of early-onset (< 50) BC, CRC, and bladder CA. *BRIP1* VUS were also identified among several patients with striking PHX and negative panel testing: BC < 40 (*N*= 3), bilateral BC (*N*= 4), TNBC (*N*= 2), CRC < 40 (*N*= 3), and a patient with 3 CAs < 40 (CRC, BC, and Mel). All FCCC families with a *BRIP1* PV and select VUS families (*N*= 6) are seen in the Table. In the MGL population, 0.3% (1,678/586,740) carried a *BRIP1* PV. Logistic regression analyses found that female *BRIP1* PV carriers have significantly increased risk for OC (OR 2.40, 95% CI 1.93-2.98) and TNBC (OR 1.93, 95% CI 1.52-2.46). Data were insufficient for testing risk of bladder or prostate CA. Findings did not support associations of *BRIP1* with CRC, melanoma, endometrial, pancreatic or gastric CA. **Conclusions:** *BRIP1* PV and VUS may be identified in patients with diverse CA histories. These results confirm studies showing that *BRIP1* PV are associated with an ~2-fold increased risk of OC and TNBC, but do not support increased risks of CRC, melanoma or endometrial CA in *BRIP1* PV carriers. Research Sponsor: Myriad Genetic Laboratories, Inc.

FCCC *BRIP1* families.

	Variant	Carrier	1st Degree Relatives
PV	R798X (*N*= 5)	BC 40	OC 50
		BC 44	CRC 86, Prostate 77
		BC 77	Pancreas 71
		Mel 78	BC 66
		--	
	T997Rfs	BC 55	
	K998E	BC 34, Bladder 37	
	S624X	--	BC 45
	R439X	--	Prostate 70
	K703Ifs	--	CRC 40
Notable VUS	G569R	CRC 36, Mel 37, BC 38	CRC 60
	I902M	CRC 28	
	I482V (*N*= 4)	Bilat BC 43/54 (1 TNBC)	TNBC 48
		Bilat BC 49/63 (1 TNBC)	BC 50, BC 67
		--	Bladder 80
		CRC 60	

All breast cancers were in women

1539 Poster Session (Board #31), Fri, 8:00 AM-11:00 AM

Effect of detection of epigenomic changes in plasma-derived cell-free DNA on multicancer classification. *First Author: Anna Bergamaschi, Bluestar Genomics, San Diego, CA*

Background: Epigenomic changes in DNA methylation patterns are more precisely delineated by active demethylation events as marked by 5-hydroxymethylation (5hmC) of cytosine residues. 5hmC appears to be dynamically modulated in tumor tissues and can be employed as a cancer biomarker. Strategies which interrogate 5hmC genome-wide patterns in a liquid biopsy context may provide efficient and precise technology for early cancer screening and detection. In this study we identified genome-wide 5hmC changes in plasma based circulating free DNA (cfDNA) from breast, colorectal, lung, pancreatic and prostate cancer patients versus non-cancer individuals. **Methods:** cfDNA was isolated from plasma, enriched for the 5hmC fraction using novel click-chemistry protocol for labelling followed by sequencing and alignment to a reference genome to construct features sets of 5hmC patterns. Regularized classification models were constructed to classify cancer samples apart from non-cancer. **Results:** > 500 non-cancer individuals and > 500 cancer patients across five cancer types (breast, colorectal, lung, pancreas and prostate) were included in this study. About 60% of the cancer samples were early stage disease (I or II). The ability to classify non-cancer versus cancer patients was evaluated by 5-fold cross validation of our trained prediction models. Our models were able to classify all breast cancer with a test auROC of 0.86 while prediction model classification for ER negative samples had an auROC of 0.92. Colorectal performance auROC was 0.9; lung auROC = 0.92, pancreatic auROC = 0.97 and prostate auROC = 0.91. Overall sensitivity range, when allowing 2% false positive, was between 85% and 52%. Further using 5hmC signal in blood we were able to identify several signaling pathways specifically relevant to the biology of the cancers investigated. **Conclusions:** These findings further demonstrate that 5hmC changes in cfDNA enable non-invasive detection of breast, colorectal, lung pancreatic, and prostate cancers. Further, 5hmC signals enabled the identification of a suite of cancer signaling pathways differentially enriched in cancers versus non-cancers. These data suggest that dynamic changes in tumor cell methylation, detectable through 5-hydroxymethylation, are contained in the circulating blood and signal active disease biology. Research Sponsor: None.

1540 Poster Session (Board #32), Fri, 8:00 AM-11:00 AM

First year outcomes of an initiative to increase *BRCA* testing among NCCN guideline-eligible breast cancer patients within a large community OCM practice. *First Author: David Michael Waterhouse, OHC (Oncology Hematology Care)/US Oncology Network, Cincinnati, OH*

Background: Pathogenic variants in *BRCA1/BRCA2* can affect a breast CA pts care: preventative interventions, surgical decisions, medical treatments, screening, and family counseling. National data suggests significant non-adherence to NCCN testing guidelines, with only 1/3 of eligible pts referred for genetic services. In 2018, OHC (Cincinnati) launched an APP-centric genetics program. Specially trained APPs carry out genetic counseling and order NCCN-compliant testing. Early data suggested a significant deficit in physician-driven referrals. From 1/01/18 - 07/31/18, 138 new breast pts were estimated to be NCCN guideline-eligible. Only 28 (20%) pts received genetic services. **Methods:** In 2019, the OHC genetics team implemented a standardized screening process for every new breast CA pt. An EMR template (iKnowMed G2) that included NCCN guidelines was created for initial breast CA consultation and Oncology Care Model (OCM) treatment planning. All pts, not just OCM pts, are subject to OCM treatment planning. This automated screening method ensured all breast CA pts were screened, drastically increasing compliance. Through integration of genetics screening into the templates, pts meeting NCCN criteria for testing are reflexively referred for genetic counseling. With USON/McKesson, integrated data fields were developed in the EMR to automate data collection. **Results:** From 01/01/19 – 12/31/19, 717 new breast CA pts were seen at OHC. 676/717 (94%) were screened. Of those screened, 279 new breast CA pts met NCCN criteria for *BRCA* testing. 140 (50%) eligible new pts had appts with the genetics team. Another 50 (18%) had confirmed testing outside of OHC. 57 (20%) refused appts and/or testing. 32 (11%) did not have appts, representing screen fails. Referrals in non-breast CA pts also increased by 127%; 604 (2019) vs 264 (2018) suggesting a halo effect. Analyses suggest the program to be economically viable, with a financial growth rate of 127%. **Conclusions:** EMR templates embedded with the NCCN guidelines for reflex genetics referral can appropriately increase the utilization of genetic services. Breast genetics screening and resultant appt/testing rates increased significantly 2019 vs 2018. Success in BRCA testing in breast CA will lead to expansion to other cancers and genes. Implementation of structured EMR genetics data fields can automate data collection and measure compliance. Integration of genetics screening into universal OCM treatment planning is feasible, economically viable and scalable. Research Sponsor: Pfizer/ACCC.

1541 Poster Session (Board #33), Fri, 8:00 AM-11:00 AM

Return of results after somatic tumor mutation profiling in advanced cancer: Psychological impacts. *First Author: Phyllis Butow, The Chris O'Brien Lifehouse, Camperdown, Australia*

Background: Somatic tumor mutation profiling (STMP) is entering clinical practice. We aimed to investigate psychological impacts of receiving results. **Methods:** Eligible participants had: advanced solid cancers of any histological type; accessible tissue for STMP; and enrolled in the Molecular Screening and Therapeutics (MoST) Program. 1074 participants (91%) completed a baseline assessment prior to STMP (T0), of whom 570 (47%) received results and completed a post-result assessment (T1) of impact of genetic results (MICRA), anxiety and depression (HADS), cancer-specific anxiety (IES), and satisfaction with decision to have STMP. Linear regression models controlling for age, gender, parental status, cultural diversity, education and ECOG status explored associations between result received and psychological outcomes. **Results:** 360 participants received an actionable result and were recommended personalised treatment: 152 via a MoST sub-study (G1) and 208 via their treating oncologist (G2). 210 received a non-actionable result (G3). At T1, G3 were significantly more distressed and less positive about their result (MICRA subscales) and less satisfied with their decision to have STMP than both G1 and G2; G2 was less positive than G1. IES and HADs were not impacted by type of result. Interactions between gender and age, and result were non-significant for all psychological outcomes. Perceived self-efficacy in coping with results (p=0.015) and knowledge (p=0.04) at T0 was significantly correlated with satisfaction with decision at T1; self efficacy (T0) was also correlated with MICRA total (T1) (p=0.006). **Conclusions:** Pathway to treatment receipt is less important to advanced cancer patients than actionability. Patients' self-efficacy to cope with results prior to testing can identify patients vulnerable to distress post-receipt of STMP results who should be offered psychological counseling. Ensuring good knowledge of STMP at consent may avoid decisional regret. Research Sponsor: National Health and Medical Research Council of Australia grant.

	G1: Actionable, Tx via MoST (N=152)	G2: Actionable, Tx via oncologist (N=208)	G3: Non-actionable (N=210)	t statistic	p-value
MICRA, Distress	6.44 (7.0)	6.08 (7.0)	7.95 (6.7)	1.47	p=0.049[1vs3]
Mean (SD)				1.77	p=0.009[2vs3]
MICRA,	4.77 (3.8)	5.92 (4.6)	8.69 (4.4)	3.99	p<0.001[1vs3]
Positive experience				2.83	p<0.001[2vs3]
Mean (SD)				1.16	p=0.014[1vs2]
MICRA, Total	25.75 (16.1)	25.89 (15.6)	32.07 (14.3)	5.92	p<0.001[1vs3]
				5.50	
Total				5.92	p<.001[2vs3]
Mean (SD)				5.50	
Satisfaction with decision	26.75 (4.2	26.03 (5.0)	25.36 (4.4)	1.31	p=0.009[1vs3]
Mean (SD)					

* All other comparisons were non-significant.

1542 Poster Session (Board #34), Fri, 8:00 AM-11:00 AM

Test of an online tool to facilitate NCCN guideline-compliant access to cancer genetics care. *First Author: Kara J. Milliron, University of Michigan, Ann Arbor, MI*

Background: Minority populations experience inequities of access to cancer genetics. We developed and tested an online family history collection and interpretation tool, InheRET, to determine acceptability, validity and utility.Patients are mostly unable to recall accurate family history in clinic and providers have little time to collect the 3-generation pedigree. Thus, ~90% of high risk patients remain unidentified. We evaluated the impact InheRET has on facilitating National Comprehensive Cancer Network (NCCN) Guideline-compliant referrals for cancer genetic counseling. **Methods:** Patients from 3 clinics were consented online to participate. A user experience survey for patients and providers followed the health history questionnaire. **Results:** 628 patients were consented over a year, 555 (>88%) completed the tool. 439 (79%) completed the post-questionnaire user experience. Review of Inheret's recommendations by a genetic counselor found 100% accuracy. Ease of Use: 84-87% of patients reported tool was easy to use. Understandability: 92-97% of patients reported tool was easy to understand. No significant differences were reported between those with high school (n=28, avg age 50.1 yrs) compared to those with advanced degrees (n=139, avg age 45.4 yrs); patients age 70+ experienced increased difficulties. Among primary care patients (n=135), 43 established patients were newly identified as meeting NCCN referral criteria. Healthcare providers found InheRET useful, did not require extra clinical time, and all wish to continue to use it. The patient provided data were more complete and encompassed more family members than with paper forms. Turnaround-times to receive the patient's information were decreased from 4-6 weeks to ~ 72 hours. A patient scheduling backlog of 400 patients was cleared using InheRET. Previously, 40% of cancer genetics patients were lost to follow up, due to not completing their intake forms. This number was reduced to 6.5%. **Conclusions:** Patients find InheRET to be easy to use and understand and they complete this health history tool more frequently and in greater detail than by paper forms. InheRET provides accurate results, verified by in person interviews, in a timely fashion, saving clinical time, possibly enabling increase in earned clinical revenues (under analysis), and improving patient care overall. Importantly, the 43 primary care patients identified to be at increased risk were already established patients, who had not been previously identified as such by their healthcare providers as being at increased risk. Research Sponsor: U.S. National Institutes of Health, Private investors.

1543 Poster Session (Board #35), Fri, 8:00 AM-11:00 AM

Potential germline findings identified during somatic tumor testing: Room for improvement. *First Author: Sundas Khan, University of Vermont Medical Center, Burlington, VT*

Background: Genomic testing, useful for treatment planning and identification of patients for clinical trials, may indicate the presence of a germline mutation. We sought to evaluate the incidence of potentially actionable germline mutations detected via genomic testing and determined rates of germline testing among patients with potential germline mutations. **Methods:** This was a retrospective review of patients undergoing genomic testing at The University of Vermont Cancer Center (UVMCC) between 03/02-11/19. Testing was reviewed for mutations in 60 genes associated with hereditary cancer and recognized as clinically actionable by the American College of Medical Genetics. Records were reviewed for clinical follow-up. Positive (pathogenic or likely pathogenic) genomic test results were evaluated with descriptive analyses. Proportions with 95% confidence intervals are presented and comparisons made using a χ^2 test. **Results:** 342 patients underwent genomic testing at UVMCC over the study period, with a median age of 61. Common tumor types include: CNS (19%), NSCLCA (17%), ovarian (8%), and sarcoma (7%). 59% (203/342) had a mutation in $\geq$ 1 gene associated with hereditary cancer. Most common tumor types with potential germline mutations include: NSCLCA (25%), CNS (18%), ovarian (8%), sarcoma (8%), and endometrial (7%). Potential germline mutations were most commonly identified in TP53, CDKN2A, PTEN, and RB1 (each with mutations in >6% of patients). 58 patients in the cohort have undergone germline testing, of which 19% were positive for germline mutations. Of patients with mutations in the highly penetrant BRCA, PALB2, and Lynch genes, 71% were positive for germline mutations. Young age ($<$ 50) did not enrich for germline mutations ($p > 0.05$). Only 18% (36/203) of patients with potential germline results were referred for genetic counseling. **Conclusions:** Genomic testing can reveal hereditary cancer syndromes. While the majority of patients with tumor mutations in genes associated with hereditary cancer will not have germline mutations, genetic testing is the only way to confirm this. 19% of patients who underwent genetic testing in this cohort had a pathogenic germline mutation. This was enriched to 71% when considering genes rarely mutated in tumors (BRCA, PALB2, and Lynch genes). Only 17% of this cohort underwent genetic testing, representing a significant missed opportunity given the implications of these findings for both patients and families. Patients and their providers should be aware of the potential for germline findings when genomic testing is performed. Research Sponsor: None.

1544 Poster Session (Board #36), Fri, 8:00 AM-11:00 AM

Outcome of patients with breast cancer and a germline *BRCA* mutation in a prospective cohort. *First Author: Banu Arun, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: There are limited large prospective single institution studies on outcome of breast cancer in patients with germline *BRCA1* and *BRCA2* mutation. The primary aim of this study was to determine the effect of a germline *BRCA1* or *BRCA2* mutation on recurrence-free survival (RFS) and overall survival (OS) in patients with breast cancer. **Methods:** This is a prospective cohort study of patients with invasive breast cancer recruited from the UT MD Anderson Cancer Center Breast Medical Oncology and Clinical Cancer Genetics Center. For the purpose of this analysis, newly diagnosed breast cancer patients who have had germline *BRCA1* and *BRCA2* testing within 12 months were included. Clinical and pathological data, and data regarding outcomes were collected in this prospective cohort. The Kaplan-Meier method and corresponding log-rank test were used to estimate OS and RFS and to compare survival by mutation status. **Results:** Between 1996 and 2015, 3026 patients were recruited. Median age at diagnosis was 45 (19-87) years. A germline *BRCA* mutation was detected in 361 (11.9%) patients (207 with *BRCA1*, 154 with *BRCA2*). After a median follow-up time of 5.3 (0.04-20.7) years, 437 (14.4%) patients recurred and 340 (11.2%) were deceased. At median follow-up time 5 years, 79.3% of *BRCA1*, 91.4% of *BRCA2* and 89.6% of *BRCA* negative patients were disease free; this difference was significant ($p = 0.0001$). Difference in OS between *BRCA1/2*-positive and *BRCA*-negative patients was also significant ($p = 0.0001$), with 81.2% of *BRCA1*, 93.4% of *BRCA2* and 90% of *BRCA* negative patients being alive at 5 years. Amongst 600 patients with triple negative breast cancer (TNBC) patients, DFS and OS were not significantly different between the 3 groups. Of those patients diagnosed under 40 years (n = 937), RFS and OS was significantly different between 3 groups at 5 years (0.001 for RFS and OS); 75% *BRCA1*, 92% *BRCA2* and 86% *BRCA* negative patients were disease free and 77% *BRCA1*, 94% *BRCA2* and 88% *BRCA* negative patients were alive. **Conclusions:** Patients with *BRCA1* or *BRCA2* mutations have different survival outcomes. The prognosis of the first cancer needs to be taken into consideration when deciding for preventive surgeries to prevent second primary breast cancers in these patients. Furthermore, for *BRCA1* mutation carriers more effective therapy strategies need to be evaluated to improve outcome. Research Sponsor: None.

1545 Poster Session (Board #37), Fri, 8:00 AM-11:00 AM

Tumor detection rates in screening carriers with *SDHx*-related hereditary paraganglioma-pheochromocytoma syndrome based on prior tumor history. *First Author: Samantha Greenberg, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT*

Background: Patients with germline pathogenic variants (PVs) in the *SDHx* genes have increased risk for paragangliomas/pheochromocytomas (PGL/PCC), renal cell carcinomas, and gastrointestinal stromal tumors. Expert recommendation suggests individuals with *SDHx* PVs undergo biennial whole-body imaging and annual biochemical testing. This study aimed to evaluate tumor detection rate using standard biochemical and imaging protocols for individuals with *SDHx* PVs, particularly in those with and without *SDHx*-related tumor history, and in those with biochemical testing data. **Methods:** A retrospective longitudinal observational study at the Universities of Michigan, Pennsylvania, and Utah Huntsman Cancer Institute was conducted from the start of each center's screening program through March 1, 2018. Individuals with *SDHx* PVs had clinical imaging with whole body MRI/CT and biochemical testing per expert recommendation. *SDHx*-related tumors identified during clinical screening were measured. **Results:** A total of 263 individuals with *SDHx* PVs completed 491 screens. Individuals with *SDHB* PVs were the most prevalent (n = 188, 71.5%). The average number of screens per subject was 1.87 (range 1-7). A majority (n = 194, 73.7%) of individuals did not have a prior history of PGL/PCC. Overall, *SDHx*-related tumors were detected in 17.1% (n = 45) of the cohort. Of the 46 scans that identified an *SDHx*-related tumor, 85% of them (n = 39) were baseline scans. *SDHx*-related tumors were identified in 18.6% (n = 36/194) of individuals that did not have a prior history of PGL/PCC, whereas they were identified in 13.0% (n = 9/69) of individuals that did have a prior history of PGL/PCC ($p = 0.39$). Biochemical testing was available for 70% (n = 343) of imaging screens, of which 18% (n = 61) had positive biochemistry. Of those with positive biochemistry, 19 tumors were identified on imaging (6%). Sixteen tumors were identified on imaging with negative biochemistry (5%) with a sensitivity of 54% and a specificity of 94%. Utilizing a cut-off of two times the upper limit of normal, 9.91% (n = 34) biochemical tests were positive, and 15 (44.12%) had an *SDHx*-related tumor on corresponding imaging. **Conclusions:** Current *SDHx* screening protocols are effective at identifying *SDHx*-related tumors. Tumors were detected in subjects with a prior history of PGL/PCC and those with no prior history. This suggests lifelong screening is important for all *SDHx* carriers. Imaging is a crucial piece of *SDHx* screening given biochemical testing's sensitivity and specificity. Research Sponsor: None.

1546 Poster Session (Board #38), Fri, 8:00 AM-11:00 AM

Germline alterations other than *BRCA* in triple negative breast cancer (TNBC) patients who underwent neoadjuvant therapy (NAT) on a prospective clinical trial. *First Author: Banu Arun, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Previous studies have related germline *BRCA* mutations to pathologic complete response (pCR) in TNBC cohorts. However, prospective data is lacking on the frequency of non-*BRCA* germline mutations and pCR in TNBC patients who received neoadjuvant therapy (NAT). The aim of this study was to describe germline alterations in comparison with pCR in a prospective cohort of TNBC receiving NAT. **Methods:** Pre-NAT blood was drawn from patients enrolled in a clinical trial of genomically tailored NAT (ARTEMIS: NCT: 02276443, per eligibility patients had to have negative clinical *BRCA* tetsing). Germline DNA was extracted and sequenced on a HiSeq4000 sequencer (Illumina, coverage 60X). Reads were aligned to human reference hg19. Variants were filtered against public databases of normal cohorts: esp6500, 1000 genome, ExAC with a frequency cutoff at 1% in any ethnicity. Two integrative scores were used to evaluate the deleteriousness of the missense variants and the variants predicted to be damaging by both scores were included in the analyses. A 105 pan-cancer susceptibility gene panel was selected based on literature data and commercially available gene panels. NAT included anthracycline and taxane based chemotherapy +/- targeted therapy based on tumor genomic expression. Univariate logistic regression models were used to fit pCR for individual mutations, excluding genes mutated in fewer than three patients. All statistical analyses were performed using R version 3.6.1. with a significance of p=0.05. **Results:** Germline results and pCR were available for 152 patients. Median age was 55 yrs (range: 24-77). 7.9% were stage (st) I, 65.8% st II, 26.3% st III. 55 pts (36%) had pan-cancer associated germline mutations, whereas 33 (21%) had a breast-cancer associated mutation. Greater than 1% mutations were seen in seventeen genes (Table). There was no significant difference in pCR rate after NAT among pts with different germline mutations versus without mutation. **Conclusions:** Breast cancer related germline mutations other than *BRCA* in TNBC are relatively common supporting at least a breast panel (not only *BRCA1/2*) testing. Treatment implications of different germline mutations and their impact on pCR is ongoing on an extended series. Research Sponsor: None.

Gene	% pos	Gene	% pos	Gene	% pos
APC	2.6	*MSH2*	2	*SDHA*	2
BRIP1	1.3	*MSH6*	1.3	*BRCA1*	1.3
ERBB2	1.3	*MUTHY*	2.6	*TSC2*	4
MITF	1.3	*NTHL1*	1.3	*WT1*	1.3
MLH3	3.3	*PMS1*	2	*XRCC3*	1.3
PHB	1.3	*PMS2*	2		

1547 Poster Session (Board #39), Fri, 8:00 AM-11:00 AM

Ancestry-specific gene expression profiles in TNBC tumors. *First Author: Windy Marie Dean-Colomb, Lousiana State University School of Medicine, New Orleans, LA*

Background: Due to persistent disparities in breast cancer mortality, there has been a renewed focus on investigating tumor biology. Deeper exploration has exposed distinctions in tumor biology based upon self-reported race and ancestry. The disparities associated with Triple Negative Breast Cancer (TNBC) across the modern African Diaspora suggests that there is a genetic ancestry connection between its aggressive tumor biology and clinical outcomes. Understanding this connection could hold the key to improving clinical outcomes in this group. **Methods:** We investigated 75 TNBC primary tumors using Self-Reported Race (SRR) groups: African American (AA, n = 42) and European American (EA, n = 33). Using best practices established by TCGA, we analyzed bulk RNA sequencing to measure changes in genome-wide expression levels. We next quantified global ancestry in a novel manner using RNAseq variants using 1000 Genomes as the reference data. We then identified African and European ancestry-associated genes using a logistic regression (adjusted FDR $p < 0.05$) between quantified ancestry and gene expression levels. **Results:** We identified > 150 genes associated with quantified African ancestry. We also found using quantified ancestry was a more robust method to screen for differentially expressed genes than SRR. Using an updated TNBC subtyping method, we noted higher incidences of Basal-like 2 tumors in AAs. Pathway analyses indicated several canonical cancer pathways; including, TP53, NFKB1 and AKT, have altered functionality in patients of African descent. For example, TP53-associated genes were activated in TNBC tumors of AA versus EA. This upregulation, rather than loss of function, is suggestive of polymorphic and/or ancestry-specific expression regulation, likely driven by population-private genetic variants. Lastly, we used TCGA data to validate a subset of African ancestry-specific genes that were upregulated in AA patients in our cohort. Specifically, PIM3, ZBTB22 and PPP2R4 each retained significant upregulation, in our cohort, but also TNBC tumors from TCGA (p = 0.0018, 0.023 and 0.022, respectively). **Conclusions:** Our study has uncovered ancestry-specific gene expression profiles in TNBC tumors. The distinct distribution of TNBC subtypes and altered functional oncologic pathways are evidence that biological underpinnings in TNBC can be driven by shared genetic ancestry. These findings emphasize the need to investigate patient populations of various ancestral origins in order to fully appreciate the molecular diversity in tumor biology for precision of disease management. Research Sponsor: Susan G Komen.

1548 Poster Session (Board #40), Fri, 8:00 AM-11:00 AM

Outcomes of Lynch syndrome (LS) patients treated with immune checkpoint inhibitors (ICI). *First Author: Shahla Bari, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: LS is caused by a germline mutation in one of several DNA mismatch repair (MMR) genes: MLH1, MSH2, MSH6 or PMS2 (d-MMR). A minority of LS patients have MMR proficient tumors (p-MMR). ICI therapy has dramatically changed outcome of d-MMR (majority of LS patients. However, data about response to ICI in LS patients, irrespective of their tumor MMR status is scarce. The aim of this study was to evaluate outcomes of ICI therapy in all LS associated Cancer. **Methods:** This was a retrospective analysis of LS associated cancers treated with one of the 6 ICIs at our center. We also looked at age, sex, microsatellite status, response and survival. **Results:** Out of 262 LS patients analyzed, 194 had cancer and 22 received ICIs. Among the patients analyzed, the mean age at diagnosis of 1st cancer was 51 yrs. There were 10 females (47%). 10 patients had colorectal (45%), 3 urothelial (14%), 2 renal cell, 2 cholangiocarcinoma and one each of esophageal, ovarian, uterine, glioblastoma multiforme and pancreatic cancer. One patient died from progressive disease after receiving a single dose and was not included in the analysis. 17 patients (80%) received Pembrolizumab, 11 patients were microsatellite unstable (MSI), 3 were microsatellite stable (MSS) while 7 were unknown. 2 patients achieved complete response (CR) (10%), 1 patient had partial response (PR) (5%), 13 had stable disease (62%) while 5 had progressive disease (23%) leading to a disease control rate (DCR) of 76%. Of the 3 known MSS Lynch syndrome patients, 2 did not respond while the 3rd continues to respond at 9 months of therapy. Of the 5 patients who had PD, 2 were MSS, 2 unknown and 1 MSI. Among the 16 patients who responded, 15 of 16 (94%) had sustained response and have not experienced disease progression or relapse. 3 of these patients have been off therapy (1 due to immune related adverse evet) and have had no relapse. One responder progressed after 18 cycles of therapy. The DCR was 71% at 12 months as well as 48 months of follow up. Median progression survival has not been reached. Similarly, median overall survival has not been reached. **Conclusions:** Our study is the one of the largest reported analysis of LS associated cancer patients treated with ICIs and included LS patients with both MSI and MSS tumors. Though small, our data suggests robust DCR and prolonged responses in Lynch associated MSS tumors treated with ICI. This encouraging response in MSS tumors along with higher response rates in LS associated cancers as compared to non-LS MSI tumors, suggests that there may be additional drivers of response to ICI in LS patients leading to superior responses. Research Sponsor: None.

1549 Poster Session (Board #41), Fri, 8:00 AM-11:00 AM

Clinicopathologic features of invasive breast cancer (BC) diagnosed in carriers of germline *PALB2*, *CHEK2* and *ATM* pathogenic variants. *First Author: Danika Scott, Stanford University School of Medicine, Stanford, CA*

Background: While germline pathogenic variants (PVs) in *BRCA1/2* account for a large proportion of hereditary breast cancer (BC), PVs in *PALB2*, *CHEK2* and *ATM* are increasingly detected. However, the phenotype and clinical features of invasive BC with these PVs have not been fully described. **Methods:** We identified patients with a PV or likely PV in *PALB2*, *CHEK2* or *ATM* tested clinically at Stanford between 2014 - 2019 who provided informed consent to be included in a prospective cancer genetics registry. Data on baseline demographics, genetic testing history, and clinicopathologic features of diagnosed BC were collected. For patients with a subsequent diagnosis of metastatic BC, we calculated disease-free interval (DFI). **Results:** 130 patients met inclusion criteria for analysis: *ATM* (N=39), *CHEK2* (N=58), *PALB2* (N=33). Nearly all (98.5%) were women, with 2 male BC in *ATM* carriers. Non-Hispanic White ethnicity was most common in *ATM* (64.1%, 95% CI 48.4%-77.3%) and *CHEK2* carriers (69.0%, 95% CI 56.1%-79.4%), but comprised only 39.4% (95% CI 24.7%-56.4%) in *PALB2* carriers. Asian/Pacific Islander (24.2%, 95% CI 12.6%-41.3%) and Hispanic (30.3%, 95% CI 17.3%-47.5%) ethnicities were enriched among *PALB2* mutation carriers. In total, 97.7% learned of their PV status only after a preceding diagnosis of BC and 43.1% were diagnosed with BC at age ≤ 45. Data regarding invasive BC subtypes, incidence of subsequent primary BC, and metastatic recurrence are listed below in the table. Additional data on stage, grade and sites of metastatic spread will be presented. **Conclusions:** We observed clinically important differences in the spectrum of BC subtypes among carriers of *ATM*, *CHEK2* and *PALB2* PVs, in addition to racial/ethnic differences with Asian/Pacific Islander and Hispanic ethnicity enriched among carriers of *PALB2* PVs. Research Sponsor: BRCA Foundation.

	% ATM (N=39)	95% CI	% CHEK2 (N=58)	95% CI	% PALB2 (N=33)	95% CI
Invasive BC Subtype ER and/or PR positive, HER2-negative	71.8%	56.1%-83.6%	86.2%	74.8%-93.1%	60.6%	43.7%-75.4%
Any HER2-positive	25.6%	14.4%-41.2%	13.8%	6.9%-25.2%	3%	<0.01%-16.7%
TNBC	2.6%	<0.01%-14.3%	0.0%	0.0%-7.4%	36.4%	22.1%-53.4%
Diagnosed with Subsequent Primary BC	12.8%	5.1%-27.2%	19%	10.8%-31.0%	21.2%	10.4%-38.1%
Diagnosed with Metastatic BC	5.1%	0.5%-17.8%	17.2%	9.4%-29.1%	24.2%	12.6%-41.3%
Percent Relapse-Free ≥ 5 years	0%	0.0%-48.9%	50%	23.7%-76.3%	12.5%	0.11%-49.2%
Median DFI (years)	4.3		6.4		1.7	

1550 Poster Session (Board #42), Fri, 8:00 AM-11:00 AM

A noninvasive multi-analytic approach for lung cancer screening of patients with pulmonary nodules. *First Author: Hong Zheng, Department of Thoracic Surgery, Xinqiao Hospital, Chongqing, China*

Background: Low-dose computed tomography (LDCT) is an effective approach for lung cancer screening of high-risk patients with pulmonary nodules, however with varying false positive rates depending on the somewhat subjective judgement of the practice professional. Artificial intelligence derived from machine learning of comprehensive patient profiles, including multi-omics and clinical data, has the potential to provide more objective assessment of patient's risk in order to aid clinician's decision making. We have developed a multi-analyte algorithm-based assay (MAAA) that incorporates ctDNA mutation, ctDNA methylation, and protein biomarker profiles evaluated through non-invasive blood-based testing, as well as patient's clinical information, to improve the diagnostic efficacy of lung cancer. **Methods:** 98 high-risk patients with pulmonary nodules were enrolled in two independent cohorts (68 for training/testing and 30 for independent validation). The malignancy of the pulmonary nodules were established through pathology of surgical-removed nodules. Prior to surgery, each patient was also subject to cell-free DNA-based sequencing for DNA mutation and DNA methylation profiling, as well as serum protein biomarker profiling. On the training/testing patient cohort, machine-learning-based predictive models were first built for malignancy status prediction based on each type of molecular or clinical features. A final ensemble model was then constructed to incorporate the measurements based on molecular and clinical markers to provide the ultimate recommendation on the malignancy of the pulmonary nodule. The performance of each individual model and the final ensemble model was benchmarked on the training/testing cohort, and also validated on the independent validation cohort. **Results:** On the 30-patient independent validation cohort, individual prediction models based on clinical information, protein marker, ctDNA mutation, and ctDNA methylation profiles achieved predictive AUC of 0.59, 0.48, 0.71, and 0.84, respectively. The final ensemble model achieved predictive AUC of 0.86, which has strongly indicated that an integrative, algorithm-based approach of multi-analytic molecular and clinical profiles greatly outperforms any single-analytic profiling. **Conclusions:** Multi-analyte algorithm-based approach can be utilized to assist in lung cancer screening for patients with pulmonary nodules. It has demostrated a high accuracy through independent validation, and has outperformed any single-analyte testing in our study. Research Sponsor: None.

1551 Poster Session (Board #43), Fri, 8:00 AM-11:00 AM

Green tea extract to prevent colorectal adenomas in men and women: Results of the MIRACLE trial. *First Author: Thomas Jens Ettrich, Ulm University, Department of Internal Medicine I, Ulm, Germany*

Background: Prevention of colorectal adenomas (CA) can reduce colorectal cancers (CRC). Epidemiological and experimental data suggest that the green tea catechin epigallocatechingallate has an antineoplastic effect in the large bowel. MIRACLE is the largest trial so far to examine the effect of three-year daily intake of green tea extract (GTE) on the incidence of metachronous CA in a Caucasian population. **Methods:** Prospective, parallel group, double-blinded, placebo-controlled, randomized multicenter trial (40 German centers, recruitment 11/2011-6/2015). Patients (n = 1001, age 50-80y), polypectomy ≤ 6 months and tolerating GTE well (one-month run-in) were randomized to receive decaffeinated GTE standardized to EGCG (150 mg bid, capsules) or placebo (P) for 3 years. Primary endpoint: Incidence of metachronous CA at the 3-year follow-up colonoscopy. Secondary endpoints: Occurrence, number, localization, size, histological subtype of CA, frequency of CRC, biomarker and safety. Strata: study center, low-dose aspirin (≤100 mg/d). **Results:** Clinical parameters were well balanced. CA incidence at the 3-year follow-up colonoscopy was analyzed in the modified ITT set (modITT; n = 309 patients (GTE), n = 323 (placebo), timely follow up colonoscopy) and the per protocol set (PP, modITT set without major protocol violations). Incidence of CA was 55.7 % (P) and 51.1% (GTE), (modITT, adj. RR 0.905, one sided, p = 0.081), respectively 54.3 % (P) and 48.3% (GTE) (PP, adj. RR 0.883, one sided, p = 0.058). These differences did not reach statistical significance. In the preplanned exploratory analysis regarding gender incidence of CA in females was 47.9% (P) and 47.6% (GTE) in the modITT-set (adj. RR 0.989; 95%-CI: 0.753,1.299; p = 0.935), respectively 45.4% (P) and 46.9% (GTE) in the PP-set (adj. RR 1.014; 95%-CI: 0.748, 1.373; p = 0.930). In contrast, in the male population incidence of CA in the follow-up colonoscopy was 60.4% (P) and 52.9% (GTE) in the modITT-set (adj. RR 0.846; 95% CI 0.717, 0.999); p = 0.048), respectively 59.1% (P) and 49.1% (GTE) in the PP-set (RR 0.803, 95% CI: 0.666, 0.969; p = 0.022). Thus, GTE intake was associated with a significant, 12.4 relative and 7.5% absolute reduction of metachronous CA in the male modITT population. There were no differences with respect to safety between the groups. **Conclusions:** GTE reduced the incidence of metachronous CA. However, a significant effect was only observed in the in the male population whereas there was no effect in the female population. Clinical trial information: NCT 01360320. Research Sponsor: German Cancer Aid Foundation (Stiftung Deutsche Krebshilfe).

1552 Poster Session (Board #44), Fri, 8:00 AM-11:00 AM

Non-invasive detection of urothelial carcinoma (UC) by cost-effective low-coverage whole genome sequencing from urine exfoliated cells DNA. *First Author: Shuxiong Zeng, Changhai Hospital, Navy Medical University, Shanghai, China*

Background: Urothelial carcinoma (UC) is a malignancy with frequent chromosomal aberrations. The FISH assays were more sensitive as compared to cytology tests. Here we investigated cost-effective whole genome sequencing technology, which is able to detect all chromosomal aberrations for UC diagnoses. **Methods:** UC patients and control group are prospectively recruited in trial NCT03998371. First-morning-voided urine were freshly collected before TURBT or cystectomy. Urine Exfoliated Cells DNA was analyzed by illumina HiSeq X10, followed by genotyping by bioinformatics workflow UCAD. **Results:** 195 individuals were prospectively recruited. 121 UC patients and 67 non-tumor diseases were included in this study. 7 other malignancies as confirmed by pathological testing were excluded. Frequent chromosome copy number changes were found in cancer patients as compared non-tumor controls, including chromosome 3 gain, 17 gain, 7 gain and 9p loss used in FISH assays were found. In addition to that, chr9q loss, 8q gain, 5q loss, 17p loss, 11p loss, 1q gain, 8p loss, 10q loss, 6q loss, 4q loss and 11q loss were also frequent in cancer patients (AUC > 0.65). Metacentric chromosomes showed better AUC compared to acrocentric and telocentric chromosomes (P = 1.7e-03). A novel diagnosis model UCAD was built by incorporating all the chromosomal changes. The model reached performance of AUC = 0.933. At the optimal cutoff |Z| > = 3.16, the sensitivity, specificity and accuracy were 84.7%, 97.9% and 89.0% respectively. The prediction positivity was found correlated with urine microscopy visible epithelial cells (P = 0.00069), tumor invasiveness (Ta/Tis vs the other, P = 0.0048) and tumor grade (P = 0.0030), but not microscopy RBC/WBC findings, urine culture findings, smoke and drinking history. The UCAD model outperformed cytology tests by predicting all 16-cytology positive and 12 cytology negative tumors with comparable specificity. The model found 75.0% more tumors. And UCAD identified more upper urinary tract cancer (P = 0.012) and smaller tumors (< 3cm, P = 5.9e-04). The adding of cytology to UCAD did not improve diagnosing sensitivity and specificity. UCAD reproduce the diagnoses among morning - void urine, morning, afternoon urine samples with correlation coefficient $R^2 > 0.98$. All the urine samples showed high concordances with matched tumor samples ($R^2 > 0.85$). **Conclusions:** UCAD could be a high specific, robust UC diagnoses method with improved sensitivity as compared to cytology tests. Clinical trial information: NCT03998371. Research Sponsor: None.

1553 Poster Session (Board #45), Fri, 8:00 AM-11:00 AM

Relationship between *CYP2D6* genotype, tamoxifen metabolites, and adverse events, tumor biomarkers and breast cancer recurrence in a low-dose phase III trial in noninvasive disease. *First Author: Andrea De Censi, Division of Medical Oncology, E.O. Galliera Hospital, Genoa, Italy*

Background: Low dose tamoxifen (T, 5 mg/d) given for 3 years halved recurrence in 500 women with non-invasive disease (DeCensi et al. JCO 2019). Retrospective studies with 20 mg/d have shown an association between low levels of endoxifen (9-16 nM) or Z-4OHtam (3.26 nM) and recurrence, but recent prospective studies have not confirmed these findings. We measured *CYP2D6* genotype and 8 metabolite levels to determine their associations with adverse events, tumor biomarkers (IGF-I, SHBG, C-reactive protein, CRP) and breast cancer recurrence. **Methods:** CYP2D6 genotyping was performed in the T arm (n = 183) as previously described (Johansson H et al. BCRT 2016). T and metabolites were measured at 1 (n = 169) and 3 y (n = 152) as previously described (Helland T et al. BCR 2017). We tested linear relationships between metabolite levels and biomarkers, adjusting for age, BMI, treatment compliance and baseline biomarker levels. Cumulative incidence of recurrence according to endoxifen levels was calculated by the Cox model. **Results:** Endoxifen concentrations were associated to CYP2D6 metabolizer status (p < 0.001). Median (IQR) endoxifen levels were 8.4 (5.2-11.3) and 8.8 (5.8-11.5) at 1 and 3 y, with only 42% and 47% of subjects reaching 9 nM. Median endoxifen levels were related to pill count (5.5, 7.1 and 9.0 nM/L for medication possession rate < 83.3%, 83.4-99.9%, 100%, respectively). There was no difference in metabolite levels and menopausal symptoms. There was an inverse relationship between endoxifen and endometrial thickness at 3 y (p = 0.04), and between endoxifen or tamoxifen levels and IGF-I levels at 3 y (p = 0.001). T levels were positively associated with SHBG levels in postmenopausal women (p-interaction = 0.04). Endoxifen, T and 4OHtam decreased CRP, with a greater effect in premenopausal women (p-interaction = 0.02). An increase in CRP after 3 years was associated with a HR of 4.37 (95% CI, 1.14-16.73, P = 0.03) of recurrence compared to women with no increase of CRP. Median (IQR) endoxifen levels at year 1 were 8.4 (5.3-11.4) in patients who recurred vs 7.5 (5.1-10.2) in those who did not recur (p = 0.6), although this comparison was underpowered. **Conclusions:** T levels themselves may contribute to clinical activity by decreasing IGF-I and increasing SHBG. Elevated CRP is a predictive factor for recurrence which is down-regulated by T and metabolites. Endoxifen is below 9 nM in the majority of subjects treated with 5 mg/day, although this threshold was obtained in studies up to 20 years. Clinical trial information: NCT01357772. Research Sponsor: Italian Ministry of Health, Italian Association for Cancer Research (AIRC).

1554 Poster Session (Board #46), Fri, 8:00 AM-11:00 AM

Mammography adherence among medically underserved women undergoing cancer genetic risk assessment. *First Author: Candice Schwartz, University of Illinois at Chicago College of Medicine, Division of Medical Oncology, Chicago, IL*

Background: Medically underserved women bear a disproportionate burden of breast cancer (BC) mortality. Early detection is vital for reducing BC deaths. Cancer genetic risk assessment (CGRA) provides an opportunity to identify women at highest risk so that risk-adapted screening can be implemented. The effect of CGRA on mammography adherence among underserved women is unknown. **Methods:** We conducted a study to test the feasibility of performing cancer genetic risk assessment (CGRA) as part of standard primary healthcare at two Federally Qualified Health Centers in Chicago, IL. Racial/ethnically diverse women age 25-69 without a personal history of BC underwent CGRA at the time of an annual well-visit and received the result from their PCP. Medical record review provided data on mammography adherence. Demographic data and measures of perceived BC risk, BC cultural beliefs, fatalism, and BC worry were collected with an enrollment survey. McNemar's test compared the rate of adherence to screening mammography before and after implementation of CGRA, defined as completing a screening mammogram within 18 months prior to or following CGRA, resp., among women eligible for screening (age $>$ 40 at study enrollment). Logistic regression models tested for associations between mammography adherence and demographic characteristics/health beliefs. **Results:** Data was available for 90 participants with increased BC risk (IR) who were eligible for screening and 98 eligible, average risk (AR) participants (in total, 61% black and 37% Latina). Overall, adherence improved from 38% at baseline to 49% following CGRA ($p = 0.03$). Adherence increased from 35% to 51% among IR participants ($p = 0.04$), and from 40% to 47% among AR participants ($p = 0.39$). Data on predictors of adherence will be presented. **Conclusions:** Implementing CGRA as a standard component of primary healthcare improved adherence to screening mammography among racial/ethnically diverse underserved women. The effect was seen primarily in those with increased risk. This intervention could be used to improve uptake of mammography in the subgroup of underserved women who benefit the most from screening. Research Sponsor: None.

1555 Poster Session (Board #47), Fri, 8:00 AM-11:00 AM

A sensitive and quantitative multimodal blood test for the detection of colorectal adenomas and cancer: Correlation with size and number of polyps. *First Author: Shai Friedland, Stanford University Medical Center Gastroenterology and Hepatology, Stanford, CA*

Background: Colonoscopic polypectomy is the primary reason for declining colorectal cancer incidence and mortality. Epidemiological evidence has ordered the timing and risk of pre-cancerous adenomas, localized and invasive cancer along a 7-10 year continuum. The increased size and number of index polyps are correlated with an increased probability of progression to cancer and informs surveillance colonoscopies. **Methods:** A single-center, IRB-approved, prospective, blinded study was conducted at the VA Palo Alto Health Care System. Results for 354 patients with no prior diagnosis of CRC who were scheduled for colonoscopy are presented. Indications for colonoscopy were 86% asymptomatic and 14% with symptoms or positive-FIT. Patients had blood drawn immediately prior to colonoscopy. The test analyzes three biomarkers: circulating gastrointestinal epithelial cells (CEC), validated somatic mutations, and methylation (SEPTIN9) of cell-free DNA and uses incident risk to calculate a CMx Score, scaled from 0 to 100. Multivariate regression methods were used to assess the degree of association between the pre-defined CMx Scores and polyp sizes and number, adjusting for both DNA mutation and DNA methylation status. **Results:** There is a significant association between CMx Scores and polyp size (F value = 5.80, p-value = 0.017). DNA mutation (F value = 1.29, p-value = 0.263) and methylation status (F value = 0.34, p-value = 0.560) were non-significant. Similarly, there is a significant association between CMx Scores and number of polyps (F value = 23.71, p-value $<$ 0.0001). Again, DNA mutation (F value = 1.57, p-value = 0.210) and methylation status (F value = 1.34, p-value = 0.248) were non-significant. These results suggest that CMx Scores, which incorporate CEC, are providing predictive information of polyp sizes and number above and beyond DNA mutation and methylation status alone. **Conclusions:** A novel non-invasive multimodal blood-based assay that analyzes cell-free DNA for somatic mutations and methylation, CEC and integrates SEER incidence risk is significantly associated with polyp size and number. The opportunity to track progression and potentially inform colonoscopy interval is notable. Research Sponsor: CellMax Life.

Disease Category	Subject	Sensitivity (%)	Mean Index Polyp Size (mm)	Mean Polyp Number	Mean CMx Score
Colorectal Cancer	11	100	38.3	4.0	71.3
Advanced Adenomas	53	75.5	17.6	5.2	49.9
Non-advanced Adenomas	178	48.3	5.1	3.1	35.6
Non-Neoplastic Findings	33	9.1	4.4	1.8	20.0
Negative Colonoscopy	79	**Specificity** (%) 89.9	-	0	18.1

1556 Poster Session (Board #48), Fri, 8:00 AM-11:00 AM

3,3'-Diindolylmethane (DIM): A nutritional intervention and its impact on breast density in healthy BRCA carriers compared to non-treated carriers—A prospective clinical trial. *First Author: Rinat Yerushalmi, Davidoff Cancer Center, Rabin Medical Center, Petah Tikva, Israel*

Background: Women who carry the *BRCA* mutation are at high lifetime risk of breast cancer, but there is no consensus regarding an effective and safe chemoprevention strategy. A large body of evidence suggests that 3,3-diindolylmethane (DIM), a dimer of indole-3-carbinol (I3C) found in cruciferous vegetables, can potentially prevent carcinogenesis and tumor development. The primary aim of this prospective study was to investigate the effect of DIM supplementation on breast density, a recognized predictive factor of breast-cancer risk. **Methods:** Participants were 23 healthy female *BRCA* carriers (median age 47 years; 78% postmenopausal) who were treated with oral DIM 100 mgx1/d for one year. The amount of fibroglandular tissue (FGT) and background parenchymal enhancement (BPE) on magnetic resonance imaging (MRI) performed before and after the intervention were scored by two independent expert radiologists using the Breast Imaging and Reporting Data System (BI-RADS). Each woman in the cohort was matched by age (within 3 years) and menopausal status to a woman attending the clinic who was not participating in the study and who underwent breast MRI in parallel year. **Results:** A decrease in the average score for FGT amount from 2.8 ± 0.8 at onset to $2.65 \pm 0.842.8$ after one year ($p = 0.031$), with no significant change in BPE ($p = 0.429$). A group of DIM-untreated age- and menopausal-status-matched clinic patients did not show a significant change in FGT amount ($p = 0.33$) or BPE ($p = 0.814$) in a parallel year. Mean estradiol level decreased from 159 to 102 pmol/L ($p = 0.01$), and mean testosterone level, from 0.42 to 0.31 pmol/L ($p = 0.007$). Side effects were grade 1. **Conclusions:** One year's supplementation with DIM 100 mgX1/d in *BRCA* carriers was associated with a significant decline in FGT amount on MRI. Larger randomized studies are warranted to corroborate these findings. Clinical trial information: NCT02197000. Research Sponsor: Israel Cancer Association.

1557 Poster Session (Board #49), Fri, 8:00 AM-11:00 AM

Development of a novel liquid biopsy test to diagnose and locate gastrointestinal cancers. *First Author: Yuying Wang, BGI Genomics, Shenzhen, China*

Background: Cancers of the gastrointestinal (GI) system, including esophagus, stomach, pancreas, gallbladder, liver, bile duct, colon, and rectum are estimated to account for 38% of all cancer incidences and nearly 46% of cancer-related deaths in China. We conducted a multi-center study to evaluate the feasibility of using genetic and epigenetic abnormalities in plasma cfDNA to diagnose and locate GI cancers. **Methods:** We performed parallel genetic and epigenetic profiling of plasma cfDNA from hepatocellular carcinoma (HCC), colorectal cancer (CRC) and pancreatic cancer (PC) patients as well as age-matched healthy individuals by ultra-deep sequencing targeting cancer driver genes, and by targeted bisulfite sequencing covering genome-wide CpG islands, shelves, and shores. **Results:** Using a pre-specified mutation scoring system, we found that cfDNA mutation profiling achieved a sensitivity of 59.6%, 67.2%, and 46.8% for detecting HCC (n = 322), CRC (n = 244) and PC (n = 141) respectively, with a specificity of 95% in healthy controls (n = 207). For 901 plasma cfDNA samples that underwent methylome profiling, we first applied a machine learning approach to classify each cancer type versus healthy controls in the training cohort (HCC: n = 125; CRC: n = 105; PC: n = 97; healthy individuals: n = 84). Random Forest models with 10-fold cross validation achieved an AUC of 0.96 ± 0.04,0.89 ± 0.06, 0.91 ± 0.07 for HCC, CRC, and PC, respectively. Further analyses were performed on the validation cohort, including 172 HCC patients, 162 CRC patients, 60 PC patients, and an independent cohort of healthy individuals (HCC validation: n = 63; HCC independent validation: n = 109; CRC validation: n = 104; CRC external validation: n = 58; PC validation: n = 60; healthy controls: n = 96). The trained model achieved a sensitivity of 83.1% (specificity = 95.8%), 89.5% (specificity = 95.8%), and 76.7% (specificity = 91.7%) for HCC, CRC, and PC, respectively. Using regional methylation markers from diagnostic models for individual cancer types, we built a tissue-of-origin classification model, which achieved a cross-validation accuracy of 83.3% in the training cohort and an accuracy of 80.1% in the validation cohort in assigning correct cancer types. **Conclusions:** Plasma cfDNA methylome profiling identified effective biomarkers for the detection and tissue-of-origin determination of GI cancers, and outperformed mutation-based detection approach. Therefore, a liquid biopsy test capable of detecting and locating GI cancers is feasible and may serve as a valuable tool for early detection and intervention. Research Sponsor: BGI Genomics.

1558 Poster Session (Board #50), Fri, 8:00 AM-11:00 AM

Evaluation of a mobile cervical cancer screening program in São Luis, Maranhão, Brazil: Impact and challenges. *First Author: Rachel Jorge Dino Cossetti Leal, Hospital do Câncer Aldenora Bello, São Luís, Brazil*

Background: Cervical cancer (CC) still represents a public health priority in Brazil, with estimated incidence of 15,43 cases per 100.000 women. CC is the most frequent cause of cancer and cancer-related mortality in women in the state of Maranhão. The Brazilian national screening program recommends cervical cytology (Pap test) every 3 years in women 25-64 years old. Although of public access, the screening program continues to be non-organized. This was a real-life CC screening intervention through a mobile screening unit (MSU) in communities of São Luis, Maranhão. **Methods:** Prospective, intervention-based, analytic study, from April to August, 2018. Women in the assisted communities were offered Pap tests. Tests were collected and results were retrieved within 4 weeks along with further screening recommendations. Quality control and monitoring of the test were done. A structured questionnaire was applied. **Results:** 960 tests were collected and 545 women answered the questionnaire. Median age: 43 (34 – 52), with 88.2% of women within the target age. Socioeconomic charachteristics: 47.3% completed high school education; 37.8% were housewives, 16.1% were unemployed; 56.3% were married; 59.8% had a monthly family-income up to 1 minimum wage ($ 250,00). Previous Pap tests and difficulties: 94.1% had at least one previous test; 78,2% had a test within the past 3 years; 48.4% referred to dificculties to scheduling, 23.3% time constraints, 11.2% being ashamed, and 10.4% financial restrains. There were 65 (6.9%) abnormal results (LSIL in 3%, HSIL in 0.7%, and in situ adenocarcinoma in 1 case), for whom further investigation was recommended. Follow-up was possible in 31 of these cases. More than 50% were still awaiting for additional screening tests at time of contact (>6 month interval). **Conclusions:** MSU strategy faccilitated the access to Pap tests, their results and recommendations. Although Pap test was easily available, the non-organized process of invitation, follow-up and referal of positive cases for further investigation, as offered by the Brazilian public health services, limit screening efficacy and CC control. Research Sponsor: None.

1559 Poster Session (Board #51), Fri, 8:00 AM-11:00 AM

Evaluation of circulating miRNAs for earlier cancer detection through machine-learning expression profiling. *First Author: Jason Chia-Hsun Hsieh, Chang Gung Memorial Hospital, Guashan Township, Taoyuan County, Taiwan*

Background: Earlier cancer diagnosis leads to higher patient survival rate and reduces financial burdens for patients and their families. Over the past five years, liquid biopsy has demonstrated tremendous promise in the early detection of tumor presence. In addition to circulating tumor cells and circulating tumor DNAs, extracellular microRNAs (miRNAs) have also been shown to be promising diagnostic biomarkers. Through machine-learning profiling, we sought to determine whether or not we could use individuals' miRNA expression to distinguish between healthy subjects and cancer patients. **Methods:** Blood samples were collected from healthy donors and from patients of various cancer types. Plasma samples were purified within two hours of sample collection, followed by miRNA extraction. After performing reverse transcription of miRNAs into cDNAs, expression analysis of miRNAs was done using a novel multi-gene, amplification-based detection system that simultaneously analyzes over 160 miRNAs. For subsequent data processing, miRNAs without amplification signals across all profiles were first removed, resulting in 135 miRNAs. These 135 resulting miRNAs were then used as features in Support Vector Machine (SVM) to build OncoSweep classifier, a proprietary prediction algorithm for classification of the samples. Ten-fold cross validation was used to evaluate the performance of OncoSweep. **Results:** 344 healthy donor samples and 417 cancer patient samples were collected for the study. The prediction algorithm, OncoSweep, was derived based on the miRNA expression patterns of the healthy and the patient samples. The algorithm scored an overall accuracy for cancer prediction of 86.47%, with a sensitivity of 91.4%, a specificity of 85%, a PPV of 85% and an NPV of 88.5%. **Conclusions:** Utilizing machine-learning method of analyzing circulating miRNA expression profiles, the derived algorithm OncoSweep shows significant promise in cancer prediction. Validation is currently being performed in a larger study. We believe circulating miRNAs, through stringent sample processing and machine-learning methodology, are powerful biomarkers for earlier cancer detection. Research Sponsor: Quark Biosciences, Inc.

1560 Poster Session (Board #52), Fri, 8:00 AM-11:00 AM

Epigenetic control of breast cancer susceptibility. *First Author: Natascia Marino, Indiana University School of Medicine, Indianapolis, IN*

Background: Epigenetic mechanisms such as DNA methylation are important regulators of gene expression and are frequently dysregulated early in breast carcinogenesis. The relationship between DNA methylation aberrations in normal breast tissue and breast cancer risk remains unclear. **Methods:** Disease-free breast tissue cores donated by 71 high-risk (Tyrer-Cuzick lifetime risk ≥20%) and 79 average-risk women were obtained from the Komen Tissue Bank and processed for whole methylome (Diagenode's MethylCap Library and single-end 75-bp sequencing on Illumina Nextseq) and whole transcriptome (Illumina Nextseq) profiling. Reads from RNA-seq data were aligned to the human genome reference, GRCh38.p12 using STAR v.2.5.2b and tested for differential gene expression using DESeq2 ver. 1.24.0. For DNA methylation data, difference of variation in deduplicated read coverage among 250-bp fixed sized bins spanning CpG islands between high- and average-risk libraries was computed as z-ratios to identify differentially methylated regions. Pathway analysis was performed using IPA v06_01. **Results:** We identified 1355 CpGs that were differentially methylated between high- and average-risk breast tissues ($\Delta Z > 0.5$, FDR < 0.05). Hypomethylated CpGs were overrepresented in high-risk tissue and were found predominantly (68%) in non-coding regions. Hypermethylated CpG sites were found equally in the gene body and non-coding regions. Transcriptomic analysis identified 112 differentially expressed genes (fold change≥2, FDR < 0.05), involved in chemokines signaling, metabolism and estrogen biosynthesis. Among those, FAM83A (logfc = 2.3, FDR = 0.004) was previously described as epigenetically dysregulated in multiple cancers and transforms breast epithelial cell *in vitro*. Methylation-expression correlations revealed 11 epigenetically regulated genes including cellular transformation-associated BMPR1B. Two hypomethylated/upregulated long non-coding RNAs were also identified in high-risk breasts. **Conclusions:** This is the first gene expression/DNA methylation analysis of normal breasts from women at either high or average risk of breast cancer. Our discovery of epigenetically regulated genes associated with breast cancer risk provides an opportunity to mechanistically dissect breast cancer susceptibility and risk-associated molecular alterations. Unlike the current focus of identifying germline mutations or single nucleotide polymorphisms responsible for higher risk, our studies reveal an epigenetic mechanism, which is not discernable through simple genomic sequencing. Research Sponsor: Breast Cancer Research Foundation, Catherine Peachy Fund.

1561 Poster Session (Board #53), Fri, 8:00 AM-11:00 AM

Adoption of opportunistic salpingectomy for ovarian cancer prevention: Results from a nationwide sample of privately insured women. *First Author: Pritesh S Karia, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD*

Background: Recent evidence indicates that the Fallopian tube is the site of origin for many high-grade serous ovarian cancers, particularly in *BRCA* carriers. This has led to the emergence of opportunistic salpingectomy (OS) as a novel ovarian cancer prevention strategy. Despite limited data, some national societies now recommend OS for ovarian cancer prevention during benign hysterectomy or in place of tubal ligation for sterilization in average-risk women. We assessed patient characteristics associated with increased likelihood of OS and national trends in OS adoption before and after release of recommendations. **Methods:** Data from MarketScan were used to identify women who underwent hysterectomy, tubal ligation, and OS from 2010-2017. Rates of OS were compared and interrupted time series analysis with segmented Poisson regression was used to examine immediate and persistent changes in OS rates before and after recommendations. Rates were calculated quarterly and models were adjusted for age and seasonality. **Results:** A total of 309,574 tubal ligations, 13,574 OS for sterilization, 293,000 hysterectomies, 22,798 hysterectomies with OS were included. Quarterly rates of OS for sterilization and hysterectomy with OS were 3.13 and 4.82 per 100,000 women, respectively. About 92% of OS for sterilization and 56% of hysterectomy with OS were performed in women < 45 years. The most common indication for hysterectomy with OS was uterine fibroids (46%). About 8% of OS for sterilization and 10% of hysterectomy with OS were performed in women with a family history of breast or ovarian cancer. After adjusting for age and seasonality, there was a 250% immediate increase (RR: 3.50; 95% CI: 2.59-4.72) followed by a 14% (RR: 1.14; 95% CI: 1.10-1.18) persistent increase in the quarterly rate of OS for sterilization after versus before recommendation release. There was a 109% immediate increase (RR: 2.09; 95% CI: 1.15-3.81) in the quarterly rate of hysterectomy with OS after versus before recommendation release. No persistent change in the rate of hysterectomy with OS was observed. Significant declines in hysterectomy and tubal ligation rates were observed and these declines were temporally associated with the release of recommendations. **Conclusions:** OS for ovarian cancer prevention has rapidly diffused into clinical practice with the speed of adoption bolstered by recommendations from national societies. Future studies evaluating the overall efficacy and long-term complications of OS are needed to support its continued widespread use. Research Sponsor: None.

1562 Poster Session (Board #54), Fri, 8:00 AM-11:00 AM

Breast cancer events in women with atypical ductal hyperplasia who do not undergo surgical excision. *First Author: Lyndsey Jo Kilgore, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Atypical ductal hyperplasia (ADH) found on core needle biopsy is associated with an upgrade to carcinoma in 10-30% of women, thus surgical excision remains the standard of care. We sought to review the incidence of breast cancer in women with ADH managed by either observation or surgical excision over a 15 year period. **Methods:** Our prospectively maintained registry was reviewed to identify patients with ADH diagnosed by core needle biopsy between 1/2004 and 10/2018. Observed patients were deemed low risk for upgrade after multidisciplinary review confirmed adequate sampling, limited atypia and concordance between imaging and histology. Surgical patients were excluded if upstaged to carcinoma following excision. Patients with $<$ 1 year follow-up were excluded. Subsequent breast cancer was classified as ipsilateral or contralateral to the previous ADH and was further classified as index site if the new cancer was identified in the same quadrant as prior ADH. Multivariate logistic regression models were used to assess potential predictors of subsequent breast cancer events. **Results:** Four hundred and seventy-eight women with 483 ADH lesions met criteria; 305 were observed and 173 underwent excision. Median follow-up was 5.2 years, range 1.1-15.3. At the time of ADH diagnosis, 91 women had a personal history of breast cancer. Age $<$ 50 was the only statistically significant difference between the groups (24.6% vs. 33.3%, p = 0.04). Race, receipt of chemoprevention, prior breast cancer history and median follow-up were not significant between the groups. Prior history of breast cancer was associated with subsequent breast cancer risk in multivariate analysis (OR 2.25, 95% CI 1.04-4.87, p = 0.04). After excluding patients with a history of breast cancer, multivariate analysis demonstrated no association of age, race, use of chemoprevention or surgical excision with future cancer risk. Among the 387 patients without a prior breast cancer history, 21 patients developed a subsequent cancer; 10 in the surgical group and 11 in the observed group (7.3% vs. 4.4% respectively, p = 0.2). Two cancers were identified at the index site in the surgery group (2/137, 1.5%) and three in those observed (3/250, 1.2%). **Conclusions:** Observation, rather than surgical excision, is safe in selected women that have a core biopsy diagnosis of ADH. Index site failures are rare and are superseded by cancer risk elsewhere in the breast. National screening and diagnosis recommendations should consider recommending observation for this select group of patients with ADH. Research Sponsor: None.

1563 Poster Session (Board #55), Fri, 8:00 AM-11:00 AM

Mammography utilization among women with a negative circulating tumor DNA-based early cancer detection test. *First Author: Claire Jones, Geisinger Health System, Danville, PA*

Background: Blood-based tests may enable minimally invasive detection of multiple cancer types. One such test, CancerSEEK, employs ctDNA and protein biomarkers for this purpose. Test performance has been evaluated in women without a history of cancer in an ongoing prospective study called DETECT-A. The introduction of such blood tests holds promise, and their future utility lies in augmenting, not displacing, standard-of-care (SOC) cancer screening. One important safety concern is that a negative test result could provide false reassurance that discourages adherence to SOC cancer screening. To investigate this possibility, we studied delivery of mammography to DETECT-A participants before and after receipt of a negative CancerSEEK result. **Methods:** DETECT-A screened 10,000 women aged 65-75 using CancerSEEK. Participants completed a survey about cancer screening at enrollment and at one-year post-enrollment. We analyzed only those participants who had received a negative CancerSEEK result, were insured by Geisinger Health Plan (GHP), and had completed both surveys. GHP claims data were used to identify mammograms performed within one year prior-to and post-enrollment. Overall utilization was determined by combining claims and survey data at enrollment and one-year post-enrollment. In addition to comparing SOC screening rates pre- versus post-testing, we evaluated the impact of primary care physician (PCP) type (Geisinger versus any other institution), as screening reminder mechanisms differ between institutions. **Results:** Of the 2,241 participants who met analysis criteria, 73.6% (n = 1,650) had a mammogram in the year before enrollment while a significantly great number (79.3%, n = 1,777) did so during the one-year follow-up ($\chi^2(1) = 59.05$, $p < 0.001$). At enrollment, there were 591 participants who had not had a mammogram completed in the previous year, but 404 (68.4%) of them did have a mammogram during the one-year follow-up. The rate of change in mammography utilization did not differ between those who had a Geisinger versus a non-Geisinger PCP ($\chi^2(2) = 1.83$, p = 0.40). **Conclusions:** Participants in a study using a novel blood test for earlier cancer detection had a significantly higher rate of annual mammography after study enrollment and testing. These results indicate that introduction of a minimally invasive ctDNA and protein biomarker-based cancer screening test may engender greater, not lesser, utilization of SOC cancer screening. Further study is required to understand the root causes of increased utilization in this context. Research Sponsor: Marcus Foundation.

1565 Poster Session (Board #57), Fri, 8:00 AM-11:00 AM

Mediation of black/white disparities in triple negative breast cancer by socioeconomic position, reproductive factors and diabetes in the Nurses' Health Study Cohorts I & II. *First Author: Lydia Marcus, University of Wisconsin Milwaukee, Milwaukee, WI*

Background: The higher rates of triple negative (TN) breast cancer (BC) observed among black compared to white women may be attributable to social and reproductive factors, as well as biological conditions like diabetes mellitus type 2. We examine the extent to which the black/white race disparity in TNBC is transmitted through these factors. **Methods:** Data are from the Nurses' Health Study I and II prospective cohorts and include non-Hispanic (nH) black (n = 97) and nH white (n = 8,876) women aged 25-55 years at enrollment with invasive BC diagnoses. Participant characteristics are self-reported or drawn from medical records. We estimated average controlled direct associations (ACDA) using logistic regression with model-based standardization to evaluate the age/body mass index (BMI)-adjusted prevalence difference for TN versus luminal A/B type BC by race, and performed a series of ACDA (with comparison of rescaled coefficients (RC)) controlling for diabetes, mean family income before diagnosis (cont.), husband's education ($<$ college, college, graduate school), parental ownership of participant's childhood home (yes/no), age at menarche (cont.), age at first birth (cont.), parity (integer), and breastfeeding (BF) (parous/never BF, parous/ever BF). **Results:** Compared to nH whites, nh black women had higher prevalence of TNBC (24.5% v. 45.4%; $p < 0.01$), higher prevalence of diabetes (5.5% v. 11.3%; p = 0.01), lower prevalence of BF (59.2% v. 46.6%; p = 0.02), higher mean BMI (26.1 v. 29.9; $p < 0.01$), and lower mean family income ($17,304 v. 15,750; $p < 0.01$). BMI, age, and menopause were positively associated with prevalence of diabetes. In the age/BMI adjusted model, nH black women were 20%-points more likely than nH whites to have TNBC (95% Confidence Interval (CI): 0.11, 0.29). This disparity was reduced to 18.1% after also adjusting for BF (95% CI: 0.09, 0.28), to 13.7% after additionally adjusting for socioeconomic indicators (95% CI: 0.02, 0.25), and to 13.3% after adjusting for all potential mediators (95% CI: 0.01, 0.26). Based on the method of RC, socioeconomic indicators accounted for the largest fraction of mediated effects and BF accounted for most of main effect attenuation associated with reproductive factors; diabetes accounted for negligible effect. **Conclusions:** Our findings support the hypothesis that observed racial differences in TNBC diagnoses may be at least partially mediated by differences in socioeconomic position and reproductive patterns, namely breastfeeding. Research Sponsor: University of Wisconsin.

1566 Poster Session (Board #58), Fri, 8:00 AM-11:00 AM

Projection of cancer incidence and death to 2040 in the US: Impact of cancer screening and a changing demographic. *First Author: Lola Rahib, Cancer Commons, Los Altos, CA*

Background: Coping with the current and future burden of cancer requires an in-depth understanding of cancer incidence and death trends. As of 2020, breast, lung, prostate, and colorectal cancer are the most incident cancers, while lung, colorectal, pancreas, and breast cancer result in the most deaths. Here we integrate observed cancer statistics and trends with observed and estimated US demographic data to project cancer incidences and deaths to the year 2040. **Methods:** Demographic cancer-specific delay-adjusted incidence and death rates from the Surveillance, Epidemiology, and End Results Program (2014-2016) were combined with US Census Bureau population growth projections (2016) and average annual percentage changes in incidence (2011-2015) and death (2012-2016) rates to project cancer incidences and deaths through the year 2040. We examined the 10 most incident and deadly cancers as of 2020. We utilized Joinpoint analysis to examine changes in incidence and death rates over time relative to changes in screening guidelines. **Results:** We predict the most incident cancers in 2040 in the US will be breast (322,000 diagnoses in 2040) and lung (182,000 diagnoses in 2040) cancer. Continuing decades long observed incident rate trends we predict that melanoma (173,000 diagnoses in 2040) will become the 3rd most common cancer while prostate cancer (63,000 diagnoses in 2040) will become the 5th most common cancer after colorectal cancer (139,000 diagnoses in 2040). Lung cancer (61,000 deaths in 2040) is predicted to continue to be the leading cause of cancer related death, with pancreas (45,000 deaths in 2040) and liver & intrahepatic bile duct (38,000 deaths in 2040) cancer surpassing colorectal cancer (34,000 deaths in 2040) to become the second and third most common causes of cancer related death, respectively. Breast cancer deaths (29,000 in 2040) are predicted to continue to decrease and become the fifth most common cause of cancer death. Joinpoint analysis of incidence and death rates supports a significant past, present, and future impact of cancer screening programs on the number of cancer diagnoses and deaths, particularly for prostate, thyroid, melanoma incidences, and lung cancer deaths. **Conclusions:** We demonstrate marked changes in the predicted landscape of cancer incidence and deaths by 2040. Our analysis reveals an influence of cancer screening programs on the number of cancer diagnoses and deaths in future years. These projections are important to guide future research funding allocations, healthcare planning, and health policy efforts. Research Sponsor: None.

1567 Poster Session (Board #59), Fri, 8:00 AM-11:00 AM

Malignancies associated with DPP4 inhibitors and GLP1 receptor agonists: Data from a large real-world database. *First Author: Jiasheng Wang, Met-MetroHealth Medical Center, Cleveland, OH*

Background: DPP44 inhibitors (DPP4i) and GLP1 receptor agonists (GLP1Ra) control type 2 diabetes (T2DM) by promoting GLP-1 pathway; its activation can lead to dysplasia or tumor inhibition based on tissue types. Moreover, DPP4 can act as a tumor suppressor or activator. Few studies have looked at the risk of DPP4i and GLP1Ra on various types of cancer. **Methods:** We inquired an aggregated electronic health record database, Explorys (IBM, NY). Patients (Pts) diagnosed with T2DM from 1/05 to 6/19 were included and followed for 5 years after starting DPP4i, GLP1Ra, or metformin. Odds ratio (OR) were calculated after 6mo of lag time. **Results:** We identified 344,550, 112,000, and 1,245,930 pts in the DPP4i, GLP1Ra, and metformin group, respectively. The three groups were well balanced except pts in the GLP1Ra group had higher BMI. Within 5 years, 24,260 pts (9.5%) in DPP4i, 5,580 (8.7%) in GLP1Ra, and 57,490 (9.3%) in metformin group developed any types of cancer. When adjusted for sex, age, smoking status, alcohol abuse history, hemoglobin A1C ($\leq$9.0% vs $>$ 9.0%) and BMI ($<$ 30 vs $\geq$30 kg/m^2) around initiation of antidiabetic agents, the aOR was 1.01 (95%CI .94-1.08) for DPP4i and 1.06 (95%CI .93-1.20) for GLP1Ra, comparing with the metformin group. For specific cancer types, DPP4i users were associated with significantly higher risk of bladder, kidney, liver cancer and melanoma; while the risk of breast, lung and prostate cancer were reduced. GLP1Ra users were associated with higher risk of thyroid cancer; while the risk of bladder, colon, lung, and prostate cancer were reduced. **Conclusions:** DPP4i and GLP1Ra were not associated with increased cancer risk overall. However, they were associated with increased or decreased risk of specific cancer types. Research Sponsor: None.

	DPP4i		GLP1Ra	
Cancer	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Bladder	1.18 (1.09-1.29)	$<$ .01	.69 (.58-.83)	$<$ .01
Brain	1.00 (.84-1.19)	.98	1.10 (.82-1.47)	.54
Breast	.90 (.85-.94)	$<$ .01	.99 (.91-1.07)	.75
Colon	.97 (.91-1.04)	.38	.73 (.64-.83)	$<$ .01
Esophagus	.86 (.73-1.00)	.06	1.02 (.78-1.32)	.91
Kidney	1.13 (1.04-1.23)	$<$ .01	1.13 (.98-1.31)	.09
Liver	1.14 (1.02-1.26)	.02	.91 (.75-1.11)	.37
Lung	.91 (.86-.97)	$<$ .01	.60 (.53-.68)	$<$ .01
Lymphoma	.98 (.91-1.05)	.51	.92 (.81-1.05)	.21
Melanoma	1.12 (1.04-1.21)	$<$ .01	.98 (.85-1.12)	.75
Ovary	.91 (.78-1.06)	.23	.82 (.61-1.09)	.17
Pancreatic	.94 (.86-1.04)	.23	.84 (.70-1.00)	.05
Prostate	.87 (.82-.91)	$<$ .01	.65 (.59-.82)	$<$ .01
Stomach	1.03 (.88-1.21)	.70	.74 (.54-1.03)	.07
Thyroid	.89 (.79-1.01)	.08	1.39 (1.16-1.68)	$<$ .01
All cancer	**1.01 (.94-1.08)**	**.84**	**1.06 (.93-1.20)**	**.40**

1568 Poster Session (Board #60), Fri, 8:00 AM-11:00 AM

A comparison of patients' and physicians' expectations regarding precision oncology tests. *First Author: Navdeep Dehar, University Of Calgary, Calgary, AB, Canada*

Background: With the increasing number and frequency of biomarker and genetic tests that are offered to patients with cancer, it is important to ensure that they fully understand the implications of these tests. In this survey study, we aimed to compare the attitudes and expectations of patients and cancer physicians about the role of biomarker and genetic testing in clinical decision-making. **Methods:** Two separate, complimentary, self-administered questionnaires for cancer patients and their physicians, respectively, were collected in Calgary, Alberta, Canada. Survey responses from patients were subsequently matched with those of their corresponding oncologists to form patient–oncologist dyads. We determined the concordance rates between responses of patients and those of their oncologists. **Results:** A total of 113 patients and 15 physicians participated in the study from July to September 2019. Patients demonstrated good understanding of general cancer biology (79%) and diagnostic processes (91%) associated with precision oncology. About 70% patients were willing to undergo minor procedures, and participate in research involving biomarker or genetic testing; however, this was over-estimated by their physicians in 82% of cases. Many patients felt that their tumor should be tested to guide treatment (70%) and were not bothered by potential delays in treatment due to testing (23%). These views from patients were largely shared by their oncologists (concordance 64%). While only 28% patients thought that they had enough knowledge to make informed decisions, majority (68%) said that they needed more information. Importantly, knowledge and expectations regarding the applications of biomarker or genetic test results on actual diagnosis and prognosis were grossly discrepant between patients and their oncologists (concordance 26% and 36%, respectively). **Conclusions:** Patients and cancer physicians tend to be aware of the advances in precision oncology and are willing to participate in biomarker and genetic testing and research. However, they do not consistently agree about the roles and applications of these tests, which may result in misplaced expectations. Strategies to improve education and communication are needed to align these expectations and improve the quality of clinical decision-making. Research Sponsor: None.

1569 Poster Session (Board #61), Fri, 8:00 AM-11:00 AM

Protein intake and breast cancer incidence and mortality. *First Author: Kathy Pan, Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center, Torrance, CA*

Background: Associations between dietary protein intake and breast cancer are unclear, in part due to limitations of dietary self-report. Women's Health Initiative (WHI) investigators compared the accuracy of food frequency questionnaire (FFQ) data on energy and protein intake with objective measures of dietary intake using biomarkers (doubly labeled water for energy and urinary nitrogen for protein [n=544]). Subsequently, regression equations incorporating participant characteristics were developed acknowledging differential reporting dietary data errors based on participant characteristics (Neuhouser Am J Epidemiol). FFQ findings were then used to determine biomarker- adjusted animal vs vegetable protein ratios. **Methods:** We examined associations of energy and protein intake with breast cancer incidence and mortality in Women's Health Initiative (WHI) participants 50-79 years of age at entry between1993-1998, with breast cancers verified by medical record review and survival enhanced by serial National Death Index (NDI) searches through 2016. Associations between sources of protein intake (animal versus vegetable) quintiles and breast cancer incidence and mortality were estimated using multivariable Cox proportional hazards regression. **Results:** With 100,024 eligible participants, after 14 years follow-up, women with higher total protein intake had greater body mass index, were more likely White, menopausal hormone therapy users with higher total energy intake and fat intake. With 6,340 incident breast cancers, 764 deaths from breast cancer and 2,059 deaths after breast cancer, higher vegetable protein intake was associated with significantly lower breast cancer incidence (P for linear trend = 0.01) while higher animal protein intake was associated with significantly higher breast cancer incidence (P for linear trend = 0.03). Higher vegetable protein intake was also associated with significantly lower risk of death after breast cancer (P $<$0.001) but not with lower risk of deaths from breast cancer (breast cancer followed by death attributed to breast cancer). Animal protein intake was not associated with deaths from breast cancer or deaths after breast cancer. **Conclusions:** Based on findings from biomarker-calibrated determination of protein intake by source, higher vegetable protein intake was associated with significantly lower risk of breast cancer incidence and of death after breast cancer while higher animal protein intake was associated with significantly higher risk of breast cancer incidence, but not mortality. Research Sponsor: U.S. National Institutes of Health.

1570 Poster Session (Board #62), Fri, 8:00 AM-11:00 AM

Dietary advanced glycation end products (AGEs) and breast cancer mortality in the women's health initiative (WHI). *First Author: Lindsay Leuthen Peterson, Washington University in St. Louis, St. Louis, MO*

Background: Breast cancer (BrCa) is the second leading cause of cancer death and constitutes about 14% of total cancer deaths among US women. Advanced glycation end-products (AGEs) are implicated in chronic diseases including cancer and cardiovascular diseases (CVD). AGEs are naturally found in animal products and processed foods, and preparing food at high temperatures increases AGE formation. Our goal was to assess the association between post-diagnosis dietary N$^{\varepsilon}$-carboxymethyl-lysine (CML)-AGE intake, a common measure of AGE, and mortality from all-causes, BrCa and CVD among participants with invasive BrCa in the Women's Health Initiative (WHI). **Methods:** The WHI enrolled postmenopausal women aged 50 to 79 years from 1993-1998 into randomized controlled trials and a prospective observational study to examine causes of morbidity and mortality. In this analysis, we included 2,073 women diagnosed with invasive BrCa during follow-up who completed a food frequency questionnaire (FFQ) after diagnosis, had energy intakes between $\geq$600 kcal/day and $\leq$5000 kcal/day, and had CML-AGE intake data available. Women were followed from BrCa diagnosis until death or censoring through March 2018. Cox proportional hazards regression models estimated the hazard ratios (HR) and 95% CIs of mortality risk from all-causes, BrCa and CVD by tertiles of dietary CML-AGE intake with adjustment for age, income, race/ethnicity, study arm, time from diagnosis to FFQ completion, education, physical activity, smoking, BMI, ER/PR status, diagnosis stage, postmenopausal hormone use, intake of energy, alcohol, fat, red and processed meats. **Results:** After a median 15.1 years of follow-up, 642 deaths were reported including 198 BrCa-specific and 129 CVD-specific deaths. The average time from BrCa diagnosis to FFQ completion was 1.5 years. Compared to the lowest tertile of CML-AGE intake, there was an increased risk in the highest tertile for all-cause mortality (HR: 1.51, 95% CI: 1.17-1.94), BrCa (HR: 1.86, 95% CI: 1.19-2.91) and CVD (HR: 2.14, 95% CI: 1.19-3.84) mortality. **Conclusions:** Higher dietary AGE intake after BrCa diagnosis in postmenopausal women was associated with increased risk of mortality from all-causes, BrCa and CVD. Exposure to AGEs could be modified through dietary counseling and evaluated in relation to reduced mortality risk after BrCa diagnosis. Research Sponsor: Susan G. Komen, Other Foundation.

1571 Poster Session (Board #63), Fri, 8:00 AM-11:00 AM

Metabolic syndrome, metabolic comorbid conditions, and risk of early-onset colorectal cancer. *First Author: Hanyu Chen, Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St. Louis, MO*

Background: The etiology and contributors to the rising incidence of early-onset colorectal cancer (CRC diagnosed under age 50), driven largely by distal and rectal cancer, remain largely unknown. Metabolic syndrome is associated with higher risk of CRC diagnosed at older ages; however, its association with early-onset CRC remains unclear. **Methods:** We conducted a nested case-control study among participants aged 18-50 years with ≥2 years of enrollment and prescription drug coverage in the IBM MarketScan Commercial Databases (2006-2015). Incident CRC cases were identified using ICD-9-CM diagnosis codes. Controls without any cancer were identified using frequency matching on age, sex, geographical region, and duration of insurance enrollment. Metabolic syndrome was defined using either ICD-9-CM diagnosis codes or the presence of at least 3 of the following: obesity, hypertension, hyperlipidemia, and hyperglycemia/type 2 diabetes. In addition to ICD-9-CM codes, hypertension, hyperlipidemia, and hyperglycemia/type 2 diabetes were also defined based on regular use of medications. Multivariable logistic regressions were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). **Results:** A total of 4,673 early-onset CRC and 40,832 controls were included. Metabolic syndrome was associated with increased risk of early-onset CRC (OR: 1.33, 95% CI 1.16-1.52), after adjusting for a range of potential confounders. The number of metabolic comorbid conditions was positively associated with risk of early-onset CRC in a dose-response fashion. Compared to individuals without any conditions, individuals with 1, 2, ≥3 metabolic conditions had a 13% (OR: 1.13, CI 1.04-1.22), 18% (OR: 1.18, CI 1.07-1.31), and 40% (OR: 1.40, CI 1.22-1.61) higher risk of early-onset CRC (P_{trend}<0.001), respectively. These associations were driven by proximal (OR for ≥2 vs 0 metabolic comorbid conditions: 1.40, CI 1.15-1.69) and distal colon cancer, OR ≥2 vs 0: 1.25, CI 1.03-1.53), but not rectal cancer (OR≥2 vs 0: 1.07, CI 0.92-1.24). **Conclusions:** Metabolic syndrome and metabolic comorbid conditions were associated with increased risk of early-onset CRC, largely driven by proximal and distal colon cancer. Metabolic dysregulations may contribute to the rising incidence of early-onset CRC. Research Sponsor: U.S. National Institutes of Health.

1572 Poster Session (Board #64), Fri, 8:00 AM-11:00 AM

Is there a genomic fingerprint of Radon (Rn)-induced lung cancer (LC)? Comparison of genomic alterations in LC specimens from high and low Rn zones. *First Author: Hina Khan, Rhode Island Hospital-The Warren Alpert Medical School of Brown University, Providence, RI*

Background: Rn-222 is a radioactive gas found in rocks and soil. It emits alpha particles that cause dsDNA breaks and increase potential for carcinogenesis. Rn is the 2nd leading cause of LC in the US after smoking. EPA estimates >15,000 deaths/yr (9% of LC deaths) from Rn. We hypothesize that the impact of Rn exposure may be reflected in LC gene mutation (mut) profiles. **Methods:** Using commercial NGS assays, we retrospectively analyzed genomic DNA alterations in FFPE specimens from 159 LC patients (pts) from the Lifespan Cancer Institute in Rhode Island (2014- 2019), followed by validation in a larger cohort of 5,532 pts using Caris platform. Based on EPA Rn maps, we identified counties with high indoor Rn levels (>4 pci/L; HR), and compared gene mut patterns with those from low Rn zones (<4 pci/L; LR). Based on pt's zip code of residence, we categorized them to HR and LR. In the validation cohort, p values adjusted for multiple comparison (q) of < .05 were considered significant. **Results:** In the pilot cohort, 35 pts (22%) were in HR and 124 (78%) in LR zones. Adenocarcinoma histology was most frequent (73%) and smoking prevalence was high (75%) in both groups. Most prevalent alterations were *TP53, KRAS* and *CDKN2A* muts. In the HR, we noted more frequent recurrent muts in 2 DNA repair genes (DDR): *ATM* (11 vs 1%, p= .00086) and *CHEK2* (6 vs 0%, p= .047) when compared to LR group. When classified into major pathways implicated in lung carcinogenesis, higher frequency of mutations were seen in DDR in HR zones vs. LR (29 vs 13%, p= .038). In the validation cohort, 1,433 (26%) pts were in HR and 4099 (74%) in LR zones. Among the DDR genes, *ATM* muts in HR group tended to be more frequent (4.7 vs 3.4% in LR, p= .03) as well as *PALB2* (0.9 vs 0.4%, p= .02) while no difference seen in *CHEK2*. Other genes with significantly higher prevalence in HR were *TP53, SMARCA4 and NFE2L2* (q< .05); while *KMT2D, KEAP1, CDKN2A, MET, NF2, DNMT3A, CCND1 and FAS* show a trend (p< .05). *EGFR* muts were significantly more frequent in LR zones (8.4 vs 14.6%, q= .001). Similar to the pilot cohort, DDR pathway alterations trend to be higher in HR zones (14 vs 12%, p= .05). Using a high TMB cut-off >10, tumors from HR zones had significantly higher TMB when compared to LR zones (56 vs 48%, q= .0005). **Conclusions:** To our knowledge, this is the first attempt to elucidate the pathobiology of Rn induced LC using gene mut analyses. Our observations suggest that LC associated with higher Rn exposure may have disabled DNA repair pathways and higher TMB. Assuming uniform tobacco smoke exposure, higher Rn was not associated with EGFR mut. Research Sponsor: institutional finances.

1573 Poster Session (Board #65), Fri, 8:00 AM-11:00 AM

The increasing incidence of colorectal cancer in younger patients in the United States: Who, what, when, and where? *First Author: Mary Kathryn Abel, UCSF School of Medicine and Department of Surgery, San Francisco, CA*

Background: Prior studies have shown an increase in the rate of colorectal cancer (CRC) in young individuals in the United States. However, few studies have evaluated the health disparities that exist in this population, particularly using large, national cohorts. We examined differences in age, race, stage, region, and tumor location in younger and older patients with CRC. **Methods:** Data were extracted from the United States Cancer Statistics (USCS) for individuals diagnosed between 2001 and 2014. CRC incidence data among individuals < 50 years old were compared to those > 50 years old. Age-specific and age-adjusted incidences and trend analyses reported as annual percent change (APC) were performed using SEER*Stat and Joinpoint regression. **Results:** Of 1,886,441 individuals, the overall age-adjusted incidence of CRC decreased from 52.59 (per 100,000) in 2001 to 35.22 in 2014, with an APC of -3.24. Although over 35% cases were diagnosed in the Southern United States, the Northeast had the highest age-adjusted incidence at 45.26 per 100,000 patients. Younger patients were diagnosed with distant disease at 25.8% compared to only 18.4% in older patients. Younger patients were also more likely to have sigmoid or rectal cancers compared to older patients (64.3% vs. 45.7%). Of the 170,244 individuals < 50 years, 90,855 (53.4%) were men and 79,389 (46.6%) were women. The age-specific incidence in this younger cohort increased from 5.63 to 6.48 between 2001-2014, with an APC of +1.24 in 2001-2008 compared to +2.55 in 2012-2014. The incidence of CRC in patients aged 0-29, 30-39, and 40-49 years was 0.41 (per 100,000), 6.08, and 21.09, respectively. Black individuals < 50 years had the highest age-specific incidence of CRC (7.16 per 100,000) compared to Asian (6.43), White (6.07), or Hispanic (4.76) individuals. **Conclusions:** Our data suggests that CRC is increasing in young patients, particularly for those between 40-49 years and Black individuals. In our younger cohort, CRC was more commonly found in the sigmoid colon and rectum compared to older patients. Further research is warranted to direct resources towards improved colonoscopy or sigmoidoscopy screening for younger patients at risk. Research Sponsor: None.

1574 Poster Session (Board #66), Fri, 8:00 AM-11:00 AM

Geographic disparity of outcome in patients with cancer over decades: The surveillance, epidemiology, and end results. *First Author: Kenichi Sakurai, Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Improvements in prevention, early detection and therapy of cancer have decreased cancer related mortality yet health disparities continue to exist. We investigated the impact of such disparities in cancer survival. **Methods:** In the Surveillance, Epidemiology, and End Results, we identified 784,341 patients with cancer from 1990 to 2016 in Georgia; 68,493 in 1990-1999, 371,353 in 2000-2009, and 322,932 in 2010-2016. We assessed overall survival (OS) of patients with all cancers, chronic myeloid leukemia (CML), and lung cancer given the dramatic improvement in patient outcomes in CML since 2000 compared to the consistently poor outcome in lung cancer. We assessed distance from each county to the one National Cancer Institute-designated cancer center (NCI-CC) in Georgia. **Results:** The 5-year OS of patients with any cancer was 55% with median OS 80 months; the 5-y OS of each county ranged from 33% to 82% (interquartile range[IQR], 51%-65%)(P < 0.001). The improvement of OS was minimal over decades: 5-year OS was 52%, 55%, and 55% in 1990-1999, 2000-2009, and 2010-2016, respectively; the median was 69 months, 80 months, not reached, respectively (P < 0.001). In patients with lung cancer and CML, the 5-year OS was 15% and 52% with the median of 9 months and 67 months, respectively. The geographic difference between counties was relatively small and constant over time in patients with lung cancer, represented by the width in the range and IQR: range 5%-17%, IQR 9%-13%, median 13% in 1990-1999; range 2%-24%, IQR 10%-14%, median 14% in 2000-2009; and range 4%-24%, IQR 12%-17%, median 17% in 2010-2016. However, the geographic difference was more prominent in patients with CML and widened after introduction of modern therapy: range 20%-42%, IQR 26%-34%, median 32% in 1990-1999; range 14%-83%, IQR 38%-64%, median 53% in 2000-2009; and range 14%-80%, IQR 40%-57%, median 57% in 2010-2016. Multivariate Cox regression showed age (hazard ratio[HR],1.040;95% confidence interval[CI],1.039-1.040;P < 0.001), median county income (HR,0.919; 95% CI,0.916-0.921;P < 0.001), African American (HR,1.021;95% CI,1.210-1.227;P < 0.001), and distance to NCI-CC (each 100 kilometers) (HR,1.021;95% CI,1.017-1.025;P < 0.001) as predictive factors. **Conclusions:** The disparity of cancer care exists between geographic locations. The geographic difference of survival seems more prominent when highly effective therapies are available. Research Sponsor: None.

1575 Poster Session (Board #67), Fri, 8:00 AM-11:00 AM

Population genetic screening for hereditary breast and ovarian cancer in at-risk patients: A novel testing and prevention model for community hospitals reveals high mutation rates rurally. *First Author: Charles Hendrix Shelton, Vidant Health, Nags Head, NC*

Background: Genetic testing for at risk non-cancer patients continues to increase (Guo F, et al Cancer 2020). We identified a high risk of familial breast and ovarian cancer in rural eastern North Carolina, and created a systematic approach for genetic screening, counseling and testing. **Methods:** A family history questionnaire was designed to assess for the risk for hereditary breast and ovarian cancer (HBOC) using NCCN guidelines, and used at key intake points within the unaffected population to determine eligibility for genetic testing. First it was offered at the time of all mammograms. Second, we offered it in the primary gynecology care setting to capture younger patients not participating in screening mammography. Patients meeting HBOC criteria were sent a letter and two phone calls to schedule genetic counseling. Analysis via descriptive statistics. **Results:** 3000 rural women screened using our systematic approach to genetic risk assessment. 22.4% (673/3000) of female patients met NCCN criteria for HBOC panel testing. All offered consultation and counseling. With a backlog to see patients due to higher than expected accrual, 217 patients have completed pre-test genetic counseling, 201 completed local 19-gene panel test, and 201 had post-test counseling. Germline mutations (=>1) that predict for genetic susceptibility to cancer(s) occur in 7.8% of our screened and tested population. Currently 1 in 400 patients screened in our unaffected population carry a BRCA mutation, and 1 in 200 carry some pathogenic mutation that increases risk for HBOC. **Conclusions:** This rural model of screening and prevention of at risk patients for HBOC is successful at detecting pathogenic mutations in unaffected patients before they are diagnosed with cancer. Interestingly, the rate of positivity in the unaffected population (meeting criteria) is as high as the known breast cancer population rate of germline mutations (5-10%), validating the use of testing guidelines with our model. Discovering this susceptibility before a cancer diagnosis resulted in appropriate high risk management with prevention and risk reduction strategies. We plan to expand this model to the male screening population in 2021, and streamline genetic assessment and testing for the larger population at risk by engaging more rural primary care clinics over time to increase testing compliance. We also plan to consider broader gene panels as newer mutations become linked to HBOC. Clinical trial information: UMCIRB 19-001052. Research Sponsor: Pfizer and ACCC.

1576 Poster Session (Board #68), Fri, 8:00 AM-11:00 AM

Burden of genetic testing in an academic biobank by pathological and family history-based criteria in prostate cancer (PCa). *First Author: James Ding, University of Pennsylvania, Philadelphia, PA*

Background: Approximately 5% of localized PCa and 12% of metastatic PCa are associated with germline mutations in DNA repair genes. The National Comprehensive Cancer Network (NCCN) issued genetic testing guidelines to identify PCa patients (pts) likely to harbor a germline DNA repair mutation. The overall burden of this guideline-based, resource-intensive genetic testing is unknown. Using supervised phenotype-genotype information extraction algorithms, we determined the projected genetic testing burden at a single institution adhering to NCCN PCa genetic testing guidelines. **Methods:** A PCa cohort of 2127 pts was identified from the Penn Medicine BioBank via ICD 9/10 codes. Phenotypic data were extracted from the Penn Medicine Cancer Registry and electronic health record systems via natural language processing and manual chart review. Pts were classified based on 9 germline genetic testing criteria outlined in the NCCN PCa guidelines (Version 4.2019). **Results:** 895/2127 pts met at least 1 of the 9 NCCN genetic testing criteria, corresponding to a 42.1% overall genetic testing burden. 35.2% qualified for testing via high-risk localized PCa and 6.4% qualified via metastatic disease. Of the pts with localized PCa (n=2014), 15.1% qualified for genetic testing via high Gleason score, 5.1% via high-risk family history, 3.7% via PSA>20ng/mL, 8.7% via Ashkenazi Jewish descent, and 0.8% via intraductal/ductal histology. **Conclusions:** In this single-center PCa cohort, germline genetic testing was NCCN-guideline recommended for a larger proportion of pts than would otherwise be expected based on previously published reports. Future studies are needed to validate the sensitivity and specificity of these criteria for identifying germline mutations. Our study also highlights a need for novel methods to improve the efficiency of genetic testing for a large cohort. Research Sponsor: Penn Medicine Basser Center Grant.

Number of pts in a biobank meeting individual genetic testing criteria.

	Criteria[1]	# of pts meeting criteria	Total pts with data for criteria	% of pts
1	Regional: Any T, N1, M0	28	1178	2.4%
2	Metastatic: Any T, Any N, M1	113	1763	6.4%
3	High risk: T3 or T4	380	1081	35.2%
4	High risk: Gleason score 8-10	361	1929	18.7%
5	High risk: PSA at diagnosis >20ng/mL	109	1589	6.9%
6	Very high risk: Gleason primary 5	40	1928	2.1%
7	Ashkenazi Jewish	187	1773	10.6%
8	≥3 cancers on same side of family	111	2113	5.3%
9	Intraductal/ductal histology	20	2127	0.9%

[1] Not included due to lack of data: Brother, father, or multiple family members with PCa (not clinically localized grade 1) diagnosed <60 years old or who died from PCa

1577 Poster Session (Board #69), Fri, 8:00 AM-11:00 AM

Video vs. in-person genetic counseling for men considering germline prostate cancer testing: A patient-choice study. *First Author: Veda N. Giri, Departments of Medical Oncology, Cancer Biology, and Urology, Cancer Risk Assessment and Clinical Cancer Genetics Program, Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA*

Background: Germline testing (GT) for prostate cancer (PCA) is rapidly increasing with higher demand for genetic counseling (GC). Alternate GC strategies need to be studied to address pretest informed consent. Here we conducted a patient-choice study of pretest video-based genetic education (VBGE) or in-person GC (IPGC) and assessed men's preference and patient-reported outcomes from the first cohort of the Evaluation and Management for Prostate Oncology, Wellness, and Risk (EMPOWER) study. **Methods:** Eligibility for EMPOWER includes any male with PCA or at-risk for PCA based on family history or African American race. Men may choose pretest IPGC or VBGE. All receive results by a genetic professional. Demographics and PCA features were collected at baseline. The following outcomes and scales were assessed: baseline anxiety (GAD-7 scale), change in cancer genetics knowledge from baseline (Giri 2019), decisional conflict for GT (O'Connor 1993), and satisfaction (DeMarco 2004). Understanding of personal GT results was assessed after disclosure (Giri 2019). Descriptive statistics summarized results with counts and percentages for categorical variables and mean and standard deviation for continuous variables. Data were compared with Fisher's exact, Chi-squared, or Wilcoxon two-sample tests, as appropriate. Mean change in cancer genetics knowledge was compared with t-tests. Significance level was set a priori at 0.05. All analyses were performed with SAS 9.4 (Cary, NC). **Results:** At the time of this analysis, 94 men were enrolled. Characteristics of the cohort were: White (88.3%), bachelor's degree (67%), PCA diagnosis (93%), mean age of consent 59 years (IPGC) and 61 years (VBGE), Gleason > = 8 (32%), and > = T3 (31%). The majority preferred VBGE (77%) vs. IPGC (23%). Men who opted for IPGC had lower educational levels (< = high school/GED) (18% IPGC vs 7% VBGE) and reported higher baseline anxiety (45% IPGC vs. 24% VBGE). Cancer genetics knowledge improved significantly with IPGC vs. VBGE (+2.5 vs +0.8; $p < 0.01$). No differences were observed in decisional conflict, satisfaction, or understanding of personal GT results between IPGC vs. VBGE. Both groups had high rates of GT uptake (IPGC 91%, VBGE 93%). Pathogenic mutations were identified in 15% in IPGC group and 10.4% in VBGE group. **Conclusions:** A substantial proportion of men opted for VBGE, and results suggest that VBGE is comparable to IPGC for men considering PCA GT. IPGC may be more suitable for men with lower knowledge of cancer genetics and greater levels or anxiety. Further study is warranted. Research Sponsor: TIPS Pilot Funds, Sidney Kimmel Cancer Center, Thomas Jefferson University.

1578 Poster Session (Board #70), Fri, 8:00 AM-11:00 AM

Implementation of systematic germline genetic testing (GT) for metastatic prostate cancer (mPC) patients at the Puget Sound VA prostate oncology clinic. *First Author: Alexandra Sokolova, University of Washington, Seattle, WA*

Background: There is increasing clinical relevance for GT in patients with mPC to evaluate the 2-fold possibilities of molecularly targeted therapies and implications for relatives. NCCN guidelines recommend GT for subsets of men, including those with mPC. While exciting, there are new logistical challenges around workflows for delivering GT services. We sought to address these challenges through a prospective pilot study designed to systematically deliver GT to all men with mPC receiving care at the Puget Sound VA prostate cancer (PUG-VA PC) Clinic. Our hypothesis was that systematic universal GT for men with mPC would identify similar prevalence rates of germline pathogenic/likely pathogenic variants (P/LPV) among veterans compared to previously reported cohorts. **Methods:** We conducted an IRB-approved, prospective trial testing feasibility of a systematic workflow to identify all veterans with mPC seen at PUG-VA PC Clinic between 11/2016-1/2020 to discuss and offer GT. A research coordinator pre-screened each clinic schedule to identify patients with mPC, notified the oncologist to discuss pretest education and GT with the patient at the appointment. Consenting patients provided a saliva sample same day in clinic for the CLIA-certified Color Genomics 30-gene cancer gene panel. Results were issued to patients and providers, and results were discussed by email and phone with a genetic counselor. Uptake of GT and prevalence of P/LPV was measured and compared to previously reported data from the retrospectively tested UW TAN cohort. χ^2-test was performed. **Results:** 84% (190/227) of approached veterans with mPC consented and 80% (182/227) completed GT. 6.6% (12/182) of men were found to carry P/LPV in DNA repair genes: 3 in *BRCA2,* 2 in *BRCA1*, 4 in *ATM,* and 3 in *CHEK2*. Overall, 6.6% rate of P/LPV in DNA repair genes was comparable to the 8.8% previously reported in the UW TAN cohort ($p = 0.69$). **Conclusions:** Dedicated clinic-based strategies to offer and provide GT and services for veterans with mPC is feasible and results in high GT consent and uptake, especially with direct oncologist involvement. Proportion of consenting to proceed with GT was nearly identical to a referral-based specialty Prostate Cancer Genetics Clinic (Pouv, Sokolova, and Cheng, unpublished). The proportion of P/LPV in the PUG-VA PC population was comparable to a geographically similar retrospective cohort. Updated data, including detailed demographics and GT results, will be reported at final presentation. Research Sponsor: U.S. National Institutes of Health, Prostate Cancer Foundation.

1579 Poster Session (Board #71), Fri, 8:00 AM-11:00 AM

Development and validation of the PREMMplus clinical prediction model for multigene hereditary cancer risk assessment. *First Author: Matthew B. Yurgelun, Dana-Farber Cancer Institute, Boston, MA*

Background: Current clinical prediction models provide syndrome-specific numeric estimates of an individual's likelihood of having a specific hereditary cancer syndrome (e.g., $PREMM_5$ for Lynch syndrome; BRCAPRO for *BRCA1/2*). With the emergence of multigene panel testing (MGPT), there is a need to evaluate individuals' risk of carrying a pathogenic variant in a diverse array of cancer susceptibility genes in parallel. This study's aim was to develop and validate the PREMMplus clinical prediction model for multigene cancer risk assessment. **Methods:** PREMMplus was developed in a cohort of 7296 individuals who had undergone germline MGPT at a single center. Logistic regression models were used to examine candidate predictive variables – including age, sex, ethnicity, and personal/family history of cancer – to provide a numeric estimate of an individual's likelihood of carrying a pathogenic/likely pathogenic germline variant in one of 18 cancer susceptibility genes (11 high- [*APC*, *BRCA1/2*, *CDH1*, *EPCAM*, *MLH1*, *MSH2*, *MSH6*, biallelic *MUTYH*, *PMS2*, and *TP53*] and 7 moderate-penetrance [*ATM*, *CDKN2A*, *CHEK2*, *PALB2*, *PTEN*, *RAD51C*, and *RAD51D*]). Model performance was validated in an independent dataset of 14845 individuals who had undergone MGPT at a commercial laboratory. **Results:** Using clinical characteristics, including personal/family history of 18 cancers plus colorectal adenoma burden, PREMMplus demonstrated an excellent ability to predict pathogenic variants in high penetrance genes at 90% sensitivity. PREMMplus had acceptable performance with the addition of 7 moderate penetrance genes. PREMMplus was well-calibrated and demonstrated comparable performance in the external validation dataset. **Conclusions:** PREMMplus is the first validated risk assessment model to quantify an individual's likelihood of carrying pathogenic variants in a wide diversity of cancer risk genes, and can be used to select individuals who should undergo MGPT. As expected, PREMMplus's discriminatory capacity was reduced with the inclusion of moderate penetrance cancer risk genes. Research Sponsor: U.S. National Institutes of Health.

Cohort	Outcome	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	# Needed To Test to Detect 1 Carrier	AUC (95% CI)
Development	11 high penetrance genes	90%	34.8%	7.4%	98.4%	13.5	0.74 (0.71-0.77)
Development	18 high/ moderate penetrance genes	90%	23.9%	10.6%	96.0%	9.4	0.67 (0.65-0.69)
Validation	11 high penetrance genes	90%	22.8%	5.5%	97.9%	18.3	0.69 (0.66-0.71)
Validation	18 high/ moderate penetrance genes	90%	17.8%	9.8%	94.8%	10.2	0.62 (0.60-0.64)

1580 Poster Session (Board #72), Fri, 8:00 AM-11:00 AM

Hereditary leiomyomatosis and renal cell cancer syndrome (HLRCC): Genotype and phenotype characteristics in a cohort of 197 patients. *First Author: Ana Beatriz Sanchez-Heras, Cancer Genetic Counseling Unit. Hospital General Universitario de Elche, Elche, Spain*

Background: HLRCC is a hereditary condition with autosomal dominant inheritance due to germline mutations in the fumarate-hydratase gene (*FH*). It is characterized by skin leiomyomas (SLM) in 48-84% of individuals, uterine leiomyomas (ULM) in 30-72%, renal cysts (RCy) and renal cell cancer (RCC) in 15-34%. We aimed to describe the genetics, the clinical features and the potential genotype-phenotype associations in the largest cohort of *FH* mutation carriers from Spain. **Methods:** We performed a multicenter, observational, retrospective study of individuals with genetic or clinical diagnosis of HLRCC. We collected clinical information from medical records. We analyzed genetic variants and looked for genotype-phenotype associations. Statistical analyses were performed by IBM-SPSS Statistics-v.22. **Results:** We included 197 individuals (113 women, 84 men), 74 index cases and 123 relatives. Twenty-seven different variants were detected, 26 pathogenic (12 missense, 5 frameshift, 4 large-deletions, 3 splice-site and 2 nonsense) and 1 variant of unknown significance (missense). Of 182 patients with full skin examination, 64.8% presented SLM (median age 36 years; range 8-85). ULM were diagnosed in 90.3% of 103 women with gynecologic exam (median age 30 years; range 17- 55). Hysterectomy was performed in 62.9% (median age 34 years; range 21-54). Of 153 patients with radiological records, 37.3 % presented RCy. Nineteen patients (10.9%) presented RCC, 11 males and 8 females (median age 37 years; range 10-67). The histological diagnoses were: 14 papillary, of which 10 were type 2; 3 clear cell carcinoma and 2 unclassified carcinoma. Six tumors had stage I, 2 stage II, 3 stage III, 4 stage IV, and 4 not available. The median overall survival among patients at stages 3-4 was 2.9 years [1.3-4.5]. Patients with missense pathogenic variants showed higher risk of developing SLM ($p = 0.043$) and ULM ($p = 0.002$) than those with loss of function variants. **Conclusions:** In our cohort, the frequency of RCC (10.9%) is lower than that published in cohorts of similar sample size. The most frequent histology was the papillary type-2; however, other histological patterns do not exclude HLRCC. Individuals with missense pathogenic variants show higher incidence of SLM and ULM. Research Sponsor: None.

1581 Poster Session (Board #73), Fri, 8:00 AM-11:00 AM

Using sequential next-generation sequencing assays to identify germline cancer predisposition variants. *First Author: Ira Lignugaris Kraft, University of Chicago, Chicago, IL*

Background: Next-generation sequencing (NGS) increasingly guides clinical care in hematological malignancies by identifying DNA mutations that change dynamically over time. Clinical samples contain variable numbers of malignant and non-malignant cells. So, careful interpretation is required to determine if a particular variant is somatic, germline, or clonal hematopoietic in origin. **Methods:** The University of Chicago uses a targeted NGS assay of ~1200 genes, reporting 150 as a clinical test. We aimed to identify individuals with hereditary predisposition by detecting persistent variants on sequential assays regardless of disease state. **Results:** 943 NGS assays from July 2017 – Feb. 2020 on 711 patients [ages 1 mo – 95 yrs, median 65 yrs] were included. 2,320 variants in 33 genes were identified with 144 patients having the same variant identified on more than one assay. Single nucleotide variants (SNVs) with variant allele frequency (VAF) ≥ 0.3 were prioritized. The first candidate gene identified with potential germline SNVs was *CSF3R*. 28 unique SNVs in *CSF3R* were found, 14 were confirmed as germline, 6 somatic, and 8 were unconfirmed due to lack of available tissue. At least 2 confirmed germline *CSF3R* variants were likely deleterious based on functional testing. Sequential SNVs were quantified using the coefficient of variation, characterizing each by change in VAF over time. Using a worst-case-scenario analysis, in which unconfirmed variants were not counted as germline, a computer algorithm was designed to identify potential germline variants (specificity 0.89, PPV 0.75). Via an iterative method, the algorithm compares new assays to a pool of previously reported tests, flagging patients with potential germline mutations so that biopsies may be studied in the lab, records reviewed, and referrals placed to genetic counselors. To date, 61 patients with 89 likely germline variants have been identified. Known hereditary hematological malignancy genes, such as *ATM, ASXL1*, *CHEK2*, *DDX41*, *TSC1*, and *RUNX1,* had the most variants identified. Limitations include the challenge in distinguishing variants that do not change over time, reliance on a targeted NGS panel, and normalizing VAF data prior to analysis. **Conclusions:** These data highlight the utility of NGS of bone marrow and peripheral blood samples to identify patients suspected of having germline DNA variants. In addition to identifying known predisposition syndromes, one may discover new inherited cancer syndromes and help guide clinical practice in real time. Research Sponsor: None.

1582 Poster Session (Board #74), Fri, 8:00 AM-11:00 AM

Value of multigene panel retesting of families with *BRCA1/2* mutation-negative hereditary breast and ovarian cancer (HBOC). *First Author: Ekaterina Meshoulam Nikolaeva, Mutua Terrassa, Terrassa, Spain*

Background: Despite the use of clinical eligibility criteria and mutation predictive models, a great proportion of families are negative for germline mutations in *BRCA1/2* genes. Traditionally, risk assessment of inconclusive results included the recommendation of high-risk surveillance protocol, the update of incident cancer cases in the family and the consideration of additional testing to rule out the possibility of phenocopy. More recently, next generation sequencing multigene panels have become a standard practice in cancer genetics clinics worldwide. We addressed the value of multigene panel retesting of *BRCA1/2* negative HBOC families in our institution. **Methods:** After genetic counseling session and informed consent, a total of 137 individuals (119 probands and 18 extra cancer-affected relatives) from distinct *BRCA1/2* negative families were retested using a panel containing 11 breast and ovarian cancer susceptibility genes (*BRCA1/2, PALB2, ATM, CHEK2, PTEN, TP53, STK11, BRIP1, RAD51C, RAD51D*). **Results:** According to the BOADICEA model, the remaining probability of mutation in *BRCA1/2* or *PALB2 genes* in our cohort was 5.5% (0.1-61). The reasons for considering retesting were the addition of any incident cancer diagnosis in 33 cases (24%), a prior study with a low sensitivity screening technique (dHPLC) in 6 families (5%) and the expansion of the study to other putative breast and ovarian susceptibility genes in 98 families (71%). Overall, 3 pathogenic (2 *BRCA2*, 1 *CHEK2*) and 8 likely pathogenic variants (1 *BRCA2*, 4 *CHEK2* and 3 *ATM*) were found. The prevalence was 8%. The detection rate among 19 families with a $> 10\%$ remaining probability of mutation in *BRCA1/2* and *PALB2* genes was 26%. The 3 clinically significant variants in *BRCA2* were detected in 2 families and 1 updated cancer family history (BOADICEA remaining probability of 59, 61 and 12%, respectively). Cascade testing was subsequently done in 15 relatives resulting 8 in mutation carriers and 9 true negatives. **Conclusions:** Our results support the value of updating cancer incident cases and considering expanded panels in selected families. Research Sponsor: None.

1584 Poster Session (Board #76), Fri, 8:00 AM-11:00 AM

Effect of genetic testing results on patient-reported quality of life among patients undergoing panel testing for newly diagnosed ovarian cancer. *First Author: Sarah S. Lee, New York University School of Medicine, New York, NY*

Background: This study compared patient-reported stress, anxiety, and depression between newly diagnosed ovarian cancer patients with pathogenic genetic testing results versus patients with non-informative results (i.e., variants of uncertain significance (VUS) or negative). **Methods:** Patients underwent genetic testing (GT) via a facilitated referral pathway (Frey et al, Gynecol Oncol 2020) through which they were referred for genetic counseling and GT by their gynecologic oncologist within six weeks of diagnosis from 10/2015 to 5/2019. English-speaking patients completed three quality of life (QoL) instruments: Impact of Events Scale (IOES), State-Trait Anxiety Questionnaire (STAI), Hospital Anxiety and Depression Scale (HADS) immediately pre-and post-GT and 6 months post GT. Two-way mixed ANOVA was performed to analyze effect of GT results on QoL over time with significance $p < 0.05$. **Results:** One hundred ten patients were enrolled in the pathway and 83 (76%) patients underwent GT. Among these, 15 (18%) had potentially actionable pathogenic mutations (*BRCA1*-8, *BRCA2*-4, *MSH2-2*, *MRE11A*-1); 26 (31%) had VUS results; 3 (4%) had both a pathogenic mutation and a VUS result; and 42 (51%) had negative results. Sixty patients (72%) completed QoL assessments pre and post GT, and 37 (44%) patients at 6-9 months post GT. For all patients, GT results did not affect QoL scales across our time points. By mean scores across all-comers, patients demonstrated mild stress at each time point and clinically significant anxiety immediate post-GT. All patients had a statistically significance decrease in HADS depression scores over time from pre-GT to 6 months post-GT (mean score 4.98 vs 2.97, $p = 0.020$). Patients with VUS had lower HADS mean anxiety scores across time (3.62) compared to patients with pathogenic (7.44) or negative mutations (6.83, $p = 0.029$). For patients without mutations, there was a significant decrease in clinically significant anxiety by STAI-state score at 6 months ($p = 0.002$) and a decrease in borderline anxiety by HADS scores at 6 months ($p = 0.005$). This effect was not present for patients with pathogenic mutations or VUS. **Conclusions:** A pathogenic result does not impact QoL scales immediately pre or post GT or at 6 months post GT, though patients with negative mutations were more likely to show a decrease in anxiety over time. Patients should be recommended GT at time of diagnosis of ovarian cancer without concern of increased stress, anxiety, or depression based on GT results. Research Sponsor: NYU Langone Health, Pharmaceutical/Biotech Company.

1585 Poster Session (Board #77), Fri, 8:00 AM-11:00 AM

Genetic testing and referral patterns of non-*BRCA* mutation carriers at increased or uncertain risk of ovarian cancer. *First Author: Sarah S. Lee, New York University School of Medicine, New York, NY*

Background: While the management of *BRCA1/2* is clear, management of non-BRCA mutations with increased risk or uncertain risk of ovarian cancer (OC) is not well established. Previously, we reported that referral to a gynecologic oncologist (GO) resulted in a 30-fold increased uptake of risk reducing surgery (RRS). We aimed to identify trends in genetic testing (GT) and referral to a GO of patients (pts) with such mutations. **Methods:** In this retrospective cohort study at 3 satellite sites within 1 institution from 2014 to 2018, pts were identified by ICD-10 codes Z15.01, Z15.02, Z15.09, Z15.89, C50.919, Q99.8, and C54.1. Pts with mutations with increased risk of OC (*MLH1, MSH2/6, PMS2, EPCAM* (LS genes), *RAD51C/D, BRIP1, STK11)* and uncertain risk of OC (*PALB2, ATM, BARD1, NBN)* were included; *BRCA1/2* and variants of uncertain significance were excluded. Outcomes of interest were patterns of GT and referral to a GO. Chi square and logistic regression were used with $p < 0.05$. **Results:** Of 20,000 pts with above ICD-10 codes, 240 pts had genes of interest. Mutations in increased risk of OC included: LS genes, 131; *BRIP1*, 14; *RAD51D*, 8; *RAD51C*, 5; *STK11*, 1. Mutations associated with uncertain risk of OC were: *ATM,* 43; *PALB2*, 23; *NBN*, 10; *BARD1,* 5. Pts with known mutations prior establishing care at our institution (N = 69) were less likely to be referred to a GO (22% vs 78%, $p = 0.015$). Pts with LS genes were more likely to be referred to a GO (52% vs. 25%, $p < 0.001$), to be tested by a GC (52% vs 25%, $p < 0.001$), and to be tested for family history (FH) of known mutation (69% vs 30%, $p < 0.001$). Provider performing GT included: genetic counselor (GC), 66 (28%); medical oncologist, 44 (18%); general obstetrician-gynecologist, 44 (18%); breast surgeon, 6 (3%), and primary care provider, 5 (2%). Of 66 pts tested by a GC, 46 (70%) were referred to GO, vs 48/105 (45%) pts who underwent GT by non-GC ($p = 0.001$). Reasons for GT among pts were: FH of cancer, 113 (47%); personal history of cancer, 56 (23%); known FH of a mutation, 49 (20%); and unknown indication, 22 (9%). When controlling for age, parity, race, insurance, GT provider, and reasons for GT, mutations with increased risk of OC were associated with referral to a GO (OR 3.55, 95% CI 1.88-6.72), along with pts who were tested by a GC (OR 2.65, 95% CI 1.27-5.51). **Conclusions:** Only ~30% of pts underwent GT by a GC, which was associated with increased referral to a GO. LS genes are better known and were associated with higher uptake of GO referral. Education of OC risks of these newer mutations among providers performing GT may increase referral to a GO and uptake of RRS. Research Sponsor: None.

1586 Poster Session (Board #78), Fri, 8:00 AM-11:00 AM

Comparison of genomic instability test scores used for predicting PARP activity in ovarian cancer. *First Author: Kirsten M Timms, Myriad Genetic Laboratories, Inc., Salt Lake City, UT*

Background: Clinical trials have explored the utility of various genomic instability (GI) scores or gene panels to assess deficiencies in the homologous recombination (HR) DNA repair pathway and support PARP inhibitor use in ovarian cancer; however, these methods of assessing homologous recombination deficiency (HRD) may not be equivalent. The myChoice HRD test is the only analytically and clinically validated, FDA-approved HRD test that includes *BRCA1/2* mutation status and three measures of GI. We compared the proportion of patients identified as candidates for PARP inhibitor use by two measures of HRD [percent loss of heterozygosity (%LOH), 11-gene panel] to myChoice HRD. **Methods:** Whole-genome SNP analysis was used to reconstruct ovarian tumor genomic profiles to calculate the myChoice HRD score and %LOH in 2 cohorts (clinical laboratory cohort, N = 3,278; SCOTROC4 trial, N = 248). Mutation screening for a set of 11 genes in the HR pathway (*ATM*, *BARD1*, *BRCA1*, *BRCA2*, *BRIP1*, *CHEK2*, *MRE11A*, *NBN*, *PALB2*, *RAD51C*, *RAD51D*) was performed for a subset of tumors from the SCOTROC trial (n = 187). Samples were considered positive if the myChoice HRD score was above the threshold (threshold scores of 42 and 33 were assessed), %LOH above the threshold (16%), or a pathogenic variant in one of the 11 HR genes. The correlation between positive results from %LOH and the 11-gene panel were compared to myChoice HRD. Percent positive agreement (PPA) was the proportion of positive test results from myChoice HRD that were also positive by %LOH or the 11-gene panel. **Results:** The table shows the correlation and PPA between myChoice HRD, %LOH, and the 11-gene panel. Overall, 19%-61% of patients identified as positive by myChoice HRD would have been missed by %LOH or the 11-gene panel in these two cohorts. **Conclusions:** These data show that HRD tests used in published and ongoing clinical trials are not equivalent, and they should not be considered interchangeable in predicting PARP inhibitor response in clinical practice. Research Sponsor: Myriad Genetic Laboratories, Inc.

	%LOH	11-gene panel
Clinical testing dataset		
Correlation	0.845	-
PPA – myChoice HRD ≥42	67.7%	-
PPA – myChoice HRD ≥33	53.5%	-
SCOTROC4 cohort		
Correlation	0.89	n/a*
PPA – myChoice HRD ≥42	80.88%	53.06%
PPA – myChoice HRD ≥33	60.61%	38.57%

*Could not be calculated because positive results by the 11-gene panel were not continuous

1588 Poster Session (Board #80), Fri, 8:00 AM-11:00 AM

Effects of initiating in-office germline testing in safety net clinic patients with epithelial ovarian cancer. *First Author: Scott Jordan, University of Miami-Sylvester Comprehensive Cancer Center, Miami, FL*

Background: Germline genetic mutations occur in approximately 25% of women with epithelial ovarian cancers. Recent advances in frontline maintenance therapy for patients with hereditary breast and ovarian cancer syndrome make timely germline testing critical. Adherence to genetic testing remains low (approximately 30% nationally), including at our safety net hospital where germline testing by a genetic counselor was performed in only 38% of patients. After initiating in-office genetic testing, our aim was to compare current patients with historical controls to determine whether this intervention shortened the time to testing and results. **Methods:** IRB approval was obtained. Patients seen for a diagnosis of epithelial ovarian cancer between 4/1/2018 and 12/31/2019 were identified. Patients with only one visit or those who received testing elsewhere were excluded. Patient and visit data were abstracted for each visit during the study period. Comparison was made between patients treated before (control cohort) and after in-office testing was initiated (intervention cohort) on 5/21/2019. Categorical variables were compared using Chi Squared and Fisher's Exact test. Mann Whitney U test was used to compare time from first clinic visit to the date of genetic testing and to the reporting of test results in the chart. All tests were two-sided and significance was set at $p = 0.05$. **Results:** 74 patients were identified and 504 clinic visits were analyzed. 57 (77%) patients were White Hispanic, 15 (20.3%) were Black, and 2 (2.7%) were White non-Hispanic. 56 (75.7%) underwent germline testing. Overall median time to testing from the first clinic visit was 21.2 weeks, and median time to reporting of results was 37 weeks. Though there was no significant difference in testing rate between the cohorts, the time to the date of genetic testing in the intervention group was approximately one-third as long as in the control group (9.6 vs 32.1 weeks, $p < 0.001$). Among the 52 patients with reported genetic results, results were recorded in a clinic note at 4.1 weeks from first visit in the intervention group, compared with 28.8 weeks in the control group ($p < 0.001$). In the intervention group, during clinic visits without genetics performed to date, testing was performed at that visit 25% of the time. **Conclusions:** By initiating in-office testing, time to testing and receipt of results were meaningfully shortened. Removing delays to test results will greatly improve the ability of our patients to receive potentially life-saving maintenance therapy following front line treatment. Research Sponsor: None.

1589 Poster Session (Board #81), Fri, 8:00 AM-11:00 AM

Prospective agnostic germline testing in pediatric cancer patients. *First Author: Elise Fiala, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: We report our large cohort of pediatric cancer patients undergoing prospective agnostic germline sequencing. Our dataset is a significant addition to the 1,573 children reported to date who have undergone agnostic germline sequencing in previous large sequencing studies, each with ascertainment bias. **Methods:** 676 patients with pediatric solid tumors underwent matched tumor-normal targeted DNA sequencing from July 2015 to February 2020. At least 76 genes associated with cancer predisposition were analyzed in the germline, and variants were classified per American College of Medical Genetics guidelines. Pathogenic and likely pathogenic (P/LP) variants were reported to patients/families, who were offered genetic counseling and cascade testing with screening recommendations and referral to a surveillance clinic as appropriate. **Results:** One or more P/LP variants were found in 17% (115/676) of individuals when including low, moderate and high penetrance mutations in recessive and dominant genes, or 12% (81/676) when including moderate and high penetrance mutations in dominant genes. P/LP variants were detected in 40% (21/53) of patients with retinoblastomas, 8% (13/161) with neuroblastomas/ganglioneuroblastomas, 13% (14/112) with brain/spinal tumors, 8% (20/245) with sarcomas, and 12% (13/105) with other solid tumors. The most frequent mutations were in *RB1* (n = 28) and *TP53* (n = 8) in patients with associated tumors. Of patients with moderate/high penetrance mutations, 30% (24/81) had unexpected tumor types, with potential therapeutic relevance in 58% (14/24) including *BRCA1* n = 2, *BRCA2* n = 3, *RAD51D* n = 1, *ATM* n = 1 *MLH1* n = 1, *MSH2* n = 1, *MSH6* n = 1, *PMS2* n = 3, and *SUFU* n = 1. Two patients received immunotherapy based on their germline finding. **Conclusions:** P/LP germline variants are frequently present in patients with pediatric cancer. We are contributing significantly to the cohort size of agnostic sequencing in pediatric cancers. Our experience is similar to other studies with a ~12% detection rate of moderate and high penetrance mutations. Moderate/high penetrance mutations were concordant with the patient's cancer history in 70% of cases, higher than previously reported, likely due to an enrichment of retinoblastoma. While many mutations are identified in patients with associated tumor types, a large proportion of mutations are unexpected based on the patient's history. Clinical actionability of these findings may include screening, risk reduction, family planning, and increasingly targeted therapies. Research Sponsor: Marie-Josee and Henry R. Kravis Center for Molecular Oncology, the Neihaus Center for Inherited Cancer Genomics, the Crawford fund, and the Corning fund.

1590 Poster Session (Board #82), Fri, 8:00 AM-11:00 AM

Streamlining the genetics pipeline to increase testing for patients at risk for hereditary prostate cancer. *First Author: Barry Tong, UCSF, San Francisco, CA*

Background: Metastatic prostate Cancer (mPCa) is increasingly recognized as a heritable disease and germline genetic testing has increasingly become a part of standard of care. At the University of California at San Francisco (UCSF) Genitourinary (GU) Medical Oncology clinic, approximately 850 new patients with mPCa are seen annually. A feasibility pilot Genetic Testing Station (GTS) was developed to expand access to genetic testing among this high-risk population. GTS is facilitated by Genetic Counselor Assistants (GCA) under the supervision of genetic counselors. **Methods:** This is a feasibility pilot of a GTS model among patients with mPCa. In this model, all patients with mPCa are offered a same day GTS visit with a GCA. At the GTS, the patient receives pre-test education via videos developed by genetic counselors. The patient provides informed consent, a family history, and a saliva sample for Invitae's 87-gene panel. All positive results trigger a genetic counselor visit while non-positive results either receive a letter or a genetic counselor visit (in person or via telehealth). To evaluate the model, testing frequency and laboratory turnaround time (TAT) was assessed before and after the pilot. **Results:** In the first four months of the GTS pilot (10/14/2019 – 02/10/2020), 94 patients were referred and received genetic testing. Eight germline positives were identified (BRCA2, CHEK2, HOXB13 MSH6, RECQL4). The average TAT was 8 days. 9.3% of patients were found to have pathogenic mutations through the prostate GTS which is comparable to previously published rates of germline mutations in metastatic prostate cancer patients. In a 4-month time frame the prior to the intervention (10/01/2018-1/31/2019), 26 genetic testing orders were placed. The average laboratory TAT in this prior process was 17 days. Rates of positive germline mutations in the prior model was 8.6%. **Conclusions:** The GTS is a feasible method to increase access to germline genetic testing among a high-risk population. It may reduce barriers to testing and facilitate real-time discussion of treatment and prevention strategies with patients and family members. As a result, we will continue to operate the GTS. This model provides a framework for scaling access for and cascade testing in other high-risk patient groups. Research Sponsor: None.

1591 Poster Session (Board #83), Fri, 8:00 AM-11:00 AM

Diagnostic yield of germline genetic testing following tumor testing in prostate cancer patients. *First Author: Kingshuk Das, Invitae, San Francisco, CA*

Background: NCCN guidelines recommend germline testing for patients with localized or advanced prostate cancer meeting family history or clinical/pathologic criteria. However, the guidelines for somatic molecular analysis generally consider advanced disease only, primarily to inform therapy. As the analytical and clinical specifications of both testing modalities differ accordingly, we examined the results of germline testing following prior somatic testing. **Methods:** We reviewed somatic and germline variants in an otherwise unselected consecutive series of patients who: (a) had a current or previous diagnosis of prostate cancer; (b) had undergone tumor sequencing; and (c) were referred for germline testing. Indications for germline testing included: potential germline origin of somatic test result, treatment or surgical planning, personal or family history, and patient concern. **Results:** 208 patients met study criteria of whom 81 (39%) harbored a pathogenic germline variant (PGV) in a cancer predisposition gene. Certain genes were more likely to harbor germline variants, and 98% (81) of PGVs were potentially actionable (Table). 9.6% of PGVs were not reported by somatic testing, reflecting analytical limitations of the somatic testing. Of note, 11 patients (14%) had PGVs identified after diagnosis of a subsequent primary malignancy. **Conclusions:** The high PGV rate of 39% was unexpected, given reported rates of 11.8% in patients with metastatic prostate cancer and 6% in high-risk localized disease (NCCN)--even considering potential clinician ascertainment bias. This finding, the potential clinical utility of 98% of PGVs identified, the significant proportion unreported by somatic testing, and the fraction of patients diagnosed with a PGV after a subsequent malignancy all suggest that germline testing is an underutilized tool in the care of prostate cancer patients and their families. Research Sponsor: None.

Germline and somatic findings.

Gene	#Findings Total	#Germline (%Total)	NCCN	Utility
BRCA1/2	142	52 (37)	Yes	M,T,C
ATM	19	10 (53)	Yes	M,C
MSH6,PMS2	16	4 (25)	Yes	M,T,C
CHEK2	13	5 (38)	Yes	M,C
PALB2	7	3 (43)	Yes	M,C
NBN	5	3 (60)	No	C
BRIP1	4	2 (50)	No	M,C
CDKN2A	5	1 (20)	No	M
Others	3	3 (100)	No	Varies
	214	83		

NCCN: NCCN recommended prostate cancer germline panel constituent. Utility: Germline findings associated with management guidelines (M), approved therapy (T), clinical trial eligibility (C). Other genes: CFTR, MITF, RAD51C. Genes without germline findings not shown.

1592 Poster Session (Board #84), Fri, 8:00 AM-11:00 AM

Cancer risk and overall survival in APC I1307K carriers. *First Author: Stephen B. Gruber, City of Hope National Medical Center, Duarte, CA*

Background: The germline variant *APC* I1307K is one of the most commonly identified pathogenic variants on germline genetic testing panels. The purpose of the Molecular Epidemiology of Colorectal Cancer study was to quantify the risk of colorectal cancer among carriers, characterize the clinical, pathologic, and molecular features of colorectal cancers arising in patients with *APC* I1307K, and to describe the overall and disease-specific survival of carriers with colorectal cancer. Here, the final results of the Molecular Epidemiology of Colorectal Cancer Study are reported with respect to *APC* I1307K. **Methods:** We consented 6,006 incident, pathologically confirmed cases of colorectal adenocarcinoma and 5,023 age, sex, and ethnicity matched controls without colorectal cancer between March 31, 1998 and July 1, 2017 within a geographically defined area of Northern Israel. Comprehensive, in-person epidemiologic interviews were conducted for cases and controls, with uniform histopathologic review, detailed molecular analysis, medical record review and clinical follow-up for up to 21 years. **Results:** The demographic and clinical features of incident colorectal cancer cases matched the population distribution of colorectal cancer in Israel. *APC* I1307K was identified in 429 (7.1%) of cases and 201 (4.0%) of controls. The estimated relative risk of colorectal cancer among carriers was 1.89 (95% confidence interval, 1.59 - 2.24), $p < 0.0001$. The prevalence and odds ratios differed by ethnic group. Homozygous carriers were at especially high risk, with an odds ratio of 3.90 (95% confidence interval 1.11–13.71). *APC* I1307K carriers were significantly less likely to have microsatellite instable tumors ($p = 0.04$). Overall survival of *APC* I1307K carriers was not significantly different than survival of non-carriers, after adjustment for age, stage, sex, ethnicity, and microsatellite instability. **Conclusions:** *APC* I1307K is an actionable germline mutation that confers meaningful lifetime risk of colorectal cancer in heterozygous and homozygous carriers. *APC* I1307K is not an independent prognostic factor for overall survival or disease specific survival and is not associated with the MSI phenotype. Cumulative lifetime risk estimates inform genetic counseling and provide data for policies regarding the timing and frequency of screening and other preventive strategies. Research Sponsor: U.S. National Institutes of Health.

1593 Poster Session (Board #85), Fri, 8:00 AM-11:00 AM

Relative and absolute risk of second primary neoplasms of the central nervous system. *First Author: Elisa Liu, NYU School of Medicine, New York, NY*

Background: Cranial radiation is known to increase the relative risk for developing a second primary neoplasm, but existing analyses do not take into account differential survival or follow-up. The absolute risk, or true incidence, of developing a second primary neoplasm in the central nervous system (CNS) is not well characterized. **Methods:** Patients diagnosed with cancer from between 1976 and 2016 were sampled using the Surveillance, Epidemiology, and End Results (SEER) Program. Relative risks were estimated using standardized incidence ratios (SIRs) and absolute risks were estimated using cumulative incidence (CI) functions with death as a competing risk. Among CNS primaries, comparison groups were matched by age, sex, year of diagnosis, primary histology, and lesion location. **Results:** Over 3.8 million patient records, including 13,167 second primary CNS tumors, were extracted from SEER. The relative risk of developing a second primary CNS neoplasm is elevated in all patients diagnosed with a CNS primary cancer (SIR = 9.6), but higher in those who received radiation (SIR = 13.1) or chemotherapy (SIR = 12.6). The absolute risk of developing a second primary CNS neoplasm at 25-years is highest in CNS and endocrine cancers (CI 1.0% and 0.50%, respectively). Among long-term ($>$ 10-year) survivors of CNS primaries, the 25-year CI of a second primary CNS neoplasm was 4.4%. Cranial radiation increased the incidence of second primary tumors in pediatric patients (25-year CI 4.8% vs 1.2%, p = 0.007), but not adults (25-year CI 5.1% vs 4.9%, p = 0.85). Chemotherapy did not increase CI in either pediatric (25-year CI 7.0% vs 5.4%, p = 0.87) or adult (25-year CI 3.6% vs 5.8%, p = 0.11) populations. Meningiomas (39.3% vs 22.0%, p = 1e-6) and glioblastomas (21.1% vs 14.6%, p = 0.03) represent a greater proportion of the second primary CNS tumors in those who received cranial irradiation. **Conclusions:** The risk of developing a second primary CNS neoplasm is elevated in patients with a prior CNS cancer. Cranial irradiation increased the CI of second primary tumors in pediatric patients but did not affect adult patients. The association between radiation therapy and risk for subsequent cancers may be limited to the pediatric population. Research Sponsor: None.

1594 Poster Session (Board #86), Fri, 8:00 AM-11:00 AM

Results of a prospective phase II national study: Prophylactic radical fimbriectomy (NCT01608074), in women with a documented high risk of breast/ovarian cancer—Final pathological results and outcomes. *First Author: Eric Leblanc, Centre Oscar Lambret, Lille, France*

Background: Risk-reducing salpingo-oophorectomy (RRSO) is the gold standard in surgical prophylaxis of pelvic high-grade serous carcinoma (HGSC) for women at risk of breast/ovarian cancer. Due to significant adverse effects of early oophorectomy, 20-30% of women delay or deny performing this operation. Recent data highlight the fallopian origin of most pelvic HGSC, especially its fimbrial part. Thus, we suggested a new two-step risk-reducing procedure: the radical fimbriectomy (RF) with delayed oophorectomy (DO) (Leblanc et al Gyn Oncol 2011), leading to the current RF/DO Phase 2 study. We present the definitive results on primary and secondary objectives of this trial. **Methods:** *BRCA1/2* carriers or any women with a documented familial risk of breast/ovarian cancer were first counseled to perform a classical laparoscopic RRSO. If they denied, they were offered to enter the RF/DO study. All specimens were submitted to the SEE-FIM pathological protocol. Pathological data along with all intra- and 30-day and beyond post-operative adverse events were prospectively recorded. Follow-up consisted in an annual clinical breast and gynecological examination, with tumor markers and hormonal status assessment. Primary endpoint was the rate of pelvic serous carcinoma. Secondary endpoints were procedure morbidity, rates of tubal abnormalities, breast cancer, secondary oophorectomy. **Results:** From January 2012 to October 2014, 121 RF were performed: 120 by laparoscopy, 1 laparotomy (concurrent myomectomy). An occult neoplasia was found in 3 cases with 1 invasive HGSC. Intraoperative complications were two grade1 bleedings without transfusion with no grade $\geq$3 early post-operative or delayed complication. With a median follow-up of 5.3 years (0.2 -7.6), no patient developed any pelvic HGSC, 21 patients developed a breast cancer (3 de novo, 18 recurrences/contralateral.). 1 cancer-free *BRCA1*-mutated lady delivered safe twins, after an uneventful post-RF pregnancy obtained with assisted reproductive technology (ART). Overall, 29 women underwent DO (by choice: 12 or menopause: 17) resulting in grade 3b complication in 1 case, but no pathological abnormality. **Conclusions:** RF/DO appears as a safe, well tolerated and effective procedure in terms of occult neoplasia detection. A successful pregnancy with ART was possible after radical fimbriectomy. Longer follow-up and larger cohort are necessary to confirm its efficacy in terms of ovarian cancer prophylaxis. Clinical trial information: NCT01608074. Research Sponsor: PHRC 2011.

1595 Poster Session (Board #87), Fri, 8:00 AM-11:00 AM

Outcomes of lung cancer screening among cancer survivors: An NCCN institution experience. *First Author: Bradley Maller, University of South Florida, Morsani College of Medicine, Tampa, FL*

Background: In 2013, the USPTF recommended low-dose CT (LDCT) screening for individuals at high risk of lung cancer based on data from the National Lung Screening Trial. However, the trial excluded participants with cancer diagnosis $<$ 5 years except for non-melanoma skin cancer, making it unclear whether the data will be generalizable to cancer survivors. This population, while at increased risk of secondary lung cancer, may be prone to false positive results due to anatomic defects or recurrent cancers. Our NCCN institution serves a large number of cancer survivors. We evaluated the outcomes of LDCT screening and the adherence to annual screening among cancer survivors, compared with individuals without cancer history (IWC). **Methods:** Prospectively maintained database of LDCT screening participants was analyzed. Eligibility was per NCCN criteria and cancer survivors needing regular chest CT were not offered LDCT. Participants were asked to complete a self-administered questionnaire on risk factors. Positive result was defined as Lung-RADS $\geq$3, corresponding to nodule $\geq$6 mm. Adherence to LDCT screening was defined as having T1 screening, excluding those $<$ 18 months from T0 at time of analysis. Predicted risk of lung cancer was calculated per PLCOm2012 model. **Results:** To date, 454 subjects have undergone LDCT screening. Positive results occurred in 60 subjects (13.2%) at T0; lung cancer was diagnosed in 10 subjects (2.2%); and other cancers were diagnosed in 5 subjects (1.1%). There were 152 cancer survivors, including survivors of breast (52), prostate (26), bladder or kidney (19), lung (14), and head and neck cancer (13). The median time from cancer treatment to LDCT screening was 6 years (range 0-55). Cancer survivors were older than IWC: median age 67.4 vs. 63.5 years ($p<$ 0.001) and more likely to be active smokers: 37.5% vs. 29.5%, ($p=$ 0.09). The median predicted risk of lung cancer at 6 year was 5.5% vs. 3.2%, ($p=$ 0.15). No significant difference in the screening outcomes was found between groups. Among cancer survivors (N = 152), positive screening occurred in 15 (9.9%); lung cancer was diagnosed in 1 (0.7%); and other cancers were diagnosed in 3 subjects (1.9%). Non-adherence to LDCT screening occurred in 31 out of 152 cancer survivors (20.4%), compared with 81 out of 262 (30.9%) IWC, ($p=$ 0.02). **Conclusions:** About one-third of LDCT screenings at this NCCN institution occurred among cancer survivors. We found no evidence of increased false positive results. However, a higher rate of adherence to annual screening was observed among cancer survivors than IWC. Research Sponsor: James Esther King Biomedical Research.

TPS1597 Poster Session (Board #89), Fri, 8:00 AM-11:00 AM

ECOG-ACRIN tomosynthesis mammographic imaging screening trial (EA1151). *First Author: Etta Pisano, Beth Israel Deaconess Medical Center, Boston, MA*

Background: This randomized trial is intended to determine whether tomosynthesis (TM) should replace the current standard for breast cancer (BC) screening, digital mammography (DM). It is hypothesized that the population of women assigned TM screening for 3-5 rounds will have fewer advanced cancers than the population assigned to DM screening. **Methods:** 164,946 women, ages 45 to 74 years who present for screening mammography and consent to participate will be enrolled across 150 sites in the US, Canada and abroad. Women will be randomized to TM or DM. The frequency and number of screening examinations over a five year period will vary based on menopausal status and whether they have specific risk factors, including - hormone use, family history of BC, deleterious genes, prior benign breast biopsy with diagnosis of LCIS or atypia any kind, or dense breasts. Blood and buccal cells will be collected from as many enrolled women as are willing to provide the samples. All breast biopsies during the trial will undergo gene expression analysis for the PAM50 and other progression pathways (PAM50-plus). All subjects enrolled will be followed long term for at least eight years. The primary endpoint is the proportion of participants who have an advanced breast cancer diagnosed at any time within 4.5 years of randomization in to the trial. Secondary endpoints include measures of diagnostic and predictive performance; rates of recall, biopsy, and interval cancers, prevalence of breast cancer subtypes, and tumor subtype based on PAM50-plus analysis. As of January 17th 2020, there are 104 sites open and 21,452 women enrolled in the trial. The DSMC last reviewed the trial in June 2019 and suggested that the trial continue as planned. Clinical trial information: NCT03233191. Research Sponsor: U.S. National Institutes of Health.

2000 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Intervention combining nurse navigators (NNs) and a mobile application versus standard of care (SOC) in cancer patients (pts) treated with oral anticancer agents (OAA): Results of CapRI, a single-center, randomized phase III trial. *First Author: Olivier Mir, Gustave Roussy Cancer Institute, Villejuif, France*

Background: Various interventions aiming to improve a safe use of oral anti-cancer agents have previously been reported. These retrospective studies involved nurse-led follow-up and use of health technologies. However, the potential impact of these combined strategies is limited by a lack of rigorous methodology. **Methods:** We performed a randomized phase 3 trial comparing an intervention combining NNs and a mobile application vs. SOC in cancer pts treated with OAA (excluding hormonal therapy) in our tertiary cancer center. Pts initiating OAA (all types of cancer, PS $<$ 3, life expectancy $>$ 6 months), were randomized in a 1:1 basis. The intervention combined a nursing-led follow-up and a mobile application for patients. NNs provided regular phone follow-ups to manage symptoms and assess toxicities, adherence and supportive care needs. Pts had access to a mobile application to record tracking data, contact NNs via secure messaging or a dedicated phone line. The intervention lasted 6 months. The primary endpoint was the Relative Dose Intensity (RDI). Secondary endpoints included adherence, toxicity, response and survival, quality of life, pts experience (PACIC Score), end-of-life support, and economic estimation of the use of healthcare resources. **Results:** From October 2016 to May 2019, 609 pts (median age: 62 years, 20-92; PS2: 11.8%) were included. 39% were receiving oral chemotherapy, and 61% other OAA. The RDI was significantly higher in the CAPRI arm (93.4% $\pm$0.26 vs. 89.4% $\pm$0.19, p = 0.04). The CAPRI intervention also improved PACIC scores (mean: 2.94$\pm$0.83 vs. 2.67$\pm$0.89, p = 0.01), the number of unplanned hospitalizations (15.1% vs. 22.0%, p = 0.04), hospitalization duration (mean: 2.82$\pm$6.96 days vs. 4.44$\pm$9.60, p = 0.02), and treatment-related grade$\geq$3 toxicities (27.6% vs. 36.9%, p = 0.02). **Conclusions:** Compared to SOC, the CAPRI intervention improved RDI, pts experience, hospitalizations and their duration, as well as the rate of treatment-related grade$\geq$3 toxicities. This type of intervention should represent a new standard in pts receiving OAA. Clinical trial information: NCT02828462. Research Sponsor: Fondation Philanthropia Lombard Odier, Other Government Agency, Pharmaceutical/Biotech Company.

2001 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Chemotherapy remote care monitoring program (CRCMP): Integration of an SMS text patient-reported outcome (PRO) in the electronic health record (EHR) to identify patients needing pharmacist intervention for chemotherapy-induced nausea and vomiting (CINV). *First Author: Shannon Hough, University of Michigan, Ann Arbor, MI*

Background: CINV is a feared side effect of cancer therapy. Despite advances in management, CINV is a common cause for emergency department (ED) evaluation and other unplanned health care utilization. The University of Michigan Rogel Cancer Center initiated the CRCMP to proactively identify patients (pts) experiencing CINV and intervene prior to the need for urgent evaluation. **Methods:** Pts receiving highly emetogenic chemotherapy are identified by administration of a NK1 antagonist. Once enrolled in the CRCMP, pts receive a daily text message survey for 7 days after treatment. The survey is based on the validated MASCC anti-emesis tool (MAT). Responses are stored within a flowsheet in the EHR. Responses above a set threshold trigger a message to the team pharmacist for intervention. Data presented was reviewed from EHR and claims data. **Results:** In 8 mo, 652 pts received a NK-1 antagonist (2244 total cycles) and 387 pts enrolled in the CRCMP (59%). Each pt enrolled for an average of 1.8 cycles of chemo (range 1-8). Of patients enrolled, 61.4% were female and 86.2% were Caucasian. Chemotherapy intent was curative for 51.7% and palliative for 48.3% of pts. Pts enrolled most commonly received cisplatin-based (29.7%) followed by carboplatin-based (22.5%), and 5-fluoruracil-based (20.9%) therapy. Text message response rate was 94% (N=18,143 responses of 19,256 total messages sent). During 861 cycles of therapy, 7% of responses noted vomiting and 33% of responses noted nausea. Since implementation of CRCMP, total hospitalization, ED, and urgent care use has decreased (p=0.029) compared to historical data. When utilization for nausea-related diagnoses was considered, the reduction was more notable (Table). **Conclusions:** Pts engaged in the CRCMP for CINV, allowing for rapid assessment of PROs by a pharmacist. Health care utilization related to nausea was reduced following implementation of CRCMP. While these changes were numerically small, reduction in unnecessary care utilizing PROs can contribute to high value care for cancer patients. Research Sponsor: None.

Claims-based review of health care utilization before and after CRCMP.

	BEFORE CRCMP (n=3504 doses)	AFTER CRCMP (n=2244 doses)	p value
Admissions (ED/IP/OBS)	124	80	0.958
Nausea-Related Admissions	22	7	0.1
Urgent Care	110	38	0.001
Nausea-Related Urgent Care	23	7	0.077
Total visits	234	118	0.029
Total Visits: Nausea-Related	45	14	0.015

IP: inpatient;OBS:observation

2002 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Home-based management of cancer patients (CPs) experiencing toxicities while on anticancer treatment: The impact of a nurse-led telephone triage (NTT). *First Author: Lorenzo Calvetti, Department of Oncology, San Bortolo General Hospital, Vicenza, Italy*

Background: Novel organization models are needed to ensure early management of new treatment-related toxicity of anticancer treatments. Aim of this prospective observational study was to evaluate the impact of the introduction of NTT in reducing hospitalization of CPs. **Methods:** CPs on active medical treatment at the Department of Oncology of San Bortolo Hospital (Vicenza, Italy) were given instructions to refer to NTT in case of treatment-related adverse events (TRAEs). The service was opened Mon to Fri from 8am to 8pm. Assessment of TRAEs was performed by trained oncology nurses according to the CTCAE scale and subsequent actions were taken according to the severity of the events. The assessment was made under supervision of a medical oncologist in charge of the service while on duty. Primary endpoint of the study was to compare the rate of hospitalization of CPs on anticancer treatment after the introduction of NTT compared to 2017-2018 period. **Results:** From September 2018 to September 2019 1,075 patients received systemic anticancer treatment (versus 936 patients in the equivalent 2017 – 2018 period). Total consultations at NTT were 429; 581 TRAEs were reported. 117 patients reported more than one TRAE. CTCAE were graded as G1 237 (40.8%), G2 231 (39.8%) or G3-G4 113 (19.4%). The most common grade $\geq$ 3 TRAE was fever (38 events (33.6%) that resulted a febrile neutropenia in 7 cases) followed by cancer pain (15 (13.3%)) and fatigue (9 (8%)). In the observation period, 109 CPs on treatment were hospitalized versus 138 in the 2017-2018 period with a normalized hospitalization rate of 10.1% versus 14.7 % (p = 0.002, chi-square) with a reduction of normalized number of hospitalizations of 44 (estimated cost savings of 380.160 euros). **Conclusions:** Our results provided evidence of successful implementation of the NTT system in reducing rates of hospitalization through emergency room in cancer patients receiving modern medical treatments. Research Sponsor: None.

2003 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Changes in cancer mortality rates after the adoption of the Affordable Care Act. *First Author: Anna Lee, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: The Affordable Care Act (ACA) was designed to improve health status in the US primarily through improving access to health insurance. As adoption of Medicaid expansion varied at the state level, this study aims to compare cancer mortality rates over time between states who did (EXP) and did not adopt (NonEXP) Medicaid expansion. **Methods:** Age-adjusted mortality rates per 100,000 were gathered from the National Center for Health Statistics from 1999-2017 to establish trends. Only deaths due to cancer in patients less than 65 were included. Absolute change in cancer mortality was calculated from 2011-2013 and then from 2015-2017 with 2014 as washout year. Changes within subpopulations (gender, race, ethnicity) were also assessed. Mortality changes between EXP and NonEXP groups were via "difference in differences" analysis. **Results:** Overall age-adjusted cancer mortality in the US fell from 1999-2017 from 66.9 to 48.8 per 100,000. EXP states had higher population (157 vs 118 million) with less black/African Americans (19.2 vs 21.8 million) and more Hispanics (33.0 vs 21.7 million) than NonEXP states (all examples from 2017). The overall age-adjusted cancer mortality was consistently worse in NonEXP states, cancer mortality fell from 64.7 to 46.0 per 100,000 in EXP states and from 69.0 to 51.9 per 100,000 in NonEXP states from 1999-2017 (both trends p $<$ 0.001, comparison p $<$ 0.001). Comparing the mortality changes in the peri-ACA years (2011-2013 vs 2015-2017) between the 2 cohorts, the difference in differences between EXP and NonEXP states was -1.1 and -0.6 per 100,000 respectively (p = 0.006 EXP, p = 0.14 NonEXP). The estimated overall cancer mortality benefit gained in EXP states after Medicaid expansion ($\Delta\Delta\Delta$) is -0.5 per 100,000 (p = NS). In EXP states, this translates to an estimated 785 less cancer deaths in 2017. Age-adjusted cancer mortality per 100,000 was worse in NonEXP states for black patients (58.5 EXP vs 63.4 NonEXP in 2017) however there was no differential mortality benefit after ACA expansion when comparing between the peri-ACA years. Of the subpopulations assessed, Hispanics in EXP states had the highest differential cancer mortality benefit at -2.1 per 100,000 (p = 0.07). **Conclusions:** This is the first study to show a directly measured cancer survival benefit from the ACA on a national scale using a comprehensive database. Hispanic populations appear to have the highest differential cancer mortality benefit after Medicaid expansion. Further study is needed to elucidate why other populations like black patients did not appear to reap the same mortality decrease. Research Sponsor: None.

2004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Survival impact of multidisciplinary thoracic oncology care in a regional healthcare system. *First Author: Raymond U. Osarogiagbon, Multidisciplinary Thoracic Oncology Program, Memphis, TN*

Background: Much-advocated, the value and impact of multidisciplinary care and planning (MDC) needs greater evidence. We compared non-small cell lung cancer (NSCLC) patient characteristics, treatment patterns and survival in a large community healthcare system spanning 3 US states with some of the highest lung cancer incidence and mortality rates. **Methods:** We identified MDC patients in the Tumor Registry NSCLC data from 2011-2017. Because the MDC program was located in metropolitan Memphis, we separated non-MDC patients by location of care resulting in 3 cohorts: MDC, non-MDC metropolitan care and non-MDC regional care. Using National Comprehensive Cancer Network guidelines, we categorized treatment by stage as 'preferred', 'appropriate' (allowable under certain circumstances). We compared demographic and clinical characteristics across cohorts using chi-squared tests and compared survival using Cox regression with Bonferroni adjustment. We repeated survival analysis with propensity matched cohorts. **Results:** Of 6259 patients, 14% received MDC, 56% metro care and 30% regional care; MDC had the highest rates of African Americans (34% v 28% v 22%), stage I-IIIB (63 v 40 v 50), urban residents (81 v 78 v 20), stage-preferred treatment rates (66 v 57 v 48), stage-appropriate treatment rates (78 v 70 v 63;), and lowest non-treatment rates (6 v 21 v 28). All $p<0.001$. Compared to MDC, the hazard for death was higher in metro (1.4, 95% confidence interval 1.3-1.6) and regional (1.7, 1.5-1.9); hazards were higher in regional care v metro (1.2, 1.1-1.3); all $p<0.001$ after adjustment. Results were similar for MDC comparisons after propensity matching with and without adjusting for preferred treatment. No differences in regional and metro cohorts. **Conclusions:** In this large community-based healthcare system, receipt of MDC for NSCLC was associated with significantly higher rates of guideline-concordant care and survival, providing strong evidence for recommending rigorous implementation of MDC. Research Sponsor: PCORI.

Care Setting Cohorts*	Hazard Ratio (95% Confidence Interval)	Pvalue	Bonferroni Adjusted Pvalue
Propensity matched†			
Metro v MDC	1.5 (1.2, 1.8)	0.001	0.003
Regional v MDC	1.7 (1.4, 2.2)	<.001	<.001
Regional v Metro	1.2 (1.0, 1.4)	0.058	0.139
Propensity matched adjusting for preferred treatment			
Metro v MDC	1.4 (1.1, 1.8)	0.006	0.018
Regional v MDC	1.5 (1.15, 1.9)	0.003	0.007
Regional v Metro	1.1 (0.9, 1.3)	0.525	0.800

*MDC-multidisciplinary care, Metro-non-MDC metropolitan care, Regional- non-MDC regional care; †matched on age, race, sex, insurance, rurality, and clinical stage.

2005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Barriers to prescribing targeted therapies for NSCLC patients with highly actionable gene variants in the VA National Precision Oncology Program. *First Author: Vishal Vashistha, Duke University Health System/Durham VA Health Care System, Durham, NC*

Background: Next-Generation Sequencing (NGS) gene panels are often completed to guide therapeutic decisions for patients with advanced stage non-small cell lung cancer (NSCLC). Patients with highly-actionable gene variants may experience improved therapeutic treatments and reduced toxicities with use of targeted agents. Ensuring appropriate prescription of targeted therapies is therefore of high importance. We sought to identify barriers to targeted agent use within the Veterans Health Affairs' (VHA) National Precision Oncology Program (NPOP). **Methods:** A retrospective evaluation examined the cohort of NSCLC patients who underwent NGS multi-gene panels through NPOP between July 2015 and February 2019. A level of evidence for drug actionability was assigned to each observed oncogenic gene variant using an artificial intelligence offering (IBM Watson for Genomics: WfG). WfG level 1 and 2A evidence was reviewed by NPOP staff to exclude gene variants that did not conform to NPOP level 1 and 2A definitions. Anti-neoplastic drug prescriptions and oncology provider notes were obtained for all included patients from the VHA Corporate Data Warehouse. Review of clinical notes of patients who did not receive targeted agents was performed to categorize the reason(s). **Results:** Of 1764 NSCLC patients who successfully underwent NGS gene panel testing, 156 (8.9%) received therapeutic level 1 (7.3%) or 2A (1.6%) options for targeted agents based on WfG evidence analysis. In total, 117 (6.6%) patients had NPOP level 1 and 2A gene variants, all within *ALK*, *BRAF*, *EGFR*, *ERBB2*, *MET*, and *RET*. Of these, 49 (41.2%) patients were not prescribed available targeted agents. The three most common reasons were: (1) treating provider did not comment on NGS results (30.7%), (2) patient did not carry a diagnosis of advanced stage disease (18.4%), and (3) patient had begun an alternative systemic therapy prior to completion of sequencing (16.3%). No patient was denied access to a level 1 or 2A targeted drug due to utilization-management review. **Conclusions:** A substantial minority of patients with advanced NSCLC bearing highly-actionable gene variants are not prescribed available targeted agents. Further provider- and pathologist-directed educational effort are needed, as well as implementation of health informatics systems to provide near real-time decision support for test ordering and interpretation. Research Sponsor: None.

2006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Launch prices and price developments of cancer drugs in the United States and Europe. *First Author: Kerstin Noëlle Vokinger, Harvard Medical School, Program on Regulation, Therapeutics, and Law/University of Zurich, Boston, MA*

Background: Cancer drug costs are rising in the US and Europe. While drug manufacturers set prices without restriction in the US, European countries have regulations that allow national authorities to directly negotiate drug prices at launch and over time. We analyzed and compared the launch prices and price developments of cancer drugs in the US, Germany, Switzerland and England. **Methods:** We identified new drugs indicated to treat solid tumors in adults that were FDA-approved between 2009 and 2019 and had also been approved by the EMA and Swissmedic by 31 December 2019. Launch prices and post-launch price changes as of 1 January 2020 were extracted and adjusted to average sales prices for monthly treatment costs in the US and compared to comparable currency-adjusted ex-factory monthly treatment costs in Germany, Switzerland, and England. A cross-sectional analysis was conducted to infer yearly trends in launch prices and post-launch price changes across the countries. **Results:** The study cohort included 42 drugs for solid tumors, of which 40 (95%) drugs were first approved in the US compared to Germany and England, and 41 (98%) to Switzerland. Average launch prices for monthly treatment costs per patient were $15,178 in the US vs $7,049 in Germany, $7,421 in Switzerland and $8,176 in England, i.e., 215% (interquartile range [IQR] 263%-187%), 205% (IQR 202%-185%) and 186% (IQR 166%-189%) higher in the US compared to Germany, Switzerland and England respectively. Post-launch prices of 36 (86%), 40 (95%), and 38 (90%) drugs decreased over time with total savings of monthly treatment costs for all drugs in the study cohort of $86,744, $44,936, and $1744 in Germany, Switzerland, and England respectively. By contrast, prices of 8 (19%) drugs decreased, while 34 (81%) increased post-launch in the US with total additional expenses of $128,192 for monthly treatment costs. **Conclusions:** Launch prices for cancer drugs are far higher in the US than in Germany, Switzerland, or England. These price disparities continue to increase substantially after market entry since cancer drug prices, in general, decrease over time in Europe and increase in the US. Spending on cancer drugs could be reduced in the US if it adopted the principles used to more effectively negotiate drug prices in Europe. Research Sponsor: Swiss Cancer Research Foundation.

2007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

The BRCA founder outreach study: Initial results of a digital health model. *First Author: Kelly Morgan, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: NCCN now endorses BRCA founder mutation genetic testing (GT) via longitudinal studies in all Ashkenazi Jewish (AJ) individuals. The BRCA Founder OutReach (BFOR) study offers pre-GT online education with posttest engagement of primary care providers (PCPs). **Methods:** The study in 4 US cities enrolls those age > 25 with > 1 AJ grandparent. Participants enroll online with chatbot and video education, have GT at local centers, receive results from their PCP or BFOR staff, and are surveyed 12 weeks post disclosure and annually for 5 years. Univariate analyses and multivariable (MV) logistic regression models were used to evaluate characteristics associated with not completing GT, selecting PCP to disclose GT, and positive GT. **Results:** As of January 2020, 4754 participants consented (77.5% female, median age 51); 37.7% never previously considered GT. Cancer family histories (FHx) were 56.4% low risk (LR), 36.4% high risk (HR), and 7.2% had a familial mutation (FM). To date, 3658 participants (76.9%) completed and 677 (14.2%) did not complete GT; the remainder are pending. Only 34.8% of participants selected PCP to disclose GT, and 42.6% of PCPs agreed. Of the 124 mutation carriers (3.4%) identified, 60.5% had a FM. At the 12-week survey, 65.4% of mutation carriers planned to proceed with recommended screening or scheduled risk reducing surgery; 3.5% of those with negative GT and HR FHx reported further GT. Satisfaction was high (mean 9.58/10, SD 1.12) and unrelated to result ($p>.05$). **Conclusions:** A digital model for founder mutation testing engaged those with LR FHx and no prior experience with GT. Older participants were more likely to complete the study. Males were less likely to enroll but more likely to carry mutations. The majority of those who tested positive had a FM. A minority of results were disclosed by PCPs. Continued follow up is needed to determine long term outcomes. Research Sponsor: The Sharon Levine Corzine Foundation, Breast Cancer Research Foundation, Basser Center for BRCA, Nancy Ann Mellen Fund for Hereditary Cancer Research, Robin and Ken Isaacs, Brooke and Eric Meltzer, Jerold O. and Abbe Beth Young, Anonymous Donors.

Select variables included in MV analysis.

	Fail to complete GT	MV p value	Select PCP to disclose GT	MV p value	Positive GT	MV p value
Age ≥51/<51	6.5%/13.8%	<.001	39.6%/29.7%	<.001	2.8%/4.1%	NS
Male/Female	7.1%/8.9%	NS	33.9%/34.8%	NS	8.1%/2.0%	<.001
Has children (yes/no)	7.4%/11.4%	NS	36.1%/30.1%	NS	2.9%/5.1%	0.044
FHx LR	9.0%	ref	34.7%	ref	1.0%	ref
FM	4.8%	<0.006	26.5%	0.015	27.1%	<0.001
HR	8.1%	NS	36.1%	NS	2.2%	0.003
Baseline cancer specific distress ≤/>5.0 (median)	7.7%/8.5%	NS	34.8%/35.5%	NS	2.7%/4.0%	0.013
Provider previously recommended GT (yes/no)	8.1%/8.5%	NS	46.0%/33.8%	0.004	4.2%/3.3%	NS
Has PCP (yes/no)	9.5%/12.8%	NS	37.9%/4.6%	<0.001	3.1%/6.1%	NS

NS= not significant by MV analysis ref= reference for FHx comparisons

2008 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Randomized trial of web-based genetic education versus usual care in advanced cancer patients undergoing tumor genetic testing: Results from the ECOG-ACRIN NCI Community Oncology Research Program (NCORP; EAQ152) COMET trial. *First Author: Angela R. Bradbury, University of Pennsylvania, Philadelphia, PA*

Background: Enthusiasm for precision oncology may obscure the complex psychosocial and ethical considerations for tumor genetic testing. Low patient genetic knowledge has been documented and heightens the risk for adverse experiences. We developed a web-based intervention to increase genetic knowledge and decrease distress among advanced cancer patients undergoing tumor genetic testing. **Methods:** 594 patients (80% from NCORP Community Sites) were recruited and randomized to web-intervention (n = 293) or usual care (n = 301), prior to receipt of tumor genetic test results. Primary outcomes were genetic knowledge, anxiety, depression, and cancer-specific distress measured at T0 (prior to intervention), T1 (post-intervention), T2 (after receipt of tumor results) and T3 (3 months post receipt of tumor results). Secondary outcomes included satisfaction, regret and disappointment. The effect of web-intervention was evaluated using t-test, multiple linear regression and logistic regression, with an intent-to-treat approach. **Results:** Patients randomized to web-intervention had better knowledge improvement than those randomized to usual care (T1-T0, $p < 0.0001$; T2-T0, $p = 0.003$). No difference was observed in change scores for anxiety, depression or cancer-specific distress. To find the moderators of intervention effect (including sex, age, education, and literacy) two 2-way interactions were noted with statistical significance: higher depression among those in the intervention arm versus the control arm for patients with lower literacy ($p = 0.03$); and lower cancer-specific distress among women in the intervention arm than with usual care but no such effect noted in men ($p = 0.01$). 71% of patients reported receiving tumor test results and this did not differ by arm. Only 20% of patients reported regret and disappointment at T2, which was more likely for those without a mutation of interest (MOI) detected vs those with a MOI detected (OR = 2.08, 95% CI, 1.13 to 3.83, $p = 0.02$). **Conclusions:** Web-based education prior to receipt of tumor genetic test results increases patient understanding of tumor genetic testing. While the intervention did not significantly reduce distress, results suggest that women who received the intervention had lower cancer-specific distress than those with usual care. Future refinements to the web-intervention are needed to address low literacy groups, men and patients with no actionable results. Clinical trial information: NCT02823652. Research Sponsor: U.S. National Institutes of Health.

2009 Poster Discussion Session; Displayed in Poster Session (Board #1), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Prospective validation of a machine learning algorithm to predict short-term mortality among outpatients with cancer. *First Author: Chris Manz, University of Pennsylvania, Philadelphia, PA*

Background: Oncologists accurately identify only 35% of patients with cancer who will die in six months. There is an urgent need for automated, accurate prognostic systems to inform treatment and advance care planning in oncology. We assessed the prospective performance of a previously described ML algorithm (Parikh et al, JAMA Netw Open, 2019) to predict short-term mortality in a cohort of general oncology outpatients. **Methods:** Our prospective cohort consisted of patients aged ≥18 years who had a medical or gynecologic oncology encounter between March 1 and April 30, 2019 in either a tertiary academic practice or one of twelve community practices within a large academic cancer system. We used a retrospectively validated gradient-boosting ML algorithm, based on 559 structured electronic health record (EHR) variables, to predict 180-day mortality prior to each oncology encounter. For patients with multiple encounters, we selected the last encounter to assess performance. We assessed several performance metrics, including area under the receiver operating curve (AUC), area under the precision-recall curve (AUPRC), scaled Brier score (sBrier; a measure of calibration ranging from 0 [random] to 1 [perfect]), and positive predictive value (PPV). **Results:** Of 25,537 unique patients, median age was 64.4 (interquartile range 53.3 – 73.0), 76.8% were White, 56.5% were treated at a community center, and 4.1% died within 180 days. The ML algorithm had an AUC of 0.89 (95% confidence interval [CI] 0.88-0.90), AUPRC 0.34, and sBrier 0.29. At a prespecified threshold of 40%, observed 180-day mortality was 44.5% (95% CI 40.7 – 48.4%) in the high-risk group vs. 3.0% (95% CI 2.8% – 3.3%) in the low-risk group. There was an 85-fold difference in mortality (13.6% vs. 0.16%) in the top vs. bottom risk quartiles. The model was well-calibrated for mortality risks ≤40% and slightly under-calibrated for mortality risks > 40%. Performance varied across cancer types in the tertiary hospital but did not vary by race or practice type (Table). **Conclusions:** In this prospective cohort study among outpatients with cancer, a ML prognostic algorithm based on EHR data had better discrimination and calibration that published cancer-specific models. This is one of the first ML prognostic models to be prospectively validated in oncology. Research Sponsor: University of Pennsylvania Center for Precision Medicine.

	AUC	PPV
OVERALL	0.89	0.45
Tertiary center	0.89	0.45
· **Breast**	0.96	0.56
· **Myeloma**	0.91	0.59
· **Lymphoma**	0.91	0.46
· **Genitourinary**	0.88	0.38
· **Gastrointestinal**	0.85	0.40
· **Thoracic**	0.82	0.40
Community practices	0.89	0.44
Black	0.91	0.46
White	0.89	0.45

2010 Poster Discussion Session; Displayed in Poster Session (Board #2), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Multi-institutional comparative effectiveness of advanced cancer longitudinal imaging response evaluation methods: Current practice versus artificial intelligence-assisted. *First Author: Andrew Dennis Smith, University of Alabama at Birmingham, Birmingham, AL*

Background: Current-practice methods to evaluate advanced cancer longitudinal tumor response include manual measurements on digital medical images and dictation of text-based reports that are prone to errors, inefficient, and associated with low inter-observer agreement. The purpose of this study is to compare the effectiveness of advanced cancer longitudinal imaging response evaluation using current practice versus artificial intelligence (AI)-assisted methods. **Methods:** For this multi-institutional longitudinal retrospective study, body CT images from 120 consecutive patients with multiple serial imaging exams and advanced cancer treated with systemic therapy were independently evaluated by 24 radiologists using current-practice versus AI-assisted methods. For the current practice method, radiologists dictated text-based reports and separately categorized response (CR, PR, SD, and PD). For the AI-assisted method, custom software included AI algorithms for tumor measurement, target and non-target location labelling, and tumor localization at follow up. The AI-assisted software automatically categorized tumor response per RECIST 1.1 calculations and displayed longitudinal data in the form of a graph, table, and key images. All studies were read independently in triplicate for assessment of inter-observer agreement. Comparative effectiveness metrics included: major errors, time of image interpretation, and inter-observer agreement for final response category. **Results:** Major errors were found in 27.5% (99/360) for current-practice versus 0.3% (1/360) for AI-assisted methods ($p < 0.001$), corresponding to a 99% reduction in major errors. Average time of interpretation by radiologists was 18.7 min for current-practice versus 9.8 min for AI-assisted method ($p < 0.001$), with the AI-assisted method being nearly twice as fast. Total inter-observer agreement on final response categorization for radiologists was 52% (62/120) for current-practice versus 75% (90/120) for AI-assisted method ($p < 0.001$), corresponding to a 45% increase in total inter-observer agreement. **Conclusion:** In a large multi-institutional study, AI-assisted advanced cancer longitudinal imaging response evaluation significantly reduced major errors, was nearly twice as fast, and increased inter-observer agreement relative to the current-practice method, thereby establishing a new and improved standard of care. Research Sponsor: None.

2011 Poster Discussion Session; Displayed in Poster Session (Board #3), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Prospective study of an AI enabled online intervention to increase delivery of guideline compliant cancer care, on the ground. *First Author: C. S. Pramesh, Director, National Cancer Grid, Mumbai, India*

Background: Despite survival benefits of guideline compliant cancer care, under treatment and over treatment are prevalent. Navya is an AI enabled online intervention that matches a patient's medical record with NCCN and NCG guidelines (National Cancer Grid, India) and layers live multidisciplinary expert review to recommend actionable treatment plans. It was developed to standardize care and mitigate morbidity and mortality, by delivering on-t ime, guideline based expert treatment plans. **Methods:** From July 2019 to January 2020, all patients who received a Navya treatment plan based on guidelines and live expert review were included. Intended treatment plans were prospectively collected from the patient. Compliance of intended plans with NCCN (including Resource Stratified Framework) or NCG was measured. Noncompliant intended plans were categorized as overtreatment or undertreatment. After delivery of Navya plan, prospective phone follow up assessed whether noncompliant intended plans were changed to guideline compliant care. **Results:** Of 1707 consecutive patients who received a Navya plan, 1549 intended plans were available. Patients were diverse with respect to geographic, socioeconomic, and primary tumor distribution: West of India: 28%, North: 26%, East: 21%, South: 15%, Central: 7%, International: 3%; 35% of patients with income < $300/month; GI: 23%, Breast: 14%, Head & Neck: 11%, Thoracic: 10%. Of the 1549 intended plans, 441 (28.47% (95% CI ± 0.26%)) were not compliant with NCCN or NCG. Undertreatment was 35%, overtreatment 26%, incomplete staging workup 28% and 11% could not be categorized. Of 441 patients with noncompliant intended plans, 80.19% (± 0.97%) shared the Navya plan with their treating oncologists and 50.40% (± 0.88%) changed their intended plan to receive the Navya treatment plan. Intervention with Navya increased on-the -ground guideline compliance by ~15% (from 71.53% ±0.42% to 85.87% ± 1.73%). **Conclusions:** Guideline compliant care ensures best achievable clinical outcomes with existing therapies. A technological earthshot that significantly increases adoption of guideline based care is the first step towards cancer moonshots. Research Sponsor: None.

2012 Poster Discussion Session; Displayed in Poster Session (Board #4), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Four distinct patient-reported outcome (PRO) trajectories in longitudinal responses collected before, during, and after chemotherapy. *First Author: Douglas W. Blayney, Stanford University, Stanford, CA*

Background: Cancer chemotherapy, whether given with curative or palliative intent, is toxic. Toxicity is routinely captured in clinical trials by investigator observation and increasingly by PRO. The ability to capture PRO in the routine treatment workflow has been standard at Stanford since 2015 (Roy et al ASCO 2020). Analysis of longitudinally captured, real world PRO and prospectively identifying patients (pts) whose quality of life (QOL) is at risk of deteriorating either permanently or temporarily is needed. Routine serial PRO measurement should enhance precision care delivery, precision toxicity detection and management. **Methods:** We identified patients undergoing chemotherapy at Stanford and analyzed PROMIS (PRO Measurement Information System) responses. Pts with PROMIS survey information at three intervals—pre-treatment, during chemotherapy and post chemotherapy—were identified. We evaluated global physical health (GPH) and global mental health (GMH). Pts with a clinically significant decrease (CSD) in GPH or GMH scores were identified. A k-median cluster analysis was used to identify patient trajectory clusters and a machine-learning model was applied to identify risk factors for CSD and predict CSD. **Results:** We identified 670 adult oncology patients undergoing chemotherapy who completed at least one PROMIS survey in each interval. GPH scores were 48.4 $\pm$ 9.1 before, 47.1 $\pm$ 8.5 during, and 48.5 $\pm$ 8.9 after chemotherapy and GMH scores were 50.5 $\pm$ 8.2, 49.1 $\pm$ 8.5, and 50.7 $\pm$ 9.0, respectively. The majority of patients did not have a CSD in GPH or GMH post treatment compared to pretreatment scores. Pretreatment scores were the strongest predictor of a CSD in GPH and GMH. Trajectory clustering identified four distinct trajectories: Temporary Improver, Temporary Deteriorator, Improver, Inexorable Deteriorators. We were not able to predict any cluster based on pre-treatment features. **Conclusions:** Using routinely collected PROMIS surveys in a real-world setting, we are able to predict patients with post-treatment decreases in their physical and mental well-being. We further defined four novel patient trajectories during chemotherapy, which could guide personalized supportive interventions to improve patient's chemotherapy experience. Identification of patients at risk for deterioration and the patterns of deterioration could help guide efficient deployment of toxicity mitigating and supportive care interventions to patients most in need. Research Sponsor: U.S. National Institutes of Health.

2013 Poster Discussion Session; Displayed in Poster Session (Board #5), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Patient-reported care satisfaction and symptom burden in hospitalized patients with cancer. *First Author: Emilia R. Kaslow-Zieve, Massachusetts General Hospital, Boston, MA*

Background: Hospitalized patients with cancer often experience high symptom burden, which may impact their care satisfaction and use of health care services. Yet, studies describing these patients' care satisfaction, symptom burden, and health care utilization are lacking. **Methods:** We prospectively enrolled patients with cancer and unplanned hospitalizations from 9/2014-4/2017. Upon admission, patients self-reported their care satisfaction (FAMCARE items asking about satisfaction regarding speed with which symptoms are treated and coordination of care) and physical (Edmonton Symptom Assessment System [ESAS]) and psychological (Patient Health Questionnaire 4 [PHQ4]) symptom burden. We used regression models to identify patient factors associated with care satisfaction. We also explored associations between patients' care satisfaction, symptom burden, and hospital length of stay (LOS) in models adjusted for age, sex, marital status, comorbidity score, cancer type, cancer documented as curable/incurable, time since cancer diagnosis, and admission to a dedicated oncology service. **Results:** We enrolled 1,576 of 1,749 (90.1%) consecutive patients (mean age = 63.19$\pm$13.39 years, 46.3% female). Most reported being very satisfied/satisfied with the speed with which symptoms are treated (89.0%) and coordination of care (90.1%). Older age (B = 0.01, $P < .02$ for both) and admission to a dedicated oncology service (B = 0.20, $P < .01$ for both) were each independently associated with higher satisfaction with the speed with which symptoms are treated and coordination of care. Higher satisfaction with the speed with which symptoms are treated was associated with lower PHQ4 depression (B = -0.14, P = .01), PHQ4 anxiety (B = -0.11, $P < .01$), ESAS physical (B = -1.30, $P < .01$), and ESAS total (B = -2.44, $P < .01$) symptoms. Higher satisfaction with coordination of care was associated with lower PHQ4 depression (B = -0.14, P = .02), PHQ4 anxiety (B = -0.16, $P < .01$), ESAS physical (B = -1.30, $P < .01$), and ESAS total (B = -2.75, $P < .01$) symptoms. Satisfaction with the speed with which symptoms are treated (B = -0.47, P = .03) and coordination of care (B = -0.50, P = .03) were both associated with shorter hospital LOS. **Conclusions:** Most hospitalized patients with cancer reported high care satisfaction, which was associated with older age and admission to a dedicated oncology service. We found relationships among higher care satisfaction, lower symptom burden, and shorter hospital LOS, underscoring the importance of efforts to enhance symptom management and care coordination in this population. Research Sponsor: Massachusetts General Hospital Cancer Center.

2014 Poster Discussion Session; Displayed in Poster Session (Board #6), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Mapping PRO-CTCAE responses to clinician-graded adverse events, dose reductions, interruptions, and discontinuations in phase I cancer trials. *First Author: Geoffrey Alan Watson, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Typically symptomatic adverse events (sy-AEs) on clinical trials are reported by clinicians using the CTCAE. To complement clinician collected sy-AEs and understand tolerability better, the patient report outcome version of the CTCAE (PRO-CTCAE) has been developed to provide the patient (pt) perspective on severity of AEs (graded scale 0-4) and their interference in daily life (scale 0-4). The aim of this study was to correlate PRO responses with the grade (G) of AEs, dose interruptions/reductions and dose limiting toxicities (DLTs). **Methods:** Pts enrolled on phase 1 clinical trials at Princess Margaret were surveyed electronically on tablet using the full library of items for PRO-CTCAE. The PRO-CTCAE was administered at baseline (prior to therapy), mid-cycle 1, and mid-cycle 2. AEs on study were recorded by physicians using the CTCAE. The electronic medical records were analyzed for an association between reported sy-AEs and PRO score. Summary statistics were used to describe patient and disease characteristics, as well as the outcomes. Spearman's method was used to correlate PRO severity and interference responses. Logistic regression was used to assess which factors were associated with CTCAE G 3-4 vs G 2 AEs. **Results:** We analyzed 158 pts: median age 60yrs, 77 (49%) were male; all were ECOG $\leq$1 and 22, 55 and 81 pts completed 1, 2 and 3 surveys, respectively. Clinician reported G2, 3 and 4 sy-AEs occurred in 81, 47 and 3 pts, respectively and all of these were related to a PRO item except 5% (4/81), 9% (4/47) and 33% (1/3), respectively because either the AE occurred after 3rd time point or patient not able to complete the PRO (encephalitis). Sy-AEs causing dose interruptions, reductions, DLTs and discontinuations occurred in 45 (28%), 12 (7.5%), 5 (3%) and 12 (7.5%) pts, respectively; with a corresponding PRO item in 40 (89%), 12 (100%), 4 (80%) and 11(92%) pts, respectively. For patients who had CTCAE G2, G3/4 AEs, interruptions and discontinuations, their severity and inference levels were positively correlated (coefficient 0.49, $p < 0.001$; 0.45, $p < 0.001$ 0.59, $p < 0.001$, 0.86, $p < 0.001$). Dose interruptions (p = 0.0027) and reductions (p = 0.0061) were significantly associated with G3-4 compared to G2 AEs. **Conclusions:** This is the first time an association between PRO-CTCAE severity and interference; and CTCAE G2, 3, 4 AEs, dose interruptions and discontinuations has been demonstrated. Additional modelling and more patient data are being analyzed to explore the relationship. Research Sponsor: None.

2015 Poster Discussion Session; Displayed in Poster Session (Board #7), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Cancer diagnoses and survival rise as 65-year-olds become Medicare eligible. *First Author: Deven C. Patel, Stanford University, Stanford, CA*

Background: A "Medicare effect" has been described to account for increased health care utilization occurring at the age of 65, when individuals become eligible for government-sponsored health care. The existence of such an effect in cancer care, where it would be most likely to reduce mortality, has been unclear. **Methods:** Patients aged 61-69 diagnosed with lung, breast, colon, or prostate cancer from 2004-2016 were identified using the Surveillance, Epidemiology, and End Results database and dichotomized based on eligibility for Medicare (age 61-64 vs 65-69). Using age-over-age percent change calculations, trends in cancer diagnosis, AJCC staging, and survival were characterized. **Results:** 134,991 patients were identified with lung cancer; 175,558 with breast; 62,721 with colon; and 238,823 with prostate. The age-over-age growth in the number of cancer diagnoses was highest at age 65 when compared to all other ages within the decade, for all four cancers (Table: $p<0.01$, $p<0.001$, $p<0.01$, $p<0.001$ respectively). Comparing age 65 diagnoses to the 61-64 year old cohort, the greatest difference for all four cancers was seen in stage I (lung $p<0.001$; breast $p<0.002$; colon $p<0.001$; prostate $p<0.02$). The older (65-69), Medicare-eligible cohort had higher cancer specific 5-year survival than the 61-64 aged cohort for lung (22.0% vs 21.0%, $p<0.01$) and colon cancer (66.2% vs 63.2%, $p<0.01$). **Conclusions:** The 65 age threshold for Medicare eligibility is associated with more cancer diagnoses, particularly in stage I, resulting in improved cancer-specific survival for some cancers. Near-elderly individuals may be delaying care until the age of 65. A Medicare-for-all system would thus be likely to reduce cancer mortality. Research Sponsor: None.

Age-over-age percent change in number of cancer diagnoses.

		61	62	63	64	65	66	67	68	69
Lung	**Cancer**									
	Incidence	13,000	13,438	13,869	14,433	15,835	15,728	16,059	16,408	16,221
Δ	N/A	3.4%	3.2%	4.1%	**9.7%***	-0.7%	2.1%	2.2%	-1.1%	
Breast	**Cancer**									
	Incidence	20,996	20,832	20,464	19,469	21,312	19,624	18,538	17,620	16,739
Δ	N/A	-0.8%	-1.8%	-4.9%	**9.5%***	-7.9%	-5.5%	-5.0%	-5.0%	
Colon	**Cancer**									
	Incidence	6,526	6,604	6,749	6,861	7,893	7,154	7,144	7,068	6,732
Δ	N/A	1.2%	2.2%	1.7%	**15.0%***	-9.4%	-0.1%	-1.1%	-4.8%	
Prostate	**Cancer**									
	Incidence	23,772	25,112	26,019	25,888	30,183	28,392	27,794	26,667	24,996
Δ	N/A	5.6%	3.6%	-0.5%	**16.6%***	-5.9%	-2.1%	-4.1%	-6.3%	

Δ denotes age-over-age (AoA) percent change – comparing incidence for a specific age with the previous age year *P-values of T-tests comparing AoA percent change at age 65 vs all other ages: lung: < 0.01, breast: < 0.001, colon: < 0.01, prostate: < 0.001

2016 Poster Discussion Session; Displayed in Poster Session (Board #8), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Association between a national insurer's pay-for-performance program for oncology and changes in prescribing of evidence-based cancer drugs and spending. *First Author: Justin E. Bekelman, University of Pennsylvania, Department of Radiation Oncology, Philadelphia, PA*

Background: Efforts to standardize quality and control cost growth for cancer care have focused heavily on promoting evidence-based cancer drug prescribing. We evaluated the association between a national commercial insurer's ongoing pay-for-performance (P4P) program for oncology and changes in prescribing of evidence-based cancer drugs and spending. **Methods:** Retrospective difference-in-differences quasi-experimental study utilizing administrative claims data from the insurer's commercial health plans in 14 states covering 6.7% of US adults. We included patients 18 years of age or older with breast, colon, or lung cancer who were prescribed cancer drug regimens by 1,867 participating oncology physicians between 2013 and 2017. We leveraged the geographically staggered, time-varying rollout of the P4P program to simulate a stepped-wedge study design. Specifically, we estimated a patient-level model clustered by physician and used physician fixed-effects to examine pre- to post-intervention changes in evidence-based prescribing and spending for patients of participating physicians eligible earlier versus later in the period of P4P program rollout. We evaluated four categories of spending over a 6-month episode period: cancer drug spending; other (non-cancer drug) health care spending; total episode spending; and patient out-of-pocket spending. **Results:** The P4P program was associated with an increase in evidence-based regimen prescribing from 57.1% of patients in the pre-intervention periods to 62.2% in the post-intervention periods for a difference of +5.1 percentage points (pp) (95% CI 3.0 pp to 7.2 pp, $P< 0.001$). The P4P program was also associated with a differential $3,235 (95% CI $1,004 to $5,466, $P= 0.005$) increase in cancer drug spending, a differential $253 (95% CI $101 to $406, $P= 0.001$) increase in patient out-of-pocket spending, but no significant changes in other health care spending or total health care spending over the 6-month episode period. **Conclusions:** A national insurer's oncology P4P program was associated with a 5.1 percentage point increase in prescribing of evidence-based cancer drug regimens. Our findings suggest that P4P programs may be effective in increasing evidence-based cancer drug prescribing at national scale -- enhancing cancer care quality. However, they may also increase out-of-pocket expenses and may not lead to savings in total health care spending during the 6-month episode. Research Sponsor: None.

2017 Poster Discussion Session; Displayed in Poster Session (Board #9), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Out-of-pocket cost of screening with breast MRI for women at high risk for breast cancer. *First Author: I-Wen Pan, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: The prevention provision of Affordable Care Act (ACA) mandates private insurance to waive cost sharing for preventive services with grade A or B recommendations from the US Preventive Services Task Force. Although several professional societies have recommended augmenting screening mammography with MRI for women at high risk for breast cancer, the ACA prevention provision does not apply to screening MRI. This study examined the proportion of high-risk women having zero cost sharing associated with breast MRI for screening purposes and estimated out of pocket (OOP) costs as well as sources of variations. **Methods:** We identified women who underwent MRI and mammography for breast cancer screening from Marketscan database, 2009-2017. We quantified OOP costs as the sum of copayment, coinsurance, and deductible and defined zero cost sharing as having no OOP cost. We calculated the proportion of zero cost sharing for mammography and that for MRI and compared the time trend of each before and after ACA (enacted in 2010). We used multivariable logistic regression to examine factors associated with zero cost sharing for MRI use. We estimated OOP costs of MRI and examined cost variations by geographic regions or whether a woman had high deductible plans. **Results:** 25,232 women were included in the analysis. For screening mammography, the rate of zero cost sharing increased from 81% in 2009 to 91% in 2011 (post ACA) then 97% in 2017. For MRI, the rate was 41%, 37%, and 25%, respectively. The odds ratio (OR) of zero cost sharing for MRI screening was significantly lower for women with high deductible plans (OR = 0.65, 95% CI: 0.59-0.72) and for those resided in South (vs. Northeast) region (OR = 0.50, 95% CI: 0.46-0.53), after controlling for age, MSA, family breast cancer history, and year. OOP costs of MRI varied by region and insurance plan (Table); the mean OOP cost for women with high deductible plan were more than twice the mean cost for those in other plan types. **Conclusions:** With the financial protection under the ACA prevention provision applying to only screening mammography, many women at high risk for breast cancer are subject to high OOP costs for MRI screening. Those enrolled in high deductible plans and resided in the South are especially vulnerable financially. Research Sponsor: U.S. National Institutes of Health.

OOP costs (USD) for screening MRI, by insurance plan and region.

Subgroup	Category	No. of Cases	Mean	STD	P25	Median	P75
Total		25232	271	449	0	88	359
High Deductible	No	22602	240	403	0	76	323
	Yes	2630	537	682	3	246	843
Region	Northeast	7159	189	411	0	20	172
	Midwest	5183	295	459	0	123	393
	South	7994	331	486	0	162	462
	West	4896	265	412	0	113	362

2018 Poster Discussion Session; Displayed in Poster Session (Board #10), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Post-hoc power of clinical trials supporting anticancer drug approval by FDA. *First Author: Michelle Nadler, Princess Margaret Cancer Centre and University of Toronto, Toronto, ON, Canada*

Background: Regulatory approval of drugs is based typically on randomized control trials (RCTs) observing statistically significant superiority of an experimental agent over a prior standard. Statistical significance can result from large effect size and/or over-sampling (as a result of large sample size or long follow-up). Here we explore the source(s) of statistically significant results in trials supporting anti-cancer drug approval by the FDA. **Methods:** We searched Drugs@FDA to identify anti-cancer drug approvals for solid tumors (excluding lymphoma) from 2015-2019. We retrieved corresponding manuscripts and associated appendices and extracted data on study characteristics, statistical plan, primary outcomes and accrual and follow-up times. Post-hoc power was calculated based on observed results and was compared to expected effect size and power in the statistical plan. We explored associations with higher than expected power resulting from over-sampling using binary logistic regression. **Results:** We identified 75 unique drug-approvals reporting 94 endpoints. The most common tumour types were lung, breast, melanoma, and renal cell carcinoma. The most common endpoints were progression free survival and overall survival (OS). In 74 endpoints (79%), observed power was greater than expected power. The magnitude of higher than expected power ranged from 0.1 to $>$ 20%. Of these, 59 (80%) had an effect size greater than predicted in the statistical plan. In 44/74 over-powered endpoints (60%), post-trial power was 100%. When post-hoc power was calculated based on expected effect size rather than observed effect size, 50 endpoints (85%) remained over-powered. Higher than expected power resulting from over-sampling was associated with OS compared to other endpoints (OR 3.03), with targeted agents compared to immunotherapy (OR 1.63) and inversely associated with year of approval (OR 0.57). **Conclusions:** Most cancer drug approvals result from statistically significant studies which are over-powered due to greater than anticipated effect size. Approximately 1 in 5 studies are over-powered likely due to over-sampling. In this setting, benefit observed in RCTs may not translate to the real-world setting. Research Sponsor: None.

2019 Poster Discussion Session; Displayed in Poster Session (Board #11), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Methodology, results, and publication of oncology clinical trials: Insights from all the world's randomized controlled trials (RCTs) 2014-2017. *First Author: Shubham Sharma, Queen's University, Kingston, ON, Canada*

Background: Clinical cancer research is now a global effort. Most published overviews of oncology trials are restricted to a specific disease site or cohort of high-profile journals. Here we describe authorship, trial characteristics, design, and results of all oncology RCTs published globally during 2014-2017. **Methods:** A structured literature search was designed using PUBMED to identify all RCTs evaluating anti-cancer therapies published during 2014-2017. Data were captured regarding authorship, participants, study characteristics, design, and results. Among superiority RCTs that met the primary endpoint (i.e. statistically "positive"), we calculated the ESMO-MCBS to identify trials with substantial clinical benefit (MCBS scores 4/5 or A/B). Outcomes were compared with Chi Square or Fisher's Exact tests. **Results:** The study cohort included 694 RCTs. The most common cancers evaluated were breast (17%, 121/694), lung (15%, 104/694) and colorectal (8%, 58/694). Treatment intent was curative, adjuvant/neoadjuvant, and palliative in 10% (68/694), 25% (176/694), and 65% (448/694) of trials respectively. Median sample size was 443 (IQR 246-718). Seventy percent (488/694) of RCTs were supported by industry; 87% (601/694) of experimental arms tested systemic therapy. Ninety-two percent (636/694) of RCTs were led by investigators in 28 high-income countries; the most common countries leading these trials were US (27%, 174/636), France (10%, 64/636), Germany (10%, 62/636), Japan (9%, 59/636), and UK (9%, 57/636). The most common primary endpoints were PFS (32%, 220/694), OS (31%, 215/694), and DFS (11%, 79/694); Forty-six percent of all trials (318/694) met their primary endpoint. Among superiority trials with "positive" results, 33% met ESMO-MCBS threshold for substantial clinical benefit. The median impact factor (IF) of journals which published the overall study cohort of trials was 21 (IQR 7-27); trials meeting their primary endpoint were published in higher profile journals (median IF 25 vs 18, $p < 0.001$). **Conclusions:** At the global level, oncology clinical trials are dominated by high-income countries and study diseases which do not necessarily reflect the global burden of cancer. The vast majority of trials are funded by industry and only one third of "positive" trials meet ESMO-MCBS threshold for substantial clinical benefit. Research Sponsor: None.

2020 Poster Discussion Session; Displayed in Poster Session (Board #12), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Absence of optimism bias in industry-sponsored cancer trials. *First Author: Sonal S Noticewala, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Randomized controlled trials (RCTs) in oncology power their studies to detect expected effect sizes. Prior studies have shown that there is optimism bias, the *a priori* overestimation of treatment effect size among cooperative-group-supported RCTs. However, it is unknown whether such bias is present among industry-supported trials. **Methods:** All published phase 3 clinical oncology RCTs were identified through ClinicalTrials.gov. Only superiority-design RCTs assessing a therapeutic intervention to improve disease-related outcomes were included. We compared the ratio of observed to expected hazard ratio (OEHRR) between trial subgroups using the Mann-Whitney U-test; comparisons of median OEHRR to a hypothetical median of 1 was performed using the Wilcoxon Signed Rank test. **Results:** We identified 140 phase 3 trials with available hazard ratio (HR) data. Of these, 123 trials (88%) were industry-sponsored, and 38 trials (27%) were cooperative-group-supported. For all trials, the median OEHRR was 1.099 (IQR = 0.855-1.291), demonstrating evidence of optimism bias when compared to a hypothetical median OEHRR of 1 ($p = 0.018$). In the subgroup analysis, compared to non-industry-sponsored trials (median OEHRR 1.253, IQR 1.061-1.334), industry-supported trials (median OEHRR 1.061, IQR 0.829-1.274) had a significantly lower OEHRR ($p = 0.022$) and did not demonstrate optimism bias ($p = 0.15$). Similarly non-cooperative group trials (median OEHRR 1.208, IQR 1.019-1.317) had a significantly lower OEHRR ($p = 0.005$) and did not demonstrate optimism bias ($p = 0.562$) compared to cooperative group trials (median OEHRR 1.208, IQR 1.019-1.317), which did demonstrate optimism bias ($p < 0.001$). **Conclusions:** Cooperative group trials, which represent a minority of trials, suffer from optimism bias. In contrast, industry-funded trials, which account for the majority of trials, do not demonstrate evidence of optimism bias, and have very close concordance between observed and expected effect size. These findings suggest that the powering and design of industry-funded trials better models the outcomes eventually observed. The reasons for this are likely complex and multifactorial, but may include financial constraint considerations, as industry-supported trials may not be as financially-limited as cooperative group studies. Therefore, industry-supported studies may be able to power trials with sufficient participants to reflect the estimated effect size. Research Sponsor: None.

2021 Poster Session (Board #13), Fri, 8:00 AM-11:00 AM

Distress screening through PROMIS at an academic cancer center and network site: Implementation of a hybrid model. *First Author: Mohana Roy, Stanford University and Stanford Cancer Institute, Stanford, CA*

Background: The NCCN guidelines recommend routine distress screening of patients with cancer, but the implementation of such programs is inconsistent. Up to one in three such patients experience distress, however fewer than half of them are identified and referred for supportive services. **Methods:** We implemented a hybrid (electronic and paper) distress screening tool, using a modified version of the PROMIS-Global Health questionnaire. Patients received either an electronic or in-clinic paper questionnaire to assess overall health and distress at the Stanford Cancer Center and its associated integrated network site. Iterative changes were made including integration with the electronic health record (EHR) to trigger questionnaires for appointments every 60 days. A consensus "positive screen" threshold was defined, with data collected on responses and subsequent referrals placed to a supportive care services platform. **Results:** Between June 2015 and December 2017, 53,954 unique questionnaires representing 12,744 distinct patients were collected, with an average completion rate of 58%. Approximately 30% of the questionnaires were completed prior to the visit electronically through a patient portal. The number of patients meeting the positive screen threshold remained ~ 40% throughout this period. Following assessment by the clinical team, there were 3763 referrals to cancer supportive services. Among the six most common referral categories, those with a positive screen were more likely to have a referral placed (OR 6.4, 95% CI 5.8-6.9 p-< 0.0001), with a sensitivity of 80% and a specificity of 61%. However, 89% of responses with a positive screen did not have a referral to supportive care services. **Conclusions:** The hybrid electronic and paper use of a commonly available patient reported outcome tool, as a high throughput distress screening tool, is feasible at a multi-site academic cancer center. Our positive screen rate for referrals was sensitive and consistent, but with a low positive predictive value. This screening also resulted in variable clinical response and overall increased clinical burden. Future directions for our group have included refining the threshold for a positive screen and implementation of a real-time response system, especially to address acute concerns. Research Sponsor: None.

2022 Poster Session (Board #14), Fri, 8:00 AM-11:00 AM

Association of hospital type and patient volume growth with timely cancer treatment. *First Author: Zachary AK Frosch, Division of Hematology & Oncology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA*

Background: Studies have suggested superior outcomes for patients with cancer treated at National Cancer Institute (NCI) and academic hospitals, leading some to advocate for complex cancer care to be delivered at regional referral centers. However, growing demand at such centers may exceed their capacity to provide timely treatment, which could be detrimental to patient outcomes. We evaluated the relationship between hospital type, the average annual growth rate in patient volume (PV), and time to treatment initiation (TTI) trends. **Methods:** We used the National Cancer Database to identify patients undergoing initial treatment for a new diagnosis of cancer (breast, lung, prostate, colorectal, melanoma, bladder, non-Hodgkin lymphoma, renal, uterine or pancreatic) in 2007-2016. The exposure was hospital type (NCI, academic, community or integrated network). The primary outcome was TTI over time. We estimated both the average annual growth rate for PV and adjusted TTI trends by hospital type using linear mixed effects models, including a hospital type-by-time interaction and, when modeling TTI, a patient volume-by-time interaction. **Results:** We identified 4,218,577 patients treated at 1351 hospitals (49% at 897 community, 23% at 177 academic, 14% at 50 NCI and 14% at 227 integrated network hospitals). Over the study period, PV grew by 40% at NCI and 25% at academic hospitals, compared to 8% at community hospitals (p-value for trend both < 0.001). Meanwhile, mean TTI increased by 3.2 days at community, remained stable at academic (+0.3 days) and decreased by 4.3 days at NCI hospitals (p-value for trend both < 0.001 vs community). A higher annual PV growth rate was associated with a statistically but not clinically significant TTI increase (0.05 days for each 100 patient/year increase in the growth rate, $p = 0.001$). **Conclusions:** Patients with newly diagnosed cancer are increasingly receiving treatment at NCI and academic hospitals. While TTI at NCI and academic hospitals is longer than in the community, PV growth has been possible without delaying cancer treatment. Further study is needed to determine whether continued growth at this rate is sustainable. Research Sponsor: None.

	Community (ref)	Academic	NCI
Patient Volume			
Mean no. patients treated (95% CI), 2007	232 (217, 248)	505 (470, 540)*	1027 (960, 1093)*
Average annual growth rate, 2007-16 - patients/year (95% CI)	2 (0.4, 4)	14 (10, 18)*	45 (38, 52)*
Time to Treatment			
Mean no. days (95% CI), 2007	34 (34, 35)*	43 (42, 45)*	52 (49, 54)*
Average annual growth rate, 2007-16 - days/year (95% CI)	0.4 (0.3, 0.4)	0.04 (-0.1, 0.2)*	-0.5 (-0.8, -0.2)*

*$p < 0.001$ compared to ref

2023 Poster Session (Board #15), Fri, 8:00 AM-11:00 AM

Are ED visits in cancer patients preventable? Care patterns before an ED visit. *First Author: Arthur Hong, University of Texas Southwestern Medical Center, Dallas, TX*

Background: Medicare's Oncology Care Model alternative payment program participation requires 24-hr patient access to clinician phone advice. Many participating practices have established oncology urgent care clinics to reduce the frequent ED visits in the early phase after cancer diagnosis. However, little is known about patients' use of pre-ED visit clinical advice via phone. We combined EHR data on phone/secure messaging encounters, outpatient visits, and regional ED visits, to assess how often patients visit the ED without prior clinical advice, and to compare ED visit severity between those with and without preceding clinical advice. **Methods:** We linked adults ages 18+ from Parkland Health and Hospital System (PHHS), the Dallas County public safety net system, and UT Southwestern (UTSW) NACR Gold-certified cancer registry (2012-2018), to their respective EHR, and identifiably linked patients to a regional health information exchange of ED and hospital encounters. Exchange data included hospital name, ED disposition, diagnoses, and ED Severity Of Illness. We tallied ED visits within 6 months (180 days) after cancer diagnosis and EHR clinical contacts for 24 hours prior to ED visit (telephone/secure messaging, outpatient visits). After descriptive statistics, we used mixed-effects multivariate logistic regression clustering at patient level to model ED disposition after a pre-ED clinical contact. **Results:** We matched 8,289 Parkland (54% female, 78% Medicaid/charity assistance) and 10,817 UTSW patients (50% female, 12% Medicaid), who generated 21,009 and 22,696 ED visits, respectively. Two-thirds of all ED visits occurred without preceding clinical contact (70.2% PHHS, 66.7% UTSW); large shares of ED visits were to 67 other regional hospitals (22.2% PHHS, 69.5% UTSW). Telephone encounters and outpatient visits to any specialty were the most common contact before ED visit (UTSW: 28.2 and 12.4%; PHHS: 8.7 and 16.1%), but while nearly all UTSW clinic visits were to oncology, only 30% of PHHS clinic visits were to oncology. Though ED visit severity was slightly higher for ED visits without preceding clinical contact (46% vs. 43% ≥Major severity, $p < 0.01$), patients were discharged home more often if clinical contact preceded ED visits (aOR of hospitalization 0.82, 95% CI: 0.74 – 0.90). **Conclusions:** Two-thirds of ED visits occurred without prior clinical contact, and though these no-contact ED visits had higher severity of illness, they were more often discharged home from the ED. Future work should identify patient-oriented options to optimize the use of clinical care and the ED. Research Sponsor: Texas Health Resources Clinical Scholars Program, U.S. National Institutes of Health.

2024 Poster Session (Board #16), Fri, 8:00 AM-11:00 AM

The impact of early integrated supportive care on length of stay at an NCI-designated cancer center. *First Author: Jessica Kaltman, City of Hope National Medical Center, Los Angeles, CA*

Background: With movement towards value-based care, institutions seek ways to reduce costs by decreasing inpatient stays. A multidisciplinary approach to supportive care, especially when provided early, is one way to realize value-based care. We assess the impact of pre-admission versus post-admission involvement of an Integrated Supportive Care Model (ICSM) on inpatient length of stay (LOS) at a NCI-designated cancer center. **Methods:** Data was collected from 2014 to 2016 at City of Hope. The Integrated Supportive Care Model at City of Hope includes: palliative care, psychiatry, psychology, interventional pain, social work, child-life, distress screening, and couples program. "Pre-admission" was defined as seeing at least one service prior to hospital admission; "Post-admission" defined as seeing at least one service during admission. "Short LOS" for hematology patients was categorized as $\leq$ 14 days and for oncology patients as $\leq$ 3 days. Continuous LOS between patients receiving an ISCM intervention pre- and post-admission was compared using Kruskal-Wallis test. Univariate and multivariable logistic regression was done to examine association between involvement of ISCM pre- and post-admission and categorical LOS. P-values < 0.05 were considered statistically significant. **Results:** 1,627 (809 with hematologic malignancy, 818 with oncologic malignancy) patients with only one hospitalization during the study time were included. For hematology patients, involvement with the ISCM pre-admission was associated with shorter LOS ($\leq$ 14 days) compared with involvement post-admission (29.3 vs 11.1%, multivariable OR = 4.08, $P < 0.001$). Median LOS for hematology patients who participated in the ISCM pre-admission was shorter than those who received ISCM services post-admission (21 vs. 22 days, $p = 0.049$). Similarly, for oncology patients, ISCM involvement pre-admission was associated with shorter LOS ($\leq$ 3 days) compared to involvement post-admission (91.4% vs 8.6%, multivariable OR = 3.74, $P < 0.001$). Median LOS for oncology patients who received an ISCM intervention pre-admission was shorter than those who received an ISCM intervention post-admission (2 vs. 6 days, $p < 0.001$). **Conclusions:** In hematologic and oncologic malignancies, use of an ISCM prior to patient's first hospitalization is associated with significantly shorter LOS compared with those who received ISCM services during the hospital stay. This suggests efforts should be made to include an ISCM early in the trajectory of illness, prior to first hospitalization. Research Sponsor: City of Hope.

2025 Poster Session (Board #17), Fri, 8:00 AM-11:00 AM

Integrating breast cancer screening into a cervical cancer screening program in three rural districts in Rwanda. *First Author: Lydia E. Pace, Brigham And Women's Hospital, Boston, MA*

Background: In low-income countries where mammography is not widely available, optimal strategies to facilitate earlier breast cancer detection are not known. We previously conducted a cluster randomized clinical trial of clinician trainings in Burera District in rural Rwanda to facilitate earlier diagnosis among symptomatic women; 1.3% of women evaluated at intervention health centers (HCs) were diagnosed with cancer. Early stage breast cancer incidence was higher in intervention areas. Subsequently, Rwanda Biomedical Centre, Rwanda's national health implementation agency, adapted the program in 3 other districts, offering screening clinical breast exams (CBE) to all women aged 30-50 years receiving cervical cancer screening and any other woman requesting CBE. A navigator facilitated patient tracking. We sought to examine patient volume, service provision and cancer detection rate in the adapted program. **Methods:** We abstracted data from weekly HC reports, facility registries, and the referral hospital's electronic medical record to determine numbers of patients seen, referrals made, biopsies, and cancer diagnoses from July 2018-December 2019. **Results:** CBE was performed at 17,239 visits in Rwamagana, Rubavu and Kirehe Districts (total population 1.34 million) over 18, 17 and 7 months of program implementation respectively. At 722 visits (4.2%), CBE was abnormal. 571 patients were referred to district hospitals (DH); their average age was 35 years. Of those referred, 388 (68.0%) were seen at DH; 32% were not. Of those seen, 142 (36.6%) were referred to a referral facility; 121 of those referred (85.2%) actually went to the referral facility. Eighty-eight were recommended to have biopsies, 83 (94.3%) had biopsies, and 29 (34.9% of those biopsied; 0.17% of HC visits) were diagnosed with breast cancer. **Conclusions:** Integrating CBE screening into organized cervical cancer screening in rural Rwandan HCs led to a large number of patients receiving CBE. As expected, patients were young and the cancer detection rate was much lower than in a trial focused on symptomatic women. Even with navigation efforts, loss-to-follow-up was high. Analyses of stage, outcomes, patient and provider experience and cost are planned to characterize CBE screening's benefits and harms in Rwanda. However, these findings suggest building health system capacity to facilitate referrals and retain patients in care are needed prior to further screening scaleup. In the interim, early diagnosis programs targeting symptomatic women may be more efficient and feasible. Research Sponsor: Breast Cancer Research Foundation.

2027 Poster Session (Board #19), Fri, 8:00 AM-11:00 AM

Pilot program of remote monitoring for high-risk patients on antineoplastic treatment. *First Author: Robert Michael Daly, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Early detection and management of symptoms in patients with cancer improves outcomes, however, the optimal approach to symptom monitoring and management is unknown. This pilot program uses a mobile health intervention to capture and make accessible symptom data for high-risk patients to mitigate symptom escalation. **Methods:** Patients initiating antineoplastic treatment at a Memorial Sloan Kettering regional location were eligible. A dedicated staff of RNs and nurse practitioners managed the patients remotely. The technology supporting the program included: 1) a predictive model that identified patients at high risk for a potentially preventable acute care visit; 2) a patient portal enabling daily ecological momentary assessments (EMA); 3) alerts for concerning symptoms; 4) an application that allowed staff to review and trend symptom data; and 5) a secure messaging platform to support communications and televisits between staff and patients. Feasibility and acceptability were evaluated through enrollment (goal $\geq$25% of new treatment starts) and response rates (completion of $>$ 50% of daily symptom assessments); symptom alerts; perceived value based on qualitative interviews with patients and providers; and acute care usage. **Results:** Between October 15, 2018 and July 10, 2019, the pilot enrolled 100 high-risk patients with solid tumors and lymphoma initiating antineoplastic treatment (median age: 66 years, 45% female). This represented 29% of patients starting antineoplastics. Over six months of follow-up, the response rate to the daily assessments was 56% and 93% of patients generated a severe symptom alert (Table). Both patients and providers perceived value in the program and 5,010 symptom-related secure messages were shared between staff and enrolled patients during the follow-up period. There was a preliminary signal in acute care usage with a 17% decrease in ED visits compared to a cohort of high-risk unenrolled patients. **Conclusions:** This pilot program of intensive monitoring of high-risk patients is feasible and holds significant potential to improve patient care and decrease hospital resources. Future work should focus on the optimal cadence of EMAs, the workforce to support remote symptom management, and how best to return symptom data to patients and clinical teams. Research Sponsor: None.

Prevalence of symptoms reported at moderate and severe levels on one or more days % (n = 100).

Symptom	Moderate	Severe
Pain	73%	74%
Anxiety	73%	21%
Depression	70%	14%
Functional status	66%	53%
Diarrhea	62%	12%
Decreased Oral Intake	61%	18%
Nausea	58%	25%
Dyspnea	38%	22%
Emesis	24%	9%

2028 Poster Session (Board #20), Fri, 8:00 AM-11:00 AM

Interest in cessation treatment and survival among smokers in a community-based multidisciplinary thoracic oncology program. *First Author: Meghan Meadows, University of Memphis, School of Public Health, Memphis, TN*

Background: Tobacco cessation is essential to high quality oncology care. Many patients smoke when diagnosed and continue to smoke during treatment, which adversely affects treatment response and survival. Although most patients are motivated to quit, few receive effective cessation therapy. The multidisciplinary clinic (MDC), where patients, their caregivers, and key specialists coordinate care, is an ideal setting to integrate a cessation program. To assess the need for cessation services within a MDC setting, we surveyed incoming patients about their smoking status, interest in quitting, and willingness to participate in a clinic-based cessation program. **Methods:** The study was conducted in the Multidisciplinary Thoracic Oncology Program at Baptist Cancer Center, Memphis TN. We evaluated sociodemographic/clinical characteristics, smoking status, and tobacco dependence of consecutive new patients diagnosed with lung cancer from 2014-2019, who completed a social history questionnaire. Current smokers reported their interest in quitting and their willingness to participate in a cessation program. Chi square tests and logistic regression models were used to compare characteristics of those who would participate vs. those who would not/were unsure. Kaplan-Meier curves and multivariable Cox regression were used to evaluate the association between willingness to participate in a cessation program and overall survival, adjusted for age, sex, race, and total pack-years of smoking. **Results:** Of 641 patients, the average age was 69 years (range: 32-95), 47% were men, 64% white/34% black, and 17% college graduates; 90% had ever smoked, 34% currently smoked, and 24% quit smoking within the past year. Among current smokers, 60% were very interested in quitting and 37% would participate in a clinic-based cessation program. Willingness to participate was associated with greater interest in quitting ($p = 0.0010$) and greater overall survival (log rank $p = 0.01$;HR: 0.48, 95% CI: 0.24-0.95) but was not associated with any sociodemographic, clinical, or smoking-related characteristics. **Conclusions:** Over half (58%) of patients in a community-based MDC program were current smokers/recent quitters. Willingness to participate in a cessation program was associated with improved survival, suggesting patients with favorable prognoses are especially interested in receiving cessation support. There is considerable need for cessation services and relapse-prevention support within a coordinated, MDC lung cancer care setting. Research Sponsor: Patient-Centered Outcomes Research Institute (PCORI).

2029 Poster Session (Board #21), Fri, 8:00 AM-11:00 AM

Nickel and dimed: Parking fees at NCI-designated cancer centers. *First Author: Anna Lee, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Nonmedical costs from cancer treatment can be a significant out-of-pocket expense. As treatment may span over months, parking costs can become a significant burden on patients and caregivers. This cross-sectional study aims to report parking fees at National Cancer Institute (NCI)-designated cancer centers and to project parking costs for the treatment duration of certain cancers. **Methods:** Parking fees from NCI treatment centers were obtained via online search or phone call in Fall of 2019. City cost of living, median city household income, and discount availability were documented. Pearson correlation was used between parking costs and city variables. Parking costs were estimated for treatment of node positive breast cancer (12 daily rates plus 20 1-hr rates), definitive head and neck cancer (35 1-hr rates) and acute myeloid leukemia (AML) (42 daily rates). RStudio Version 1.2.5033 was used for analyses. **Results:** Parking costs were obtained for 100% of the 63 NCI centers included. Median city cost of living relative to New York City was 75.0 (out of 100); median city household income was $55,295 (range $28,974-$120,573). Twenty-five (40%) of NCI centers did not have detailed parking cost information online. Average parking costs were $3.55/hr (median $2, range 0-$15) and $7.79/day (median $5, range 0-$40). Twenty centers (32%) offered completely free parking for patients. Free parking was available at 43 (68%) centers for radiation appointments and 34 (54%) centers for chemotherapy appointments. Averaged estimated parking costs including discounts for a course of treatment for breast cancer was $122.03 (range 0-$800); head and neck cancer, $85.56 (range 0-$665); and AML hospitalization, $327.33 (range 0-$1470). City cost of living was positively correlated with daily parking costs ($R = 0.7$, $p < 0.01$) and negatively correlated with both free daily parking ($R = -0.33$, $p = 0.02$) and free parking during radiation ($R = -0.34$, $p = 0.02$) or chemotherapy ($R = -0.37$, $p < 0.01$). The median city household income was correlated with the daily parking costs ($R = 0.30$ $p = 0.02$) but not with free daily parking ($R = -0.19$, $p = 0.16$), free parking for patients on radiation ($R = -0.23$, $p = 0.09$) or on chemotherapy ($R = -0.21$, $p = 0.14$). **Conclusions:** Patients may face significant nonmedical costs through parking fees, even at centers that reflect the highest standard of care. There was high variability in costs with the potential for patients to pay hundreds of dollars in parking in order to receive their care. Efforts to minimize financial toxicity should focus on this potentially under-reported patient concern. Research Sponsor: None.

2030 Poster Session (Board #22), Fri, 8:00 AM-11:00 AM

Implementation of Symptom Care Clinic (SCC) for acute symptoms management at outpatient oncology ambulatory centers. *First Author: Han Xiao, Memorial Sloan Kettering Cancer Center, Basking Ridge, NJ*

Background: With improved overall cancer survival, increasing number of cancer patients are undergoing active treatment. This, in return, add burden in acute symptom management related to disease and treatment. This has resulted in increasing unplanned emergency room (ER) visits and negatively impacted patients experience and health cost. We establish Symptom Care Clinic (SCC) embedded in suburban ambulatory oncology centers to reduce unplanned ER lists and to improve patient experience. **Methods:** Together with all stakeholders, we developed six SCCs at regional ambulatory centers in NY and NJ. Clearly defined work flow and algorithm were developed to ensure appropriate patient referral. On-site radiology and laboratory services are available. The SCCs are staffed with combination of Advanced Practice Provided (APP) and physicians or APP alone supported by on site medical oncologist or remote central Urgent Care Center Attendings. We evaluated clinic volumes, reduction ins unplanned ER visits and patient experience. **Results:** From October 2017 to December 2019, total of 17,542 SCC visits were documented. Total of 17,479 lab and 5,355 radiology tests as well as 3,915 infusions were performed. The top five most common laboratory tests are CBC, blood cultures, CMP, respiratory panel and urine culture. The most common symptoms are fever, nausea/vomiting/dehydration, rash and pain. Among all SCC visits during this period, 83% were discharged home and 17% were transferred to ER or hospitals. During 2019, total 10,736 SCC visits were recored, APP evaluated 73.7% of visits and physicians 16.3% with comaprable recidivism rate, 2.52% and 2.75%, respectively. Conservatively, we estimated that approximately 40% of visits would have been Er visits based on numbers of CBC and other testes performed. Qualitative feedbacks from patients indicated positive experience in convenient access, cohesive care coordination and time saving from traveling to and waiting in ER. **Conclusions:** We successfully implemented an effective acute symptom management system in busy ambulatory oncology centers that is patient centric. Out data showed that SCC reduced unplanned ER visits and that APP/physician model has low recidivism rate. Research Sponsor: None.

2032 Poster Session (Board #24), Fri, 8:00 AM-11:00 AM

Impact of an immuno-oncology (IO) education/monitoring program on patient's self-efficacy and adverse event reporting from immune checkpoint inhibitors (ICIs). *First Author: Parneet Kaur Cheema, William Osler Health System, University of Toronto, Brampton, ON, Canada*

Background: ICIs have unique side effects of immune related adverse events (irAEs). For early detection and management of irAEs, at a large community hospital we implemented a standard IO nursing baseline assessment, education and monitoring program. We studied it's impact on a patient's irAE reporting and self-efficacy (confidence to manage symptoms) of ICIs. **Methods:** Prospective study conducted at William Osler Health System, Brampton, Canada from May 2018-December 2019. Patients aged $> = 18$, English speaking that received an ICI for cancer were included. Patients underwent a standardized baseline nursing assessment and education class. Patients identified at the assessment as high risk (risk of grade 3/4 irAE $>20\%$) had weekly nurse proactive calls. Cancer Behaviour Inventory – Brief Version (CBI-B) (Heitzmann et al, 2011) was used to evaluate patient's self-efficacy. **Results:** Eighty patients were enrolled. Median follow up of 4.1 months. Baseline demographics: median age 69, 70% males, 77% Caucasian, 81% ECOG 0/1, 66% had English as their first language and 19% highest education was elementary, 30% high school, 26% trade diploma and 21% post-secondary. Fourty-one percent had limited cancer health literacy (measured by CHLT6 (Dumenci et al, 2014)). ICIs prescribed were 70% monotherapy anti-PD1/PDL1, 13% combination nivolumab/ipilimumab, 17% anti-PD1/PDL1 + chemotherapy/other therapies. Majority had a diagnosis of non-small cell lung cancer (55%), melanoma (19%) and renal cell carcinoma (9%). A statistically significant improvement in the average CBI-B scores were found pre and post baseline assessment/education ($p < 0.001$) and this improvement was maintained over time at follow-up visits (non-significant change in scores from post education results). Fourty-three percent of patient's experienced $>$ 1 irAE. Most were grade 1/2 at time of detection (65%). Method of detection was mainly by patient self-reporting (62%), followed by proactive calls (27%). Only 3 patients had detection of an irAE with an ER visit. Rate of discontinuation of ICIs due to toxicity was 8.8%. **Conclusions:** In this diverse patient population with almost half of patients having limited cancer health literacy, a standardized IO baseline assessment, education and monitoring program resulted in improved patient self-efficacy with most irAEs detected by self-reporting and proactive calls. Our IO program can be a model for other oncology programs. Research Sponsor: None.

2033 Poster Session (Board #25), Fri, 8:00 AM-11:00 AM

Evaluating barriers to uptake of comprehensive genomic profiling (CGP) in advanced cancer patients (pts). *First Author: Kortnye Maureen Smith, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia*

Background: Despite increasing evidence of benefit supporting CGP in personalizing cancer therapy, its widespread uptake remains limited. Barriers include low patient understanding, unmet patient expectations related to low utility, clinician concerns over cost-effectiveness, perceived value, and discomfort in management of complex genomic results. **Methods:** This prospective cross-institutional demonstration study was designed to evaluate implementation of CGP in the care of adult and paediatric advanced cancer pts, incorporating pt reported outcomes (PROMs), discrete choice experiment (DCE), ongoing process optimization and clinician evaluations. DNA sequencing of FFPE tumor and matched blood was completed with CGP (PMCC Comprehensive Cancer Panel; 391 genes) via central laboratory. A tumor board reported results weekly with emphasis on therapeutic relevance. Oncologists performed consent and results delivery. Pts completed pre-and post-test surveys, including validated and study-specific questions, DCE and if eligible, semi-structured interviews. Qualitative interviews were undertaken with study clinicians and laboratory staff to evaluate processes. **Results:** 86% (315) of 365 enrolled pts had successful CGP; of these 63% (199) had relevant therapeutic, diagnostic or germline results. 50 (16%) had treatment change at 6m, 49 (16%) had germline mutations. 293 (88% of adult pts) completed PROMs. 17 of 19 clinicians/laboratory staff approached consented to an interview. At consent pts cited multifaceted value in testing, showed good understanding of basic concepts, but most (69%) overestimated the likelihood of result-led change. Post-test pts remained consistently satisfied with accessing CGP; valuing research contribution, taking opportunities and information for family. 21% struggled with understanding results but there were low levels of decisional regret following participation (89% had nil/mild regret). Pt-elicited preferences (via DCE) indicated priority for high rates of clinical utility and timeliness. Clinicians sited collaboration and communication as critical to delivery of CGP. **Conclusions:** Pts undergoing CGP are generally satisfied, and derive value on its use beyond potential therapeutic benefit. Our results suggest that to improve test utility and delivery of CGP with value to pts and investing institution, focus must be placed on addressing the additional barriers to its wider implications including efforts to improve process efficiencies, clinician genomic literacy and decision-making support. Research Sponsor: Melbourne Genomic Health Alliance, Other Foundation.

2034 Poster Session (Board #26), Fri, 8:00 AM-11:00 AM

Effect of a supportive medicine program for cancer patients on patient connectivity to care and health care utilization. *First Author: Brooke Worster, Sidney Kimmel Cancer Center, Philadelphia, PA*

Background: The benefits of supportive medicine (SM) for cancer patients include improved quality of life, increased patient satisfaction, improved symptom management, increased cost savings and improved survival rates. At one NCI-designated cancer center, all patients were screened for distress; those who screened positive or were directly referred by a provider were enrolled into our multi-disciplinary SM program. Here, we document the impact of the supportive medicine program on outcomes of emergency department (ED) visits, hospital readmission, and non-billable touchpoints associated with patient navigation and resource referrals. **Methods:** The program systematically screened for biopsychosocial distress utilizing the National Comprehensive Cancer Center Distress Thermometer (DT) and the Problem Checklist (PC) to identify practical, emotional, spiritual and physical issues. Patients were categorized into three types: screened and enrolled in the SM program, and screened and not enrolled in the SM program, or provider referral into the SM program. Data included patient's age, number of hospital admissions, emergency department visits, and non-billable touchpoints at 90 and 180 days after the distress screening or referral. Descriptive data were analyzed with counts and percentages for categorical variables and summarized with mean and standard deviation for numerical variables. For investigation of the effects of time and patient type on the change in utilization rate, generalized estimation equations for Poisson regression were conducted for each outcome. **Results:** In all, 2,738 patients were included in the analysis. Patients who were referred from a provider tended to be younger ($p < .01$) and more likely to die within 90 days ($p < .001$). At 180 days, ED visits decreased 18% for patients referred to the SM program and 42% for patients screened into the SM program, compared to a 3% decrease in ED visits among those not enrolled in the SM program ($p < .01$). Similarly, hospital admissions decreased 34% for patients referred to and 39% screened into the SM program, compared to a 4% increase for patients not enrolled in the SM program ($p < .01$). Non-billable touchpoints increased among all types of patients. **Conclusions:** An SM program reduces hospital admissions and ED visits, therefore improving outcomes and potentially reducing the cost of care for cancer patients. Future research should link this data to claims data to definitely evaluate the impact of SM programs on cost. Research Sponsor: None.

2037 Poster Session (Board #29), Fri, 8:00 AM-11:00 AM

Disparities in the treatment of brain metastases from breast cancer: Insights from the National Cancer Database. *First Author: Zena Chahine, Allegheny General Hospital, Pittsburgh, PA*

Background: Breast cancer is the most common malignancy in women accounting for over 300,000 cases per year. Unfortunately, brain metastases are found in a sub-group of patients with breast cancer even at presentation. Management of brain metastases typically includes radiotherapy with conventional whole brain radiation therapy (WBRT) or more focused stereotactic radiosurgery (SRS). We queried the National Cancer Database (NCDB) to analyze the incidence of brain metastases at diagnosis in breast cancer patients, as well as trends in radiation use/technique. **Methods:** The NCDB was queried for patients who were diagnosed with breast cancer between 2004-2015 and had brain metastasis at presentation (N = 4,491). We excluded patients without brain radiation and inadequate follow up. Odds ratios were calculated to identify factors associated with treatment. Multivariable cox regression was used to determine predictors of survival. **Results:** Using the eligibility criteria above 1,505 patients were identified in the NCDB. The cohort had a median age of 58 years. A small portion were uninsured (7%) population uninsured and 81% of radiation treatments were delivered in metropolitan areas. Two hundred sixty-one (17.3%) patients received SRS while 1,244 (82.7%) received WBRT. Those patients with private insurance, higher income, metro location, and having care delivered at an academic center were more likely to receive SRS. Conversely, the likelihood of receiving WBRT was significantly higher in those with luminal type cancer, African Americans, the uninsured, and those located in urban areas or treated at a community cancer center. On Cox regression, predictors of worse survival were age > 60 with Hazard Ratio (HR) 1.3 (95% CI 1.17-1.49), a comorbidity score > 2 with HR 1.45 (95% CI 1.1-1.9), and extra cranial metastatic disease with HR 1.33 (95% CI 1.15-1.54). **Conclusions:** This analysis of the NCDB demonstrates socioeconomic and demographic disparities in the treatment of patients with brain metastases from breast cancer. There is a continued need to reduce these disparities and improve access to care for at-risk populations affected by this highly prevalent malignancy. Research Sponsor: None.

2039 Poster Session (Board #31), Fri, 8:00 AM-11:00 AM

Affordable Care Act Medicaid expansion does not reduce guideline concordant cancer care disparities in vulnerable populations. *First Author: Michelle Ju, UT Southwestern, Dallas, TX*

Background: The receipt of timely, guideline concordant cancer amongst racial/ethnic and socioeconomic vulnerable populations remains a significant health policy issue. The Affordable Care Act (ACA) with implementation of Medicaid Expansion sought to reduce cancer disparities by reducing uninsured rates, theoretically improving healthcare access and delivery. We assessed the impact of Medicaid expansion on racial/ethnic disparities in the receipt of timely guideline concordant cancer care. **Methods:** We identified patients between 40-64 years of age with all stages of cancer (lung, colorectal, breast, uterine, and cervical) in the National Cancer Database, 2012-2015. Patients were assigned to Medicaid expansion cohort based on state of residence and whether Medicaid expansion was enacted at date of diagnosis in that state. Guideline concordant care was defined based on NCCN guidelines. We constructed an ecological model with multivariate regression analysis on rate of guideline concordant care receipt with covariates including race/ethnicity, Medicaid expansion, SES, gender, Charlson-Deyo score, and treatment facility type. **Results:** We identified 445,952 patients, 12% Black, 6% Hispanic white, median age 55 years. Patients in the lowest SES quartile following Medicaid expansion had the greatest increase in rates of insured status, although all SES quartiles had increased insured rates compared to non-Medicaid expansion regardless of race/ethnicity. In our ecological model, the rate of receipt of guideline concordant care declined by 0.5% per year between 2012-2015. After adjusting for covariates, Asians were 2.8% less likely to receive guideline concordant care than non-Hispanic whites, Blacks 3.8% less likely, and Hispanics 6.3% less likely ($p < 0.0001$). Racial/ethnic disparities in receipt of guideline concordant cancer care remained after Medicaid expansion with no differential benefit. **Conclusions:** Insurance gains under the ACA Medicaid expansion did not affect the rate of guideline concordant care receipt. Significant racial disparities persist in the likelihood of receiving guideline concordant care, particularly among Hispanics. Further studies are needed to determine additional barriers to cancer care access/delivery and identify key targets aimed at improving equity. Research Sponsor: None.

2040 Poster Session (Board #32), Fri, 8:00 AM-11:00 AM

Dynamic 30-day readmission prediction for cancer patients via clinical embeddings. *First Author: Chi Wah Wong, City of Hope National Medical Center, Duarte, CA*

Background: Existing models typically predict unplanned 30-day readmission for cancer patients at discharge[1]. Performing prediction dynamically during hospital stay may allow earlier intervention for high risk patients. In addition, readmission risk may be associated with the outcome of a variety of labs and diagnoses. Models including all those elements may not be practical due to large number of variables relative to number of samples. Embeddings have the potential to represent medical concepts in low dimensional spaces[2]. In this study, we developed a machine learning model utilizing embedding representations of ICD and LOINC codes to dynamically predict readmission risk. **Methods:** This is a single institutional study examining inpatient 30-day unplanned readmissions from Jan 2013 to Dec 2016 (n = 16361 total, n = 5685 in hematology). The readmission rate was 18% (24% for hematology). We used gradient boosted trees models with 10-fold cross validation and included baseline factors that are typically available shortly after admission: gender, age, service, admission count within 6 months, insurance, emergency admission, admission year, allogeneic or autologous stem cell transplant (hematology only). For dynamic factors, we randomly selected a timepoint (TP, median = 2.4 days) during each visit. We utilized publicly available clinical embeddings[2] to generate 300 dimensional representations for ICD9s and LOINCs in the patients' Electronic Medical Records. We considered diagnoses (ICD9) between 6 months prior to admission and TP, and lab tests (LOINC) ordered between admission time and TP. We used records from Jan 2017 to Dec 2017 for prospective validation (n = 3785 total, n = 1424 in hematology), with 17% readmission rate (22% for hematology). **Results:** Prospective validation Area Under Receiver Operating Characteristic Curve (AUC) using baseline factors were 0.72 (average precision "AP" = 0.33) and 0.65 (AP = 0.32) for overall and hematology populations, respectively. By including dynamic factors, we obtained AUCs of 0.74 (AP = 0.4) and 0.7 (AP = 0.39) for overall and hematology populations, corresponding to 3% and 8% AUC (21% and 22% AP) improvements, respectively. **Conclusions:** We found that dynamic readmission prediction utilizing clinical embeddings improves the prediction performance comparing with using baseline factors only. The model shows potential to improve patient care and reduce costs by predicting and preventing readmissions when the patient is still in the hospital. [1] J Surg Oncol 2018; 117:1113-1118. [2] AMIA Jt Summits Transl Sci Proc. 2016;41-50. Research Sponsor: None.

2041 Poster Session (Board #33), Fri, 8:00 AM-11:00 AM

Prediction of mental health disorder onset and impact on emergency visits following a cancer diagnosis. *First Author: William Chen, UCSF Department of Radiation Oncology, San Francisco, CA*

Background: Cancer patients are at increased risk of mental and emotional distress. The aim of this study is to investigate risk factors and timing of mental health disorder (MHD) onset following a cancer diagnosis, and evaluate its impact on emergency visits. **Methods:** All patients with a new onset diagnosis of malignancy (*ICD*-10 codes C00-C97, with conversion of *ICD*-9 codes) were identified from an institutional de-identified electronic health data warehouse. Demographic data, Charlson comorbidity index excluding cancer, mortality, and time to onset of a new MHD diagnosis (*ICD*-10 codes F00-F99) and emergency visits were extracted and used to calculate rates and Cox-model hazard ratios. A predictive logistic model of MHD was tested on an internal hold-out sample (25%). **Results:** A total of 110,306 patients with 338,208 person-years of follow up were identified with a new diagnosis of cancer from February 1980 to July 2019, of which 95,474 (86.5%) had no prior diagnosis of MHD. Actuarial rates of new MHD among previously MHD-free patients were 8.1% at 6 months, and 14.1% and 20.8% at 2 and 5 years. Median time to onset of MHD was fastest among head and neck cancer (57 days, HR 2.32 [2.1-2.6]), urinary organ cancer (94 days, HR 2.21 [2.0-2.4]), and lung and thoracic cancers (99 days, HR 2.47 [2.2-2.7]), compared to skin neoplasms (987 days, HR 1.0). Median time to onset was less than one year for all malignancies except for skin neoplasms and male genital cancers (840 days). Male sex, older age, Charlson score, divorce or legal separation, self-identification of a gender-neutral partner, African American or American Indian race, Hispanic ethnicity, current or former smoking status, and self-identification as Christian were associated with higher risk of MHD onset, while married status and native Hawaiian or Pacific Islander race were protective. A logistic model predicted new MHD with an AUROC of 0.72. Onset of new MHD was associated with greater rates of emergency visit (HR 1.92 [1.8-2.0], adjusted for cancer type and Charlson score), and patients with new MHD who experienced an emergency visit had a mean of 3.75+/-0.03 (SEM) total emergency visits versus 2.65+/-0.02 ($p < 0.0001$). Finally, onset of new MHD was associated with greater mortality even after adjusting for age, Charlson score and cancer type (HR 1.29, [1.23-1.35]). **Conclusions:** Onset of new mental health diagnosis after a cancer diagnosis was correlated with greater rates of emergency visits and mortality. Cancer patients with risk factors identified here may benefit from increased social and mental health support. Research Sponsor: None.

2042 Poster Session (Board #34), Fri, 8:00 AM-11:00 AM

Predicting the risk of VISIT emergency department (ED) in lung cancer patients using machine learning. *First Author: Pablo Rodriguez-Brazzarola, Grupo de Inteligencia Computacional en Biomedicina, ETSI Ingeniería Informática, Universidad de Málaga, Málaga, Spain*

Background: Lung cancer patients commonly need unplanned visits to ED. Many of these visits could be potentially avoidable if it were possible to identify patients at risk when the previous scheduled visit takes place. At that moment, it would be possible to perform elective actions to manage patients at risk to consult the ED in the near future. **Methods:** Unplanned visits of patients in active cancer therapy (i.e. chemo or immunotherapy) are attended in our own ED facilities. Our Electronic Health Record (EHR) includes specific modules for first visit, scheduled visits and unplanned visits. Lung cancer patients with at least two visits were eligible. The event of interest was patient visit to ED within 21 or 28 days (d) from previous visit. Free text data collected in the three modules were obtained from EHR in order to generate a feature vector composed of the word frequencies for each visit. We evaluate five different machine learning algorithms to predict the event of interest. Area under the ROC curve (AUC), F1 (harmonic mean of precision and recall), True Positive Rate (TPR) and True Negative Rate (TNR) were assessed using 10-fold cross validation. **Results:** 2,682 lung cancer patients treated between March 2009 and October 2019 were included from which 819 patients were attended at ED. There were 2,237 first visits, 47,465 scheduled visits (per patient: range 1-174; median 12) and 2,125 unplanned visits (per patient: range 1-20; median 2). Mean age at diagnosis was 64 years. The majority of patients had late stage disease (34.24 % III, 51.56 % IV). The Adaptive Boosting Model yields the best results for both 21 d or 28 d prediction. **Conclusions:** Using unstructured data from real-world EHR enables the possibility to build an accurate predictive model of unplanned visit to an ED within the 21 or 28 following d after a scheduled visit. Such utility would be very useful in order to prevent ED visits related with cancer symptoms and to improve patients care. Research Sponsor: Pfizer.

	AUC (95%CI)	F1 (95%CI)	TPR (95%CI)	TPN (95%CI)
21 d	0.75 (0.74-0.76)	0.77 (0.773-0.779)	74.3% (74.2%-74.4%)	67.9% (64.8%-65%)
28 d	0.75 (0.74-0.76)	0.77 (0.775-0.776)	73.7% (73.6%-73.8%)	65% (64.9%-65.1%)

2043 Poster Session (Board #35), Fri, 8:00 AM-11:00 AM

Development and validation of natural language processing (NLP) algorithm for detection of distant versus local breast cancer recurrence and metastatic site. *First Author: Yasmin Karimi, Division of Medical Oncology, Stanford School of Medicine, Stanford, CA*

Background: Electronic health records (EHR) are used for retrospective cancer outcomes analysis. Sites and timing of recurrence are not captured in structured EHR data. Novel computerized methods are necessary to use unstructured longitudinal EHR data for large scale studies. **Methods:** We previously developed a neural network-based NLP algorithm to identify no recurrence vs. metastatic recurrence cases by analyzing physician notes, pathology and radiology reports in Stanford's breast cancer database, Oncoshare (Cohort A). To validate this algorithm for local vs. distant recurrence, we identified a distinct Oncoshare cohort (Cohort B). Cases were manually curated for longitudinal development of local or distant recurrence and metastatic sites. A two-sided t-test was used to compare mean probabilities between local and distant recurrence cases. Next, we combined cases in Cohorts A and B to train and validate a novel NLP classifier that identifies metastatic site. The combined cohort was randomly divided into training and validation sets. Sensitivity and specificity were calculated for the NLP algorithm's ability to detect metastatic sites compared to manual curation. **Results:** In Cohort B: 350 metastatic cases were identified. Mean probability for local and distant recurrence was 0.43 and 0.79, respectively and differed significantly for patients with local vs. distant recurrence ($p<0.01$). In Cohorts A and B: 632 metastatic cases were used for determination of sites. Sensitivity and specificity were highest for detection of peritoneal metastasis followed by liver, lung, skin, bone and central nervous system (table). **Conclusions:** This NLP algorithm is a scalable tool that uses unstructured EHR data to capture breast cancer recurrence, distinguishing local from distant recurrence and identifying metastatic site. This method may facilitate analysis of large datasets and correlation of outcomes with metastatic site. Research Sponsor: None.

Sensitivity & specificity of extracting recurrence sites.

	Bone	Liver	Lung	Lymph Nodes	CNS	Peritoneum	Skin
N (cases)	252	98	94	101	37	15	16
Sensitivity	0.84	0.97	0.93	0.82	0.9	0.94	0.97
Specificity	0.77	0.77	0.6	0.6	0.5	1.0	0.5

2044 Poster Session (Board #36), Fri, 8:00 AM-11:00 AM

Improved prognostication for lung cancer patients from computed tomography imaging using deep learning. *First Author: Felipe Torres, University of Toronto, Toronto, ON, Canada*

Background: Clinical TNM staging derived from computed tomography (CT) imaging is a key prognostic factor for lung cancer patients when making decisions about treatment, monitoring, and clinical trial eligibility. However, heterogeneity among patients, including by molecular subtypes, may result in variability of survival outcomes of patients with the same TNM stage that receive the same treatment. Artificial intelligence may offer additional, individualized prognostic information based on both known and unknown features present in CTs to facilitate more precise clinical decision making. We developed a novel deep learning-based technique to predict 2-year survival from pretreatment CTs of pathologically-confirmed lung cancer patients. **Methods:** A fully automated, end-to-end model was designed to localize the three-dimensional (3D) space comprising the lungs and heart, and to learn deep prognostic features using a 3D convolutional neural network (3DCNN). The 3DCNN was trained and validated using 1,841 CTs of 1,184 patients from five public datasets made available in The Cancer Imaging Archive. Spearman's rank correlation (R) and concordance index (C-index) between the model output and survival status of each patient after 2-year follow-up from CT acquisition was assessed, in addition to sensitivity, specificity and accuracy stratified by staging. **Results:** 3DCNN showed an overall prediction accuracy of 75.0% ($R = 0.32$, C-index = 0.67, $p < 0.0001$), with higher performance achieved for stage I patients (Table) . 3DCNN showed better overall correlation with survival for 1,124 patients with available TNM staging, in comparison to TNM staging only ($R = 0.19$, C-index = 0.63, $p < 0.0001$); however, a weighted linear combination of both TNM staging and the 3DCNN yielded a superior correlation ($R = 0.34$, C-index = 0.73, $p < 0.0001$). **Conclusions:** Deep learning applied to pretreatment CT images provides personalized prognostic information that complements clinical staging and may help facilitate more precise prognostication of patients diagnosed with lung cancer. Research Sponsor: None.

3DCNN performance by staging.

	Stage I	Stage II	Stage III	Stage IV	All Patients*
Number of Patients Survived >2 years	400	137	164	165	919
Number of Patients Died within 2 years	53	38	132	35	265
AUC	0.81	0.69	0.76	0.55	0.74
Accuracy	79.2%	66.3%	67.7%	66.7%	75.0%
Specificity	0.81	0.56	0.54	0.61	0.62
Sensitivity	0.73	0.65	0.81	0.52	0.70

*Includes 60 additional patients where staging was not available.

2045 Poster Session (Board #37), Fri, 8:00 AM-11:00 AM

Driving quality improvement: How clinical decision support can facilitate compliance with evidence-based pathways. *First Author: Debra A. Patt, McKesson Specialty Health and US Oncology Network, The Woodlands, TX*

Background: Cancer care is changing rapidly with more detailed understanding of disease and more numerous therapeutic choices. As treatment choice is more complex, mechanisms to improve compliance with evidence based treatment can improve the quality of cancer care. **Methods:** A retrospective cohort study was conducted from January 2014-May 2016 evaluating the impact of a clinical decision support system (CDSS) on compliance with evidence based pathways (EBP) across 9 statewide community based oncology practices. These EBP are developed with physician input on efficacy toxicity and value and incorporated in to a CDSS that is used within the Electronic Health Record (EHR) at point of care to alter the choice architecture a clinician sees when prescribing therapy. A multi-level logistic regression model was used to adjust for group effects on physician or practice behavior. SAS 9.4 software was used and GLIMMIX was applied. Individual physician benchmark compliance was evaluated using McNemar's test. **Results:** Regimen compliance with EBP was measured pre- and post-implementation of the CDSS tool across a large network encompassing 9 statewide practices and 633 physicians who prescribed over 30,000 individual patient treatment regimens over a 6 month period. The CDSS that is incorporated within the EHR significantly improved compliance with EBP across the entire cohort of practices, and in individual practices (see Table). Individual oncologists reached a target of 75% compliance more often (58% vs 72%) after implementation of the tool ($p < 0.001$). **Conclusions:** CDSS is a tool that improves compliance with EBP that is effective at improving targets of compliance broadly, at the practice, and at the individual clinician level. Clinical informatics solutions that influence physician behavior can be inclusive of physicians in design, iterative in process, and nudge as opposed to force clinician behavior to drive quality improvement. These clinical informatics solutions grow in importance as the complexity of cancer care continues to increase and we seek to improve upon the quality and value of care delivery. Research Sponsor: Texas Oncology, US Oncology.

Label	Odds Ratio of Regimen Compliance	95% LCL	95% UCL	Pr > |t|
Overall Post vs. Pre	1.48	1.25	1.76	0.0007
Practice A	1.60	1.33	1.94	0.0004
Practice B	1.13	0.88	1.45	0.2930
Practice C	1.39	1.08	1.79	0.0160
Practice D	1.85	1.53	2.24	< .0001
Practice E	1.76	1.32	2.36	0.0021
Practice F	1.71	1.38	2.11	0.0004
Practice G	1.23	0.96	1.57	0.0897
Practice H	1.37	1.12	1.67	0.0066
Practice I	1.46	1.30	1.63	< .0001

2046 Poster Session (Board #38), Fri, 8:00 AM-11:00 AM

Identifying and overcoming clinical trial enrollment barriers: Can an integrated clinical pathways tool help bridge the gap? *First Author: Mishellene McKinney, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: Barriers to clinical trial (CT) enrollment continue to be a national challenge, with only about 3% of adult cancer patients treated within a CT. A key recommendation from the 2013 NCI-ASCO Cancer Trial Accrual Symposium was to use information technology to enhance identification of potentially eligible patients for CTs. We assessed if the implementation of a Clinical Oncology Pathways System (COP) with integrated CT information increased enrollment of CT's, and categorized physician-identified reasons for non-enrollment. **Methods:** In 2018, Roswell Park Comprehensive Cancer Center (RP) implemented ClinicalPath pathways (formerly Via Oncology) for medical oncology. The COP software embeds interventional CTs that are open to accrual at RP in the pathway specific to a patient's disease type, stage and biomarkers. The provider is presented with relevant CTs and must select screening for the trial or provide a reason for bypassing the CT from a drop-down list prior to being presented standard care options. CT screening requests from the COP system from 6/1/18-5/31/19 were reviewed. Screening requests and actual enrollment data were matched. The accrual-to-study ratio (ASR), defined as the number of consented accruals divided by the number of CTs open to accrual at RP at any time during the period, was calculated for the study period and the baseline from 6/1/14-6/1/18. The reasons physicians did not elect to screen for CTs were summarized. **Results:** There can be multiple trials presented for each pathway decision.There were 1,606 decision points with at least one embedded trial. Of these, 1,289 decision points matched 2,242 CTs that were not selected for screening. 317 trials were selected for screening. The most common reasons for not screening were patient ineligibility (41%), provider bypassing the CT by selecting treatment "off pathway" (28%), patient not interested (12%), patient already on CT (8%) and "other" (9%). Audits confirmed that the majority of ineligible patients had co-morbidities such as organ dysfunction or brain metastasis that precluded them from the CT. Among the 317 trials selected for CT screening, 108 (34%) patients enrolled in CTs. The ASR increased from the four-year historical average baseline of 4.08 to 4.33 one year post-implementation. **Conclusions:** The use of COP with embedded CT was associated with a modest increase in ASR. Stringent eligibility criteria was the primary barrier to enrollment. Adopting a broader set of clinical trial eligibility criteria could increase enrollment to CT. Research Sponsor: Genentech.

2047 Poster Session (Board #39), Fri, 8:00 AM-11:00 AM

Machine learning algorithms to predict financial toxicity associated with breast cancer treatment. *First Author: Chris Sidey-Gibbons, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Financial burden caused by cancer treatment is associated with material loss, distress, and poorer outcomes. Financial resources exist to support patients but objective identification of individuals in need is difficult. Accurate predictions of an individual's risk of financial toxicity prior to initiation of breast cancer treatment may facilitate informed clinical decision making, reduce financial burden, and improve patient outcomes. **Methods:** We retrospectively surveyed 611 patients who had undergone breast cancer therapy at MD Anderson Cancer Center to assess the financial impact of their care. All patients were over 18 and received either a lumpectomy or a mastectomy. We collected data using the FACT-COST patient-reported outcome measures alongside other financial indicators including income and insurance status. We extracted clinical and perioperative data from the electronic health record. Missing data were imputed using multiple imputation. We used this data to train and validate a neural network, LASSO-regularized linear model, and support vector machines. Data were randomly partitioned into training and validation samples (3:1 ratio). Analyses were informed by international PROBAST recommendations for developing multivariate predictors. We combined algorithms into a voting ensemble and assessed predictive performance using area under the receiver operating characteristics curve (AUROC), accuracy, sensitivity, and specificity. **Results:** In our validation sample, 48 of 203 (23.6%) women reported FACT-COST scores commensurate with significant financial burden. The algorithm predicted significant financial burden relating to cancer treatment with high accuracy (Accuracy = .83, AUROC = .82, sensitivity = .81, specificity = .82). Key clinical predictors of financial burden from linear models were neo-adjuvant therapy ($\beta_{regularized}$ 0.12) and autologous, rather than implant-based, reconstruction ($\beta_{regularized}$ 0.10). **Conclusions:** Machine learning models were able to accurately predict the occurrence of financial toxicity related to breast cancer treatment. These predictions may be used to inform decision making and care planning to avoid financial distress during cancer treatment or to enable targeted financial support for individuals. Further research is warranted to further improve this tool and assess applicability for other types of cancer. Research Sponsor: None.

2048 Poster Session (Board #40), Fri, 8:00 AM-11:00 AM

Semi-automated discovery of real-world patient pathway from U.S. electronic health records: Advanced non-small cell lung cancer (aNSCLC). *First Author: Fei Yang, Roche Diagnostics Information Solutions, Basel, Switzerland*

Background: A good understanding of cancer care continuum presents opportunities to uncover unmet medical needs and improve outcomes and clinical workflow efficiency. However, patient care is poorly understood in real-world clinical practice. This study aimed to discover real-world patient pathways for advanced non-small cell lung cancer (aNSCLC). **Methods:** This study included patients diagnosed with aNSCLC (stage IIIB and above) at their initial diagnoses between 2011-2018 from the Flatiron Health electronic health records (EHR)-derived deidentified database. Overall survival (OS) was calculated using the Kaplan-Meier method. We also explored the application of process mining analytics (Heuristics Miner & Directly-Follows Graphs) to describe and visualize real-world patient pathways, following patients from initial diagnosis, through any National Comprehensive Cancer Network guideline-recommended companion diagnostics (CDx; including EGFR, ALK, ROS1, KRAS, BRAF, or PD-L1) and treatment patterns, until death or end of the study. **Results:** A total of 39,156 eligible patients were included. During a median follow-up of 0.78 years (interquartile range [IQR] 1.27), 28,801 (73.6%) patients died (median OS 11.6 months [95% CI 11.4 -11.8]). We established a semi-automated process discovery pipeline that transforms high-dimensional EHR datasets in table format as input into real-world event logs and produces a series of patient pathway graphs as output. The patient pathway graphs showed 19,878 (50.8%) patients had CDx testing within a median 11 days (IQR 18) and 29,241 (74.7%) patients started first-line therapy within a median 1.2 months (IQR 1.2) after the initial diagnosis. When we stratified analysis by years of initial diagnosis (2011-2014 vs 2015-2018), 38.8% (6808 of 17546) vs. 60.5% (13070 of 21610) patients had their first CDx testing within median 12 days (IQR 21) vs. 10 days (IQR 17) respectively. **Conclusions:** This study suggested an uptake of 56% increase of CDx utilization over the last 8 years in real-world clinical setting and that patient pathways can be analyzed and visualized in a semi-automated fashion. Research Sponsor: ROCHE DIAGNOSTIC INFORMATION SOLUTION.

2049 Poster Session (Board #41), Fri, 8:00 AM-11:00 AM

Concordance study of treatment guidance from an online patient assistance algorithm (OCPAP) and treatment recommendation of a multidisciplinary panel of oncologists in India. *First Author: Amit Kumar Jotwani, Netdox Health Private Limited (Onco.com), Hyderabad, India*

Background: OCPAP (online cancer patient assistance pathway) is an algorithm-based online platform for patients to help them understand their treatment options. It is based on basic inputs like cancer type, stage, patient's performance status and treatment received. It is developed by a team of oncologists from onco.com based on standard guidelines. Till date, more than 30,000 users from 18 countries have used OCPAP platform to get directional treatment recommendations. Onco.com also provides onco tumour board (OTB) services to help patients to get a detailed opinion from a multidisciplinary panel of oncologists. We presented initial data on development of OCPAP™ at the ASCO Breakthrough Summit 2019 (OCPAP Breakthrough Abstract). Here we present a concordance analysis of treatment recommendations from OCPAP platform against opinion of OTB panel. **Methods:** We analysed data from 448 eligible cases (those with 15 types of solid cancers) where an OTB opinion was provided and compared it with OCPAP treatment recommendation. We entered data from 448 anonymised OTB case records in to the OCPAP platform and recorded the output in terms of treatment recommendations. The study was blinded by its very design as we took data of cases from the time when the platform was non-existent. **Results:** We compared and analysed the recommendation provided by OCPAP in terms of surgery, chemotherapy, targeted therapy, radiation, clinical trials, palliative care or best supportive care against the opinion of OTB panel. Overall the concordance rate was found to be 93% for all cases and it was above 90% for all types of cancers included, except for brain tumors where it was 78% mainly due to variation in surgical operability and imaging findings influencing the treatment recommendation. The concordance rate was above 90% for all stages of disease and was highest for metastatic disease where it was 95%. The reasons for discordance were mostly related to availability of more detailed insights about the disease for OTB, like clinical details, performance status, imaging findings, molecular data and oligometastasis. **Conclusions:** The treatment direction recommended by OCPAP was found to be consistent with the one provided by OTB panel for most solid cancers. This indicates that OCPAP is an effective and simple online tool for patients to understand their treatment options, validate their ongoing treatment and be able to actively participate in their treatment decisions. Research Sponsor: None.

2050 Poster Session (Board #42), Fri, 8:00 AM-11:00 AM

Ranking of therapeutic regimens for hormone receptor-positive, HER2-negative, metastatic breast cancer (MBC) using information theoretic network meta-analysis. *First Author: Xuanyi Li, Vanderbilt University, Nashville, TN*

Background: Hormone receptor-positive (HR+), HER2-negative (HER2-) metastatic breast cancer (MBC) is treated with targeted therapy, hormone therapy, chemotherapy, or combinations of these modalities. Evaluating the increasing number of treatment options is challenging, especially since few regimens have been compared head-to-head in randomized clinical trials (RCTs). Potential solutions include expert-driven guidelines (e.g. NCCN guidelines), algorithmic scales (e.g. the ASCO and ESMO Value Frameworks), traditional Bayesian network meta-analysis (NMA), and information theoretic (IT) NMA, a graph theory-based approach that also enables dynamic ranking of regimens over time. **Methods:** We used IT-NMA to rank regimens for HR+/HER2- MBC. The analysis includes RCTs of regimens identified from HemOnc.org and a recent large traditional NMA (Giuliano et al. 2019). Variables used in ranking include primary endpoints, no. of patients enrolled, p-value, hazard ratio for time-based outcomes (e.g. overall survival) or odds ratio for fixed endpoints (e.g. response rate), and year of publication. **Results:** The analysis included 238 RCTs enrolling 92,971 patients published between 1974-2019. There were 277 unique regimens, taking into account variations in dosage, frequency, and no. of cycles. As of 2019, out of 85 ranks, combinations of targeted therapy and hormone therapy (e.g. letrozole & palbociclib) are ranked the highest (Table). Over time, we observe that novel treatments tested in escalation trials tend to rise to the top of the rankings (e.g. paclitaxel & bevacizumab in 2007, driven by ECOG E2100), and monotherapy approaches tend to fall to the bottom. **Conclusions:** In 2019, the combinations of hormone or chemotherapy and targeted therapy are ranked higher than hormone therapy or chemotherapy alone. Our ranking result is similar to previous studies with a notably larger number of comparisons (Giuliano et al. is the largest published study, with 131 regimens/50,029 pts analyzed). Informatic theoretic NMA is a promising method of indirect rankings of treatment that also enables dynamic regimen ranking over time. Research Sponsor: U.S. National Institutes of Health.

Five highest and five lowest ranked regimens.

Rank	Value*	Regimen
1	22.8	Letrozole & Palbociclib
2	16.6	Letrozole & Ribociclib
3	11.1	Paclitaxel & Bevacizumab
4	9.7	Capecitabine, Paclitaxel, Bevacizumab
5	9.6	Anastrozole & Ribociclib
81	-15.6	Weekly paclitaxel
82	-15.8	Fulvestrant 500
83	-16.4	Letrozole
84	-17	Fulvestrant 250
85	-42.1	Tamoxifen 20

*Unitless number; higher is better

2051 Poster Session (Board #43), Fri, 8:00 AM-11:00 AM

An automated EHR-based tool for identification of patients (pts) with metastatic disease to facilitate clinical trial pt ascertainment. *First Author: Jeffrey J. Kirshner, Hematology-Oncology Associates of Central New York, Syracuse, NY*

Background: Efforts to facilitate patient identification for clinical trials in routine practice, such as automating electronic health record (EHR) data reviews, are hindered by the lack of information on metastatic status in structured format. We developed a machine learning tool that infers metastatic status from unstructured EHR data, and we describe its real-world implementation. **Methods:** This machine learning model scans EHR documents, extracting features from text snippets surrounding key words (ie, 'Metastatic' 'Progression' 'Local'). A regularized logistic regression model was trained, and used to classify patients across 5 metastatic status inference categories: highly-likely and likely positive, highly-likely and likely negative, and unknown. The model accuracy was characterized using the Flatiron Health EHR-derived de-identified database of patients with solid tumors, where manually abstracted information served as standard accurate reference. We assessed model accuracy using sensitivity and specificity (patients in the 'unknown' category omitted from numerator), negative and positive predictive values (NPV, PPV; patients 'unknown' included in denominator), and its performance in a real-world dataset. In a separate validation, we evaluated the accuracy gained upon additional user review of the model outputs after integration of this tool into workflows. **Results:** This metastatic status inference model was characterized using a sample of 66,532 patients. The model sensitivity and specificity (95%CI) were 82.% (82, 83) and 95% (95, 96), respectively; PPV was 89% (89, 90) and NPV was 94% (94, 94). In the validation sample (N = 200 originated from 5 distinct care sites), and after user review of model outputs, values increased to 97% (85, 100) for sensitivity, 98% (95, 100) for specificity, 92 (78, 98) for PPV and 99% (97, 100) for NPV. The model assigned 163/200 patients to the highly-likely categories, which were deemed not to require further EHR review by users. The prevalence of errors was 4% without user review, and 2% after user review. **Conclusions:** This machine learning model infers metastatic status from unstructured EHR data with high accuracy. The tool assigns metastatic status with high confidence in more than 75% of cases without requiring additional manual review, allowing more efficient identification of clinical trial candidates and clinical trial matching, thus mitigating a key barrier for clinical trial participation in community clinics. Research Sponsor: Study sponsored by Flatiron Health, which is an independent subsidiary of the Roche group.

2052 Poster Session (Board #44), Fri, 8:00 AM-11:00 AM

Novel artificial intelligence (AI)-based technology to improve oncology clinical trial fulfillment. *First Author: TJ Bowen, Deep Lens, Inc., Columbus, OH*

Background: Less than 5% of US adult cancer pts are enrolled on clinical trials. Challenges in clinical trial fulfillment limit available treatment options, slow enrollment and ultimately delay new therapies from reaching market. Pt screening requires multiple clinical team members to find pts that meet strict inclusion/exclusion criteria. We evaluated the impact of new technology, Deep Lens VIPER, in identifying more qualified pts for clinical studies, and reduction of staff burden. **Methods:** We implemented Deep Lens VIPER at Hoag Hospital (Newport Beach, California), accessing the electronic medical records and pathology systems (EMR/LIS) to effectively identify pts who are candidates for 20 ongoing recruiting clinical studies. VIPER was fed pt data from 5,706 surgical pathology pts over a 4-month period (October 1, 2019 - January 31, 2020). Proprietary AI identification and matching technology was configured to align cancer pts with those 20 clinical studies, each with unique study criteria. Following an initial machine-assisted triage step, a research coordinator was alerted when pts who met protocol criteria were ready for final approval steps. Results were analyzed and a qualitative assessment of usability was also performed. **Results:** VIPER was able to triage all 5,706 surgical pathology cases (100%), identifying 1,045 pts (18.3%) with malignant neoplasms that would qualify for further analysis for clinical trials enrollment. Further triage based on inclusion and exclusion criteria led to the identification of 150 previously unidentified pts for 16 of the 20 studies. The 16 different studies for which potential pts were identified, included 11 tumor types, 12 biomarkers and 3 basket studies. Working with the VIPER system, 1 novice care team member performed initial identification of all 150 previously unidentified pts. The VIPER system increased monthly candidate pt catchment for 16 of the 20 studies under investigation, which is approximately 600 patients annually added for final triage for studies being conducted. **Conclusions:** We demonstrate the use of an AI-based platform to identify pts for clinical trial enrollment who would be missed using traditional recruiting methods. One staff member effectively triaged participants from 20 different studies with unique inclusion/exclusion criteria. These studies were previously managed by 6 different care team members with limited time for recruitment. Scaling this platform to additional institutions and more studies is ongoing to validate these findings. Research Sponsor: Deep Lens, Inc.

2053 Poster Session (Board #45), Fri, 8:00 AM-11:00 AM

Model selection applied to 750 outpatient ICD-9 codes identifies hazards important for all-cause cancer mortality in 2 million veterans with 14 years of follow-up. *First Author: Benjamin McMahon, Los Alamos National Laboratory, Los Alamos, NM*

Background: Cost-benefit analysis before undergoing cancer treatments can involve a broad array of factors, yet existing statistical algorithms are limited to a few of the most commonly observed competing risks. Using 20 years of Veteran medical records from the Veteran's Administration, we identify a broad array of outpatient descriptors providing contributions to computed mortality comparable in size to common cancers. **Methods:** 1,911,632 Veterans born between 1927 and 1968 with medical records extending from October 1, 2000 until either recorded death after October 1, 2005 (47%) or observation during CY 2019 were split equally into age-matched test and training sets. The 20 year-long record was split into three intervals: 5 years during which ICD codes were tallied, 14 years of waiting, and establishment of continuation in care during 2019. The 750 most common outpatient ICD9 codes were recorded as present/absent for each patient and used in a generalized linear model to predict subsequent mortality, subject to LASSO model selection and 10-fold cross validation. Gender was included as a covariate as well as age at time of prediction, up to the 4^{th} power. **Results:** The C-statistic for predicting mortality in 14 years of follow-up was 0.835 on training data and 0.833 on test data when using the 498 codes selected by LASSO. Prevalent codes with the largest model coefficients were (ICD 9 code: model coefficient, # alive/# deceased in test set) congestive heart failure (428.0: 0.66, 9k/48k), chronic airway obstruction (496.: 0.60, 42k/105k), and tobacco use disorder (305.1: 0.54, 107k/123k), while the prevalent codes most protective in comparison to baseline were hyperlipidemia (272.4: -0.21, 211k/225k) and colon cancer screening (V76.51: -0.16, 49k/39k). In comparison, observed cancer ICD 9 coefficients were lung (162.9: 1.03, 1k/7k), colon (153.9: 0.18, 3.1k/7.0k), and prostate (185.: 0.06, 16k/32k). 74 predictors contribute with coefficients greater than colon cancers, such as 'no household member able to render care' (V60.4: 0.28, 1.1k/4.2k). **Conclusions:** A wide variety of structured data contribute at a similar level of importance in prediction of 14-year mortality. While various selection biases, co-linearity of predictors, differences in treatments, and missing data are significant impediments to utilization of predictive models in clinical practice, we have demonstrated an ability to identify and quantify predictors from a large data set with model selection techniques. Research Sponsor: This work was supported by Department of Veterans Affairs, Office of Research and Development, Million Veteran Program MVP000 and MVP017.

2054 Poster Session (Board #46), Fri, 8:00 AM-11:00 AM

Novel evidence synthesis system to support living systematic reviews and living guidelines for cancer immunotherapy. *First Author: Irbaz Bin Riaz, Mayo Clinic, Rochester, MN*

Background: Systematic reviews that summarize the toxicity of Immune checkpoint inhibitors (ICIs) become outdated very soon after publication. Therefore, we reported results of a toxicity meta-analysis at 2019 ASCO meeting and informed the intent to create a living systematic review (LSR). LSRs combine human and machine effort and support rapid evidence synthesis and living clinical practice guidelines. Now, we report our experience maintaining a LSR on toxicity of ICIs. **Methods:** Steps include quarterly literature searches to identify new clinical trials reporting ICI-associated adverse events (AEs), AI-enabled screening of new citations which meet the inclusion criteria, automated cumulative meta-analysis and an online reporting platform. Standard data formats and protocols were designed for inputting text, tables and graphics. Software was written to interpret these data and output the information in the appropriate format, such as a forest plot and summary tables. Finally, a dynamic interface that enables user inputs and displays the associated output was designed. **Results:** The LSR is continuously updated incorporating toxicity data from new clinical trials as it becomes available. We have screened 8000 relevant citations and summarized the odds of Grade 3 or higher AEs and AEs of special interest in patient receiving ICIs. The results are updated on quarterly basis and are available online. The results are updated on quarterly basis and will be available on a website at the time of publication. Prototype with dummy data is available at this link. This interface can also be manipulated via user input to organize and sort data tables and forest plots by type of cancer, name or mechanism (PD-1 or PD-L1) of ICI agent, single agent or combination, type of control arm, line of treatment and several other clinically relevant filters. For example, a user can instantaneously generate a meta-analysis summarizing the risk of colitis or pneumonitis in metastatic lung cancer trials with pembrolizmuab. **Conclusions:** This LSR engine can prospectively synthesize toxicity data from ICI trials in an efficient manner providing accurate and timely information for advanced clinical decision support at point-of-care. Efforts are ongoing to improve efficiency of screening, improve AI-enabled processes for automated screening and data abstraction, and test across multiple clinical questions. Research Sponsor: None.

2055 Poster Session (Board #47), Fri, 8:00 AM-11:00 AM

Fragility index of trials supporting approval of anti-cancer drugs in common solid tumors. *First Author: Alexandra Desnoyers, Princess Margaret Cancer Centre & University of Toronto, Toronto, ON, Canada*

Background: The Fragility Index (FI) quantifies the reliability of positive trials by estimating the number of events which would change statistically significant results to non-significant results. Here, we calculate the FI of trials supporting approval of drugs for common solid tumors. **Methods:** We searched Drugs@FDA to identify randomized trials (RCT) supporting drug approvals by the US Food and Drug Administration between January 2009 and December 2019 in lung, breast, prostate, gastric and colon cancers. We adapted the FI framework (Walsh et al. J Clin Epidemiol 2014) to allow use of time to event data. First, we reconstructed survival tables from reported data using the Parmar Toolkit (Parmar et al. Stat Med 1998) and then calculated the number of events which would result in a non-significant effect for the primary endpoint of each trial. The FI was then compared quantitatively to the number of patients in each trial who withdrew consent or were lost to follow-up. Multivariable linear regression was used to explore association between RCT characteristics and the FI. **Results:** We identified 69 RCT with a median of 669 patients (range 123-4804) and 358 primary outcome events (range 56-884). The median FI was 26 (range 1-322). The FI was $\leq$10 in 21 trials (30%) and $\leq$20 in 31 trials (45%). Among the 69 RCT, the median number of patients who withdrew consent or were lost to follow up was 27 (range, 6-317). The number of patients who withdrew consent or were lost to follow-up was equal or greater than the FI in 42 trials (61%). There was statistically significant inverse association between FI and trial hazard ratio (p0,001) and a positive association with number of patients who were lost to follow-up or withdrew consent (p0,001). There was no association between trial sample size, year of approval or reported p-value and the FI. **Conclusions:** Statistical significance of trials supporting drug approval in common solid tumors relies often on a small number of events. In most trials the FI was lower than the number of patients lost to follow up or withdrawing consent. Post-approval randomized trials or real-world data analyses should be performed to ensure that effects observed in registration trials are robust. Research Sponsor: None.

2057 Poster Session (Board #49), Fri, 8:00 AM-11:00 AM

Core limitations in clinical trials leading to anticancer drug approvals by the U.S. Food and Drug Administration. *First Author: Talal Hilal, University of Mississippi Medical Center, Jackson, MS*

Background: To date, a comprehensive evaluation of core limitations in clinical trials leading to anti-cancer drug approvals by the US Food and Drug Administration (FDA) has not been undertaken.The aim of this analysis was to assess the percentage of clinical trials with core limitations, defined as lack of randomization, lack of overall survival data, inappropriate use of crossover, and use of sub-optimal control arms that led to FDA approvals from 2014 to 2019. **Methods:** This observational analysis included all approved anti-cancer drug indications by the FDA from July 2014 through July 2019. All indications were investigated and each clinical trial evaluated for design, enrollment period, primary endpoints, and presence of core limitations. The standard of care therapy was determined by evaluating the literature and published guidelines 1-year prior to start of clinical trial enrollment. Crossover was examined and evaluated for optimal use. We then calculated the percentage of approvals based on clinical trials with any or all core limitations. **Results:** A total of 187 anti-cancer approvals were evaluated. The number of anti-cancer drug approvals doubled over time with 68 in first half of study period (June 2014 to December 2016) to 119 in second half of study period (January 2017 to July 2019). Of those, 125 (67%) were based on a clinical trial with at least one core limitation. 64 (34%) approvals were based on a single-arm clinical trial. Of the remaining 123 approvals based on randomized trials, 60 (32%) had a core limitation. Of all randomized trials, 37 (30%) lacked overall survival benefit, 31 (25%) had a sub-optimal control, and 17 (14%) used crossover inappropriately. **Conclusions:** The majority of cancer drugs are approved based on clinical trials with core limitations. Efforts to minimize core limitations at the time of clinical trial design are essential to ensure that new anti-cancer drugs being marketed truly improve patient outcomes over current standards. Research Sponsor: None.

2058 Poster Session (Board #50), Fri, 8:00 AM-11:00 AM

Gender-based disparities in clinical trials supporting FDA approval of oncology drugs. *First Author: Marjorie Zettler, Cardinal Health, Dublin, OH*

Background: Adequate gender representation in clinical trials of new drugs is critical in order to accurately detect possible differences in response and toxicity (Özdemir et al, JCO 2018). The under-representation of women in oncology clinical trials has been previously described, however data on registrational trials, which are the basis for drug approval and inform the prescribing information, is lacking. We conducted an analysis of the trials supporting Food and Drug Administration approval of oncology drugs over a 5-year period to evaluate the representation of women vs. men. **Methods:** Prescribing information for novel new drugs approved from 2014-2018 was reviewed for the proportions of men and women in the evaluable population of the supporting clinical trials. Sex-specific cancers were excluded. Prevalence estimates for the indications were obtained from the Surveillance, Epidemiology and End Results database and the published literature. A participation to prevalence ratio (PPR) was calculated for each trial by dividing the percentage of women in the trial by the percentage of women in the disease population. A PPR value closer to unity represents even gender distribution and the range 0.8-1.2 is considered to reflect an acceptable representation of women. Data are presented using descriptive statistics. **Results:** A total of 46 oncology drugs were approved based on 56 trials enrolling 13,862 patients (7941 [57%] men; 5,921 [43%] women). Of the 56 trials, 38 (68%) had a PPR within the 0.8-1.2 range, 15 (27%) fell between 0.4-0.7, and 3 (5%) had a PPR of 1.3. The proportion of trials with unbalanced gender representation was comparable for hematological malignancy and solid tumor indications and did not improve over time. Fewer unbalanced trials were Phase III or employed a randomized design. Nine of the 18 (50%) unbalanced trials enrolled <100 subjects, compared to 3 of the 38 (8%) balanced trials. **Conclusions:** A third of registrational trials for oncology drugs lacked balanced gender distribution. Of the trials lacking balance, the vast majority (80%) had under-representation of women. Phase I-II trials and smaller trials had greater gender disparity, a concerning finding in a precision medicine environment where an increasing number of registration trials have double digit accrual. Further research is needed to understand the implications of unbalanced gender accrual in registrational trials, and to develop strategies for preventing disparities. Research Sponsor: Cardinal Health.

2059 Poster Session (Board #51), Fri, 8:00 AM-11:00 AM

Performance status restriction in phase III cancer clinical trials. *First Author: Ramez Kouzy, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Patients with good performance status (PS) tend to be favored in randomized clinical trials (RCTs), possibly limiting the generalizability of trial findings. We sought to characterize trial-related factors associated with the use of eligibility criteria that restrict patients by PS, and analyze patient accrual breakdown by PS. **Methods:** We searched ClinicalTrials.gov for phase III RCTs between 2003-2018. Randomized multi-arm trials assessing a therapeutic intervention in cancer patients were included. PS data were extracted from corresponding manuscripts. Trials with PS restriction Eastern Cooperative Oncology Group (ECOG) ≤1 were identified. Factors associated with PS restriction were determined, and trial patient accrual was analyzed. **Results:** Six-hundred trials were included with PS data for 238,213 patients. In total, 527 studies (87.8%) specified an upper PS restriction cutoff as part of their exclusion criteria, and 237 studies (39.5%) had a strict inclusion criterion of patients with ECOG PS ≤1. Enrollment criteria restrictions based on PS (ECOG PS ≤1) were more common among industry-supported trials (P< 0.001) and lung cancer trials (P < 0.001). Nearly half of trials that led to subsequent FDA approval included strict PS restrictions. Binary logistic regression revealed stable use of restrictive PS eligibility criteria between 2007-2018 (P= 0.789). The vast majority of patients enrolled across all trials had an ECOG PS of 0 to 1 (96.3%). Even among trials that allowed patients with ECOG PS ≥2, only 8.1% of enrolled patients had a poor PS (ECOG 2 or higher).Trials of hematologic cancers had the largest proportion of patients with ECOG PS ≥2 (8.7%), while lung, breast, gastrointestinal and genitourinary trials all included less than 5% of patients with poor PS (P< 0.001). Only 4.8% of patients enrolled in trials that led to subsequent FDA approval had a poor PS. **Conclusions:** The use of PS restrictions in oncologic RCTs is pervasive, and exceedingly few patients with poor PS are enrolled. The selective accrual of healthier patients has the potential to severely limit and bias trial results. Future trials should consider a wider cancer population with close toxicity monitoring, to ensure generalizability of results, while maintaining patient safety. Research Sponsor: None.

2060 Poster Session (Board #52), Fri, 8:00 AM-11:00 AM

Trends in FDA cancer registration trial design over time, 1969-2020. *First Author: Jeremy Lyle Warner, Vanderbilt-Ingram Cancer Center, Nashville, TN*

Background: The FDA has issued hundreds of cancer drug indications, with many new drugs, expanded indications, and biosimilars approved in recent years. While the gold standard for regulatory approval is the randomized controlled trial (RCT), RCT design including selection of control arms can differ considerably. We sought to investigate trends and patterns in RCT trial design used to support FDA approvals in oncology. **Methods:** We reviewed the available FDA package inserts of oncology drugs (N=258) for RCTs cited to support initial and expanded indication approvals as of January 2020; biosimilars were excluded. RCTs were linked to the HemOnc ontology, which contains trial-level metadata including publication year, endpoints, and trial design. Log-linear regression was performed to evaluate trends in approvals over time by endpoint. Study drugs were categorized as cytotoxic therapy, targeted therapy, or immunotherapy. RCTs were categorized by four designs: escalation (adding a drug or increasing the drug dose in an established regimen), in-class comparison (comparing two drugs in the same therapeutic class), out-of-class switch (comparing drugs in distinct therapeutic classes), and de-escalation (removing a drug or reducing the drug dose in an established regimen). **Results:** We identified 556 registration trials, 372 (67%) of which were RCTs. Approvals have been increasing exponentially over time (R^2 0.9, p<0.001), both for RCTs reporting overall survival (OS) endpoints (R^2 0.77, p<0.001), and non-OS endpoints (R^2 0.67, p<0.001). Of the three most common trial designs (Table), in-class comparisons were least likely to report OS (28%; escalations 47%; out-of-class switches 43%, p=0.01 by Chi-squared). Class switches were common in immunotherapy trials compared to targeted or cytotoxic therapy. **Conclusions:** Despite growth in FDA approvals, a minority of registration trials report paradigmatic shifts in therapeutic approach (out-of-class switches), with the relative exception of immunotherapy trials. Escalation is the most common route to FDA approval, even though this design inevitably increases cost and toxicity. This suggests that new oncology drug approvals are not alone a useful metric of practice-changing innovation. Research Sponsor: U.S. National Institutes of Health.

Distribution of RCT design by therapeutic category.*

	All trials, n (%)	Cytotoxic therapy, n (%)	Targeted therapy, n (%)	Immunotherapy, n (%)
Escalation	217 (58)	99 (63)	154 (60)	26 (50)
In-class comparison	93 (25)	45 (29)	51 (20)	4 (8)
Class switch	54 (14)	5 (3)	51 (20)	**22 (42)**
De-escalation	11 (3)	9 (6)	2 (<1)	0 (0)

*some trials tested multiple categories

2061 Poster Session (Board #53), Fri, 8:00 AM-11:00 AM

Use of real-world data to understand barriers to interventional clinical trial enrollment in community oncology clinics (COC). *First Author: Johnetta Blakely, Tennessee Oncology, Nashville, TN*

Background: Increasing enrollment in clinical trials remains a national priority, yet there are limited data from COCs on the degree to which common trial exclusion criteria (EC) and socioeconomic factors play a role in low enrollment rates. **Methods:** We analyzed data from the nationwide Flatiron Health electronic health record (EHR) derived de-identified database. COC were eligible if they had given a clinical trial study drug to ≥2 patients (pts)/year. We included pts with one of eight advanced or metastatic solid tumors who received ≥1 line of systemic anticancer therapy between 1/1/2014 and 11/30/2019. We defined EC as either: creatinine > 1.5 mg/dl or CcI < 45 ml/min, Hb < 9 g/dL, ANC < 1500/ul, plts < 100,000/ul, bilirubin > 1.5 upper limit of normal (uln) or AST/ALT > 2.5 uln within 30 days or ECOG performance status (PS) ≥ 2 within 60 days prior to start of therapy. We calculated the percentage of pts with ≥1 EC relative to the group of candidate pts, stratified by therapy line (1L, 2L, 3L+). We used multivariate logistic regression models to evaluate the effect of EC and socioeconomic factors (age, race, Medicaid) on the likelihood of receiving a clinical study drug for each line of therapy. **Results:** In this sample of 35 COCs, 26,988 pts received ≥1 systemic therapy. Pts with ≥ 1 EC: 28.4% in 1L, 34.2% in 2L, 37.4% in 3L. Percentages of pts with an ECOG PS ≥ 2 were: 15.6% (1L), 18.2% (2L), 19.8% (3L). Pts receiving a clinical study drug: 1.7% of 26,988 in 1L, 2.0% of 12,738 in 2L, 2.9% of 5,333 in 3L+, and 3.1% in any line. Excluding pts with ≥1 EC from the denominator modestly improved overall accrual: 2.0% of 19,729 in 1L, 2.3% of 8,588 in 2L, 3.7% of 3,470 in 3L+. In multivariate logistic regression, ECOG PS ≥ 2 was strongly associated with not receiving a study drug [odds ratio (95% CI); 1L: 0.25 (0.16-0.4); 2L: 0.28 (0.17-0.49); 3L: 0.21 (0.1-0.44)]. The likelihood of receiving a clinical study drug (any line) was lower for pts who are Black [0.63 (0.48-0.82)], Latino [0.49 (0.32-0.75)], and pts older than 70 years [0.63 (0.54-0.72)]. Medicaid pts were not significantly less likely to receive study drug [0.83 (0.64-1.07)]. **Conclusions:** In COC, common trial EC reduce pt availability for trials by > 25%. Poor PS is highly prevalent and influential. These EC and complex trial requirements challenge COC's ability to recruit representative pt populations. Future efforts to increase enrollment in trials must consider common EC along with well known barriers to enrollment of unrepresented groups. Research Sponsor: Flatiron Health, Inc.

2062 Poster Session (Board #54), Fri, 8:00 AM-11:00 AM

A pilot study of a wearable monitoring system as an adjunct to geriatric assessment in older adults with cancer. *First Author: Karlton Wong, UCLA, Santa Monica, CA*

Background: Advances in health technology provide potential tools that can aid in assessing and monitoring the functional status of the growing older adult population diagnosed with cancer. We piloted a novel wearable monitoring platform, Sensing in At-Risk Populations (SARP), which consists of a smartwatch, software application for health monitoring, and a central data processing and analytics engine. **Methods:** This is a prospective single center, single arm study, utilizing the SARP platform to risk stratify older adults with cancer and determine correlation with treatment-related adverse events and healthcare utilization. Pts age ≥60 undergoing active treatment, were offered participation. Pts were instructed to wear the smartwatch for ≥7 days. We used Kruskal-Wallis to correlate wearable data with clinical outcomes: toxicity, ED visits, hospitalizations, and mortality. We also compared SARP data to independently collected ECOG PS, CARG score, ADLs, and IADLs. **Results:** From 8/2016 to 8/2017, 54 older adults were consented, and 26 had wearable data available for analysis. The average age was 72 years, with 18 males and 8 females. 12 pts had ECOG PS of 0, 12 with ECOG of 1, and 2 with ECOG of 2. 4 pts had CARG score of low, 17 intermediate, and 3 high. Energy intensity was significantly correlated with ED visits, with an effect size of 0.95 (p = 0.04). Similarly, energy intensity and hospitalizations had an effect size of 0.87 (p = 0.06). The CARG scores were noted to be significantly correlated with dose delay and dose reduction with an effect size 0.45 (p = 0.05) and 0.4 (p = 0.05), respectively. Spearman correlation analysis demonstrated that walking time, active time, and energy intensity positively correlate with ADLs and IADLs, and inversely correlated with ECOG PS and CARG risk. **Conclusions:** Though this is a limited study due to sample size, the overall trend demonstrated that the SARP platform offers an adjunct tool in assessing and risk stratifying older patients with cancer undergoing active therapy. Additional cohorts are now enrolled with an at-home monitoring system. Research Sponsor: AHRQ R01HS024394.

	Dose Delay		Dose Reduction		ED Visits		Hospitalizations	
	Effect Size	p-Value	Effect Size	p-Value	Effect Size	p-Value	Effect Size	p-Value
ECOG	0.08	0.78	0.11	0.81	0.24	0.68	0.03	0.94
CARG	**0.45**	**0.05**	**0.40**	**0.05**	0.92	0.40	1.18	0.18
ADL	0.46	0.43	0.50	0.29	0.46	0.42	0.44	0.48
IADL	0.20	0.83	0.12	0.99	0.18	0.71	0.07	0.89
Energy	0.56	0.36	0.10	0.85	**0.95**	**0.04**	**0.87**	**0.06**
Active	0.15	0.99	0.48	0.31	0.11	0.85	0.41	0.41
Walking	0.68	0.22	0.23	0.43	0.68	0.14	0.59	0.28
Stationary	0.68	0.22	0.23	0.43	0.68	0.14	0.59	0.28

2063 Poster Session (Board #55), Fri, 8:00 AM-11:00 AM

Home ePRO compliance in prostate cancer clinical studies. *First Author: Sarah Tressel Gary, ERT, Boston, MA*

Background: Patient-reported outcomes (PRO) and electronic PRO (ePRO) play an important role in the development and approval of cancer products. Regulatory agencies are encouraging the inclusion of PRO-based endpoints that are indicative of clinical benefit in terms of patient symptoms and overall quality of life (QOL). Compliance with completion of ePRO assessments is an important component for obtaining accurate and high-quality data when conducting clinical trials. Traditionally, ePRO data in oncology trials has been collected mainly at clinic visits due to concerns over poor compliance at home. However, since symptoms and QOL can vary widely through a treatment course, it is often necessary to collect ePRO data more frequently in between clinic visits. It has been hypothesized that home completion, length of time in a study, and number of assessments may affect compliance. **Methods:** To address this hypothesis, ePRO compliance data was analyzed from two clinical studies in prostate cancer. Both studies used a handheld smartphone that contained an application to collect ePRO data. At the randomization visit, subjects completed ePRO assessments in clinic (2-3 questionnaires). Subsequently, all assessments were completed at home, including a daily diary and 1-4 questionnaires completed every 4-8 weeks for up to 14 months. Compliance was calculated as the number of assessments received divided by the number of assessments expected in a given assessment period. To evaluate assessment burden, each assessment period was categorized as requiring a lower number (daily diary and 1 questionnaire) or higher number (daily diary and 2-4 questionnaires) of assessments. **Results:** A total of 1,040 patients were included in the analysis. Overall compliance at the single clinic visit was 100%, which was expected since it was a required randomization visit. Overall compliance at home over 14 months was 80%. Compliance ranged from 78% to 89% over the duration of the studies, with no effect of time in the study on compliance. Compliance remained high even as patient numbers declined. Compliance when patients were required to complete a lower number of assessments (80%) was similar to compliance when patients were required to complete a higher number of assessments (79%). Compliance by region varied from 72% (Middle East) to 87% (Asia and Eastern Europe). **Conclusions:** The collection of ePRO at home provided high compliance that did not vary with length of time in the study or due to assessment burden. At home ePRO assessments provide an effective and feasible approach for recording symptoms and QOL in prostate cancer patients. Research Sponsor: ERT.

2064 Poster Session (Board #56), Fri, 8:00 AM-11:00 AM

Self-reported overall wellbeing (OWb), physical function (PFn), and PRO-CTCAE symptom scores in post-operative and chemotherapy patients. *First Author: Hannah Hazard, West Virginia University, Morgantown, WV*

Background: A standardized, validated tool for capturing symptoms from cancer patients, PRO-CTCAE, has been used to reduce symptom burden, decrease acute care needs, and preserve quality of life. The association between specific PRO-CTCAE symptom scores and single item measures of OWb and PFn were characterized to understand symptom constellations. **Methods:** A novel Epic-based symptom management program (eSyM) was deployed for GI, GYN, and thoracic cancer patients starting chemotherapy (Memphis Baptist) or having surgery (WVU Medicine). Patients received automated prompts to complete surveys via the patient portal (MyChart) on a fixed schedule, approximately twice/week. Each survey included one OWb item, one PFn item, and at least 6 PRO-CTCAE items (pain, nausea, vomiting, fatigue, anxiety, insomnia). The OWb and PFn items, which were created *de novo*, included 5 ordinal response options with corresponding pictograms (emojis from very happy to very sad for OWb; a figure walking to one prone in bed for PFn). Composite scores were generated: 0 for no symptoms, 1-2 for mild/moderate symptoms, and 3 for severe symptoms. We describe OWb and PFn and analyze associations between these items and PRO-CTCAE symptom scores. **Results:** Between 9/10/19-1/22/20, we collected 908 eSyM responses from 166 chemotherapy patients at Baptist (Age, M = 65), and 480 eSyM responses from 97 postoperative patients at WVU (Age, M = 57). The OWb and PFn scores demonstrated moderate correlation with PRO-CTCAE symptom scores (Baptist r = 0.63; WVU r = 0.75), and moderate correlation with mean symptom scores among surgery patients at WVU (r = 0.74); but lower correlation among chemotherapy patients at Baptist (r = 0.53-0.55). Scores improved over time following surgery, but not after initiation of chemotherapy. Among the 730 eSyM responses with none/mild values for both OWb and PFn (52.9% of all responses), only 4.5% reported any severe symptom; among 651 responses with impairment of OWb and/or PFn, 45.2% reported at least one severe symptom. **Conclusions:** Integration of eSyM into the Epic EHR enabled tracking of OWb, PFn, and PRO-CTCAE items. When asked alongside PRO-CTCAE symptom items, two single item OWb and PFn measures provided distinct information and correlated with symptom burden. These results demonstrate the feasibility of integrating ePRO collection into routine post-operative and medical oncology care and that PRO-CTCAE items provide information that is distinct from that obtained from global metrics of well-being. Clinical trial information: NCT03850912. Research Sponsor: U.S. National Institutes of Health.

2065 Poster Session (Board #57), Fri, 8:00 AM-11:00 AM

Mobile apps: Breaking barriers to early cancer detection in underserved communities. *First Author: Carlos A. Munoz-Zuluaga, Mercy Medical Center, Baltimore, MD*

Background: Despite being potentially curable with early detection and timely treatment, breast (BC) and cervical cancers (CC) remain leading causes of death for Colombian women. Lack of cancer screening education, tedious administrative processes, and geographical limitations hinder early cancer detection. Today, technological tools permeate all levels of society and could gather data for user risk stratification, deliver clear and customized information, and help with care coordination, tracking, and addressing communication, transportation, and financial barriers. We aimed to assess the effectiveness of a free mobile application (mApp) to reach women, understand misconceptions about cancer screening, identify users at risk for BC and CC, and coordinate screening tests in Cali, Colombia. **Methods:** The mApp, Ámate, was developed over 4 months and advertised to women (≥14 years) in waiting rooms of 4 healthcare facilities in Cali, Colombia for 23 months. Ámate used educational, evaluative, and risk factor questions followed by brief explanations to assess the population's knowledge, educate users on BC and CC, and identify users in need of BC and/or CC screenings. Correct answers yielded points redeemable for cellular data. Women who required screening were subsequently navigated to a healthcare provider and enrolled in the national cancer program. **Results:** From August 2017-August 2019, 1,043 women from Cali downloaded Ámate and answered all questions. Misconceptions about BC included beliefs that BC can be prevented (87%), obesity does not increase the risk of BC (49%), deodorant causes BC (17%), and only women with a relative with BC can get BC (16%). For CC, misconceptions included that pap smears should not be performed while sexually active (64%), vaginal pain is an early sign of CC (44%), and only women contract HPV (33%). Overall, 31.5% (329) were identified as at-risk and needed a mammogram and/or pap smear. So far, 30% (98) were successfully navigated and completed their recommended screening test(s). Barriers to enrollment in these programs included patient unwillingness, using fake contact information, limited available appointments, and denied access due to healthcare coverage. **Conclusions:** Ámate is an accessible tool that identifies women at-risk for breast and cervical cancer and detects barriers to early cancer detection. Administrative obstacles exist and must be addressed to improve early cancer detection/screening. Ámate is currently being tested in other areas of Colombia and may be useful in other underserved countries. Research Sponsor: American Cancer Society, Susan G. Komen Foundation.

2066 Poster Session (Board #58), Fri, 8:00 AM-11:00 AM

MSK eConsent: Digitalizing the informed consent process to improve participant engagement and understanding. *First Author: Michael T. Buckley, Memorial Sloan Kettering Cancer Center, NY, NY*

Background: eConsent was developed to digitize the research participant consenting experience with an educational engagement model. The eConsent platform tiers consent document content in an easy-to-navigate format, using videos, images, and access to supplementary information. We hypothesize that enhancing the consenting experience improves participant engagement and comprehension. **Methods:** Here we present two projects: 1) qualitative assessment of patient engagement in the eConsent process using a standardized 5-question survey sent to all patients who used it during 9 months in 2019, and 2) a report of our preliminary findings from exempt protocol, *Assessing Participant Engagement and Protocol Education in the Consent Process* (X19-055) that quantitatively compares paper and electronic consenting and a) assesses patient agency and b) tests comprehension of key consent elements in 2 protocols: *Storage and Research Use of Human Biospecimens* (06-107) and *Genomic Profiling in Cancer Patients* (12-245). **Results:** 1) 940 patients completed the qualitative experience survey (27% response). Most respondents (777; 83%) indicated that electronic consenting was very easy (371) or easy (406) to use. Only 25 (3%) said electronic consenting was somewhat difficult to use, 3 indicated it was difficult (0.3%), and 64 were neutral. Most (896; 95%) recommended electronic consenting to other MSK patients. Those who reported a 1 unit increase in technology discomfort, only reported a .48 unit increase in eConsent discomfort ($P < .001$). 2)Quantitative 10-question electronic tests were sent to each patient's portal account within 72h after consenting via paper or eConsent to protocols 06-107 and 12-245. To date, for 06-107: 18 paper consenters completed the test with a score of 76% vs 23 eConsent users who scored 80%. For 12-245: 43 paper consenters scored 69% vs 13 eConsent users scoring 80%. Scores are a surrogate marker for patient comprehension and show that 12-245 protocol participants' average testing scores are higher when participants are consented with eConsent vs paper ($P < .01$). 06-107 protocol participants' average test scores are trending toward eConsent improving patient understanding ($P = .11$). We will follow this trend as our sample size increases to a total of 500 participants. Patient agency questions received favorable responses from most patients (100%-84%). **Conclusions:** eConsent enhances participant engagement and understanding and does not impose a digital burden on participants. Research Sponsor: None.

2067 Poster Session (Board #59), Fri, 8:00 AM-11:00 AM

A prospective trial of standard versus multimedia counseling in patients undergoing endometrial cancer surgery. *First Author: Katherine Tucker, University of North Carolina, Division of Gynecologic Oncology, Chapel Hill, NC*

Background: A patient's understanding of surgery is often limited, especially in the setting of complex oncologic procedures. A recent review found that interventions such as the use of written materials, videos, and websites, improve patients' knowledge of the procedure and their satisfaction with decision making. We sought to determine if a video-based approach in patients undergoing robotic endometrial cancer staging improves satisfaction with perioperative counseling. Secondary objectives were physician satisfaction, patient comprehension, and visit length. **Methods:** From 2018-2019, patients were randomized to standard physician education or multimedia-based education, which included watching two novel animated videos followed by focused physician counseling. Basic demographic information was collected. Patient satisfaction was assessed using the Client Satisfaction Questionnaire-8 (CSQ-8, a validated satisfaction survey, scored 8-32) and a global satisfaction score (10-point scale). Physician satisfaction was assessed using a global satisfaction score. Comprehension was assessed with a 9 question survey at 3 time points. Descriptive statistics were used to compare groups. **Results:** Of 76 patients randomized, the majority were Caucasian (68%), 50-70 years old (70%), and had at least some college education (75%). Most patients had undergone prior surgery (83%) and one fourth had a prior cancer diagnosis. Demographic variables and surgical history were similar between groups. The video patients reported higher satisfaction on the CSQ-8 (31.57 ± 1.02 vs 30.62 ± 2.09, $p < 0.05$) and global satisfaction score (9.95 ± 0.23 vs 9.74 ± 0.55, $p < 0.05$). There was no difference in comprehension scores between groups at either the initial or postoperative visit. At the time of surgery, comprehension scores were higher in the standard education group compared to the video group ($p < 0.01$). There was no difference in physician satisfaction between groups. Among the video group, there was improvement in physician satisfaction between the first and second half of patients enrolled ($p < 0.05$). There was no difference in visit length. **Conclusions:** While multimedia education improved patient satisfaction in the preoperative setting, this was not clinically significant. Provider satisfaction improved over time with the use of a video aid. Multimedia education may be implemented in perioperative counseling based on provider preference and consideration should be made for further study of satisfaction after the initial implementation period. Clinical trial information: NCT03899441. Research Sponsor: Fowler Fellowship Fund.

2068 Poster Session (Board #60), Fri, 8:00 AM-11:00 AM

The association between drug industry payments and NCCN guideline panel membership. *First Author: Aaron Philip Mitchell, Memorial Sloan Kettering Cancer Center, New York City, NY*

Background: The high frequency of financial relationships between the pharmaceutical industry and influential oncologists who author clinical practice guidelines may influence guideline recommendations. Therefore, we assessed the financial relationships held by NCCN Guidelines panelists before and after joining the panel, compared to those held by a matched set of oncologists. **Methods:** Membership of NCCN Guidelines panels for the 20 most common cancers was obtained from archival guidelines and linked manually to Open Payments records of industry payments. We identified physicians who newly joined an NCCN panel during the August 2013-December 2018 study period, and we included medical oncologists who had at least 1 year of Open Payments data before and after joining. These medical oncologists who joined an NCCN panel (panelists) were matched 1:2 to medical oncologists with the same gender, institutional affiliation, and medical school graduation year, who did not join an NCCN panel (non-panelists). The dollar value of industry payments was then calculated over the 1 year before (pre-join) and after (post-join) the date that each panelist joined. We used generalized linear models to assess differences in industry payments between the panelists and matched non-panelists in the pre-join period. We used difference-in-difference estimation (DiD) to assess whether joining an NCCN panel was associated with increased payments in the post-join period. **Results:** There were 54 panelists and 108 non-panelists (matched from 1447 eligible oncologists at NCCN institutions). Mean per-oncologist payments among panelists were greater than non-panelists in the pre-join period ($11,259 vs $3,427, p = 0.02). From the pre-join to post-join period there was a similar increase in mean per-oncologist payments among panelists and non-panelists ($2,236 vs. $1,569, DiD estimate +$667, p = 0.77). **Conclusions:** Medical oncologists who were selected to an NCCN Guidelines panel had greater financial ties to industry compared to peer oncologists who were not selected. This difference was present prior to joining; oncologists did not experience a greater increase in financial payments from industry in the 1-year period after joining an NCCN panel. These results suggest an opportunity to reduce the potential influence of industry in oncology clinical practice guidelines through the selection of guideline panelists with fewer ties to industry. Research Sponsor: None.

2069 Poster Session (Board #61), Fri, 8:00 AM-11:00 AM

Actionable policy barriers for receiving standard of care treatment among unresected stage III non-small cell lung cancer (NSCLC) patients in the United States. *First Author: Zhiyuan Zheng, American Cancer Society, Atlanta, GA*

Background: Recent data suggests that a significant number of good performance, unresectable stage III non-small cell lung cancer (NSCLC) patients do not receive standard-of-care treatment, i.e. concurrent chemoradiotherapy (cCRT) followed by durvalumab, despite being eligible. However, little is known about actionable policy barriers to delivery of cCRT to this patient population. **Methods:** The National Cancer Database (2004-2016) was used to identify unresected stage III NSCLC patients aged 18-79 years with Charlson comorbidity score ≤ 1. cCRT was defined as the initiations of chemotherapy (CT) and radiation therapy (RT) that were ≤ 14 days (n = 53,444) apart. The remaining treatment groups included sequential CRT (sCRT; n = 16,666), CT only (n = 15,416), RT only (n = 11,579), and no first course treatment (n = 16,691). Multinomial logistic regressions were used to examine the likelihoods of receiving different treatment modalities, controlling for patient demographics, Charlson comorbidity score, health insurance, facility type, social deprivation index (SDI, a comprehensive socio-economic measure; higher SDI indicates lower socioeconomic status [SES]), driving time to facility, diagnosis year, and region. **Results:** Of the total 113,796 patients assessed (median age 66 years), most were male (55.7%), non-Hispanic white (81.7%), and with SDI score ≥ 50 (51.3%). 29.5% had Charlson comorbidity score = 1 while the rest had 0. In adjusted analyses (predicted margins), 47.0% patients received cCRT (sCRT: 14.6%; CT only: 13.5%; RT only: 10.2%; no treatment: 14.7%). Compared to the privately insured, Medicaid, Medicare, and uninsured patients were more likely to receive RT only (relative risk ratios [95%CI]: 1.93 [1.77-2.11]; 1.51 [1.41-1.61]; 1.80 [1.61-2.01], respectively) and no treatment (1.84 [1.71-1.99]; 1.54 [1.45-1.63]; 2.19 [2.01-2.40], respectively) rather than cCRT (all $p < .001$). Moreover, higher SDI was associated with higher likelihood of receiving RT only (highest vs lowest SDI scores: 1.42 [1.33-1.52]), or no treatment (1.46 [1.38-1.55]) rather than cCRT (all $p < .001$). Longer driving time was associated with higher likelihood of receiving CT only (> 120 mins vs < 30 mins: 1.24 [1.10-1.39]), or no treatment (1.33 [1.18-1.50]) rather than cCRT (all $p < .001$). **Conclusions:** Health policies should focus on patients who are not privately insured and live in neighborhoods with low SES. Moreover, helping their transportation needs may also improve the likelihood of receiving cCRT. Research Sponsor: AstraZeneca.

2070 Poster Session (Board #62), Fri, 8:00 AM-11:00 AM

Opioid prescribing patterns among generalists & oncologists for Medicare Part D beneficiaries from 2013-2017. *First Author: Trevor Joseph Royce, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC*

Background: In response to the opioid crisis, recent policies aiming to reduce opioid prescribing, misuse, & abuse have generated concern that patients with cancer pain may unintentionally experience reduced access to necessary opioid therapy. It is unknown how opioid prescribing patterns have changed between generalists and oncologists during this era. **Methods:** We conducted a longitudinal repeated cross-sectional study estimating adjusted annual national trends in opioid prescribing among generalists & oncologists using the Medicare Part D Prescriber Public Use Files 2013-2017. Poisson models estimated annual adjusted predicted mean rates of opioid prescribing-per-1,000 total prescriptions & long-acting opioid prescribing per-1,000 opioid prescriptions. Poisson models estimated adjusted incidence rate ratios (aIRRs) to quantify annual changes in prescribing rates. **Results:** From 2013-2017 the annual adjusted predicted mean rate of opioid prescriptions per 1,000 total prescriptions decreased from 53.4 to 41.3 among generalists (aIRR = 0.78; $p < 0.01$) and from 133.2 to 105.9 among oncologists (aIRR = 0.83; $p < 0.01$). The rate of long-acting opioid fills per 1,000 opioid prescriptions decreased from 96.0 to 87.0 (aIRR = 0.87; $p < 0.01$) and 235.1 to 222.5 (aIRR = 0.95; $p < 0.01$) for generalists & oncologists, respectively (Table). **Conclusions:** We found large declines in overall opioid prescribing rates among generalists (-22%) and oncologists (-17%) from 2013-2017. Long-acting opioid prescribing rates decreased over 2.5-times more among generalists than oncologists. Opioid policy & advocacy have been effective in reducing the extent of opioid prescribing in the Medicare population but how much of the decrease in prescribing by oncologists is 'appropriate' versus 'inappropriate' deserves further investigation. Research Sponsor: U.S. National Institutes of Health.

	All opioids				Long Acting opioids			
	Generalists		Oncologists		Generalists		Oncologists	
	aIRR (95%CI)	P	aIRR (95%CI)	P	aIRR (95%CI)	P	aIRR (95%CI)	P
2013	Ref		Ref		Ref		Ref	
2014	0.98 (0.97-0.99)	< .01	0.97 (0.95-0.98)	< .01	0.98 (0.97-0.99)	< .01	1.00 (0.98-1.02)	1.00
2015	0.92 (0.91-0.92)	< .01	0.92 (0.91-0.94)	< .01	0.94 (0.93-0.95)	< .01	1.01 (0.99-1.04)	0.24
2016	0.85 (0.85-0.86)	< .01	0.88 (0.87-0.90)	< .01	0.92 (0.91-0.93	< .01	0.99 (0.97-1.02)	0.52
2017	0.78 (0.77-0.78)	< .01	0.83 (0.82-0.85)	< .01	0.87 (0.86-0.88)	< .01	0.95 (0.93-0.98)	< .01

2071 Poster Session (Board #63), Fri, 8:00 AM-11:00 AM

Timing of US Food and Drug Administration (FDA) cancer drug approvals relative to publication of clinical trial results. *First Author: Ali Raza Khaki, University of Washington, Seattle, WA*

Background: Publication of clinical trial results in peer reviewed literature is essential to inform clinicians regarding the use of new anti-cancer treatments, which often have a low therapeutic ratio and require careful assessment of risks and benefits. Publication of registration trials should precede FDA approval to facilitate evaluation and implementation of new therapies. The timing of trial publication relative to FDA drug approvals has not been systematically investigated. **Methods:** We collected all FDA drug approvals for a cancer indication between 2000-19. Trials were identified using FDA labels as well as drugs and publications indexed on HemOnc.org. Approvals for generics/biosimilars, non-oncology indications and label revisions without supportive evidence were excluded. Dates of approval, the approval pathway, approval type (new vs expansion), and the first full publication related to the registration were recorded. Trials and approvals were matched using available metadata. We calculated the proportion of drugs approved prior to publication overall and for those receiving accelerated approval (AA). We used logistic regression to compare rates of pre-publication approval by approval pathway and by new vs expanded approval. **Results:** Among a total of 378 drug approvals, 139 (37%) had pre-publication approval. Of these, the median overall time from approval to publication was 140 days (IQR 64-281 days). For those with approval after publication, median time from publication to approval was 157 days (IQR 72-359 days). The number of drugs approved pre-publication rose by 27% between the first and last quarters of the study period, though, the proportion decreased as more anti-cancer drugs have been approved in recent years (Table). More drugs were approved pre-publication through AA than regular approval (46% vs 34%, OR 1.66 [95% CI 1.03-2.70], p=0.04) and as new approvals vs. expanded approvals (45% vs 32%, OR 1.76 [95% CI 1.15-2.70], p=0.01). **Conclusions:** A substantial minority of FDA approvals occur before trial results are published, with the odds being higher for drugs receiving AA and for new approvals. Since clinicians rely upon published results to inform risk/benefit decisions, efforts are needed to ensure trial results are published by the time of FDA approval of new cancer drugs and indications. Research Sponsor: U.S. National Institutes of Health.

Years	Fraction of pre-publication approvals, n/N (%)	Fraction of AA pre-publication approvals, n/N (%)
2000-05	30/46 (67)	10/15 (67)
'06-10	33/61 (55)	5/14 (36)
'11-15	38/103 (37)	15/28 (54)
'16-19	38/170 (22)	11/32 (34)

2072 Poster Session (Board #64), Fri, 8:00 AM-11:00 AM

Mismatch between mortality burden and number of FDA registration trials in highly lethal cancers. *First Author: Bishal Gyawali, Brigham and Women's Hospital, Boston, MA*

Background: Treatment successes in cancer are achieved through new drugs tested in clinical trials. However, drug discovery has been disparate across cancer types for various reasons. We sought to investigate if the number of trials used to support United States Food and Drug Administration (FDA) drug approvals is proportional to the incidence and mortality burden of highly lethal cancers, i.e. those with an expected relative mortality of >5% per *Cancer Statistics, 2020* (Siegel et al.). **Methods:** All FDA labels for 258 antineoplastic cancer drugs approved as of January 2020 were reviewed for citations of registration trials supporting initial approval and additional indications. Trials were identified by matching described characteristics (e.g., patients enrolled, clinical trial NCT codes) to publications indexed on HemOnc.org. Trials were labeled by cancer type studied and type of trial (randomized vs non-randomized). **Results:** We identified 559 registration trials in total. Results for the six highly lethal cancers are shown in the table. The percent of registration trials was roughly proportional to incidence, but not mortality burden. For example, despite the 22% expected mortality burden of lung cancer, it had a share of only 11% of registration trials whereas breast cancer has an expected 7% mortality burden, with a share of 14% of registration trials. Chronic myeloid leukemia is expected to cause 1,130 deaths in 2020 (0.2%) and has had 20 registration trials (3.6%). The highly lethal cancers had a higher rate of randomized trials supporting approval than other cancers (84% vs 56%, p<0.001 [Chi-square]). **Conclusions:** While the findings may in part be due to disease biology (e.g., pancreatic ductal adenocarcinoma has proven resistant to many novel therapies), our evaluation highlights a potential mismatch between resources and needs. Randomized trials were more often used to support new drug approvals in highly lethal cancers. These findings will be important in regulatory policy. Research Sponsor: U.S. National Institutes of Health.

Cancer type	Expected Cases, 2020 (%)	Expected Deaths, 2020 (%)	Registration Trials (%)	Of which, Randomized (%)
Lung*	228,820 (13)	135,720 (22)	59 (11)	46 (78)
Colorectal	147,950 (8)	53,200 (9)	33 (6)	26 (79)
Pancreas**	57,600 (3)	47,050 (8)	9 (2)	8 (89)
Breast	279,100 (15)	42,690 (7)	80 (14)	74 (92.5)
Prostate	191,930 (11)	33,330 (5)	31 (5)	25 (81)
Liver & Bile duct	42,810 (2)	30,170 (5)	7 (1)	5 (71)
Subtotal	948,210 (52)	342,160 (56)	219	184 (84)
Total	**1,806,590**	**606,520**	**559**	**375 (67)**

*Includes small cell and non-small cell histologies **Includes adenocarcinoma and neuroendocrine histologies

2073 Poster Session (Board #65), Fri, 8:00 AM-11:00 AM

Reliability and correlations among quality measures for lung, breast, and colorectal cancer. *First Author: Jessica Cleveland, Dana-Farber Cancer Institute, Boston, MA*

Background: Alternative payment models for oncology seek to improve quality and reduce spending. Yet the ability to measure high-quality care across oncology practices remains uncertain. We characterized quality of care for oncology practices using registry and claims-based measures of processes, utilization, end-of-life care, and survival and assessed correlations of practice-level performance across measure type and cancers. **Methods:** Using SEER-Medicare data, we studied individuals with newly diagnosed lung (N = 95,635), breast (N = 78,736), or colorectal (CRC, N = 51,385) cancers in 2010-2015 treated in oncology practices with ≥20 patients (502, 492, and 347 practices, respectively). We measured receipt of guideline-recommended treatment and surveillance (processes), hospitalizations or emergency department visits during 6-month chemotherapy episodes (utilization), care intensity in the last month of life (EOL), and 12-month survival (lung and CRC only). We calculated summary process, utilization, and EOL measures for each patient (number of measures met divided by the number for which the patient was eligible). We used hierarchical linear models with practice-level random effects to estimate summary measures and survival for each practice. We calculated practice-level reliability (a measurement's reproducibility) for each measure based on the between-measure variance, within-measure variance, and sample size. **Results:** Few practices had ≥20 patients eligible for most measures (38%, 37%, and 31% of practices had ≥20 patients for any lung, breast, and CRC measures, respectively). Measure reliability was low. Only 13%, 7%, and 20% of measures for lung, breast, and CRC, respectively, had a median reliability across practices ≥0.7. Among practices with ≥20 patients with summary measures of each type within cancer, correlations across measure types were low (all correlation coefficients (r)≤0.21 except a weak correlation of the CRC process summary measure with 1-year CRC survival, r = 0.38, $p < 0.001$). Summary process measures were minimally or not correlated across cancer type (lung, breast, CRC; all correlation coefficients ≤0.16). **Conclusions:** Claims-based measures of care processes, utilization, EOL care, and survival are limited by small numbers of fee-for-service Medicare patients across practices, even after pooling 6 years of data. Measures have poor reliability and are poorly correlated across measure or cancer type. Additional research is needed to identify reliable quality measures for practice-level alternate payment models. Research Sponsor: Arnold Foundation.

2074 Poster Session (Board #66), Fri, 8:00 AM-11:00 AM

Physician whistle-blower's experiences in hematology-oncology safety litigation against pharmaceutical companies. *First Author: Ashley Caitlin Godwin, University of South Carolina College of Pharmacy, Columbia, SC*

Background: Some clinicians have reported initial series of severe or fatal adverse drug reactions (ADRs) that affected large hematology-oncology patient numbers and for which pharmaceutical manufacturers subsequently paid large settlements or fines for allegedly failing to inform physicians about such ADRs. Based on their large human costs (> 1,000 serious illnesses or deaths) and large financial costs (> $100 million in settlements or fines), we have termed these ADRs as titanic ADRs. At a Senate hearing on one titanic, Vioxx, (a COX-2 inhibitor that was evaluated for colorectal cancer prevention), the clinician reporter was termed a "whistleblower" by a senator although this individual had not filed a formal whistleblower lawsuit. We identified physicians who would fit this characterization of whistleblowers and had published titanic hematology-oncology ADR reports in high impact journals. **Methods:** Hematology-oncology titanic ADRs were identified by collaborators with two NIH-funded drug safety networks (RADAR and SONAR (1998-2019)). Exclusion criteria included having also filed a whistleblower lawsuit. Qualitative research analyses evaluated content of statements made by whistleblowers to national reporters or at congressional hearings. **Results:** 18 physicians who reported titanic hematology/oncology-associated ADRs in peer-reviewed literature and discussed their findings in national news media outlets are included. Titanic ADRs included death, nephrogenic systemic fibrosis, coronary artery disease, and venous thromboembolism related to COX-2 inhibitors, heparin, gadolinium dye, thalidomide, lenalidomide, epoetin, and darbepoetin. Related financial settlements ranged from $100 million to $4.85 billion. Whistleblowers were from the United States, Denmark, and Germany. Primary motivations were public health and medical awareness. Whistleblowers reported having gone through lawsuits and having had executives request that the whistleblowers' university terminate employment. One whistleblower was quoted saying "I believe that the lawsuit is an attempt to silence me." **Conclusions:** Clinician whistleblowers of titanic hematology-oncology ADRs experienced reputational, financial, and personal threats. Motivations for reporting titanic ADRs were mainly public health and medical awareness focused. This differs from our previous study on clinicians publishing on non-titanic ADRs, where the primary motivation was scientific curiosity. Research Sponsor: American Cancer Society.

2075 Poster Session (Board #67), Fri, 8:00 AM-11:00 AM

Resource and reimbursement barriers to comprehensive cancer care (CCC) delivery: An Association of Community Cancer Centers (ACCC) survey research analysis. *First Author: Al Bowen Benson, Northwestern Medicine, Chicago, IL*

Background: CCC delivery is recommended in guidelines, required by accreditation bodies, and essential for high-quality cancer management. Barriers, such as insufficient reimbursement and lack of specialist staff, prevent consistent access to and delivery of CCC, particularly supportive oncology services. Challenges especially persist in community programs, where access to philanthropy and similar funding is limited. ACCC conducted a representative survey of its member programs to elucidate capacity and barriers to CCC delivery in the community/academic setting in order to inform policy and value-based payment reform. **Methods:** Survey development methodology included item generation with expert review, iterative piloting and cognitive interviews to achieve content and internal validity. An online survey was piloted at the ACCC 2018 Annual Meeting and sent to member programs via email link. The final survey included 22 questions on availability and funding for supportive services. Twenty-seven supportive oncology services were assessed for availability, reasons not offered, reimbursement/funding and patient payment. Analyses were conducted with SAS. **Results:** 172 of 704 ACCC member programs responded and completed the majority of survey as of 10/7/19. Despite a high proportion of programs offering supportive oncology services, gaps between cost and reimbursement were present for all (Table). Deficits in reimbursement are compensated by patient out-of-pocket payments, grants and donations. Most centers report needing more staffing in psychology (61%), social work (60%), navigation (59%), nutrition (57%), palliative care (56%), genetic counseling (52%), and financial counseling (53%). Gaps were observed regardless of region or practice type. **Conclusions:** There is a lack of sufficient reimbursement, staffing, and budget to provide CCC across the U.S., regardless of region or practice type. Oncology care models and reimbursement policies must include CCC services to optimize delivery of care. Research Sponsor: Association of Community Cancer Centers.

Reimbursement for selected supportive services.

n variable, max n = 172	Service offered within cancer program (%)	≤50% cost covered by reimbursement (%)	≤74% cost covered by reimbursement (%)	Reimbursed, but not sufficiently (%)	Rarely/never get paid for service (%)
Distress management 22		92	33	44	43
Fertility preservation 0		42	47	47	43
Genetic counseling 11		77	29	44	66
Patient navigation	92	33	51	9	73
Palliative care	79	33	54	52	2
Survivorship care planning	86	34	49	46	22
Nutrition consults	90	37	55	35	35

2076 Poster Session (Board #68), Fri, 8:00 AM-11:00 AM

Annual trends in opioid prescribing for patients (Pts) with metastatic non-small cell lung cancer (mNSCLC): Cancerlinq data analysis, 2010 to 2017. *First Author: Judith A. Paice, Northwestern University, Chicago, IL*

Background: Despite opioid misuse and abuse, opioids remain a mainstay for management of cancer pain. Government, payers, and institutions have implemented policies to reduce opioid use. The impact of these restrictions on oncologist prescriptions (Rx) of opioids and management of cancer pain in pts with cancer is not well known. **Methods:** A retrospective, observational analysis used deidentified EHR data from ASCO's CLQ Discovery database. Study cohort included pts with mNSCLC diagnosis and >1 clinical encounter (including opioid Rx) from CLQ clinician during 2010-2017. Opioids included DEA schedule II and III opioid drugs prescribed for cancer pain, excluding cough suppressants. Annual Rx rates were defined as the number of mNSCLC pts who had ≥ 1 opioid Rx dated 2010-2017 per CLQ total mNSCLC pts who had ≥1 clinical encounter in the year. Annual rates demonstrate trends in opioid prescribing patterns over time. **Results:** 18,106 pts with mNSCLC clinical activity between 2010 and 2017 were identified. Overall, 39.8% of pts had opioid Rx in 2010-2017. Annual Rx rates increased from 2010-2015 and fell 2016-2017 (see table). Hydrocodone was the second most frequently prescribed opioid overall (N=4211 pts), but Rx rates began to decline in 2012. Tramadol and acetaminophen + codeine Rx rates gradually increased throughout the time period. DEA initially scheduled Tramadol as schedule IV in 2014. **Conclusions:** Opioids are commonly prescribed by oncologists for patients with mNSCLC. Rx rates have declined since 2015, likely due to increased government, payer, and institutional restrictions on access. Hydrocodone Rx declined since 2012, perhaps exacerbated by reclassification from schedule III to schedule II by the DEA (October 2014). Rxs for schedule IV and III opioids (known to be of lower potency) increased modestly, likely due to comparatively fewer prescribing restrictions. Additional research is needed to understand whether the decline continues and the impact on management of cancer pain, particularly among metastatic patients. Research Sponsor: ASCO and Concerto HealthAI.

Year of Activity	Number of Pts With Diagnosis N	Pts With Opioid Rx N (%)	Pts with Hydrocodone Rx Among Opioid Rx Pts	Pts with Tramadol and/or Acetaminophen + Codeine Rx Among Opioid Rx Pts
2010	2520	449 (18%)	118 (26%)	15 (3%)
2011	2647	550 (21%)	212 (39%)	22 (4%)
2012	4084	878 (21%)	324 (37%)	53 (6%)
2013	4823	1256 (26%)	440 (35%)	87 (7%)
2014	4953	1579 (32%)	535 (34%)	136 (9%)
2015	5336	1807 (34%)	589 (33%)	160 (9%)
2016	5067	1676 (33%)	541 (32%)	169 (10%)
2017	4061	1235 (30%)	398 (32%)	145 (12%)

2077 Poster Session (Board #69), Fri, 8:00 AM-11:00 AM

Pivotal trial endpoints and prices of cancer drugs in the US and Europe. *First Author: Kerstin Noëlle Vokinger, Harvard Medical School, Program on Regulation, Therapeutics, and Law/University of Zurich, Boston, MA*

Background: A key clinical outcome for new cancer drugs is improvement in overall survival (OS), defined as time from the date of randomization to the death from any cause. However, many cancer drugs are approved by regulators based on changes to surrogate measures of OS, such as progression-free survival or overall response rate. When surrogate measures are not validated, they can provide misleading information about drug efficacy. We categorized pivotal trial endpoints for recently-approved cancer drugs in the US and Europe as showing improvements in OS vs non-OS surrogates, and evaluated the correlation with drug prices. **Methods:** We identified new drugs FDA-approved between 2009 and 2018 that were indicated to treat solid and hematologic tumors in adults and that had also been approved by the EMA and Swissmedic by December 2019. Launch prices were extracted and adjusted to average sales prices for monthly treatment costs in the US and compared to currency-adjusted ex-factory monthly treatment costs in Germany, Switzerland, and England. Pivotal clinical trial primary endpoints were collected from the drug labeling and FDA medical reviews for the US, and the EMA public assessment reports for Europe, and categorized as OS in any trial vs. not. Pearson's correlation tests assessed the association between launch prices and OS vs non-OS endpoints in each country. **Results:** 54 drugs were approved by the FDA, EMA, and Swissmedic during the study period. In the US, 30 (56%) were approved based on OS by contrast to 35 (65%) in the EMA. The number of cancer drugs approved by the FDA based on OS decreased in the past years. By contrast, the number of approved cancer drugs by the EMA based on OS were stable. There was no association for the US (p = 0.05), Germany (p = 0.13) and England (p = 0.12), while Switzerland revealed an association (p = 0.03) between OS endpoint and price. **Conclusions:** Reductions in use of OS endpoints as the basis for cancer drug approval in the US is concerning. Drug pricing should be better aligned with the benefit that drugs provide to patients, as measured by clinical trial outcomes such as OS. Research Sponsor: Swiss Cancer Research Foundation.

2078 Poster Session (Board #70), Fri, 8:00 AM-11:00 AM

The clinical impact of ASCO "choosing wisely" recommendations on staging imaging for early stage breast cancers: An interrupted time-series analysis utilizing SEER-Medicare data. *First Author: Alan Baltz, University of Arkansas for Medical Sciences, Little Rock, AR*

Background: The "Choosing Wisely" (CW) list, released by the American Society for Clinical Oncology (ASCO), highlights low-value procedures. In 2012, the CW recommendations advised against the use of staging imaging, including Positron Emission Tomography (PET), Computerized Tomography (CT) and radionuclide bone scans, for the staging of early breast cancer at low risk for metastasis. The objective of this study was therefore to assess the impact of the ASCO CW recommendations on staging imaging among early stage breast cancers. **Methods:** Women above the age of 66 with an early stage incident breast cancer diagnoses between 2010 and 2015 were identified within the linked SEER-Medicare data. The primary outcome of interest was the proportion of patients with a claim for staging imaging in the six months following the breast cancer diagnosis. Negative binomial regression, adjusting for pre-recommendation trends, was performed to estimate the changes in the rate of imaging staging within each year following the release of the recommendation. **Results:** A total of 50,004 women were identified during the study period. Prior to the release of the recommendations in 2012, the staging imaging rates among women newly diagnosed with early stage breast cancers were 5% greater in 2010 ($p<.01$) and 4% greater in 2011 ($p<.01$). Following the release of the recommendations, staging imaging rates did not decrease significantly in 2013 (2%;p=0.18). Imaging rates did, however, significantly decrease by 13% in 2014 ($p<0.01$) and by 16% in 2015 ($p<0.01$). **Conclusions:** The CW recommendation was associated with a significant decrease in unadvised staging imaging among incident early stage breast cancer diagnosis in the second and third year following its release. These findings demonstrate an improvement in the proportion of potentially inappropriate staging imaging in early stage breast cancers. The creation and dissemination of resources, such as the CW recommendations, serves as a powerful tool to improve clinical practice, quality of care, and patient safety from secondary malignancies, anxiety, and overdiagnosis. Research Sponsor: UAMS Laura Hutchins Distinguished Chair in Hematology Oncology.

2079 Poster Session (Board #71), Fri, 8:00 AM-11:00 AM

Understanding practice variation with a clinical pathways system: Differences by physician and practice factors, and changes in practice over time. *First Author: Emily Foster, Dana-Farber Cancer Institute, Boston, MA*

Background: Clinical oncology pathways aim to support clinical decision-making and reduce unwarranted practice variation across an enterprise. The Dana-Farber Cancer Institute (DFCI) implemented web-based oncology pathways with DFCI-customized content in each disease center and at each of its satellites. Our pre-specified aim was an on-pathway rate of 70-85%. **Methods:** Treatment decisions were electronically captured as on- or off- pathway. Monthly metrics about usage and on-pathway rate were shared with users on a monthly basis. Physicians were categorized into quintiles based on the calculated on-pathway performance during the first 90 days of each individual's use of the platform. On-pathway rates were then calculated for days 91-360 to study changes in behavior over time. Physician and practice factors were examined to determine any differences by initial on-pathway quintile classification. **Results:** 122 physicians were eligible for inclusion in this analysis (minimum 5 navigations in each study period). On-pathway rates showed significant variability in the initial 90-day period: quintile 1 median 100%, quintiles 2-4 80.2%, and quintile 5 50% (Table). In the follow-up period, median on-pathway rates shifted into the pre-specified goal range for all groups. Physicians in quintiles 1 or 5 of initial on-pathway rate were more likely to have fewer total navigations than were physicians in quintiles 2-4 (p=0.003). While no other physician or practice characteristic differed significantly by on-pathway rate group, physicians in the first or last quintile were more likely to be in an academic setting, have a PhD, or navigate fewer pathways. **Conclusions:** Over time, the deployment of a web-based clinical pathways program resulted in greater uniformity in physician practice, based on on-pathway rate. Familiarity with the pathways platform and its navigation, monthly feedback about usage, and evolution of content over time are some factors that might have played a role. Research Sponsor: None.

Comparison of on-pathway rate between 0-90 days of use and 91-360 days of use, by quintile group.

	0-90 Days of Use			91-360 Days of Use			
Quintile Group	Range	Median (IQR)	Mean±STD	Range	Median (IQR)	Mean±STD	P-value*
Quintile 1 (n = 26)	94.7-100%	100% (100-100%)	99.4±1.7%	54.5-100%	84.0% (77.8-95.8%)	84.1±13.2%	<0.0001
Quintiles 2-4 (n = 72)	66.7-94.1%	80.2% (75.9-87.5%)	80.8± 8.1%	38.5-100%	80.6% (69.7-84.9%)	77.2±13.0%	0.024
Quintile 5 (n = 23)	37.5 – 66.0%	50% (50-58.3%)	52.2± 8.0%	48.3 – 87.5%	71.1% (60-77.8%)	70.2±11.6%	<0.0001

* Paired t-test

2080 Poster Session (Board #72), Fri, 8:00 AM-11:00 AM

Association of financial conflicts of interest with academic success among junior faculty in hematology and oncology. *First Author: Angela J. Fought, University of Colorado Denver, Denver, CO*

Background: Financial conflict of interest (COI) represents a complex issue in hematology and oncology. Little is known about when COIs develop during a career and if these correlate with early career success. We evaluated self-reported COIs for junior faculty members at 10 academic cancer centers and examined if these financial relationships with industry correlated with measures of academic career success. **Methods:** The study evaluated 229 assistant professors from the top 10 cancer centers based on the 2018 US News Cancer rankings. Faculty characteristics were determined from hospital websites including the number of years since completing fellowship. Data regarding National Institute of Health (NIH) funding were obtained. Industry funds (Sunshine Act funds; SAF) were identified from the Centers for Medicare & Medicaid Services (CMS) Open Payments database from 2013-2017. Self-reported COIs were obtained from the American Society of Clinical Oncology (ASCO) or American Society of Hematology (ASH) disclosures databases, and through review of disclosures from recent publications. Measures of academic success included h-index and number of publications. We assessed the influence of number of COIs and SAF received on measures of academic success. **Results:** Of the 229 included faculty, 45% were female, 39% graduated fellowship in 2015 or later, 35% were double-boarded, 40% had dual degrees and 15% received NIH funding. Approximately 46% of faculty had at least 1 COI. COIs (ASCO/ASH) were positively correlated with COIs self-reported in publications and total SAF (Spearman correlations 0.57 and 0.54, both $P < 0.01$). The development of COIs and the number of SAF increased with years in practice (Spearman correlations 0.37 and 0.28, both $P < 0.01$). COIs and SAF correlated with h-index (Spearman correlation 0.40 and 0.41, both $P < 0.01$). After adjusting for years since fellowship, linear regression demonstrated that log-transformed h-index and number of publications were associated with SAF ($P < 0.01$) and COIs (ASCO/ASH) ($P = 0.01$). **Conclusions:** Financial COIs were present in nearly half of the faculty and increased with more time since completing fellowship. Measures of academic success were positively correlated with COIs (ASCO/ASH) and SAF. These data suggest that cultivating industry relationships may aid faculty in establishing early academic success. Research Sponsor: None.

2081 Poster Session (Board #73), Fri, 8:00 AM-11:00 AM

Adoption of behavioral restrictions as anti-infective measures: A survey among solid tumor patients. *First Author: Eliya Shachar, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel*

Background: Despite lack of evidence, a wide range of rigorous behavioral and social restrictions are recommended in various guidelines and websites in an attempt to mitigate infections. These include patient guided sites. We aimed to study the practices of patients with solid tumors treated with active therapy. **Methods:** We conducted an anonymous survey among cancer patients treated at a tertiary care center, addressing behavioral approach to infection prevention, by assessing adopted social (seven items), environmental (five items), and dietary (eight items) limitations, as well as compliance to influenza vaccinations. Clinical data included neutropenic fever (NF), and therapy myelosuppressive potential. Multivariable Poisson regression adjusted for sex, age, disease status, therapy to estimate the impact of these restrictions. **Results:** 214 patients with solid tumors responded to the survey, the majority female (59%), with a median age of 63. The most common tumor types included breast (28%), lung (14%), and colon (9.3%). Most (68%) were treated with chemotherapy, 17% with immunotherapy, 11% with biologicals and 3% with chemo-immunotherapy. Only 6% were admitted for NF. Sources of information regarding restrictions included physicians (4%), nurses (32.9%), and internet (9.8%); the majority were self-imposed. 53% maintained environmental limitations (traveling, sun exposure, hair dying), 37% adopted social restrictions (abstained from children, public places), and 21% affirmed dietary constraints (raw vegetables, tap water consumption). Females practiced stricter environmental and dietary restraint ($p < 0.05$), with a numerical trend reflecting stricter female social measures ($p < 0.4$). With no difference in practices among patients treated for a malignant disease and curative intent, and no difference in practice across therapies, in those treated with chemotherapy and immuno-therapy. 37% affirmed difficulty in adherence to these limitations. **Conclusions:** Our findings indicate that despite lack of evidence, cancer patients adopt anti-infective behavioral measures, which have a deleterious impact on quality of life. These practices are being used even among patients at low or no risk of NF. These findings call for implementation of an education program and development of practical instructions enabling patients to resume their normal life Research Sponsor: None.

2082 Poster Session (Board #74), Fri, 8:00 AM-11:00 AM

Telemedicine visits reduce time to biopsy, travel time and costs for interventional radiology patients. *First Author: Suken Shah, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Telemedicine has been utilized to increase access to care for patients in primary care practices and more recently, specialty practices. The purpose of the study was to test the hypothesis that adding a telemedicine clinic practice could decrease the time to biopsy, travel time and cost for interventional radiology (IR) clinic patients. **Methods:** Telemedicine visits were performed by a physician or advanced practice provider (PA or NP) at a single institution, academic medical center to patients at 3 MSK regional locations in NY and NJ. Total patient encounters and data from November 2017 to October 2019 were analyzed. Primary outcome measures were wait time from the IR referral to biopsy procedure visits, patient travel time and travel cost, stratified by in-person vs telemedicine visit. Round-trip travel distance and costs for patients were calculated by determining the offset travel. Cost (economic) benefit was the sum of: Federal cost per mile for travel, toll and parking costs, and doctor visit lost wages. **Results:** There were 172 MSK Regional site telemedicine visits. There was a significant reduction in time from referral to biopsy for telemedicine visits compared to in-person visits (12 vs 17 days, $p < 0.0001$). Additionally, there was a significant reduction in travel time for telemedicine visits vs travel time to Manhattan for an in-person visit ($p < 0.0001$). Telemedicine visit patients had to travel 367 less hours than an in-person visit and saved a total of 11,222 in miles that they did not have to travel. Telemedicine patients accrued $14,652 in economic benefits due to reduced travel costs and lost wages from work. **Conclusions:** Telemedicine significantly reduced the time to biopsy, travel time and cost for Interventional Radiology patients compared to in-person visits. Telemedicine for IR patients increases access to care for patients and allow for more efficient use of physician time and resources. Research Sponsor: None.

2083 Poster Session (Board #75), Fri, 8:00 AM-11:00 AM

Documentation patterns and impact on observed side effects of the CANKADO ehealth application: An exploratory analysis of the PreCycle trial. *First Author: Tom Degenhardt, University of Munich, LMU, Munich, Germany*

Background: PreCycle (NCT03220178), a multicenter, randomized phase IV Intergroup trial evaluates the impact of ePRO assessment on quality of life (QoL) in HR+/HER2- locally advanced or metastatic breast cancer patients (pts) treated by palbociclib (P) and an aromatase inhibitor or P+fulvestrant. Pts willing to use the web/APP-eHealth solution CANKADO are eligible. Patients are randomized (2:1, stratified by therapy line) to the active (CANKADO PRO-React) or inactive inform arm. Primary endpoint is time to deterioration (TTD) of QoL. **Methods:** The trial started in 2017 and is ongoing (81 centers); regular safety reports are routinely provided to the study sponsor. Analysis of distribution of serious adverse events (SAE) was initiated by the trial leadership and performed using the Oct 15, 2019 safety report. Data that could bias primary or secondary endpoints were not analyzed. Bayesian inference (non-informative prior) was used to estimate probabilities; no corrections for potential multiplicities were made. **Results:** At data cut-off, 261/281 randomized patients had received study medication and provided CANKADO documentation. At time of evaluation, a total of 40298 days were documented. CANKADO was used on 59% (+/-10%) of all days over a 2-year period. SAEs were observed in 26/175 (14.9%) of all active-arm patients vs. 18/86 (20.9%) of inform-arm patients (90% probability of reduction in inform patients). Total SAEs were 36 (active) vs. 27 (inform); corresponding SAE incidence per hundred patients was 20.6 vs. 31.4, a relative reduction of about one-third. **Conclusions:** CANKADO is well accepted and used regularly by pts in PreCycle, so far over a 2-year period. The present (unplanned) analysis suggests a potentially substantial, clinically relevant reduction in relative SAE incidence among 1stL pts using PRO-React, with a more modest decrease overall. This analysis is preliminary, representing a snapshot, and cannot provide a definitive explanation for the observed SAE reduction. PreCycle will continue to enroll patients in order to further evaluate the potential benefits of interactive eHealth support. Collaborators: WSG WOMEN´S HEALTHCARE STUDY GROUP, CANKADO, Pfizer, AGO-TraFo, AGO-B, Deutsche Gesellschaft für Hämatologie und Medizinische Onkologie e.V. Sponsor: Palleos Healthcare GmbH Keywords: eHealth, Adverse Events, Palbociclib Clinical trial information: NCT03220178. Research Sponsor: Palleos Healthcare GmbH.

2084 Poster Session (Board #76), Fri, 8:00 AM-11:00 AM

Administration of immune checkpoint inhibitors using teleoncology model of care in Far North Queensland: A multicenter review of safety outcomes. *First Author: James Fletcher, Liz Plummer Cancer Centre, Cairns and Hinterland Hospital and Health Service, Cairns, QLD, Australia*

Background: The Teleoncology model of care, as developed and implemented across health services in Far North Queensland (Australia), improves access to specialist oncology services, including telehealth supervised administration of Oncology drugs for patients in rural/remote towns. There is limited published data regarding the safety of checkpoint inhibitor immunotherapy when it is administered via Teleoncology. Aim: Evaluate safety of immunotherapy administration via Teleoncology, including immune-related adverse events (irAE), treatment delays, hospital admissions and interhospital transfers, in comparison to a retrospective control population. **Methods:** Retrospective review of all patients treated with immunotherapy via Teleoncology as part of Cairns and Hinterland Hospital and Health Service (CHHHS) and the Townsville Teleoncology Network (TTN) between January 2015 and April 2019. A retrospective cohort treated at Townsville Cancer Centre over the same time period was used as a control group. **Results:** Fifty-one patients received a total of 624 cycles of immunotherapy (all single agent anti-PD-1/L-1) via Teleoncology. The control population included 142 patients who received 1697 cycles of immunotherapy. Baseline characteristics were well matched between groups. Compared to the control population, patients treated via telehealth did not have statistically significant differences in the rate of Grade 3+ irAE (13.7% v 8%), hospital admissions (13.7% v 7.4%) or protocol suspensions due to immune toxicity (16% v 10%). One patient with Grade 3+ irAE required interhospital transfer for investigation and management, which occurred within 24 hours of presentation to hospital. There were no treatment-related mortalities in either group. **Conclusions:** Checkpoint inhibitor immunotherapy can safely be delivered using the Teleoncology model of care in rural and remote centres. The incidence of toxicity for single agent immunotherapy was predictably low and not significantly different between groups, however the numbers in this retrospective study were small. The time to recognition and management of immune mediated toxicity in rural and remote centres is an important factor that was not assessed in this study and will be considered in future work. Research Sponsor: None.

2085 Poster Session (Board #77), Fri, 8:00 AM-11:00 AM

TeleTriage at a high-volume specialty cancer center: Aligning patient volume and need with available resource. *First Author: Stutman E Robin, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: The Memorial Sloan Kettering (MSK) Urgent Care Center (UCC) functions as the emergency room for MSK. With 23,000+ visits annually, increasing volume and acuity means more days over capacity. Patients experience increased wait times to see clinicians, complete evaluation, and transfer to an inpatient bed. The UCC TeleTriage Program is a remote triage program which aims to align patient volume and need with available resources, improve patient experience, and streamline flow through the UCC. By managing resources more efficiently and expediting initial evaluation, the program promotes timely patient access to care, while maintaining MSK's standard of care. **Methods:** UCC TeleTriage began July 2018 with the Gastrointestinal Medical Oncology service. The Service Nurse refers patients to TeleTriage on weekdays, from 9a.m.- 4:30p.m. The TeleTriage clinician contacts each patient within 30 minutes of referral, takes the history, and determines the initial plan. Patients are directed to a local ER, clinic, or UCC based on level of acuity, real-time GPS, and specific need. For stable patients coming to UCC, TeleTriage focuses on initiating testing prior to registration in UCC. **Results:** TeleTriage patients have (virtual) contact with a UCC clinician within 30 minutes of referral, whereas non-TeleTriage patients wait 110 minutes or more. TeleTriage patients are discharged from UCC up to 42 minutes more rapidly. TeleTriage patients who receive imaging prior to registration in UCC receive a final disposition up to 93 minutes sooner. About 4% of TeleTriage patients are managed at home. In a small number of TeleTriage patients with severe complications of cancer-treatment, significant morbidity was avoided due to early intervention and coordination of care. **Conclusions:** TeleTriage patients have contact with a UCC clinician measurably faster than non-TeleTriage patients. Their evaluation is also started earlier. By managing less acute patients at remote sites or at home, TeleTriage can help patients avoid unnecessary travel, (time) expenditure, and hospital contact. TeleTriage patients who come to UCC, spend less time in UCC than non-TeleTriage patients and they discharge faster. By utilizing cancer care expertise, TeleTriage can significantly impact patient outcomes and utilize resources more effectively. Research Sponsor: Memorial Sloan Kettering Cancer Center.

TPS2086 Poster Session (Board #78), Fri, 8:00 AM-11:00 AM

Implementing a clinical risk prediction tool for patients undergoing active cancer treatment. *First Author: Nathan Handley, Thomas Jefferson University, Philadelphia, PA*

Background: Acute care utilization (ACU), encompassing both emergency department visits and hospitalizations, is common in patients with cancer, with nearly three quarters of patients with advanced disease hospitalized at least once in the year after their diagnosis. Efforts to prospectively identify these patients prior to ACU have led to the development of a variety of scoring systems for specific cancer patient populations, including the elderly and those initiating palliative infusional chemotherapy. Prospectively identifying patients may enable early interventions to reduce ACU. However, few studies have demonstrated effective implementation of such prediction tools in clinical practice. We developed an oncology risk score (ORS) for active oncology patients (defined as patients with an active cancer diagnosis in the last 12 months who had a Medical Oncology encounter in a 180-day period) to prospectively determine risk of ACU. Patients are defined as high risk (18% of patients, accounting for 57% of historical ACU), intermediate risk (25% of patients, accounting for 25% of ACU), or low risk (56% of patients, accounting for 18% of ACU) by the ORS. We are currently deploying a pragmatic implementation initiative to evaluate the impact of targeted nurse navigator (NN) outreach to patients defined as high risk for ACU by the ORS. **Methods:** The ORS is embedded within the health system electronic medical record. The ORS will be queried on a weekly basis. NNs will contact identified patients, prioritizing patients not yet identified by the navigation team by other means. Following chart review, NNs will either meet patients in person (if a visit is already planned within 24 hours) or complete standard navigation outreach and documentation (consisting of phone call and barrier assessment, as well as appropriate nursing intervention) if no visit is planned. NNs will determine follow up cadence based on clinical judgement. Efficacy will be determined using a case-control method. Case patients will be OCM patients defined as high risk by the ORS (historical n = 289); control patients will be non-OCM high risk patients (historical n = 388). The total number of patients in the case and control groups, as well as the proportion of patients in the group utilizing acute care, will be monitored over time. Proportion of high risk patients known to navigation will be tracked. ACU in medium and low risk groups will also be monitored. Targeted outreach to high risk patients using the ORS began on 2/5/2019. Research Sponsor: None.

TPS2087 Poster Session (Board #79), Fri, 8:00 AM-11:00 AM

A multi-stakeholder platform to prospectively link longitudinal real-world clinico-genomic, imaging, and outcomes data for patients with metastatic lung cancer. *First Author: Michael W Lu, Genentech, Inc., South San Francisco, CA*

Background: Making personalized diagnostics and treatments a reality for every cancer patient necessitates comprehensively capturing the patient journey. Real-world data has shown promise for the future of clinical research and advancing precision medicine. However, certain limitations exist such as data quality management as well as bias and confounding factors associated with retrospective analyses. We present a multi-stakeholder platform to prospectively collect and link real-world clinico-genomic, imaging, and outcomes data to longitudinal blood genomic profiling for lung cancer. **Methods:** This study is enrolling approximately 1000 patients with metastatic non-small cell lung cancer or extensive-stage small cell lung cancer who will initiate standard-of-care systemic anti-neoplastic treatment, regardless of line of therapy, at 20 community oncology and academic practices within the Flatiron Health network. Relevant clinical data points from both structured and unstructured fields will be collected through the electronic health records via technology-enabled abstraction, eliminating the need for case report forms. Digital pathology and clinical images at standard-of-care visits will be collected. Blood samples for circulating tumor DNA (ctDNA) profiling using FoundationOne Liquid will be collected at three timepoints: enrollment, first tumor assessment, and end of treatment. Tumor tissue samples may be submitted at baseline for genomic profiling using FoundationOne CDx. Overall survival follow-up will occur until death, withdrawal of consent, loss to follow-up, or end of study. The objectives are to evaluate 1) the feasibility of building a scalable, prospective platform and 2) the associations between ctDNA and real-world clinical outcomes, including overall survival. Enrollment is ongoing. Clinical trial information: NCT04180176. Research Sponsor: Genentech, Inc.

TPS2088 Poster Session (Board #80), Fri, 8:00 AM-11:00 AM

Technology-enabled longitudinal monitoring of patient-reported outcomes (PROs) to individualize care of immune-related adverse events (irAEs) in patients (pts) treated with immune checkpoint inhibitors (ICIs). *First Author: Pavlos Msaouel, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: ICIs have become the therapeutic standard for many cancers but are associated with unique and diverse irAEs that often occur at home. Appropriately timed and specific interventions are critical to recovery. Thus, there is a need to effectively & efficiently monitor in real time pts treated with ICIs. To improve outcomes, we have activated a clinical trial developed to determine the feasibility and safety of an electronically enabled strategy to remotely monitor symptoms and prompt communication that will guide and inform specific patient-driven "course corrections" in response to potential irAEs. **Methods:** This is an adaptive prospective trial that uses a mobile irAE-specific PRO application we developed to monitor and alert the care team in real time when severe symptoms are reported. In parallel with the mobile symptom collection, serum and urine biomarkers are collected at baseline, first tumor restaging, and upon the development of irAEs. Optional stool microbiome analyses are also performed. To facilitate the generalizability of our inferences, we are using broad inclusion criteria: ECOG performance status $\leq$3; any line of ICI given as standard of care or as part of therapeutic clinical trials; elderly pts are included. Because the relationship between PROs and irAEs is currently undefined, we designed our trial to use adaptive symptom thresholds that will notify the healthcare team of suspicion for irAEs. The mobile application will use these dynamic thresholds to determine whether or not to alert the healthcare team. The positive and negative predictive value of each symptom for identifying subsequent irAEs will be assessed at scheduled interim analysis time points. The care teams' responses to the alerts, and all of the clinical outcomes for the pts over time will be collected as part of the trial. The primary goal of the trial is the assessment of the predictive power of the mobile PRO symptom collection in combination with serum and urine markers to identify grade 2 or higher adverse events that require intervention (e.g., dose modifications, hospitalizations, and therapeutic interventions) within two weeks of symptom onset. Effective remote monitoring of irAEs will leverage our understanding of ICI toxicity and empower pts to be effective partners in their care. The trial has currently enrolled 17 pts towards the enrollment target of 100 pts. Clinical trial information: PA19-0095. Research Sponsor: Project Ronin.

TPS2089 Poster Session (Board #81), Fri, 8:00 AM-11:00 AM

ApricityRx companion digital therapeutic for evidence-based mitigation and phenotype-linked molecular characterization of irAEs in patients receiving immune checkpoint therapy (ICT). *First Author: Matthew T Campbell, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Presentation of immune-related adverse events (irAEs) is heterogeneous and unpredictable in patients receiving immune checkpoint therapy (ICT). ICT has been approved for cancer patients as single agent, combination of dual ICT, ICT plus chemotherapy, and ICT plus targeted therapy. Given the ever increasing complexity in recognizing and managing irAEs, coupled with the lack of skilled resources and clinical experience in real world practice, there is increasing demand for digital solutions that can detect early toxicity and support evidence-based interventions in real world practice. To this end, we have developed ApricityRx, a companion digital therapeutic for end-to-end irAE management. In addition to (i) teaching patients about immune-related toxicities and (ii) empowering them to monitor key symptoms and vital signs, ApricityRx continuously analyzes the combined patient-reported data and longitudinal EMR data to (iii) detect symptom-triggers and lab test-triggers of irAEs, and (iv) activate the clinical team to triage, evaluate and treat in a timely fashion, while (v) providing access to synthesized longitudinal patient information and expert guidance on evidence-based management and care. In a feasibility trial conducted in a community setting, we demonstrated two-thirds of the study participants completed on average 5 eCheck-ins per calendar week (overall average 4 times per week), with 5% of the check-ins resulting in notifications alerting the clinical team to evaluate for the early signs of an irAE. **Methods:** To accelerate translational research in irAEs and to develop predictive biomarkers for risk stratification, we are launching a single-arm, open-label study that utilizes ApricityRx in patients receiving ICT alone or in combination. The objectives of the study will include (i) defining the operative characteristics of ApricityRx as an irAE mitigation strategy; (ii) identifying patients and time points for phenotype-triggered biospecimen collection and molecular characterization. The study aims to enroll initially up to 100 participants per site, with a total target of 1,000. Research Sponsor: Apricity Health.

2500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Randomized phase III study of high-dose methotrexate and whole brain radiotherapy with or without concomitant and adjuvant temozolomide in patients with newly diagnosed primary central nervous system lymphoma: JCOG1114C. *First Author: Kazuhiko Mishima, Saitama Medical University International Medical Center, Hidaka-shi, Saitama, Japan*

Background: Temozolomide (TMZ) is an oral alkylating agent that penetrates the blood-brain barrier with moderate toxicity, and has shown anti-tumor activity in primary central nervous system lymphoma (PCNSL) in single arm studies. Our goal was to determine whether the addition of concomitant and adjuvant TMZ chemotherapy to standard treatment of high-dose methotrexate (HD-MTX) and whole brain radiotherapy (WBRT) for PCNSL improves survival in a randomized controlled trial. **Methods:** We did an open-label, randomized phase III trial at 30 hospitals in Japan enrolling immunocompetent patients (pts) aged 20-70 years with histologically confirmed newly diagnosed PCNSL. Pts enrolled at step 1 registration received HD-MTX (MTX; 3.5 g/m^2 at day 1, 15, 29). Pts who received at least 1 cycle of HD-MTX were randomly assigned (1:1) at step 2 registration to receive WBRT (30 Gy) ± 10 Gy boost (control arm: A) or WBRT ± boost with concomitant TMZ (75 mg/m^2 daily) and adjuvant TMZ (150-200 mg/m^2 daily for 5 days every 28 days) for two years after initiation of HD-MTX or until tumor progression (experimental arm: B). Randomization was adjusted by institution, PS (0-1 / 2-3), age (≤60/≥61 years), presence or absence of intraparenchymal tumor after HD-MTX. The primary endpoint was overall survival (OS). The planned sample size was 130 pts in total, to provide an 80% power to detect a 0.52 hazard ratio (65% vs 80% in 2y-OS) for arm B to A and a one-sided alpha of 5%. **Results:** Between September 29, 2014 and October 15, 2018, 134 pts were enrolled, of whom 122 were randomly assigned and analyzed; 62 to arm A and 60 to arm B. At the planned interim analysis, the 2-y OS was 86.8% (95% CI: 72.5-94.0) in arm A and 71.4% (56.0-82.2) in arm B. The hazard ratio was 2.18 (95% CI: 0.95 to 4.98) with predictive probability for showing the superiority of arm B at the final analysis was calculated to be 1.3%. The study was terminated due to futility. The 2-y progression-free survival was 60.6% (43.6-73.8) in arm A and 49.9% (34.4-63.5) in arm B with a hazard ratio of 1.54 (0.88 to 2.70). The most common grade 3 and 4 toxicities were lymphopenia, observed in 7 (11.5%) pts during WBRT in arm A, 18 (30%) pts during WBRT + concomitant TMZ and 18 (37.5%) pts during adjuvant TMZ in arm B. **Conclusions:** This study failed to demonstrate the benefit of the addition of TMZ to WBRT and adjuvant TMZ in newly diagnosed PCNSL. Possible biomarkers including methylation status of the MGMT promoter in the tumors will be analyzed. Clinical trial information: jRCTs031180207. Research Sponsor: AMED.

2501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Randomized phase II study of rituximab, methotrexate (MTX), procarbazine, vincristine, and cytarabine (R-MPV-A) with and without low-dose whole-brain radiotherapy (LD-WBRT) for newly diagnosed primary CNS lymphoma (PCNSL). *First Author: Antonio Marcilio Padula Omuro, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: MTX-based chemoradiotherapy is effective in PCNSL, but carries a risk of severe neurotoxicity (NT), especially in the elderly. In a phase II single arm study, R-MPV-A chemotherapy was combined with substantially reduced doses of radiotherapy (23.4 Gy), achieving prolonged progression free survival (PFS) and overall survival (OS) with acceptable NT. Because R-MPV-A had never been tested without radiotherapy, we conducted a randomized study to determine if the low doses of radiation played a role in the observed disease control, and to characterize NT as compared to chemotherapy alone. **Methods:** Patients were stratified by MSK RPA class and randomized to receive R-MPV-A with LD-WBRT (chemoRT arm) versus R-MPV-A alone (chemo arm). MTX dose was 3.5g/m2 infused over 2 hours. Filgrastim and pegfilgrastim support was given to all patients. LD-WBRT dose was 23.4 Gy (1.8 Gy X 13). The primary endpoint was intent-to-treat (ITT) PFS. A sample size of 89 would provide 80% power to detect a hazard ratio (HR) of 0.63, with one-sided alpha level of 0.15. **Results:** A total of 91 patients were randomized, of whom 4 were ineligible. Among eligible patients, 43 were enrolled in the chemoRT arm and 44 in the chemo arm. Median age was 66 (chemoRT) and 59 (chemo). Median KPS was 80 for both arms. Response rates following R-MPV were 81% (chemoRT) and 83% (chemo). In the chemoRT arm, 37 patients (86%) received LD-WBRT. After median follow-up of 55 months (m), the median ITT PFS was 25 m in the chemo arm and not reached in the chemoRT arm (HR 0.51; 95% CI [0.27, 0.95]; p = 0.015). The 2-year PFS was 54% (chemo) and 78% (chemoRT). Salvage radiotherapy has been given to 11 patients in the chemo arm. Median OS was not reached in either arm, with data still maturing. In both arms, most common grades 3 or 4 toxicities were anemia (27%), lymphopenia (41%), neutropenia (35%), thrombocytopenia (26%), ALT (23%) and AST (13%). One patient died from sepsis (chemo arm). As per investigators' assessment, the rate of clinically defined moderate to severe NT was 11.4% (chemo) and 14% (chemoRT), p = 0.75. **Conclusions:** The study met the primary endpoint, demonstrating the addition of LD-WBRT to R-MPV-A improves PFS in newly diagnosed PCNSL. As per investigator's assessment, NT rates were not statistically significantly increased, but further neuropsychological testing and neuroimaging analyses are ongoing to characterize cognitive decline and how it compares to other consolidation treatments. Clinical trial information: NCT01399372. Research Sponsor: U.S. National Institutes of Health, Other Government Agency.

2502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Alliance A071401: Phase II trial of FAK inhibition in meningiomas with somatic NF2 mutations. *First Author: Priscilla Kaliopi Brastianos, Massachusetts General Hospital and Harvard Medical School, Boston, MA*

Background: Patients with progressive or recurrent meningiomas have limited treatment options. Clinical trials of systemic therapies for meningiomas have failed to demonstrate benefit. FAK inhibition has a synthetic lethal relationship with NF2 loss. Given the predominance of NF2 mutations in meningiomas, we evaluated the efficacy of GSK2256098, a FAK inhibitor, as part of the first genomically-driven phase II study in recurrent or progressive grade I-III meningiomas. **Methods:** Eligible patients (pts) whose tumors screened positively for NF2 mutations were treated with GSK2256098 750mg po bid until progressive disease in 2 separate cohorts: grade I or II/III meningiomas. Two co-primary endpoints were used: progression-free survival at 6 months (PFS6) and response rate (RR) by Macdonald criteria; per study design, the trial would be declared positive if either endpoint was met. RR was evaluated across the overall cohort; PFS6 was evaluated within each subgroup. Historical benchmark data was obtained from Kaley et al. Neuro Oncol 2014. In the grade I group, 12 evaluable pts provided >79% power to detect a PFS6 rate >65% (vs. null hypothesis of 25%; alpha=0.014). In the grade II/III group, 24 evaluable pts provided >85% power to detect a PFS6 >41.5% (vs. null 15%; alpha=0.02). The threshold for promising results for PFS6 was: 7+/12(grade I) and 8+/24(grade II/III) pts. For RR, 36 evaluable pts provided >94% power to detect RR >20% (vs. null 2.5%; alpha= 0.012). **Results:** Of 322 pts screened for all mutation cohorts of the study, 36 eligible and evaluable pts with NF2 mutations were enrolled. Across all grades, one pt had a partial response and 24 had stable disease as best response to treatment. In Grade I pts, the observed PFS6 rate was 83% (10/12 pts; 95% CI: 52-98%). In Grade II/III pts, the observed PFS6 rate was 33% (8/24 pts; 95% CI: 16-55%). The study met PFS6 efficacy endpoint both for the Grade I and the Grade II/III cohorts. Treatment was well tolerated. Only 7 patients had a maximum grade-3 adverse event that was at least possibly related to treatment; toxicities across these pts included: proteinuria (2), rash (1), pain (1), ALT (1), AST (1), cholecystitis (1), hypertriglyceridemia (1), apraxia (1), and lymphopenia (1) with no grade 4 or 5 events. **Conclusions:** GSK2256098 had excellent tolerability andresulted in an improved PFS6 rate in pts with recurrent or progressive NF2-mutated meningiomas. Trial endpoint was met. FAK inhibition warrants further evaluation in this patient population. Support: U10CA180821, U10CA180882; https://acknowledgments.alliancefound.org Clinical trial information: NCT02523014. Research Sponsor: U.S. National Institutes of Health.

2503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

The role of tumor markers for relapse detection in central nervous system non-germinomatous germ cell tumors (CNS-NGGCT): A pool analysis of cooperative group clinical trials. *First Author: Adriana Fonseca, The Hospital for Sick Children, Toronto, ON, Canada*

Background: CNS-NGGCT are rare tumors that have been successfully treated with multimodal therapies. With a 5-yr EFS and OS of 72-84% and 82-93% respectively, surveillance and relapse detection is essential. Tumor marker (TM) elevation has proven to be a highly sensitive method of relapse detection in extracranial-NGGCT. We aim to determine the role of TM for relapse surveillance in children and adolescents with CNS-NGGCTs. **Methods:** European and North American data from germ cell tumor trials (SIOP GCT96, SFOP-TGM TC 90/92, COG-ACNS0122 and COG-ACNS1123) were pooled for analysis. Additionally, patients treated in the UK, Germany and France under strict protocol-guidelines were included. Details regarding imaging, pathology and TM elevation at diagnosis and relapse were collected. We report the proportion of relapses detectable by TM elevation. **Results:** Four-hundred and eighty-four patients enrolled in prospective cooperative group CNS-NGGCT trials from 1989 to 2016 were pooled for analysis. One-hundred and thirteen (23%) patients experienced a relapse/progression (SIOP GCT96: n = 57; SFOP TGM TC 90-92 n = 23, COG-ACNS0122 n = 16 & COG-ACNS1123 n = 17) and constitute the population of this report. Median age at diagnosis was 13 (range:1-30) years. The most common primary location was pineal in n = 60 (53%) patients. The site of relapse was available for 100 patients, 48 patients relapsed locally, 36 relapsed with distant disease, combined relapses were seen in 22 patients and 4 patients relapsed with TM elevation alone. TM in serum and/or CSF at diagnosis was available in 93(82%) patients, and in 90(80%) patients at the time of relapse. Eighty-four patients had TM available at both timepoints. At diagnosis 81 (96%) patients had TM elevation and 3 (4%) had negative TM. At relapse, 74(94%) patients with positive TM at diagnosis had TM elevation, while 7(6%) had TM negative. Conversely, 2/3 patients with negative TM at diagnosis, relapsed with elevated TM. **Conclusions:** Herein, we have assembled the largest prospective cohort to date of relapsed intracranial germ cell tumors. TM are highly sensitive detecting relapse/progression in CNS-NGGCT patients with elevated TM at diagnosis. The routine use of TM for relapse surveillance in patients with CNS-NGGCT can decrease the frequency of cross-sectional imaging, therefore, reducing lengthy hospital visits, sedation procedures and decreasing health-care costs. Research Sponsor: None.

2504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Vorasidenib (VOR; AG-881), an inhibitor of mutant IDH1 and IDH2, in patients (pts) with recurrent/progressive glioma: Updated results from the phase I non-enhancing glioma population. *First Author: Ingo K. Mellinghoff, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Isocitrate dehydrogenase 1 and 2 mutations (m*IDH1/2*) occur in approximately 70% and 4% of low-grade gliomas (LGGs), respectively, promoting oncogenesis via increased production of D-2-hydroxyglutarate. In this ongoing phase 1 trial, VOR, a potent, oral, reversible, brain-penetrant, first-in-class dual inhibitor of mIDH1/2, is being evaluated in advanced m*IDH1/2* solid tumors, including gliomas. Safety and preliminary results were presented previously (Mellinghoff et al., J Clin Oncol 2018). Here, we report updated data for the non-enhancing glioma pt population. **Methods:** Pts with recurrent/progressive m*IDH1/2* glioma received VOR daily (continuous 28-day cycles). Key eligibility criteria included: ≥18 years; histologically or cytologically confirmed glioma with documented m*IDH1/2*; ECOG 0-2; and evaluable disease by RANO-LGG criteria. Dose escalation cohorts enrolled using a Bayesian logistic regression model (BLRM) escalation guided by the overdose control (EWOC). Tumor response was evaluated by MRI every 8 weeks using RANO-LGG criteria by local assessment. **Results:** As of 28 Nov 2019, 22 pts with non-enhancing glioma had received VOR and 8 (36%) remain on treatment. M/F, 8/14; grade 2/3, 17/5; median age, 47 years; m*IDH1/2*, 20/1; 1p19q intact, 9/22; median (range) number of prior systemic therapies, 2 (1–4). Common (≥5 pts) treatment-emergent adverse events (AEs) of any grade and regardless of causality included increased ALT/AST (63.6%/59.1%), headache (45.5%), nausea (40.9%), neutropenia (31.8%), fatigue and hyperglycemia (27.3% each), and seizures and decreased white blood cell count (22.7% each). Transaminase elevations were grade 1 in severity at dose levels < 100mg and were less frequent (5 [38.5%] of 13 pts). Three subjects had related grade ≥3 AEs; 2 discontinued due to AEs. Objective response rate was 13.6% (1 partial response, 2 minor responses), and 17 (77.3%) pts achieved stable disease. 60.5% of pts were progression free and alive at 24 months. **Conclusions:** In this previously treated population with non-enhancing glioma, VOR was associated with a favorable safety profile. The study results also show encouraging preliminary activity within that population, with PFS duration extending to 24 months or longer in 60% of participants. A global randomized phase 3 study of VOR in grade 2 non-enhancing glioma pts who have had surgery only is currently enrolling (NCT04164901). Clinical trial information: NCT02481154. Research Sponsor: Agios Pharmaceuticals, Inc.

2505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A phase Ib/II study of olutasidenib in patients with relapsed/refractory IDH1 mutant gliomas: Safety and efficacy as single agent and in combination with azacitidine. *First Author: Macarena Ines De La Fuente, Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL*

Background: Isocitrate dehydrogenase 1 mutations (mIDH1) are present in >70% of patients with Grade II/III gliomas resulting in production and accumulation of (R)-2-hydroxyglutarate causing DNA hypermethylation and promoting tumorigenesis. Olutasidenib is an oral, potent, brain penetrant (Kpuu=0.4 in intact rodent), and selective inhibitor of mutated IDH1 protein. **Methods:** Patients (pts) with relapsed/refractory (R/R) mIDH1 gliomas received olutasidenib 150 mg BID, orally either as single agent (SA) or in combination (CO) with azacitidine in a dose confirmation phase Ib followed by efficacy evaluation phase II study (NCT: 03684811). **Results:** As of 31-Oct-2019, 29 pts with R/R mIDH1 glioma were treated with olutasidenib as SA (n=24) or CO (n=5). The median age was 45 yrs (range: 23-64) & 62% were male. WHO Glioma Grade (Gr) at study entry was: II (17%), III (52%) & IV (31%). Median number of prior treatments was 2 (1-5); 86% had received prior temozolomide. mIDH1 status was locally determined (IHC, NGS or PCR): R132H (86%), R132L (7%), R132C (3.5%) & unspecified (3.5%). The median duration of olutasidenib treatment for SA & CO was 4.8 (1-11.4) & 1 (0.2-2.3) months, respectively. Fifteen pts discontinued (disease progression [n=12], AE [n=1], withdrew consent [n=1], other [n=1]). For SA, the most common (>25%) TEAEs (all grades, regardless of attribution) were: fatigue (50%), nausea (50%), diarrhea (33%), ALT increase (29%) & headache (29%). For CO, TEAEs that occurred in ≥ 2 pts were: nausea (n=4), fatigue (n=2), neutropenia (n=2), ALT increase (n=2) & AST increase (n=2). There were 2 protocol defined DLTs in the CO cohort, 1 pt with Gr 4 ALT, Gr 3 AST & Gr 3 GGT elevations & 1 pt with Gr 3 ALT elevation. No pts experienced a TEAE of QTcF prolongation. SA best responses are shown in Table; CO pts are too early for response assessment. The median PFS for SA was 8.3 months. Twenty (87%) and 11 (48%) pts were alive and progression-free at 6 & 12 months, respectively. **Conclusions:** SA olutasidenib at 150 mg BID demonstrates acceptable safety and tolerability with preliminary clinical activity in glioma pts. Evaluation of CO is ongoing. Updated safety and clinical activity, as well as evaluations of serum/CSF PK/PD will be provided. Clinical trial information: NCT03684811. Research Sponsor: FORMA Therapeutics, Inc.

Investigator Assessed Best Response per RANO, n (%)	SA (N=23)*	Independent Central Volumetric Assessment, n (%)	SA (N=22)
CR	0	≥ 50% decrease	1 (5)
PR	1 (4)	> 25% decrease but < 50% decrease	3 (14)
SD	10 (43)	≤ 25% decrease and ≤ 25% increase	6 (27)
PD	12 (52)	> 25% increase	12 (55)

* 1 pt not evaluable

2506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Temozolomide-induced hypermutation is associated with high-grade transformation, distant recurrence, and reduced survival after transformation in initially low-grade *IDH*-mutant diffuse gliomas. *First Author: Nancy Ann Oberheim Bush, University of California San Francisco, San Francisco, CA*

Background: Temozolomide, a commonly used alkylating agent to treat gliomas, can induce somatic hypermutation. The prevalence and clinical implications of this phenomenon are not well characterized. **Methods:** We used targeted and whole exome sequencing from a cohort of 82 patients with recurrent *IDH*-mutant low grade gliomas undergoing re-operation to evaluate the prevalence as well as the clinical implications of hypermutation. **Results:** Hypermutation was identified at transformation in 57% of recurrent gliomas exposed to Temozolomide, 94% of which were transformed to higher WHO grades. All patients who developed hypermutation were exposed to Temozolomide. Hypermutation was associated with transformation to higher WHO grade (OR 12.0 95% CI 2.5 – 115.5, p = 0.002) and shorter survival after transformation (HR 2.1, 95% CI 1.1-4.0, p = 0.018) compared with non-hypermutated transformed tumors, controlling for grade, molecular subtype, age, and prior radiotherapy. Patients with transformation to glioblastoma had poor survival regardless of hypermutation (p = 0.78). Hypermutated tumors were associated with development of discontiguous disease at a significantly higher frequency (p = 0.003), including four cases with spinal dissemination. **Conclusions:** TMZ-induced hypermutation is associated with high grade transformation, unique patterns of dissemination and shortened survival after transformation. Next generation sequencing should be considered in this patient population. These data have important implications for the management of newly diagnosed and recurrent *IDH*-mutant low grade gliomas. Research Sponsor: U.S. National Institutes of Health.

2507 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Utilizing phenotypic characteristics of metastatic brain tumors to predict the probability of circulating tumor DNA detection from cerebrospinal fluid. *First Author: Meichen Li, Department of Medical Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, China*

Background: Brain metastases occur in approximately 20% of tumor patients and is often associated with terminal events and poor prognosis. Cerebrospinal fluid (CSF) can be a promising source for detecting circulating tumor DNA (ctDNA) specific to the central nervous system (CNS) instead of peripheral blood due to the blood-brain barrier. However, CSF's suboptimal ctDNA detection rate might limit its clinical application. Precise screening of suitable patients is needed to maximize clinical benefit. **Methods:** We sequenced 425 cancer-relevant genes in CSF and matched extracranial tissue or blood samples obtained from 67 lung cancer patients with brain metastases. The impact of clinical factors, including age, gender, tumor size, number of lesions, and distance of lesions to the ventricle on CSF ctDNA detection was then evaluated by univariate logistic regression. To predict the probability of successful CSF ctDNA detection, best subsets regression was employed for feature selection and cross validation was used for performance assessment to determine the final model. **Results:** We detected somatic alterations in 39/67 (58%) CSF ctDNA, 57/66 (86%) plasma ctDNA and 45/49 (92%) tissue samples. Mutation detection rate of CSF ctDNA was significantly lower than that from extracranial tissue and plasma ($P < 0.001$). Univariate analysis revealed significant association ($P < 0.05$) of high CSF ctDNA detection rate with the following features: (1) intracranial lesion size (*T*), (2) shortest distance between the largest lesion and the ventricle (D_{top}), and (3) shortest distance between all intracranial lesion and the ventricle (D_{all}). We also revealed a trend of higher detection rate in patients with CNS symptoms (S_{CNS}). Subsequent best subsets analysis and cross validation suggested best prediction power with lesion size and largest lesion-ventriclar distance (area under curve [AUC], 0.76 [95% CI, 0.71 to 0.85]; accuracy, 0.75 [95% CI, 0.70 to 0.81]). Final probability can then be derived from $Logit\ P = 0.11 \times T - 0.16 \times D_{all}$ (AUC, 0.82; sensitivity, 0.91; specificity, 0.74). The detection of CSF ctDNA was significantly improved from 58% to 83% (P = 0.03) based on the model. **Conclusions:** This study established a regression model to predict the probability of CSF ctDNA that can be useful to facilitate clinical decisions and avoid excessive practice when monitoring tumor evolution in the brain. Research Sponsor: None.

2508 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

A prospective validation cohort study of baseline plasma cell-free DNA (cfDNA) as a prognostic biomarker in newly diagnosed glioblastoma (GBM). *First Author: Stephen Joseph Bagley, Abramson Cancer Center, Philadelphia, PA*

Background: Due to significant interpatient heterogeneity, survival outcomes vary widely in patients with GBM. Novel prognostic biomarkers are needed. We aimed to determine the prognostic impact of baseline plasma cfDNA concentration in patients with GBM. **Methods:** We analyzed 84 patients with newly diagnosed GBM and at least 7 months of follow-up time. The first 41 patients comprised a previously published derivation cohort (Bagley, Clin Cancer Res 2020). The subsequent 43 patients served as an independent validation cohort. cfDNA was extracted from plasma collected prior to initial surgical resection and quantified by qPCR for a 115 bp amplicon of the human ALU repeat element. Receiver operating characteristic (ROC) curve analysis was used in the derivation cohort to (1) assess the accuracy of plasma cfDNA concentration for predicting progression-free survival status at 7 months (PFS-7), a landmark based on the median PFS for newly diagnosed GBM (Stupp, N Engl J Med 2005), and (2) derive the optimal cutoff for dichotomizing patients into high- and low-cfDNA groups. In the validation cohort, logistic regression was used to measure the association of plasma cfDNA concentration (high vs. low) with PFS-7, adjusted for age, isocitrate dehydrogenase (*IDH)* 1/2 mutational status, 0-6-methylguanine-methyltransferase (*MGMT*) methylation, extent of resection, and performance status. Multivariate Cox regression was used for overall survival (OS) analysis. **Results:** In the derivation cohort, the optimal cutoff for plasma cfDNA was 25.0 ng/mL (area under the curve [AUC] = 0.663), with inferior PFS and OS in patients with cfDNA above this cutoff (PFS, median 4.9 vs. 9.5 months, log-rank p = 0.001; OS, median 8.5 vs. 15.5 months, log-rank p = 0.03). In the validation cohort, baseline plasma cfDNA concentration over the cutoff was independently associated with a lower likelihood of being alive and progression-free at 7 months (adjusted OR 0.13, 95% CI 0.02 – 0.75, p = 0.02). OS was also worse in in the validation cohort in patients with high plasma cfDNA (adjusted HR 3.0, 95% CI 1.1 – 8.0, p = 0.03). **Conclusions:** In patients with newly diagnosed GBM, high baseline plasma cfDNA concentration is associated with worse survival outcomes independent of other prognostic factors. Further validation in a larger, multicenter study is warranted. Research Sponsor: U.S. National Institutes of Health.

2509 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Single cell mapping of human brain tumors reveals tumor-specific education of tissue-invading leukocytes. *First Author: Ekaterina Friebel, Institute of Experimental Immunology, University of Zürich, Zürich, Switzerland*

Background: Brain tumors can be both of intracranial origin (e.g. gliomas) or spread from another location in the body (metastases). Tumor growth in the CNS is commonly favored by a highly immunosuppressive tumor microenvironment (TME). Whether the TME is predominantly shaped by the CNS microenvironment or by the nature of the malignancy is unknown, as is the origin and function of CNS tumor-associated macrophages (TAM). **Methods:** We have mapped the leukocyte landscape of brain tumors using high-dimensional profiling with mass cytometry (CyTOF). We designed two CyTOF panels (one lymphoid and one myeloid focused) measuring 74 parameters at the single-cell level and analyzed samples from 47 individuals with the most common tumor entities being glioblastoma and metastases from melanoma and lung cancer as well as control tissue from epilepsy surgery. **Results:** The heterogeneous composition of tissue-resident and invading immune cells within the TME alone permitted a clear distinction between glioblastoma and metastases. Tissue-invading leukocytes accumulate in metastases, whereas gliomas predominantly contain tissue-resident reactive microglia. In gliomas, isocitrate dehydrogenase 1 (IDH1) mutations are associated with minimal host responses whereas IDH1-wildtype gliomas comprise monocyte-derived macrophages (MDM) similar to metastases. These MDM show a distinctive signature trajectory indicative of tumor-driven education. **Conclusions:** The immune cell composition of the brain tumor TME is tumor entity-specific, rather than dictated by the CNS tissue. Defining the distinct immunological signature of brain tumors can facilitate the rational design of targeted immunotherapy strategies. Research Sponsor: None.

2510 Poster Discussion Session; Displayed in Poster Session (Board #1), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Controlled IL-12 in combination with a PD-1 inhibitor subjects with recurrent glioblastoma. *First Author: E. Antonio Chiocca, Brigham and Women's Hospital, Boston, MA*

Background: Monotherapy with intratumoral Ad-RTS-hIL-12 (Ad), a gene therapeutic conditionally expressing IL-12 under the transcriptional control of oral veledimex ("Controlled IL-12"), was shown in a phase 1 study (NCT02026271) to elicit a new and sustained intra-tumoral infiltration of T cells with co-expression of PD-1. We report updated findings following completion of enrollment (with follow-up ongoing) for a phase 1 substudy (NCT03636477) evaluating safety and tolerability of local, Controlled IL-12 in combination with nivolumab (nivo) in adults with recurrent glioblastoma (rGBM). **Methods:** Multicenter, open label, dose-escalation phase 1 trial to evaluate safety and tolerability of local, Controlled IL-12 with nivo in adult subjects with rGBM. Ad was administered by single intratumoral injection (2×10^{11} viral particles, Day 0 at time of resection) plus V (10 or 20 mg) PO QD x 15 with nivo (1 or 3 mg/kg) IV on Days -7, 15, then Q2W. **Results:** 21 subjects were treated (Cohort 1: V 10 mg, nivo 1 mg/kg, n = 3; Cohort 2: V 10 mg, nivo 3 mg/kg, n = 3; and Cohort 3: V 20 mg, nivo 3 mg/kg, n = 3 + 12 expansion). Safety data were similar to Ad+V monotherapy. Adverse reactions during follow-on nivo dosing were consistent with anti-PD-1 labeling, manageable, and generally reversible with no synergistic toxicities. Focusing on the 20mg V cohort (recommended phase 2 *dose)*, serum IL-12 mean ± SEM (screening, 0.4 ± 0.1 pg/mL; Day 0, 0.6 ± 0.1 pg/mL), increased after Ad+V to 8.7 ± 3.3 pg/mL on Day 3. Similarly, serum IFN-g levels did not increase due to nivo alone (screening, 0 ± 0 pg/mL; Day 0, 0 ± 0 pg/mL), increasing after Ad+V to 6.2 ± 2.3 pg/mL on Day 7. Additionally, nivo alone did not significantly increase circulating T cells ($CD3^+$ $CD8^+$%) (paired differences comparison, Day 0 to screening) 3.1%, p =0.13, whereas Ad+V significantly increased peripheral T cells (Day 28 - Day 0) 3.6%, p =0.02. Pseudoprogression followed by a decrease in size (SPD) has been shown as evidenced by serial MRIs in a subgroup of subjects. Preliminary overall survival findings will be presented. **Conclusions:** Controlled IL-12 with PD-1 inhibition is a rational combination with initial data consistent with immune-mediated effects, a favorable safety profile, and early evidence of anti-tumor effects. An additional phase 2 study combining Controlled IL-12 with cemiplimab-rwlc in adults with rGBM is ongoing. Clinical trial information: NCT03636477. Research Sponsor: Ziopharm Oncology.

2511 Poster Discussion Session; Displayed in Poster Session (Board #2), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase I/II study to evaluate the safety and clinical efficacy of atezolizumab (atezo; aPDL1) in combination with temozolomide (TMZ) and radiation in patients with newly diagnosed glioblastoma (GBM). *First Author: Shiao-Pei S. Weathers, The University of Texas MD Anderson Cancer Center, Department of Neuro-Oncology, Houston, TX*

Background: Immunotherapy strategies such as PD-1/PD-L1 inhibition may work synergistically with radiation, which is known to increase antigen presentation and promote a pro-inflammatory tumor microenvironment. This trial evaluated the safety and clinical efficacy of concurrent atezo with radiation therapy and TMZ followed by adjuvant atezo and TMZ in patients with newly diagnosed GBM, unselected for MGMT status. **Methods:** Eligibility criteria included patients with newly diagnosed GBM age > 18 yrs who had undergone only surgery. The primary endpoint was safety in Phase I (n = 10) and OS in Phase II (n = 50). Secondary endpoints included progression free survival (PFS), overall response rate (ORR), and duration of response. All 60 patients were evaluated for efficacy. Correlative endpoints include profiling of tumor immune cell populations and peripheral blood for evaluation of circulating chemokines/cytokines. **Results:** 60 patients were enrolled. With median follow-up time of 16.7 months (data cutoff = 30 Dec 2019), 24 patients had died and 32 had progressed. Median OS was 17.1 months (95% CI: 13.9, not reached). Median PFS was 9.7 months (95% CI: 7.6-15). Median PFS in MGMT methylated patients (n = 18) was 16.7 months (95% CI: 7.85, not reached) and 7.9 months (95% CI: 6.70-12.4) in MGMT unmethylated patients (n = 33). Treatment-related adverse events with maximum CTCAE grade > 3 occurred in 33 patients; the most common were LFT elevation (n = 5) and lymphopenia (n = 23). To date, 17 of the enrolled 60 patients underwent re-resection post treatment with atezo. The matched paired tumor analysis of pre and post treatment tissue will provide valuable insights into mechanisms of anti-PD-L1 therapy resistance. Tumor immunocorrelative studies are pending. **Conclusions:** Concurrent use of atezo with radiation and TMZ was tolerable and demonstrated modest efficacy. Clinical trial information: NCT03174197. Research Sponsor: Genentech.

2512 Poster Discussion Session; Displayed in Poster Session (Board #3), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Updated safety phase I trial of anti-LAG-3 alone and in combination with anti-PD-1 in patients with recurrent GBM. *First Author: Michael Lim, The Johns Hopkins Hospital, Baltimore, MD*

Background: Preclinical GBM data targeting the checkpoint molecule Lag-3 have shown promising anti-tumor immune response with resultant improved survival when combined with anti-PD-1. Here we report our experience from a multi-arm safety study in patients with recurrent GBM treated with anti-Lag-3 and in combination with anti-PD-1. **Methods:** A phase I, open label, multicenter, multi-arm dose-finding/safety study of anti-LAG-3 (BMS-986016) alone or in combination with anti-PD-1 in patients at first recurrence of GBM was carried out in The Adult Brain Tumor Consortium (ABTC) (1501). The primary objectives were safety and to define MTD (DLT rate $<$ 33%) for both the mono and combination arms. The major secondary objective was efficacy. The key inclusion criteria were: adults with first recurrence of GBM following RT+TMZ, TLC$\geq$1000/ul, KPS$\geq$ 60%, on a stable corticosteroid regimen, measurable disease, and written informed consent. Three pre specified dose levels of anti-Lag-3 at 80mg, 160mg, and 800mg were tested. Anti-PD-1was given at a flat dose of 240 mg in combination with anti-LAG-3 at 80 mg and 160 mg. **Results:** To date, the phase I portion of study completed its accrual and 33 patients were enrolled into the anti-LAG-3 alone or in combination with anti-PD-1 arms. The median age and KPS was 56 and 90 respectively. 39% tumors were MGMT methylated and the median treatment cycle was 3. The highest safe dose for Anti-LAG-3 alone is 800 mg without a DLT. Two DLT were observed in combination arms of Anti-LAG-3 +anti-PD-1 (80 mg/240mg), a grade 3 muscle weakness and a grade 4 edema. Three DLTs were observed in the higher Anti-LAG-3 + anti-PD-1 group (160 mg/240mg): grade 3 hypertension, syncope, and edema. 80% of the DLTs occurred after cycle 2 of the treatment. The estimated overall mOS was 8 months. Seven (44%) patients in the combination arm are still alive and 3 out of the 7 are living beyond 20 months suggesting a subset benefit. **Conclusions:** The phase I part of trial has completed enrollment. The MTD is 800mg for anti-LAG-3 as a monotherapy. For the combination arms, 160 mg of Anti-LAG-3 and 240 mg of anti-PD-1 was the MTD. DLTs were late onset events. Clinical trial information: NCT02658981. Research Sponsor: NCI - ABTC, BMS for correlative studies.

2513 Poster Discussion Session; Displayed in Poster Session (Board #4), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

MDNA55 survival in recurrent glioblastoma (rGBM) patients expressing the interleukin-4 receptor (IL4R) as compared to a matched synthetic control. *First Author: John H. Sampson, Duke University Medical Center, Durham, NC*

Background: MDNA55 is an engineered IL-4 fused to pseudomonas exotoxin A being developed for GBM, an aggressive, universally fatal disease. No curative therapy exists and 75% of patients are not eligible for resection at recurrence. MDNA55 targets IL4R overexpressed in GBM, the immunosuppressive tumor microenvironment, and high expression is associated with poor survival outcomes in GBM. A Ph 2b trial of MDNA55 was completed in rGBM using convection-enhanced delivery to bypass the BBB. Here we report results from the Ph 2b trial and comparison against a matched Synthetic Control Arm (SCA). **Methods:** MDNA55-05 is an open-label, single-arm study of intratumoral delivery of $\leq$ 240 μg MDNA55 as a single treatment via $\leq$ 4 catheters in *de novo* GBM without IDH1/2 mutation at 1st or 2nd recurrence not eligible for resection, tumors $\leq$ 4 cm, KPS $\geq$ 70. IL4R expression in GBM tissues was determined by H-Score using a validated IHC assay. 1^o endpoint is median overall survival (mOS); 2^o endpoint includes the impact of IL4R status on mOS. An eligibility-matched SCA was identified retrospectively from patient registries at major neurosurgery centers with access to GBM tumor tissue banks under IRB-approved protocols. **Results:** 44 subjects comprise the MDNA55 per protocol analysis population: median age 56 (35 - 77); median dose 177 mg (range 18 – 240 mg), 50% had KPS $\leq$ 80. No systemic toxicities observed, drug-related AEs were primarily neurological and characteristic of GBM, no deaths attributed to MDNA55. Median OS was 11.6 months (95% CI 7.9 – 15.2). When stratified by IL4R expression, mOS in IL4R High (n = 21) was 15 vs. 8.4 months in IL4R Low (n = 19); p = 0.2175. OS12 is 57% vs. 33%. When compared to the SCA (n = 81), MDNA55 subjects survived significantly longer: mOS 12.4 vs. 7.7 months; p = 0.0077. When comparing IL4R High groups, mOS in MDNA55 (n = 21) was 15.8 vs. 6.2 months in the SCA (n = 17); p = 0.0626. Subgroup analysis in unmethylated MGMT subjects also show better survival with MDNA55 (n = 23) than the SCA (n = 31); mOS 12.3 vs. 7.7 months (p = 0.0268), indicating that MDNA55 may be beneficial in patients resistant to temozolomide. **Conclusions:** MDNA55 subjects represent a difficult to treat population (*de novo* GBM, IDH wild-type, not eligible for surgery at recurrence). Single treatment with MDNA55 prolongs survival by nearly 10 months in a subset of rGBM expressing high levels of IL4R when compared to a matched SCA, providing an unprecedented outcome for this highly lethal disease. Clinical trial information: NCT02858895. Research Sponsor: Medicenna Therapeutics, Cancer Prevention & Research Institute of Texas.

2514 Poster Discussion Session; Displayed in Poster Session (Board #5), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

INO-5401 and INO-9012 delivered intramuscularly (IM) with electroporation (EP) in combination with cemiplimab (REGN2810) in newly diagnosed glioblastoma (GBM): Interim results. *First Author: David A. Reardon, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA*

Background: Novel T cell-enabling therapies, in combination with checkpoint inhibition, may improve OS in GBM. INO-5401 (synthetic DNA plasmids encoding for hTERT, WT-1 and PSMA), plus INO-9012 (synthetic DNA plasmid encoding IL-12), with the PD-1 checkpoint inhibitor cemiplimab, is given to patients with newly-diagnosed GBM to evaluate tolerability, efficacy and immunogenicity of the combination. **Methods:** Phase I/II, single arm, 2 cohort study (A: MGMT unmethylated, B: MGMT methylated). The primary endpoint is safety; efficacy and immunogenicity are secondary. Nine mg INO-5401 plus 1 mg INO-9012 (every 3 weeks for 4 doses, then Q9W) is given with EP by CELLECTRA 2000 with cemiplimab (350 mg IV Q3W). RT is given as 40 Gy over 3 weeks. TMZ is given with radiation (all patients), followed by maintenance (Cohort B only). **Results:** Fifty two subjects were enrolled: 32 in Cohort A; 20 in Cohort B. 35% women and 90% white. Median age 60 years (range 19-78 years). Common Grade $\geq$3 AEs reported were: platelet count decreased (11.5%), tumor inflammation (7.7%), seizure (7.7%), ALT increased (7.7%), lymphocyte count decreased (7.7.%). One Grade 5 unrelated event of urosepsis was reported. Of 69 SAEs reported there was only 1 related to the combination therapy, Grade 1 pyrexia. 48% of subjects reported irAEs, most frequently ALT increased (9.6%), AST increased (7.7%), diarrhea (7.7%), pyrexia (7.7%) and tumor inflammation (7.7%). 71% of the reported SAEs and irAEs occurred within the first 12 weeks of treatment. OS at 12 months was 84.4% (95% CI 67.2, 94.7) in Cohort A; Cohort B will be presented at ASCO. ELISpot assessments demonstrated T cell responses to INO-5401. Flow cytometry demonstrated evidence of activated INO-5401-specific CD8+T cells with lytic potential (CD38+Prf+GrzA+) when compared with baseline, post-treatment in the majority of patients assayed. **Conclusions:** INO-5401 + INO-9012 in combination with cemiplimab and RT/TMZ has an acceptable safety profile, is immunogenic and may show a survival advantage in patients with newly-diagnosed GBM. OS18 data will be presented later this year. Clinical trial information: NCT03491683. Research Sponsor: Inovio.

2515 Poster Discussion Session; Displayed in Poster Session (Board #6), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase I/II clinical trial of autologous CMV-specific T cells in glioblastoma (GBM) patients to reveal a lack of immune effector function. *First Author: Shiao-Pei S. Weathers, The University of Texas MD Anderson Cancer Center, Department of Neuro-Oncology, Houston, TX*

Background: Cytomegalovirus (CMV) antigens are present in $>$ 90% of GBMs but not in normal brain making it an attractive immunological target. **Methods:** Highly functional autologous polyclonal CMV pp65 specific T cells were expanded under GMP-compliant conditions from GBM patients and administered after 3 weeks of lymphodepleting dose-dense temozolomide (ddTMZ, 100 mg/m^2). The phase I component used a 3+3 design ascending through four dose levels (5 x 10^6 cells to 1 x 10^8 cells). Treatment was repeated every 6 weeks for a total of 4 cycles. Dose expansion was conducted in recurrent GBM patients undergoing resection and in newly diagnosed GBM patients following concurrent chemoradiation. *In vivo* persistence and effector function of the adoptively transferred CMV-specific T cells was determined by dextramer staining and multiparameter flow cytometry in serially-sampled peripheral blood and in the tumor microenvironment. **Results:** 65 patients were screened, 25 underwent leukapheresis, and 20 completed at least 1 cycle. Median age 48 (27-69), 35% were MGMT methylated, and 10% were IDH mutated. No dose limiting toxicities (DLTs) observed. Complete radiographic response was observed in 1 patient, partial responses in 2, stable disease in 9, and progressive disease in 8. The median PFS time was 1.3 months (95% CI: 0-8.3 months) and the median OS time was 12 months (95% CI: 6 months to not reached). Repeated infusions of CMV-TC were associated with significant increase in circulating CMV+ CD8+ T cells, but cytokine production reflective of effector activity (CD107a, TNFα, IFNγ, IL2) was suppressed in these cells including directly from the GBM microenvironment. **Conclusions:** Adoptive infusion of CMV-specific T cells after lymphodepleting ddTMZ was well-tolerated. However, effector function of the adoptively transferred T cells was attenuated indicating further modulation of the T cell is required to prevent its dysfunction prior to proceeding to large scale clinical studies. Clinical trial information: NCT02661282. Research Sponsor: MD Anderson Glioblastoma Moon Shots Program, Other Foundation.

2516 Poster Discussion Session; Displayed in Poster Session (Board #7), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Inefficiencies in the phase II to phase III transition as a modifiable factor that is impeding successful drug development for glioblastoma. *First Author: Adithya Balasubramanian, Olivia Newton-John Cancer Centre, Austin Health, Melbourne, VIC, Australia*

Background: Improving the outcomes of patients with glioblastoma (GBM) represents one of the most significant challenges in neuro-oncology. We have observed inefficiencies in the availability and use of phase 2 data when planning phase 3 studies, and have undertaken a detailed review of key design parameters of phase 2 and 3 trials in GBM to identify and quantify the impact of this phenomenon. **Methods:** Studies between 2005-2019 inclusive were identified though MEDLINE search using keywords and MeSH terms, and manual bibliography searches. P2Ts were restricted to those referenced by the corresponding P3Ts. Clinical, statistical and sponsor characteristics were extracted by two reviewers (AB&AG). For each P3T, corresponding Phase 2 trial (P2T) data was "optimally matched" (OM) where same drug was used in similar schedule and similar GBM population; "partially matched" (PM) where dissimilar schedule and/or treatment setting; and "lacking" in all other circumstances. The statistical data used in the P2/3 transition were compared by Pearson Correlation, Fisher's Exact or Chi-square testing as appropriate. **Results:** Of 20 P3Ts identified, 6 (30%) lacked any phase 2 data. Of the remaining 14 P3T, 9 had 1 prior P2T, 4 had 2 P2T and 1 had 3 P2T, for a total of 20 P3T-P2T pairs (called dyads). Further, there were 13 OM dyads and 7 PM dyads. OM dyads showed strong concordance for mPFS (r^2= 0.95, $p < 0.01$) and mOS (r^2= 0.84, $p < 0.01$), whilst PM dyads did not ($p > 0.05$). We identified several inefficiencies in translation from P2T to P3T. Firstly, 3 P3T had statistical assumptions of primary endpoint that may have been too optimistic. 2 of these P3Ts aimed for an expected endpoint that was higher than the actual outcomes from a matched P2T. 1 P3T was unable to reach the desired sample size. We note that 4 P3Ts had actual primary endpoint HRs that were < 0.9 but with $P > 0.05$. Finally, we investigated whether there were absolute thresholds for efficacy in P2Ts to inform whether to proceed with P3Ts. For P2Ts in the newly diagnosed setting, all those with mPFS $<$ 14 months and/or mOS $<$ 22 months had subsequent negative P3Ts. For P2Ts in recurrent disease, all those with mPFS $<$ 6 months and mOS $<$ 12 months had negative P3Ts. Applying these thresholds to the studies in our review, 10 of the 12 negative P3Ts (83%) with matched P2Ts need not have been initiated, sparing 4739 patients' from unnecessary trial participation. **Conclusions:** Our data strongly supports the vital role of properly designed P2Ts in informing P3Ts for drug development for primary CNS tumours. Research Sponsor: None.

2517 Poster Discussion Session; Displayed in Poster Session (Board #8), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

4-miRNA signature combined with *MGMT* methylation status in glioblastoma: A multicentric retrospective biomarker analysis with accompanying prospective cohort study. *First Author: Maximilian Niyazi, University Hospital, LMU Munich, Munich, Germany*

Background: Previously, we identified a prognostic 4-miRNA signature (built from let-7a-5p, let-7b-5p, miR-125a-5p and miR-615-5p) in glioblastoma patients treated according to the EORTC26981/22981-NCIC CE3 protocol. We present results of a novel external validation and will report on a completed prospective study on blood plasma samples of glioblastoma patients prior to chemoradiotherapy (CRT). **Methods:** The external validation cohort (n = 103) contained IDH1/2 wildtype tumors with known *MGMT* promoter methylation from the LMU-Munich (n = 37), the University Hospital Düsseldorf (n = 33) and TCGA (n = 33). Risk groups from the combination of miRNA signature with *MGMT* promoter methylation were analyzed for overall survival (OS) and prognostic performance using C-index. Within the prospective study (n = 52), blood samples were taken prior to RT, on d42 and d84 (22 cases analyzed up to now). Risk scores were obtained from signature miRNA expression levels in resection or biopsy specimen (retrospective, endpoint OS) and blood plasma (prospective, PFS). **Results:** The 4-miRNA signature was independent of sex and *MGMT* promoter methylation ($p > 0.1$) and defined high-risk (n = 47, med. OS: 16.4months) and low-risk (n = 56, med. OS: 26.9months) patients (HR: 2.08, 95%CI: 1.25-3.46, p = 0.004). Patients with methylated (med. OS: 23.7months, n = 54) compared to non-methylated *MGMT* promoter (med. OS: 16.8months, n = 49) had superior OS (p = 0.007, HR: 0.48, 95%-CI: 0.28-0.82). Combining the 4-miRNA signature and *MGMT* promoter methylation resulted in the signature-low-risk/*MGMT*-promoter-methylated (med. OS: 37.4months), signature-low-risk/*MGMT-promoter*-unmethylated (med. OS: 24.7months), signature-high-risk/*MGMT-promoter*-methylated (med. OS: 16.4 months) and signature-high-risk/*MGMT*-unmethylated groups (med. OS: 14.3months, Log-rank p = 0.002) with superior prediction performance. **Conclusions:** We confirmed the 4-miRNA signature as an independent prognosticator in IDH-wildtype glioblastoma while combination with *MGMT* promoter methylation outperformed other established prognostic factors. Our hypothesis is, that blood plasma samples will allow the risk stratification of glioblastoma patients before CRT. Phenotypic alterations driving its prognostic value remain to be determined and will allow for 1) risk stratified trials, 2) pathway analysis and targeting and 3) testing in healthy subjects to elucidate its screening potential. Research Sponsor: None.

2518 Poster Discussion Session; Displayed in Poster Session (Board #9), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Long-term analysis of the WHO-defined molecular subgroups of high-risk grade II gliomas treated with radiation and temozolomide on NRG Oncology/RTOG 0424. *First Author: Erica Hlavin Bell, The Ohio State University, Columbus, OH*

Background: This study sought to evaluate the prognostic significance of the three WHO-defined molecular glioma subgroups (*IDH*wt, *IDH*mt/non-codel, and *IDH*mt/codel) in NRG Oncology/RTOG 0424, a phase II trial of high-risk low-grade gliomas treated with radiation (RT) and concurrent and adjuvant temozolomide (TMZ) after biopsy/surgical resection. Notably, this is the first clinical study to evaluate the prognostic value of the WHO subgroups in RT + TMZ-treated high-risk grade II (G2) gliomas using prospectively-collected long-term survival data. **Methods:** *IDH1/2* mutation status was determined by next-generation sequencing. 1p/19q co-deletion status was determined by Oncoscan and/or 450K methylation data. Overall survival (OS) and progression-free survival (PFS) by marker status were determined by the Cox proportional hazard model and tested using the log-rank test in a post-hoc analysis. Patient pre-treatment characteristics were included as covariates in multivariate analyses. **Results:** Of all the eligible patients (N=129), 80 (62%) had sufficient quality DNA for both *IDH* and 1p/19q analyses. Of these 80, 54 (67.5%) were *IDH*mt, and 26 (32.5%) were *IDH*wt. Of the 54 *IDH*mt patients, 26 (32.5% of total, 48% of *IDH*mt) were *IDH*mt/codel, and 28 (35% of total, 52% of *IDHmt*) were *IDH*mt/non-codel. Both *IDH*mt subgroups were significantly correlated with longer PFS (*IDH*mt/co-del = 8.1yrs (5.2-not reached (NR)); *IDH*mt/non-codel = 7.5yrs (3.9-11.8); *IDH*wt = 1.0yr (0.6-1.7), $p<0.001$) and OS (*IDH*mt/co-del = 9.4yrs (8.2-NR); *IDH*mt/non-codel = 8.8yrs (5.9-NR); *IDH*wt = 2.3yrs (1.4-3.4), $p<0.001$) relative to the *IDH*wt subgroup. Upon univariate and multivariate analyses, both molecular *IDH*mt subgroup comparisons relative to *IDH*wt remained significant ($p<0.001$) even after incorporation of known clinical variables. **Conclusions:** These analyses suggest that G2 glioma patients harboring *IDH1/2* mutations, regardless of co-deletion status, demonstrated longer survival with RT + TMZ relative to *IDH*wt tumors, although sample size is limited and analyses were post-hoc. These results also support the notion that outcomes for *IDH*wt high-risk G2 gliomas remain dismal (median = 2.3yrs, similar to G3 anaplastic astrocytoma); these patients should be separated from *IDH*mt patients in future G2 glioma trials, and warrant novel treatment strategies. Funding: U10CA180868, U10CA180822, U24CA196067, CURE, PA Dept. of Health, and Merck. Also, R01CA108633, R01CA169368, RC2CA148190, U10CA180850, BTFC, OSUCCC (all to AC). Clinical trial information: NCT00114140. Research Sponsor: U.S. National Institutes of Health, Other Foundation, Other Government Agency, Pharmaceutical/Biotech Company.

2519 Poster Discussion Session; Displayed in Poster Session (Board #10), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Superior therapy response predictions for patients with glioblastoma (GBM) using Cellworks Singula: MyCare-009-03. *First Author: Patrick Y. Wen, Dana-Farber/Brigham and Women's Cancer Center, Harvard Medical School, Boston, MA*

Background: Despite using cytogenetic and molecular-risk stratification and precision medicine, the current overall outcome of GBM patients remains relatively poor. Therapy selection is often based on information considering only a single aberration and ignoring other patient-specific omics data which could potentially enable more effective treatment selection. The Cellworks Singula™ report predicts response for physician prescribed therapies (PPT) using the novel Cellworks Omics Biology Model (CBM) to simulate downstream molecular effects of cell signaling, drugs, and radiation on patient-specific *in silico* diseased cells. We test the hypothesis that Singula is a superior predictor of progression-free survival (PFS) and overall survival (OS) compared to PPT. **Methods:** Singula's ability to predict response was evaluated in an independent, randomly selected, retrospective cohort of 109 GBM patients aged 17 to 83 years treated with PPT. Patient omics data was available from TCGA. Singula uses PubMed to generate protein interaction network activated and inactivated disease pathways. We simulated PPT for each patient and calculated the quantitative drug effect on a composite GBM disease inhibition score based on specific phenotypes while blinded to clinical response. Univariate and multivariate proportional hazards (PH) regression analyses were performed to determine if Singula provides predictive information for PFS and OS, respectively, above and beyond age and PPT. **Results:** In univariate analyses, Singula was a significant predictor of both PFS (HR = 4.130, $p < 0.000$) and OS (HR = 2.418, $p < 0.0001$). In multivariate PH regression analyses, Singula (HR = 4.033, $p < 0.0001$) remained an independent predictor of PFS after adjustment for PPT (p = 0.1453) and patient age (p = 0.4273). Singula (HR = 1.852, p = 0.0070) was also a significant independent predictor of OS after adjustment for PPT (p = 0.4127) and patient age (p = 0.0003). Results indicate that Singula is a superior predictor of both PFS and OS compared to PPT. Singula provided alternative therapy selections for 29 of 52 disease progressors detected by Cellworks. **Conclusions:** Singula is a superior predictor of PFS and OS in GBM patients compared to PPT. Singula can identify non-responders to PPT and provide alternative therapy selections. Research Sponsor: None.

2520 Poster Discussion Session; Displayed in Poster Session (Board #11), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The imaging substudy of the randomized ARTE trial: MRI and 18FET PET associations with overall survival benefit from bevacizumab in elderly patients with newly diagnosed IDH wildtype glioblastoma. *First Author: Hans-Georg Wirsching, Department of Neurology, University Hospital, Zürich, Switzerland*

Background: Bevacizumab failed to demonstrate overall survival benefit despite markedly prolonged progression-free survival in glioblastoma patients. Reasons for this divergence may include suboptimal patient selection and delayed diagnosis of progression on MRI scans under bevacizumab. Imaging analyses of retrospective and uncontrolled clinical trial cohorts suggest MRI diffusion mapping as a predictor of benefit from bevacizumab. Moreover, amino acid PET has been proposed by the RANO working group for the differentiation of tumor versus edema or gliosis based on proof-of-principle studies demonstrating earlier detection of progression with PET compared to MRI. **Methods:** ARTE (NCT01443676) was a 2:1 randomized, multi-center, open-label trial of hypofractionated radiotherapy in combination with intravenous bevacizumab every 2 weeks (BEV/RT) versus RT alone in patients with newly diagnosed glioblastoma aged 65 years or older. Patients with histologically and molecularly confirmed IDH wildtype glioblastoma aged 65 years or older were analyzed. MRI was available from 67 and serial ^{18}FET PET from 30 patients in this post hoc analysis. ^{18}FET PET intensity ratios and herein reported MRI parameters including tumor volumetric analyses and ADC were analyzed blinded for outcome and study arm. **Results:** Demographic, clinical and molecular parameters were balanced between treatment arms. Overall survival benefit from bevacizumab was observed for larger contrast-enhancing tumor volumes (hazard ratio [HR] per cm^3 0.94, 95% CI 0.89-0.99, p = 0.032) and higher ADC (HR 0.18, 95% CI 0.05-0.66, p = 0.025) on pre-treatment MRI. Response in the BEV/RT arm by the standard MRI-based RANO criteria was associated with overall survival by trend (HR 0.56, 95% CI 0.30-1.10, time-dependent p = 0.094). In a multivariate model controlling for established risk factors, ^{18}FET tumor-to-brain uptake ratios (TBR) of non-contrast-enhancing tumor portions predicted inferior overall survival specifically in the BEV/RT arm (HR [per 0.1 ^{18}FET TBR] 1.50, 95% CI 1.05-2.13, time-dependent p = 0.025). Controlling for ^{18}FET TBR at first follow-up identified benefit from BEV/RT by trend (HR 0.41, 95% CI 0.16-1.07, p = 0.069). **Conclusions:** Large contrast-enhancing tumor mass and high ADC identify patients with overall survival benefit from bevacizumab. Under bevacizumab, non-contrast enhancing tumor portions can be adequately monitored by amino acid PET. Research Sponsor: Roche.

2521 Poster Discussion Session; Displayed in Poster Session (Board #12), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Estimated clinical efficacy and radiographic response characteristics of PD1 inhibition in newly diagnosed and recurrent glioblastoma in clinical practice: A report from the iRANO Working Group. *First Author: Benjamin M. Ellingson, University of California, Los Angeles, CA*

Background: Despite concerns of immunotherapy-induced inflammatory response during PD1 inhibition, questions remain as to the true incidence of inflammatory response and potential clinical implications. The goals of the project were to use GBM patients pooled from academic centers to estimate radiographic PFS and OS, as well as determine the incidence of immunotherapy-induced inflammatory response. **Methods:** 152 patients with newly diagnosed (N = 57) or recurrent (N = 95) GBM treated with either nivolumab or pembrolizumab from Dana-Farber (N = 88), UCLA (N = 35) or UCSF (N = 29) were included in this study. Radiographic progression was defined by a 25% increase in bidirectional measurements according to RANO. **Results:** Median PFS and OS for newly diagnosed patients was 162 and 520 days, respectively, while median PFS and OS for recurrent patients was 72 and 225 days, respectively. No difference in OS was observed in recurrent patients treated with nivolumab vs. pembrolizumab (P = 0.58), but recurrent patients treated with nivolumab trended toward a longer PFS (P = 0.097). Of the recurrent patients with OS and PFS data available and radiographic progression, 95% of them progressed within 6 mos of starting treatment. Median post-progression survival (PPS) in recurrent patients with PFS $<$ 6 mos was 151 days, while PPS for patients with PFS $>$ 6 mos was 178 days (P = 0.51). In the 77 recurrent patients who progressed within 6 mos, 36.4% had an OS that was $>$ 9 mos, while 63.6% had an OS $<$ 9 mos, suggesting the majority of patients with "early progression" also died early and a minority of patients had what could be considered "immune-related inflammation". Of the 81 recurrent patients with documented progression, only 2.5% showed stabilization within 3 mos of first progression, 30.9% died before the 3-month confirmation scan could be obtained, 24.7% showed continued tumor growth by 3 months, and 48.1% had no follow-up confirmatory imaging exams. Of the 70 patients who progressed within 6 mos and had documented death, 2.9% had disease stabilization, 31.4% died before the 3-month confirmation, and 75.7% had either documented tumor growth or had no follow-up confirmatory imaging exams. **Conclusions:** This study suggests immunotherapy-induced inflammation followed by a favorable PPS is uncommon in GBM. While patients treated with other types of immunotherapy may exhibit different imaging characteristics, these data provide an important basis to refine the iRANO criteria. Research Sponsor: U.S. National Institutes of Health.

2522 Poster Session (Board #13), Fri, 8:00 AM-11:00 AM

Eradication of medulloblastoma by NKG2D-specific CAR T-cells. *First Author: Hongjiu Dai, Nanjing Kaedi Biotech Co. Ltd., Nanjing, China*

Background: Medulloblastoma (MB) is a cancerous malignant brain tumor, that most often occurs in young children. Standard-of-care therapies for treating pediatric MB have long-term side effects, even in children who are cured. Recently people are exploring the potential of chimeric antigen receptor T (CAR-T) cell therapy in brain tumor, yet the clinical outcome is limited. It's reported that NKG2D ligands are wildly expressed in MB cells, which supports NKG2D system might play an important role in MB therapy. Here, we take advantage of NKG2D-specific CAR-T cells (KD-025) for MB treatment. **Methods:** HTB186, HTB185 and HTB187 MB cell lines as well as MB cancer patient samples were evaluated for NKG2D ligands expression. The KD-025 showed antigen-specific stimulation by cytokine secretion and target cell lysis. HTB186 cells, which stably express luciferase protein, were used to establish in vivo subcutaneous and xenograft models in NSG mice. Mice received a single treatment of 10 million KD-025 intravenously. **Results:** NKG2D ligands were detected on HTB186 and HTB187 cells and most of screened BM patient samples. The KD-025 was generated with CD8 hinge region and transmembrane region, 4-1BB costimulatory region and CD3 zeta region. The KD-025 expression was $>$ 50% on the surface of T cells confirmed by flow cytometry. Co-incubation of KD-025 with HTB186 cells specifically upregulates TNF-α, IFN-γ, IL-10 and IL-2 cytokines and strongly lysis tumor cells even at low E:T ratio (70-80% at 8:1). Strikingly, KD-025 markedly eliminated xenograft tumors in vivo and did not exhibit significant treatment-related toxicity in the treated mice. Regarding to T cell persistence, the CAR-T cells are barely detectable 24 days after injection, which is comparable with CD19 CAR in our experiments as well as published data. No obvious pathological changes were found in the tested organs. **Conclusions:** Our work with the KD-025 contributes to the growing body of research committed to discovering a novel therapy for MB. NKG2D ligands are highly expressed on human MB samples. KD-025 potently respond to MB and eliminate tumor in a xenograft mouse model with no obvious safety issues. The results support future clinical trial of KD-025 in patients with MB, where the need for effective treatment is great. Research Sponsor: Nanjing Kaedi Biotech, INC.

2523 Poster Session (Board #14), Fri, 8:00 AM-11:00 AM

MGMT methylation as a prognostic factor in IDH wild type anaplastic gliomas. *First Author: Enrico Franceschi, Department of Medical Oncology, Bellaria Hospital, Azienda USL - IRCCS Institute of Neurological Sciences, Bologna, Italy*

Background: Anaplastic gliomas are classified according to the presence of IDH-mutation. IDH wild type (IDH wt) is associated with poor prognosis and limited effectiveness of treatments.The aim of this study was to find out if MGMT methylation represents a prognostic factor in this setting. **Methods:** Anaplastic gliomas are classified according to the presence of IDH-mutation. IDH wild type (IDH wt) is associated with poor prognosis and limited effectiveness of treatments.The aim of this study was to find out if MGMT methylation represents a prognostic factor in this setting. **Results:** The analysis included 73 pts with grade III, IDH wt (19.3%) gliomas. Median follow-up time was 69.9 months. Median age was 50 (Range: 18-75), M/F ratio was 40(54.8%)/33(45.2%).MGMT promoter was methylated in 34 pts (46.6%) and unmethylated in 39 pts (53.4%). After surgery, 9 pts (12.3%) received RT alone, 57 pts (78.1%) received both RT and CT (sequential, concomitant or both). Median survival was 26.2 months. In multivariate analysis age (HR = 1.064, 95%CI: 1.030-1.099; P $<$ 0.001) and MGMT methylation (HR = 0.422, 95%CI: 0.210-0.848; P = 0.015) were independently associated with risk for death. **Conclusions:** IDH wild type confers a dismal prognosis in patients with grade III gliomas. MGMT methylation, as was demonstrated in glioblastoma, represents a prognostic factor that correlated with lower risk for death. Further studies will investigate potential correlations with treatments. Research Sponsor: None.

2524 Poster Session (Board #15), Fri, 8:00 AM-11:00 AM

Leptomeningeal disease after surgical resection and radiosurgery for brain metastases and neurologic death: A multi-institutional analysis. *First Author: Roshan Sudhir Prabhu, Southeast Radiation Oncology Group, PA, Charlotte, NC*

Background: Postoperative radiosurgery (SRS) has been associated with up to 30% risk of subsequent leptomeningeal disease (LMD). We previously demonstrated that radiographic pattern of LMD (classical "sugarcoating" [cLMD] vs. nodular [nLMD]) in this setting is prognostic. The association between radiographic pattern of LMD, type of salvage treatment (tx), and neurologic death (ND) has not been well described. **Methods:** The records of patients (pts) with brain metastases (BM), of which 1 was resected and treated with adjunctive SRS, and who subsequently developed LMD were combined from 7 tertiary care centers. Pts with classically radiosensitive tumors or prior or planned whole brain radiotherapy (WBRT) were excluded. ND was defined as symptomatic CNS progression around the time of death without life threatening systemic symptoms or progression. Salvage radiotherapy (RT) for LMD was categorized according to use of WBRT vs. focal cranial RT. **Results:** The study cohort consisted of 147 pts, of which 125 had died with known cause, 107 also received LMD salvage tx, and 82 also had cranial MRI follow-up. The ND rate in the 125 pts who died with known cause was 79%; the rate in pts who underwent LMD salvage tx (n = 107) was 76%. Univariate logistic regression demonstrated radiographic pattern of LMD (cLMD vs. nLMD, odds ratio [OR] 2.9, p = 0.04) and 2nd LMD failure after salvage tx (OR 3.9, p = 0.02) as significantly associated with ND. The ND rate was 86% for cLMD vs. 68% for nLMD pattern. WBRT was used in 95% of pts with cLMD vs. 52% of pts with nLMD. In the nLMD cohort (n = 58), there was no difference in ND rate based on type of salvage RT (WBRT: 67% vs. focal cranial RT: 68%, p = 0.92). Second LMD failure (vs. not) was associated with higher ND in the nLMD cohort (77% vs. 52%, p = 0.02). Of the 26 pts with nLMD who experienced 2nd LMD failure, 7 had classical 2nd LMD, of which 100% experienced ND, and 19 had nodular 2nd LMD, of which 68% experienced ND (p = 0.09). **Conclusions:** LMD after surgery and SRS for brain metastases is a clinically significant event with high rates of neurologic death. Classical LMD pattern (vs. nodular) and 2nd LMD failure after salvage tx were significantly associated with higher risk of neurologic death. In the nodular LMD cohort, radiographic pattern of 2nd LMD may be associated with risk of subsequent neurologic death. Pts with nodular LMD treated with salvage focal cranial RT or WBRT had similar risk of neurologic death. Methods to decrease LMD and the subsequent high risk of neurologic death in this setting warrant investigation. Research Sponsor: None.

2525 Poster Session (Board #16), Fri, 8:00 AM-11:00 AM

Genomic profiling of breast cancer brain metastases reveals targetable alterations. *First Author: Sheheryar Kairas Kabraji, Dana Farber Cancer Institute, Boston, MA*

Background: Genomic characterization of breast cancer brain metastases (BCBMs) has thus far been limited. The objective of this study was to describe the landscape of genomic alterations in patients (pts) with BCBMs. **Methods:** Targeted next-generation DNA sequencing of > 300 cancer-related genes (OncoPanel) was prospectively performed on primary and metastatic (met) tumors in 321 pts with a diagnosis of BCBM between August 2016 and April 2019 at Dana-Farber Cancer Institute (table). Enrichment analysis of genomic alterations was performed using a two-sided Fisher exact test and differences in tumor mutation burden (TMB) between groups were assessed using two-sided Mann-Whitney U test. Multiple comparison correction was performed using the Benjamini-Hochberg procedure. **Results:** All subtypes were represented in BCBM (25 HR+/HER2-; 24 HR+/HER2+; 27 HR-/HER2+; 18 TNBC; 5 unknown; n = 99) and extracranial (EC) samples: (96 HR+/HER2-; 32 HR+/HER2+; 22 HR-/HER2+; 41 TNBC; 31 unknown; n = 222). BCBMs were found most commonly to have mutations or copy number alterations in *TP53, ERBB2, PIK3CA, GATA3, PTEN, ESR1, CDH1, BRCA2, ARID1A, BRCA1* (>5% frequency, table). Two pts acquired *ERBB2* amplification (amp) between the matched primary breast sample and brain met. In pair-wise comparisons of BCBMs to unmatched primaries or EC mets, only *ERBB2* amp was significantly enriched (table, † = adjusted p < 0.05). There was no significant difference in TMB between BCBM and EC mets (median 9.12 vs 7.26, p = 0.15). In contrast, TMB was significantly higher in BCBMs compared to unmatched primaries (median 9.12 vs 7.26, p=0.005). **Conclusions:** BCBMs display similar mutations and copy number alterations compared to primary tumors and EC mets in pts with BCBM. These data suggest that BCBMs contain actionable genomic alterations that are most often also reflected in EC disease. Alterations in *ERBB2, PIK3CA/PTEN*, and *BRCA1/2* represent potentially targetable alterations in pts with BCBM. Research Sponsor: U.S. National Institutes of Health, Other Foundation, Other Government Agency, Pharmaceutical/Biotech Company, Fashion Footwear Association of New York.

Genomic alteration by anatomic site % (n).

	Matched		Unmatched		
Genomic alteration	**BCBM (n=16)**	**Primary (n=13), Met (n=3)**	**BCBM (n=99)**	**Primary (n=125)**	**EC met (n=85)**
***ERBB2* amp**	62.5 (10)	50 (8)	53.5 (56) †	24.8 (31)	17.6 (15)
***TP53* mut**	12.5 (2)	31.25 (5)	48.4 (48)	45.6 (57)	42.4 (36)
***PIK3CA* mut**	12.5 (2)	18.75 (3)	24.2 (24)	22.4 (28)	25.8 (22)
***ARID1A* mut**	0 (0)	6.25 (1)	7 (7)	4 (5)	5.8 (5)
***ESR1* mut**	6.25 (1)	6.25 (1)	6 (6)	1.6 (2)	12.9 (11)
***BRCA2* mut**	12.5 (2)	6.25 (1)	5 (5)	5.6 (7)	4.7 (4)
***GATA3* mut**	0 (0)	18.75 (3)	5 (5)	6.4 (8)	10.5 (9)
***CDH1* mut**	0 (0)	0 (0)	5 (5)	10 (8)	5.8 (5)
***PTEN* mut**	6.25 (1)	6.25 (1)	3 (3)	4.8 (6)	10.5 (9)
***BRCA1* mut**	0 (0)	6.25 (1)	3 (3)	0.8 (1)	4.7 (4)

2526 Poster Session (Board #17), Fri, 8:00 AM-11:00 AM

Immune microenvironment profiling of breast cancer brain metastases using multiplex immunofluorescence. *First Author: Gaia Griguolo, Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy*

Background: Despite clinical implications, the complexity of brain metastases (BM) immune microenvironment in breast cancer (BC) patients is poorly understood. Multiplex immunofluorescence (mIF), a novel imaging technique allowing simultaneous visualization and quantification of several IF labeled proteins while maintaining spatial information, holds promise to comprehensively describe BCBM immune microenvironment, potentially providing valuable information to improve treatment. **Methods:** Clinical data and archival BM samples were collected for 60 BC patients undergoing neurosurgery (2003-2018) at three institutions. BM immune contexture was characterized using a custom mIF panel, including cell subtyping (CD4, CD8, FOXP3, CD68), activation (Granzyme B) and localization (keratin for tumor recognition) markers. Mean immune cell density (cells/mm2) for each sample was determined by digital image analysis and classified in tumor and stroma areas. Associations between immune subpopulations, BC subtype and overall survival from BM diagnosis (OS) were studied. **Results:** Up to date, 30 BCBM samples have been analyzed; 33% HR+/HER2-, 20% HR-/HER2+, 10% HR+/HER2+, 37% HR-/HER2-. At a median follow-up of 46 months, BC subtype was the only clinical variable associated with OS (longest for HER2+ and shortest for HR-/HER2-, log-rank p = 0.002). In the total sample area, no significant difference in immune cell densities was observed according to BC subtype. In the tumor area, HR+/HER2- tumors showed higher densities of CD8+ and CD68+ cells compared to other subtypes (p = 0.036 and p = 0.016, respectively). In stroma, HR-/HER2- tumors presented numerically higher densities of CD4+ and FOXP3+ cells and higher ratio of CD4/CD8 and FOXP3/CD8 ratio (not statistically significant). Higher CD4/CD8 and FOXP3/CD8 ratio in the stroma was significantly associated with worse OS, even after correction by BC subtype (Table). **Conclusions:** In BCBM, immune infiltrate differs according to BC subtype. Preliminary results suggest that a more tolerogenic immune microenvironment is associated with worse OS and might represent a target for optimization of immunotherapy for these patients. Updated results for all 60 patients will be presented. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

	Univariate Cox Model for OS		Multivariable Cox Model for OS (correction by BC subtype)	
	Hazard Ratio (95% CI)	**p**	**Hazard Ratio (95% CI)**	**p**
CD4/CD8 stroma	1.46 (1.09-1.95)	0.016	1.58 (1.03-2.40)	0.034
FOXP3/CD8 stroma	1.58 (1.07-2.35)	0.039	1.83 (1.02-3.28)	0.044

2527 Poster Session (Board #18), Fri, 8:00 AM-11:00 AM

Clinical outcome of patients experiencing central nervous system progression on first-line pertuzumab and trastuzumab for HER2-positive metastatic breast cancer in a real-life cohort. *First Author: Laetitia Collet, Centre Léon Bérard, Lyon, France*

Background: Isolated central nervous system (CNS) progression on first-line systemic therapy with Trastuzumab (T) and Pertuzumab (P) for HER2-positive metastatic breast cancer (MBC) is a therapeutic challenge. Our aim was to describe the clinical outcome and current treatment strategies for such patients in a large retrospective cohort. **Methods:** Patients (pts) were selected among all MBC pts included in the French *Epidemiological Strategy and Medical Economics* (ESME) database involving 18 specialized cancer centers (NCT03275311). CNS progression-free survival (CNS-PFS), progression-free survival (PFS) and overall survival (OS) from diagnostic of brain metastases (BM) were estimated using the Kaplan-Meier method. **Results:** Between January 2008 and December 2016, 995 pts were treated with first-line T and P for their HER2-positive MBC. They were 55 years old in median, with tumors expressing hormone-receptors in 62%. A total of 132 pts (13%) experienced isolated CNS progression on T and P, with a median time from metastatic diagnosis to CNS progression of 12 months. It was the first CNS progression for 108 pts (82%) while 24 (18%) already had BM at time of metastatic relapse. After CNS progression, T and P were continued for 58% of pts (n = 73). The remaining 47 pts were switched to another HER2-directed therapy (T-DM1 for 57%, T alone or combined with chemotherapy for 36% and lapatinib for 21%). Among those 132 pts, 37% received whole-brain radiotherapy, 18% stereotactic radiation therapy, and 11% surgery. Systemic treatment was combined with CNS-directed therapy for 50% of pts. Median follow-up is 21 months (95%CI: 14.9-25.5) from the diagnosis of CNS metastases. Median OS (mOS) of the 132 pts is 35 months (95%CI: 29.2-53,6), and median PFS 7 months (95%CI: 6.3- 9.2). A total of 77 pts (58.3%) experienced a new CNS progression with a median CNS-PFS of 9 months (95%CI: 7.6-12,0). Patient who stayed on T and P had a significantly better OS in comparison to pts who were switched to another systemic HER2-directed therapy (mOS not evaluable *vs*23 months), whereas PFS and CNS-PFS were similar between groups. **Conclusions:** In this real life setting, isolated CNS progression occurred among 13% of pts with HER2+ MBC on first-line treatment with T and P, after a median time of 12 months. Following current ASCO recommendations, continuation of T and P after CNS-directed therapy, seemed to be adequate. Nevertheless, time to subsequent progression is short and better therapeutic options are needed. Research Sponsor: None.

2528 Poster Session (Board #19), Fri, 8:00 AM-11:00 AM

Radiation-induced changes in the inflammatory microenvironment composition of lung cancer brain metastases. *First Author: Ariane Steindl, Medical University of Vienna, Vienna, Austria*

Background: Radiotherapy was postulated to impact the inflammatory microenvironment composition in patients with lung cancer brain metastases (BM). **Methods:** Formalin fixed and paraffin embedded BM specimens from treatment naïve patients (group 1) and from patients treated with radiation therapy including whole brain radiotherapy and/or stereotactic radiosurgery (group 2) or prophylactic cranial irradiation (group 3) before BM resection were identified from the Vienna Brain Metastasis Registry. T cell subsets (CD3+,CD8+,CD45RO+,FOXP3+,PD-L1+) were investigated using the Ventana Benchmark Ultra system Definiens software. **Results:** Specimens from 41 patients (28/41;68.3% NSCLC, 13/41;31.7% SCLC) were included in the study. A significant difference in CD3+TIL density between group 1 (median: 964.5cells/mm2) and group 2 (median: 283.4cells/mm2; p-value=0.021; Mann-Whitney-U test), as well as group 3 (median: 168.8 cells/mm2; p-value= 0.028; Mann-Whitney-U test) were observed. Furthermore, CD8+ and FOXP3+TIL densities of group 2 (CD8+ median: 172.1cells/mm2; FOXP3+ median: 210.7cells/mm2) were numerically lower compared to group 1 (CD8+ median: 190.1 cells/mm2; FOXP3+ median: 221.2 cells/mm2). Of 10/41 (24.4%) patients further resected BM tissue specimens after initial resection were available. Here, the inflammatory microenvironment of BM treated with radiation therapy between the resections was significantly associated with lower densities of CD3+ (median: 105.1 cells/mm2) and CD8+ (median: 20.3cells/mm2) compared to radiation-naïve patients (CD3+ median: 825.4cells/mm2; CD8+median: 105.5cells/mm2; p=0.037; Mann-Whitney U-test). **Conclusions:** Radiation treatment was associated with lower densities of TIL subsets in our BM cohort. Although results have to be interpreted with caution due to the limited sample size, further studies investigating the sequencing of radiotherapy and immune modulating therapies might be of interest. Research Sponsor: Medizinisch-Wissenschaftlicher Fonds des BÃ¼rgermeisters der Bundeshauptstadt Wien.

	GROUP 1 (n=15)			GROUP 2 (n=26)		
	Median	Range		Median	Range	p-value
CD8	190.1	1.93-487.71	CD8	172.1	2.59-916.37	>0.05
CD3	964.5	99.89-2989.34	CD3	283.4	9.97-2657.64	*0.021*
CD45	197.7	23.40-2404.53	CD45	275.6	3.20-5322.71	>0.05
FOXP3	221.2	22.88-2687.82	FOXP3	210.7	0.00-694,84	>0.05
PD-L1	0	0-60	PD-L1	0	0-60	>0.05
				GROUP 3 (n=4)		
				Median	Range	
			CD8	93.9	8.69-364.73	>0.05
			CD3	168.8	9.97-499.92	*0.028*
			CD45	275.6	125.75-740.93	>0.05
			FOXP3	71.4	0.00-529.44	>0.05
			PD-L1	0.00	0.00-0.00	>0.05

2529 Poster Session (Board #20), Fri, 8:00 AM-11:00 AM

Advanced imaging to assess longitudinal vascular changes in brain metastases treated with immune checkpoint inhibition. *First Author: Albert Kim, Massachusetts General Hospital, Boston, MA*

Background: Immune checkpoint inhibitors (ICI) have recently been shown to be effective for brain metastases (BM) for melanoma and lung cancer. This breakthrough has prompted interest in evaluating ICI in BM of other histologies. However, accurately assessing intracranial response in patients undergoing ICI is a challenge, as current measures cannot distinguish pseudoprogression from true tumor progression. To shed light on potential biomarkers of response, we prospectively use perfusion MRI to identify characteristic vascular signatures in a BM-specific trial of ICI. **Methods:** As part of an ongoing phase II study of pembrolizumab for patients with untreated or progressive, previously treated BM from any histology, patients underwent advanced MRI that includes tumor volume measurements and perfusion imaging with dynamic susceptibility contrast MRI. To calculate volumetric radiographic response, all enhancing voxels were summated. A volumetric increase of >40% was categorized as progressive disease (PD), a decrease of >60% as partial response (PR), and stable disease (SD) as between -60% and +40%. **Results:** 53 patients have been enrolled, of whom 44 have received at least baseline advanced MR imaging. Histologies include 21 with breast cancer, 5 with non-small cell lung cancer, 4 with melanoma, and 13 with other cancers. At baseline, the total number of BM was 1-50+ per patient. Based on summing the entire enhancing intracranial disease burden, best volumetric responses for the 33 evaluable patients include 4 PR, 10 SD, and 19 PD. On preliminary analysis, there was a correlation between increased tumor cerebral blood volume/flow with tumor progression. Correlation of additional vascular physiologic parameters (e.g. vessel caliber, tissue oxygenation) and volumetric response to patient outcome and standardized response criteria (iRANO) are ongoing. **Conclusions:** Pembrolizumab likely has anti-tumor efficacy in BM. Our data provides potential evidence that effective ICI is associated with a decrease in perfusion. Ongoing analyses to uncover additional vascular changes – specifically longitudinal metrics reflecting vascular structure and function - within BM to ICI are pending. These findings have potential to illustrate mechanisms of efficacy for ICI and biomarkers of response in this patient population. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

2530 Poster Session (Board #21), Fri, 8:00 AM-11:00 AM

A phase II double-blind, randomized clinical trial assessing the tolerability of two different ratios of cannabis in patients with glioblastoma multiforme (GBM). *First Author: Judith Lacey, Supportive Care, Chris O'Brien Lifehouse Cancer Hospital, Camperdown, NSW, Australia*

Background: Cannabis has been used for cancer-related symptoms but few trials have assessed quality of life or tolerability, and trials assessing tumour response or survival remain scarce. Treatment for recurrent glioblastoma (rGBM) remains palliative with poor prognosis. The tolerability of THC-containing cannabis products, and their effect on symptoms and quality of life in people with rGBM patients is poorly defined but is essential before efficacy trials can be conducted. **Methods:** We conducted a randomised double-blinded trial assessing the tolerability of two preparations of cannabis in 88 people with rGBM. The two preparations used different cannabidiol (CBD) to tetrahydrocannibidiol (THC) ratios; 1:1 (5.8mg/ml:5.6mg/ml) and 1:4 (3.8mg/ml:15mg/ml). Daily evening doses were individually monitored and titrated. Outcomes included disease response by FACT-Br, MRI imaging 12 weekly, blood pathology, NCI-CTC and clinical monitoring. Symptom assessments were performed 4 weekly for 12 weeks. **Results:** 921 people volunteered for screening across Australia, with 642 excluded, 92 recruited with 88 enrolled. 61 participants completed 12-week follow-up (attrition 30%). Both cannabis oils were well tolerated. Total FACT-Br was similar for both preparations, however, statistical significance was found for the physical section (p = 0.025) and functional (p = 0.014) identifying the 1:1 ratio as the more appropriate combination. Comparing groups to baseline, participants reported improvement of sleep (p = 0.009), improved energy (p = 0.015), and contentment with QoL (p = 0.006). Total cohort compared to baseline, participants reported improvement of sleep (p = 0.0001), pain (p = 0.046), nausea (p = 0.017), anxiety (p = 0.005) and seizure activity (p = 0.022). There were no major adverse events attributable to the cannabis with main side effects noted as dizziness, drowsiness, tiredness, and dry mouth. No abnormal blood pathology nor variance in NCI-CTCAE scores were observed. **Conclusions:** A single nightly dose of THC-containing cannabis was well tolerated in patients in both groups with rGBM and significantly improved sleep and functional wellbeing and QOL in a sample of patients compared to baseline. From this trial, the 1:1 ratio has been identified as the better tolerated product with suprerior symptom and QoL outcomes compared to the 1:4 product. Clinical trial information: ACTRN12617001287325. Research Sponsor: Bioceuticals Pty Ltd.

2531 Poster Session (Board #22), Fri, 8:00 AM-11:00 AM

Concurrent nivolumab and ipilimumab with brain stereotactic radiosurgery for brain metastases from non-small cell lung cancer: A phase I trial. *First Author: Jing Li, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Nivolumab (nivo) and ipilimumab (ipi) were found in the recent phase III CheckMate 227 trial to have an overall survival benefit over chemotherapy for advanced non-small cell lung cancer (NSCLC). However, patients (pts) with untreated brain metastasis (mets) were excluded from that trial. Because 30% of NSCLC pts develop brain mets, we tested nivo/ipi with concurrent stereotactic radiosurgery (SRS) for NSCLC pts with active brain mets. **Methods:** We report the safety data from the phase I portion of an ongoing phase I/II single-institution trial in which one treatment group was given SRS with nivo (3 mg/kg) every 2 weeks (wks) plus ipi (1 mg/kg) every 6 wks x 4 cycles, followed by maintenance nivo (480 mg) every 4 wks until disease progression, unacceptable toxicity, or withdrawal of consent. Brain SRS was delivered within 7 days of initiation of nivo/ipi. The primary endpoints were safety and 4-month (mo) intracranial progression-free survival (PFS). Dose-limiting toxicity (DLT) was defined as > 15% intracranial toxicity (>G3 hypophysitis / neurologic toxicity) or > 30% extracranial toxicity (>G3 non-dermatologic non-lab toxicity or >G4 dermatologic / lab toxicity), refractory to medical management, assessed at 8 wks after treatment initiation. Target accrual for phase I was 10 evaluable pts, with enrollment suspended after every 5 pts for DLT assessment. **Results:** Since June 15, 2018, 13 pts were enrolled and 10 were evaluable for DLT. The median follow-up time was 6.8 mo (range 1.2–18). As of January 6, 2020, only 1 pt had DLT-defined toxicity and thus the predefined stopping criteria were not met. This pt had G3 seizure right after SRS that resolved within a week, and then had increased but asymptomatic CNS edema 4 wks later. Aside from DLTs, 3 pts (25%) developed treatment-related G3 (elevated liver function tests, fatigue, nausea, adrenal insufficiency, and myocarditis) or G4 events (pneumonitis/acute respiratory distress syndrome in 1 pt with confirmed influenza at 7 mos after treatment initiation). This pt subsequently died of hemophagocytic lymphohistiocytosis (considered possibly related to the study drugs). Median intracranial PFS time was 9.7 mo, and the 4-mo intracranial PFS rate was 75%. Extracranial objective response rate was 33% in the 12 evaluable pts with a median response duration of 9.1 mo. **Conclusions:** Concurrent SRS withnivo/ipi was safe for pts with active NSCLC brain mets. Preliminary analyses of efficacy were encouraging for durable intracranial and extracranial response. Clinical trial information: NCT02696993. Research Sponsor: Bristol-Myers Squibb Global Biopharmaceutical Company.

2532 Poster Session (Board #23), Fri, 8:00 AM-11:00 AM

Response assessment and outcome of combining immunotherapy and radiosurgery for brain metastasis from malignant melanoma. *First Author: Emilie Le Rhun, Lille University Hospital, Lille, France*

Background: The evaluation of response in the context of treatment with stereotactic radiotherapy (SRT) or immune checkpoint inhibitors (ICI) or both, which represent major therapeutic options for patients with melanoma brain metastases, remains challenging due to potential tumor hemorrhage, pseudoprogression, and radionecrosis. **Methods:** We reviewed clinical and neuroimaging data of 62 melanoma patients, including 26 patients with BRAF-mutant tumors, with newly diagnosed brain metastases treated with immune checkpoint inhibitors (ICI) alone (n = 10, group 1), SRT alone or in combination with other systemic therapies (n = 20, group 2) or ICI plus SRT (n = 32, group 3). Response was assessed retrospectively using RECIST 1.1, RANO or iRANO criteria. **Results:** The MRI scans of 52 patients were available for central review. Patients received steroids at BM diagnosis in 10% in group 1, 60% in group 2 and 50% in group 3. Pseudoprogression was documented in 7 patients: 3 patients in group 2 (19%) and 4 patients (12%) in group 3. Radionecrosis was documented in 7 patients: 2 patients in group 2 (12%) and 5 patients (16%) in group 3. Patients treated with ICI alone had the worst outcome. Using RANO criteria by central review instead of local investigator assessment increased the rate of progressive disease (PD) as best response for the evaluation of SRT targets but not for the evaluation of the overall brain. Using complete RANO (including clinical assessment and steroid use) instead of RECIST criteria increased the rate of PD as best response, due to clinical deterioration noted in patients with MRI findings that did not qualify for PD. This pattern was seen in patients from all three groups. In contrast, the complete response (CR) rate was unaffected by the criteria used. More PD were also observed when comparing MRI only iRANO criteria versus complete iRANO criteria including clinical status and steroid use. **Conclusions:** Pseudoprogression is uncommon with ICI alone, suggesting that growing lesions in such patients should trigger an intervention. Pseudoprogression rates were similar after SRT alone or in combination with ICI. Response assessment criteria should be considered carefully when designing clinical studies for patients with brain metastases who receive SRT. Research Sponsor: None.

2533 Poster Session (Board #24), Fri, 8:00 AM-11:00 AM

Application of machine learning algorithms for the diagnosis of primary brain tumors. *First Author: Vasilii Khammad, James Cancer Hospital and Solove Research Institute, Columbus, OH*

Background: Primary lesions of the CNS refer to a heterogeneous group of benign or malignant tumors arising in different parts of the brain and spinal cord. According to the 2016 CNS WHO classification, the accurate diagnosis of primary brain tumors requires a layered approach of histologic, anatomic and molecular features to generate an integrated diagnosis with clinical and prognostic significance. However, in the US and worldwide, scarce resources are available to perform all the required tests routinely, so methods that improve pre-test probabilities and decrease false positive results have significant clinical and financial impact. Aims: 1) validate new diagnostic workflows with implementation of modern machine learning/artificial intelligence approaches; 2) design a reliable and interactive computational platform for primary CNS tumor diagnosis. **Methods:** To achieve these goals we have developed a population model in Rstudio, "La Tabla", based on the articles from open resources of MEDLINE database and the latest version of WHO classification of CNS tumors. The data of "La Tabla" is comprised of more than 100,000 adult and pediatric cases, including rare brain tumor diagnoses, such as Gangliocytoma, Diffuse Midline Glioma and etc. **Results:** Boruta package and weights function in R have been used to distinguish the most important features for diagnosis prediction. To visualize correlation between these features (age, ki67 level, tumor location, presence of myxoid areas, calcifications, necrosis and etc.) and all diagnoses in two-dimensional space, we used a t-SNE algorithm. Models trained with decision tree algorithms (randomForest, XGBoost and C5.0) showed high overall accuracy in predicting diagnoses of "La Tabla" (95%, 94% and 92%) and 300 patients at OSUCCC-James (93%, 74% and 87%) in the absence of IHC and molecular data. Neural networks provided by keras and nnet packages predicted diagnoses using just clinical and histological findings with 94% and 88% accuracy on "La Tabla" and James patient databases respectively. Currently, we are building "Shiny" applications with R to deliver easily operated platform for pathologists and physicians. **Conclusions:** In conclusion, we managed to generate models that are able to diagnose primary brain lesions using basic clinical data (age, gender, tumor location), ki67 levels and distinct features of histological architecture. Most of the models distinguish brain tumors and associated molecular status with high accuracy and will serve as a reliable tool for second opinion in clinical neuro-oncology. Research Sponsor: Fulbright Scholarship.

2534 Poster Session (Board #25), Fri, 8:00 AM-11:00 AM

A phase I clinical trial on intratumoral and intracavitary administration of ipilimumab and nivolumab in patients with recurrent glioblastoma. *First Author: Julia Katharina Schwarze, Department of Medical Oncology, Universitair Ziekenhuis Brussel, Brussels, Belgium*

Background: Intravenous (IV) administration of ipilimumab (IPI) and nivolumab (NIVO) has low activity in recurrent glioblastoma (rGB). Intratumoral (IT) and intracavitary (IC) administration of IPI and NIVO is under evaluation in the *GIITIpNi* phase I clinical trial. **Methods:** Patients (pts) with resectable rGB were recruited to cohorts C1, C2 and C4; pts with non-resectable rGB were recruited in C3 (biopsy only). IT administration (brain tissue lining the resection cavity during surgery) of IPI (10 mg)(C1), or IPI (5 mg) plus NIVO (10 mg)(C2, C3 and C4), was followed by IC administration of NIVO at escalating doses of 1, 5 or 10 mg Q2w in both C3 and C4 (via an Ommaya reservoir). In all cohorts, pts received 10 mg NIVO IV Q2w (6x in C1/C2, and 12x in C3/C4). Corticosteroids were contraindicated. **Results:** Forty-six pts (31 male; median age 56y (38-74); IDH1 R132H mutation in 2 pts in C1/C2; NGS somatic mutation analysis for C3/C4 ongoing) with rGB following resection, RT and temozolomide were enrolled (3, 24, 13 and 6 pts in C1, C2, C3 and C4, respectively). All pts received IT administrations. Pts in C1/C2 received a median of 5 IV NIVO administrations. Study treatment has been completed in all pts in C1/C2, in 9 pts in C3, and in 3 pts in C4; pts received a median of 4 (0-10) and 3 (0-7) postoperative IC/IV administrations in C3 and C4, respectively. Two pts in C2 and 1 pt in C3 had an increased perilesional cerebral edema (G3) with neurological deterioration after surgery/IT-injection, that was reversible with steroids. Most frequent AE were fatigue (32 pts, 64%), fever (20 pts, 44%), and headache (25 pts, 50%). In 4 pts from C3, the Ommaya was removed because of bacterial colonization (asymptomatic). There were no G5 AE. There was no dose/AE correlation with increasing IC NIVO doses in C3/C4. Repetitive CSV analysis during therapy (C3/C4) revealed increased lymphocyte counts in 4 pts; scRNA- and TCR-sequencing is ongoing. Gene expression profiling for C1/C2, and pharmacokinetic analysis of NIVO and IPI in CSV for C3/C4 are ongoing. After a median FU of 62w (16-165) for pts in C1/C2, 16 pts have died; median OS is 71w (95% CI 8-134), 1- and 2y-OS% are respectively 51% (95% CI 31-71), and 34% (95% CI 10-59). OS compares favorably to a historical cohort of Belgian rGB pts (n = 469; Log-Rank p .001). After a median FU of 10w (1-37) for pts in C3/C4, 2 pts have died; median OS has not been reached. One pt in C3 achieved a PR that is ongoing at 12m. **Conclusions:** IT/IC administration of NIVO and IPI is feasible and sufficiently safe to warrant further investigation in pts with rGB. Clinical trial information: NCT03233152. Research Sponsor: None.

2535 Poster Session (Board #26), Fri, 8:00 AM-11:00 AM

Intra-operative radiation therapy as salvage treatment option for recurrent glioblastoma multiforme. *First Author: Nidal Salim, European Medical Center, Moscow, Russian Federation*

Background: Glioblastoma multiforme (GBM) is an extremely aggressive cerebral tumor with poor prognosis. The majority of patients relapse after the initial surgery plus adjuvant radiation and chemotherapy. In case of recurrence there is no established standard therapy. The optimal techniques for salvage re-irradiation are unclear, so that procedure poses a challenge. In contrast to traditional external beam radiotherapy (EBRT) intra-operative radiotherapy (IORT) may improve patient's outcome at the cost of minimal side effects and short treatment duration. **Methods:** A total of 30 patients were treated with recurrent GBM between August 2016 and June 2019. All patients underwent maximal safe resection; patients were divided into IORT and EBRT groups. 15 patients were included in each group with similar clinical characteristics. All patients in IORT group underwent maximal safe microsurgical resection with subsequent intraoperative balloon electronic brachytherapy (IBEB) and no further adjuvant treatment. IBEB was performed using Axxent electronic brachytherapy device (Xoft Electronic Brachytherapy (eBx) System, USA. Patients in EBRT group underwent same surgery followed by external beam radiotherapy. Contrast-enhanced brain MRI with perfusion was performed within 24 hours of surgery +/- brain PET-CT with 18-FDOPA and then every 3 months. Both groups were also assigned to subgroups ($\leq$ 2.5cm3 and $>$ 2.5cm3) based on post-operative contrast-enhancing volume (POCEV). Median overall survival (OS) since diagnosis and local progression-free survival (locPFS) following the second surgery were analyzed. Possible toxicities and prognostic factors were also evaluated. **Results:** Median OS was 27 months in IORT group and 21 months in EBRT group. The locPFS range between 3.5 to 39 months in IORT group and only 2 to 10 months in group with EBRT. Kaplan-Meier OS curves in patients with POCEV $\leq$ 2.5cm3 showed more favorable outcomes for patients in the IORT group ($p < 0.05$). In patients with POCEV $>$ 2.5cm3 the median OS was 17 months in IORT group and 13.5 months in EBRT group. **Conclusions:** IORT of recurrent GBM is feasible and provides encouraging local progression-free and overall survival; no high-grade radiation induced toxicities occur and further studies to establish this method are mandatory. The toxicity profile of additional IBEB was manageable. Maximal safe microsurgical resection is the most important prognostic factor and could determine the effectiveness of post-surgical IBEB. Research Sponsor: European Medical Center.

2536 Poster Session (Board #27), Fri, 8:00 AM-11:00 AM

Accelerator-based BNCT in rescue treatment of patients with recurrent GBM: A multicenter phase II study. *First Author: Shin-Ichi Miyatake, Osaka Medical College, Takatsuki, Japan*

Background: Boron neutron capture therapy (BNCT) is tumor-selective particle radiation and theoretically efficacious especially for tumors with infiltrative nature, such as glioblastoma (GBM). The aim of this study is to assess safety and efficacy of accelerator-based BNCT (AB-BNCT) using cyclotron-based neutron generator, BNCT30, and ^{10}B-boronophenylalanine (borofalan(^{10}B)) agent, SPM-011, in patients with recurrent malignant gliomas, chiefly GBM. **Methods:** The multi-institutional open-label, phase II clinical trial for recurrent 27 cases of malignant gliomas (MG) (24 cases were GBM) was conducted with above mentioned AB-BNCT system, using 500mg/kg of SPM-011 (study code, JG002). The patients were enrolled from February 2016 to June 2018. The inclusion criteria are bevacizumab-naïve MG, recurrent after standard treatment composed of XRT and chemotherapy with TMZ. Neutron-irradiation time were determined not to exceed to 8.5 Gy-Eq for scalp dose which was decided by preceding phase I trial. Primary endpoint was 1-year survival rate and secondary ones were median overall survival (mOS), median progression free survival (mPFS) and so on. The results were compared to previous Japanese domestic bevacizumab trial for recurrent GBM (JO22506) which had the similar inclusion criteria with JG002. **Results:** 1-year survival rate and mOS of recurrent GBM cases in JG002 was 79.2% (95% CI:57.0-90.8) and 18.7 months (95% CI:12.9-23.4) (data cutoff = 20 Jun 2019) respectively, while those of JO22506 was 34.5% (90% CI: 20.0-49.0) and 10.5 months (95% CI:8.2-12.4), respectively. Median PFS of JG002 and JO22506 were 0.9 and 3.3 months, respectively. Most important adverse event in JG002 was brain edema. 21 out of 27 cases were treated with bevacizumab after progress disease. **Conclusions:** AB-BNCT demonstrated acceptable safety and prolonged survival for recurrent MG chiefly GBM. AB-BNCT might produce brain edema somewhat after the treatment, which might be the unavoidable adverse event of re-irradiation for recurrent MG, however that seemed to be controlled with bevacizumab. Clinical trial information: JapicCTI-194742. Research Sponsor: Stella Pharma Corporation.

Parameter	JG002(BNCT) GBM (N = 24)	JO22506 (bevacizumab) GBM (N = 29)
1-year survival rate,% (95% CI)	79.2 (57.0-90.8)	34.5 (90%CI, 20.0-49.0)
Median OS, mo (95% CI)	18.7 (12.9-23.4)	10.5 (8.2-12.4)
Median PFS, mo (95% CI)	0.9 (0.8-1.0)	3.3 (2.8-6.0)

2537 Poster Session (Board #28), Fri, 8:00 AM-11:00 AM

Clinical outcomes of the combination of bevacizumab and ttfields in patients with recurrent glioblastoma: Results of a phase II clinical trial. *First Author: Jaleh Fallah, Cleveland Clinic Foundation, Cleveland, OH*

Background: Clinical trials of bevacizumab monotherapy and TTFields monotherapy have shown activity but limited clinical benefit in patients (pts) with recurrent glioblastoma (GBM), with median progression-free survival (PFS) of 2-4 months and median overall survival (OS) of 6-9 months with either treatment modality. In a single-arm phase II clinical trial, the efficacy of the combination of bevacizumab and TTFields in pts with recurrent GBM was investigated. **Methods:** Pts with histologically confirmed GBM or other grade IV gliomas, who had disease progression after chemoradiation were enrolled in a phase II trial of the combination of bevacizumab and TTFields. Bevacizumab was given at a dose of 10 mg/Kg intravenously every 2 weeks and TTFields was worn by the pts continuously for more than 18 hours per day. Treatment was continued until disease progression or unacceptable toxicity. The primary endpoints were PFS at 6 months and OS at 12 months. Survival outcomes were assessed using the Kaplan-Meier method and compared by log rank test. Treatment-related adverse events were reported according to CTCAE, v4.0 criteria. **Results:** From April 2013 to December 2017, 25 pts were enrolled and 23 were evaluable: 18 (78%) men and 5 (22%) women, median age 60 years (range 17–78). 21 pts were Caucasian, 1 was African American and 1 of unknown race. After a median follow up of 31.6 months (range: 4.1-59.0 months), 21 out of 23 pts died (4 women and 17 men). The median PFS was 4.1 months (95%CI, 3.6-9.5) and the median OS was 10.5 months (95% CI, 8.2-14.9). The PFS rate at 6 and 12 months were 33% and 19%, respectively. The OS rate at 6 and 12 months were 82% and 46%, respectively. Women had better OS and PFS compared to men, however, the difference was not statistically significant which can be due to the small study population (table). Grade 3 and 4 toxicities considered definitely or probably related to the treatment included hypertension (n = 1) and cerebral infarction (n = 1). Other reported grade 3-4 toxicities (n = 7) included cough, dysphagia, muscle weakness, hyperglycemia, psychosis, seizure, lymphopenia, transaminitis, and muscle weakness considered unlikely to be treatment-related. **Conclusions:** The combination of bevacizumab and TTFields in is safe and feasible and has clinical efficacy in pts with recurrent GBM. Clinical trial information: NCT01894061. Research Sponsor: NovoCure Ltd, Other Foundation.

Variable	Female (N = 5)	Male (N = 18)	P-Value
Median PFS (95% CI)	13.0 months (3.6 - not reached)	3.9 months (3.0 - 7.9)	0.06
Median OS (95% CI)	16.0 months (6.2 - not reached)	9.9 months (8.2 – 14.0)	0.09

2538 Poster Session (Board #29), Fri, 8:00 AM-11:00 AM

Phase Ib clinical trial of OKN-007 in recurrent malignant glioma. *First Author: James D. Battiste, Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK*

Background: Despite therapeutic advances, the median overall survival for patients with recurrent, high-grade gliomas remains poor. Thus, there is an urgent need for efficacious new therapies. The nitrone compound, OKN-007 (disodium 4-[(tert-butyl-imino) methyl] benzene-1,3-disulfonate N-oxide) is a promising novel anti-cancer agent. In orthotopic glioblastoma xenografts, OKN-007 reduces cell proliferation and angiogenesis, and increases apoptosis. Here we report on the safety, efficacy, and pharmacokinetics (PK) of OKN-007 in adults with recurrent glioma. **Methods:** NCT01672463 is a phase Ib trial of OKN-007 in adults with recurrent gliomas previously treated with standard therapy. Patients with recurrence, adequate performance status and organ function, receiving clinically appropriate doses of steroids, with a life expectancy greater than 8 weeks were eligible. OKN-007 was administered by IV. The study comprised a 3+3 dose escalation design followed by an expansion cohort at the maximum tolerated dose (MTD). The dose escalation drug levels were 20 (n = 3), 40 (n = 3), and 60 mg/kg (n = 3), treating on a schedule of thrice weekly for 4 weeks, then twice weekly for 4 weeks, then once weekly until progression. Drug PK was determined in the dose escalation cohorts. The expansion cohort was treated with 60 mg/kg thrice weekly for 12 weeks, then twice weekly for 12 weeks, then once weekly until recurrence (n = 6). Kaplan-Meier analysis was used to determine progression-free (PFS) and overall survival (OS). **Results:** Median age was 51 years (range, 25-62). No dose-limiting toxicities were observed and 60 mg/kg was chosen for the expansion dose. Of 123 adverse events (AE), 34 were deemed probably (1.6%) or possibly (26%) treatment-emergent (TEAE). The most commonly-occurring TEAE were fatigue (4.1%) and headache (3.3%). No drug-attributable grade 4 or 5 AE were observed. Grade 3 TEAE included headache, urinary tract infection, and increased prothrombin time (0.8% each). Only two grade 1 AE, hypokalemia and dizziness, were considered probably attributable to OKN-007. In patients receiving 60 mg OKN-007/kg, median PFS was 1.4 months and OS was 21 months (log rank p = 0.08 for comparison across doses). Systemic PK exposure was dose proportional. The average half-life of OKN-007 is 2.8 hours. **Conclusions:** OKN-007 appears safe for patients with recurrent glioma. The MTD was not reached. Our data suggest that, compared to standard therapy, OKN-007 may prolong OS in recurrent glioma. Based on new data, a trial of OKN-007 plus temozolomide is underway in patients with newly diagnosed glioblastoma (NCT03587038). Clinical trial information: NCT01672463. Research Sponsor: Oblato, Inc.

2539 Poster Session (Board #30), Fri, 8:00 AM-11:00 AM

Defining the prognostic role of MGMT methylation value by pyrosequencing assay in glioblastoma patients: A large Italian multicenter study. *First Author: Giuseppe Lombardi, Department of Oncology, Oncology 1, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy*

Background: MGMT methylation (MGMTmet) status represents an important prognostic factor for glioblastoma (GBM) patients (PTS). Quantitative pyrosequencing approach has proven to be feasible for MGMTmet testing but its value is still unclear. We performed a large, multicentre, retrospective study to identify the association between MGMTmet values and clinical outcome. **Methods:** from 9 Italian neuro-oncology centres, we collected consecutive GBM PTS with assessment of MGMTmet by pyrosequencing approach evaluating CpG islands from 75 to 84. Other inclusion criteria were: histological diagnosis of GBM, ECOG PS $\leq$2, therapy with RT+TMZ. Kaplan-Meier method was used to estimate the survival curves, time-dependent ROC curve for defining the optimal cut-off value of mean percentage of MGMTmet in terms of 2y-OS, Cox regression for multivariable analysis, and restricted cubic spline to investigate the non-linear association between methylation values and OS. **Results:** 681 PTS were enrolled; median age was 60 ys; ECOG PS was 0 in 292 PTS, 1 in 306 PTS, 2 in 83 PTS; 391 PTS (58%) had a complete resection. 8% of PTS received a second surgery. IDH was mutated in 6%. 2y-OS was 31.6%, median OS was 17.4 ms. Median MGMTmet was 3.5% (IQR 0-22%). ROC curve identified a cutoff of 15% of MGMTmet in terms of 2y-OS (sens 78%, spec 57%, AUC = 0.67). 2y-OS was 19.7% and 53.7% for PTS with MGMTmet $<$ and $\geq$15%, respectively ($p < 0.0001$). At multivariable analysis, MGMTmet $<$ 15% was associated with impaired survival (HR 2.7, 95% CI 2.1-3.4; $p < 0.00001$), adjusting for age, KPS, type of surgery and second surgery. A non-linear association between MGMT methylation and survival was identified (non-linear term: $p < 0.0001$), with lower values of MGMT methylation associated with lower survival; indeed, estimated median OS was lowest (14 months, 2ys-OS: 17.4%) with MGMTmet of 4%, 21ms (2yr-OS: 40.9%) with MGMTmet of 20%, 27ms (2yr-OS: 40.9%) when MGMTmet was 40%, then leveled around 30ms (2yr-OS: 54.5-59.8%) when MGMTmet was $>$ 40%. **Conclusions:** this study represents one of the largest trials analyzing MGMTmet by pyrosequencing approach. Lower values of MGMTmet were associated with impaired survival and the relationship was non-linear. Noteworthy, we identified a strong prognostic value of MGMTmet which could be used as stratification factor in prospective clinical trials Research Sponsor: None.

2540 Poster Session (Board #31), Fri, 8:00 AM-11:00 AM

Phase II trial of bevacizumab and temozolomide for treatment of elderly patients with newly diagnosed glioblastoma. *First Author: Donna Molaie, UCLA Health, Los Angeles, CA*

Background: Glioblastoma (GBM) in elderly patients differ molecularly as compared to younger patients, and may have increased angiogenic activity. Bevacizumab (BV) is an anti-angiogenic monoclonal antibody against vascular endothelial growth factor. We conducted a clinical trial to evaluate the efficacy and safety of BV and temozolomide (TMZ) for elderly patients with a new diagnosis of GBM, while deferring radiotherapy. **Methods:** This is a phase II, single-arm, multicenter, open label trial. Eligible patients have a tissue diagnosis of GBM with no treatment other than surgery, age $\geq$ 70, KPS $\geq$ 60, and adequate organ function. TMZ was initiated within 2 weeks of surgery and BV was initiated within 4 weeks thereafter. TMZ was administered at 150-200 mg/m^2/day for 5 days every 4 weeks and BV at 10mg/kg every 2 weeks. A historical control group of 42 patients with similar criteria who received concurrent TMZ and RT followed by adjuvant TMZ, was derived for comparison from an institutional patient database. The primary endpoint is overall survival (OS) and secondary endpoints are progression-free-survival and safety. **Results:** 50 patients were enrolled from June 2010 to January 2016. Median age is 75 (range 70-87), and median KPS is 80 (range 60-100). 17 patients had a biopsy only, 26 patients have MGMT promoter methylation, and all patients are IDH wildtype. The study and control group are well matched in terms of age and molecular markers, however, the study patients had worse initial KPS and higher baseline tumor volume. At time of analysis, all but 2 patients were deceased. The median OS was 12.6 months for study patients (95% CI, 10.9-15.9 months) and 16.3 months for control patients (95% CI, 12.9-22.4 months). In a multivariate Cox analysis, baseline tumor volume (HR = 2.6, p = 0.0001) and MGMT promoter methylation (HR = 0.49, p = 0.004) were significant prognostic markers. Treatment type did not have a significant impact on OS (HR = 1.5, p = 0.14). Treatment-related serious adverse events included: pulmonary embolism (5), cerebral hemorrhage (3), pneumonia (1), intestinal perforation (1), deep venous thrombosis (6), hypertension (2), atrial fibrillation (1), congestive heart failure (1), cardio-respiratory arrest (1), lymphopenia (2), thrombocytopenia (8), and neutropenia (5). **Conclusions:** The results of this study suggest for patients with newly diagnosed GBM age $\geq$70 and KPS $\geq$60, treatment with BV and TMZ is equivalent to standard chemoradiotherapy, and has tolerable side effects. Complete endpoint analysis will be presented with the poster. Clinical trial information: NCT01149850. Research Sponsor: Genentech, Memorial funds in honor of Jeri Weiss.

2541 Poster Session (Board #32), Fri, 8:00 AM-11:00 AM

A pediatric and young adult phase I dose escalation study of BXQ-350 for solid and central nervous system tumors. *First Author: Mohamed Abdelbaki, Nationwide Children's Hospital, Columbus, OH*

Background: BXQ-350 is a novel agent composed of the multifunctional, lysosomal activator protein Saposin C (SapC) and dioleoyl- phosphatidylserine (DOPS) and has demonstrated antitumor effects in both *in vitro and in vivo* preclinical models. Many tumors, including high-grade glioma and diffuse intrinsic pontine glioma (DIPG), and cells of tumor vasculature have aberrantly exposed phosphatidylserine (PS)-rich domains on the cell surface. BXQ-350 is an anti-tumor agent in development from Bexion Pharmaceuticals, Inc. that selectively targets tumor cell PS, particularly those translocated to the outer leaflet of the plasma membrane in tumor cells. BXQ-350 activates and participates in various cellular processes, including apoptosis and necrosis, and may also exhibit novel mechanisms leading to cell death that require further investigation. **Methods:** Nine refractory solid (2) and central nervous system (7) tumor patients (5F:4M, age 4-23 years of age) were enrolled in a 2-site dose escalation phase I first-in-pediatric trial (NCT03967093) which completed in 2019. All patients received at least one dose of BXQ-350 which was administered as an intravenous infusion. Dosing began at 1.8 mg/kg and escalated to the highest planned dose level of 3.2mg/kg. **Results:** There were no BXQ-350-related serious adverse events, dose limiting toxicities, or withdrawals. The highest planned dose of 3.2 mg/kg was achieved safely but a maximum tolerated dose was not established. One osteosarcoma patient had progressive disease prior to completing cycle one of treatment and was removed from trial. Eight patients (DIPG-3, HGG-1, GBM-1, Pineoblasotoma-1, Ependymoma-1, Osteosarcoma-1) completed at least one cycle, with one DIPG patient completing cycle five. **Conclusions:** BXQ-350 was well tolerated with no significant dose-limiting toxicities at the highest planed dose level. A pediatric phase I trial in newly diagnosed patients is planned for 2nd quarter 2020. Clinical trial information: NCT03967093. Research Sponsor: Bexion Pharmaceuticals.

2542 Poster Session (Board #33), Fri, 8:00 AM-11:00 AM

Post-marketing safety surveillance of tumor treating fields (TTFields) in patients with high-grade glioma in clinical practice. *First Author: Wenyin Shi, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA*

Background: Tumor Treating Fields (TTFields) are an antineoplastic treatment delivering low intensity, intermediate frequency, alternating electric fields through two pairs of transducer arrays locoregionally applied to tumor bed. TTFields are FDA-approved for glioblastoma (GBM; 200 kHz) and mesothelioma (150 kHz). Safety and effectiveness were demonstrated in the phase III EF-11 and EF-14 trials in recurrent GBM (rGBM) and in newly diagnosed GBM (ndGBM), respectively. The main TTFields-related adverse event (AE) was array-associated manageable skin irritation. We report AEs from TTFields-treated patients in the real-world, clinical practice setting. **Methods:** Unsolicited, global, post-market surveillance data from TTFields-treated patients (October 2011–February 2019) were retrospectively analyzed using MedDRA v21.1, stratified by region (US, EMEA [Europe, Middle East, Africa], or Japan), diagnosis (ndGBM, rGBM, anaplastic astrocytoma and anaplastic oligodendroglioma, or other brain tumors that includes brain metastases from different cancer types), and years of age ($<$18, pediatric; 18 to 64, adults; or $\geq$65, elderly). **Results:** Of 11,029 patients, 53% had ndGBM, 39% had rGBM (at any line of recurrence), 6% had anaplastic astrocytoma/oligodendroglioma, and 1% had other brain tumors. Most were adults (73%) and 26% were elderly ($\geq$65 years of age). The majority of patients were males (66.3%) compared to females (33.7%), with a ratio representative of a typical GBM population. The most reported TTFields-related AE was array-associated local skin reaction, with an incidence of 38% in ndGBM, 29% in rGBM, 38% in anaplastic astrocytoma/oligodendroglioma, 31% in other brain tumors, 37% in pediatric, 34% in adults, and 36% in elderly patients. Most skin AEs were mild to moderate and resolved with no treatment or over the counter topical ointments. Incidence of other TTFields-related AEs in patients with ndGBM and rGBM, respectively, included heat sensation (under-array warmth; 11%, 10%), electric sensation (under-array tingling; 11%, 9%), and headache (7%, 6%). **Conclusions:** This retrospective, global, TTFields safety surveillance analysis revealed no new safety signals, with favorable safety and tolerability comparable to published TTFields/GBM trials. The most common TTFields-related AE was array-associated local skin reaction. The safety profile remained consistent among subgroups (diagnosis, age, or region) and total cohort, indicating feasibility in multiple subpopulations, including elderly patients. Research Sponsor: None.

2543 Poster Session (Board #34), Fri, 8:00 AM-11:00 AM

Phase I study of BPM31510 and vitamin K in patients with high grade glioma recurrent after a bevacizumab-containing regimen. *First Author: Seema Nagpal, Stanford University, Stanford, CA*

Background: BPM31510 is an ubidecarenone-lipid conjugate nanodispersion in clinical development for advanced malignancies, including high grade glioma (HGG). BPM31510's anti-cancer effect is mediated by induction of mitochondrial superoxide and activation of cell death in glioblastoma models. Herein, we present preliminary pharmaco-kinetic and dynamic data, and survival from a phase I study of BPM31510 + Vitamin K in HGG with progression after bevacizumab (BEV). **Methods:** This was an open-label phase I study of BPM31510 continuous infusion with Vitamin K (10mg IM qweek) using a mTPI design, starting at 110mg/kg 2X/week, allowing 2 dose escalations & 1 de-escalation. Patients had received ChemoRT and were in recurrence after BEV. **Results:** Of 12 patients treated with BPM31510, 9 completed the 28-day DLT period. 2 patients came off study for progressive disease; 1 patient after asymptomatic hemorrhage into tumor bed (G1). 10 patients had primary GB, 2 had AA. Median age was 54.5yo (27-67) and KPS 70 (60-90). On Day 1 of BPM31510, a dose dependent increase in Cmax was observed; Tmax values were similar for all doses. AUC was linear with dose escalation. For all doses, Day 4 Cmax values were higher compared to Day 1. In contrast there was variable decrease in Tmax (table). Of evaluable patients, 4 patients received the highest dose 171mg/kg, where a single patient experienced DLT: G3 AST & ALT. The most common grade 1/2 AEs were elevated AST, rash, and fatigue, each occurring in 4 patients. The mOS for 9 eligible/evaluable patients was 128 days (95% CI: 48-209) while PFS was 34 days (95% CI of mean 8.9). Two patients are currently alive $>$12 months. **Conclusions:** BPM31510 + vitamin K demonstrated a safe profile to maximum dose of 171mg/kg twice/week with potential therapeutic utility in treatment-refractory HGG patients. Multi-omic molecular profiles characterizing AE and response to be reported from the study will be investigated for next phase of clinical development. Clinical trial information: NCT03020602. Research Sponsor: Berg Health, LLC.

Arithmetic mean (SD).

Dose (mg/kg)	N	Day 1 C_{max} (μg/mL)	Day 1 T_{max} (hr)	Day 1 AUC_{0-t} (hr*μg/mL)	Day 4 C_{max} (μg/mL)	Day 4 T_{max} (hr)	Day 4 AUC_{0-t} (hr*μg/mL)
110	6	236 (32.6)	4.00 (0.00)	766 (101)	377 (80.5)	1.33 (2.07)	1400 (303)
137	1	348	4.00	922	793	4.00	2860
171	5	444 (87.0)	3.60 (0.894)	1310 (264)	1200 (340)	2.00 (2.00)	4510 (1520)

2544 Poster Session (Board #35), Fri, 8:00 AM-11:00 AM

Depatuxizumab mafodotin (Depatux-M) plus temozolomide (TMZ) in recurrent glioblastoma patients: Real-world experience from a multicenter study of Italian Association of Neuro-Oncology (AINO). *First Author: Mario Caccese, Department of Oncology, Oncology 1, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy*

Background: Precision medicine is a promising tool in oncology. Depatux-M is a new antibody-drug conjugate, consisting of a specific antibody against activated EGFR and a cytotoxic agent with antimicrotubule activity. The Intellance2/EORTC 1410 phase II trial, showed interesting results for Depatux-M and TMZ combination in EGFR-amplified glioblastoma (GBM) patients (PTS) at first recurrence after RT and TMZ. In our study, we investigated clinical outcome and safety of this combination used in recurrent GBM PTS as "compassionate use". **Methods:** In this prospective observational study, PTS were enrolled from 7 centres of AINO. Major inclusion criteria were: histologically confirmed diagnosis of GBM, 1 or more prior systemic therapies, ECOG PS $\leq$ 2 and EGFR-amplified (analyzed by FISH). According to original schedule, patients received Depatux-M 1.25 mg/kg every two weeks combined with TMZ until disease progression or unacceptable toxicity. Kaplan-Meier method was used to estimate the survival curves, RANO criteria for radiological assessment, CTCAE v5.0 for drug related adverse events. **Results:** From October 2018 to June 2019, we enrolled 36 PTS: median age was 57, ECOG PS 0-1 in 88% of PTS, MGMTmet in 64%, 42% received the treatment as second-line therapy and 27% underwent further chemotherapy at progression. At the time of analysis, 13 PTS (36%) had died and 27 PTS (75%) had progressed. Median OS was 8.7ms (95%CI not available), 6ms OS was 68%; median PFS was 2.3ms (95% CI 1.8 – 2.8), 6ms PFS was 37%. All PTS were evaluable for response: disease control rate was 47%: stable disease was reported in 36% and partial response in 11% of PTS. Drug-related adverse events led to dose reductions of Depatux-M in 17% of PTS, in 28% was delayed and in 8% was permanently discontinued. The most frequent grade 3-4 adverse events were ocular toxicity in 67% and haematological toxicity in 17% of PTS; no death was considered drug-related. **Conclusions:** We report the first "real world" experience of Depatux-M plus TMZ in recurrent GBM. We showed encouraging clinical benefit, despite most patients were treated beyond the second-line of therapy. Overall the results are closed to those reported in previous phase II trial. Although toxicity was higher than expected, it was manageable and only a small group of patients discontinued the treatment due to serious adverse events Research Sponsor: None.

2545 Poster Session (Board #36), Fri, 8:00 AM-11:00 AM

Preliminary assessment of low-intensity transcranial magnetic stimulation (TMS) during the treatment for brain glioblastomas. *First Author: Ivan A. Popov, Rostov Research Institute of Oncology, Rostov-on-Don, Russian Federation*

Background: The standard treatment of malignant brain gliomas, including surgical and radiation therapies, does not provide recovery and a long-time favorable prognosis. The development of technologies and international guidelines on the introduction of electric (TTF) and electromagnetic (TMS) fields in combination treatment for glioblastomas aims to improve immediate results, as shown in experiments on human glioblastoma cell culture. The TMS protocol requires further refinement in parameters of frequency, intensity, and exposure with an assessment of the immediate results of combined treatment. **Methods:** The study included 60 patients diagnosed with MBG receiving osteoplastic craniotomy with radical (within visible unchanged tissues) tumor removal. Starting from the second day after the surgery, patients of group 1 (n = 30) received 10 sessions of magnetotherapy in the double exposure mode. For the first morning exposure, we used an ultra-low-frequency magnetic field (ULFMF) (0.03 to 9.0 Hz) on the hypothalamus projection area to induce a general antistress reaction. After 2.5-3 hours, local (on the surgical site) TMS exposure with the Neuro-MSD system (Russia) was applied in the pulse algorithm, up to 1 GHz and 5 Hz, 15 mT, 3 min. The induction was reduced exponentially (C = 0.8). The control group 2 (n = 30) did not receive ULFMF or TMS. Magnetic resonance imaging (MRI) was used to determine the volume of tumors (Vt, cm^3) and perifocal edema (Ve, cm^3) calculated according to the Shrek's formula for an ellipsoid ($V = a \times b \times c \times \pi/6$). **Results:** Before surgery, $Vt = 54.7 \pm 5.7 cm^3$ in group 1, in group 2 - $Vt = 60.9 \pm 8.5 cm^3$ (no statistical differences). After surgery and the subsequent course of ULFMF and TMS, residual tumor volumes in group 1 were 2.5 times lower than in controls ($p < 0.05$). The difference between Ve values before and after treatment was on average 80.7 cm^3 in group 1 and 41.8 cm^3 in group 2 ($p < 0.05$). **Conclusions:** The inclusion of sequential ULFMF and TMS exposures into postoperative therapy for gliomas, taking into account various vectors of the influence on the projection of centers of homeostasis regulation and the surgical field, as well as the development of programmed modes of biotropic exposure parameters, improves antitumor and anti-edematous effects. Research Sponsor: None.

2546 Poster Session (Board #37), Fri, 8:00 AM-11:00 AM

MRI changes in patients with newly diagnosed glioblastoma treated as part of a phase II trial with bavituximab, radiation, and temozolomide. *First Author: Ina Ly, Massachusetts General Hospital, Boston, MA*

Background: Glioblastoma and tumor endothelial cells express phosphatidylserine (PS), a highly immunosuppressive membrane phospholipid. Bavituximab – a chimeric monoclonal antibody – binds to β2-glycoprotein 1 (β2-GP1) to form a complex of β2-GP1 with PS, resulting in immune activation against tumor cells and anti-angiogenic effects. Phase I/II trials in other solid cancers demonstrated response rates up to 75% when bavituximab was given with cytotoxic chemotherapy. Preclinical data in glioblastoma models suggested synergistic effects of PS blockade, radiation, and temozolomide. **Methods:** 33 adult patients with *IDH*-wild-type, *MGMT*-methylated or -unmethylated newly diagnosed glioblastoma were enrolled in this phase II trial (NCT03139916) and received 6 weeks of chemoradiation, followed by 6 cycles of adjuvant temozolomide (C1-C6 aTMZ). Bavituximab (3 mg/kg) was given weekly, starting week 1 of chemoradiation, for 18 weeks with the option to continue if tolerated. Physiologic MRIs were performed pre-treatment, pre-C1, pre-C3, and pre-C5 aTMZ. Within the enhancing tumor region, median tumor K^{trans} (reflecting vascular permeability) and relative cerebral blood flow (rCBF) were measured. Median percent changes during treatment were compared to pre-treatment values. **Results:** Median progression-free survival (mPFS) was 8 months. Based on a median overall survival (mOS) of 17.1 months, patients were categorized into above-median survivors (AMS) and below-median survivors (BMS). All patients had pre-treatment scans. 31 had evaluable pre-C1, 25 had pre-C3, and 7 had pre-C5 scans. Compared to BMS, AMS had a greater reuction in enhancing tumor volume and rCBF, and a greater increase in K^{trans} during treatment (table). One patient remains on study; 23 patients have died. Bavituximab was well tolerated. **Conclusions:** mPFS and mOS in patients treated with bavituximab, radiation and temozolomide were comparable to standard chemoradiation and aTMZ. Lower rCBF in AMS may reflect decreased tumor perfusion while higher K^{trans} could imply enhanced drug delivery to the tumor. Bavituximab induces changes in tumor vasculature that may improve survival in a subset of patients. Clinical trial information: NCT03139916. Research Sponsor: Peregrine Oncologie, National Comprehensive Cancer Network.

% change in MRI parameters compared to baseline at pre-C1, pre-C3, and pre-C5 timepoints. AMS: above-median survivors; BMS: below-median survivors.

	Enhancing tumor volume		rCBF		K^{trans}	
MRI	**AMS**	**BMS**	**AMS**	**BMS**	**AMS**	**BMS**
Pre-C1	-46.4	-8.1	-33.4	-6.0	85.8	5.1
Pre-C3	-17.4	5.3	-43.0	-20.4	29.0	-11.7
Pre-C5	-27.4	26.2	-31.8	4.9	37.4	5.0

2547 Poster Session (Board #38), Fri, 8:00 AM-11:00 AM

Impact of lymphopenia on survival for elderly patients with glioblastoma: A secondary analysis of the CCTG CE.6 (EORTC 26062-22061, TROG03.01) randomized clinical trial. *First Author: Andrew Jehyun Song, Sidney Kimmel Cancer Center, Philadelphia, PA*

Background: Lymphopenia (LMP) may lead to worse outcomes for patients with glioblastoma (GBM). This study is a secondary analysis of the CCTG CE.6 trial evaluating the impact of chemotherapy and radiation on LMP, as well as the association of LMP with overall survival. **Methods:** CCTG clinical trial CE.6 randomized elderly GBM patients ($\geq$ 65 yrs) to short course radiation alone (RT) or short course radiation with temozolomide (RT + TMZ). In this study LMP (mild-mod: grade 1-2; severe: grade 3-4) was defined per CTCAE v3.0 criteria, and measured at baseline, 1 wk and 4 wks post-RT. Pre-selected key factors for the analysis included age, sex, ECOG, extent of resection, MGMT methylation, MMSE, and steroid use. Multinomial logistic regression models were used to identify factors associated with LMP and multivariable Cox regression models were used to study effect of LMP on survival. **Results:** A total of 562 patients were included for analysis (281 RT vs 281 RT+TMZ). At baseline, both arms (RT vs RT+TMZ) had similar rates of mild-mod (21.4% vs 21.4%) and severe (3.2% vs 2.9%) LMP. The 1 wk post-RT LMP rates were also similar (p = 0.25). However, RT+TMZ pts were more likely to develop both mild-mod LMP (18.2% vs 27.9%) and severe LMP (1.8% vs 9.3%) [$p < 0.001$] at 4 wks post-RT. Developing mild-mod and severe LMP post-RT were both associated with baseline LMP ($p < 0.001$) and RT+TMZ ($p < 0.001$). Severe LMP at 4 wks post-RT was also associated with biopsy only ($p < 0.02$). After adjusting for confounding factors, 4 wks post-RT LMP was not significantly associated with PFS or OS regardless of severity. However, baseline LMP (HR 1.3) was significantly associated with worse OS (HR: 1.30, 95% C.I.: 1.05-1.62, p = 0.02), regardless of MGMT status. Other factors significantly associated with worse outcome included: males (HR 1.41), biopsy only (HR 1.59), and lower MMSE (HR 1.03). **Conclusions:** Short course RT alone does not lead to LMP after treatment. Development of LMP post-RT is associated with addition of TMZ and baseline LMP. However, only baseline LMP is associated with worse OS regardless of MGMT status. This may be considered as a prognostic biomarker for elderly GBM patients and warrants further validation. Clinical trial information: NCT00482677. Research Sponsor: None.

2548 Poster Session (Board #39), Fri, 8:00 AM-11:00 AM

Association of peripheral blood CD4+ T-cell depletion under temozolomide with inferior survival of patients with IDH wildtype glioblastoma. *First Author: Michael Weller, Laboratory of Molecular Neuro-Oncology, Department of Neurology, and Neuroscience Center Zürich, University Hospital and University of Zürich, Zürich, Switzerland*

Background: Standard first line chemoirradiation with temozolomide is associated with distinctive peripheral blood immune cell profiles in IDH wildtype glioblastoma. Whether such profiles at recurrence are associated with survival has not been studied in detail. **Methods:** Peripheral blood mononuclear cells of 21 healthy donors and of 91 patients with IDH wildtype glioblastoma were analyzed by flow cytometry at 1st recurrence. Patients received either (i) standard chemoirradiation with temozolomide (TMZ) followed by dose-intensified TMZ at first recurrence within the phase II trial DIRECTOR (N = 52) or (ii) hypofractionated radiotherapy with or without bevacizumab (N = 39) followed by investigators' choice within the phase II trial ARTE. Patients were classified based on unsupervised analyses of PBMC profiles at 1st recurrence. Associations with survival were explored in multivariate Cox models controlling for established prognostic and predictive factors. **Results:** At 1st recurrence, two patient clusters were identified in the DIRECTOR cohort which differed in CD4+ T-cell fractions, but not with respect to CD8+ T-cells, CD4+;CD25+;FoxP3+ regulatory T-cells, B-cells or monocytes. The composition of CD4+, CD8+ or regulatory T-cell fractions was similar in both clusters. All control samples clustered with the $CD4_{high}$ cluster. Patients in both clusters did not differ by established prognostic factors, including age, O6-methylguanine-DNA-methyl-transferase (*MGMT*) gene promoter methylation, tumor volume, Karfnosky performance score or steroid use. Progression-free survival was similar ($CD4_{high}$ *vs* $CD4_{low}$ 2.1 *vs* 2.4 months, p = 0.19), whereas post-recurrence overall survival was longer among the $CD4_{high}$ cluster (12.7 *vs* 8.7 months, p = 0.004). At 2nd recurrence after dose-intensified TMZ re-challenge, monocyte fractions increased, whereas memory CD4+ T-cell fractions decreased. Higher memory CD4+ fractions were associated with longer overall survival at 2nd recurrence (p = 0.004). The reported associations were retained in multivariate Cox models controlling for established prognostic factors. In the ARTE cohort, CD4+ T cell fractions at 1st recurrence did not differ compared to diagnosis (p = 0.91) and there were no associations with bevacizumab (p = 0.28) or survival (p = 0.74), supporting that the effects observed in the DIRECTOR cohort were driven by TMZ. **Conclusions:** We conclude that TMZ-associated memory CD4+ T-cell depletion may have deteriorating effects on the survival of glioblastoma patients. Research Sponsor: MSD.

2549 Poster Session (Board #40), Fri, 8:00 AM-11:00 AM

Molecular features of gliomas with high tumor mutational burden. *First Author: Joanne Xiu, Caris Life Sciences, Phoenix, AZ*

Background: TMB-H in gliomas is caused by molecular alterations or alkylator treatment- induced genomic changes characterized by a large number of G:C>A:T transitions. Our study describes the molecular features of TMB-H gliomas. **Methods:** Gliomas were tested with NextGen sequencing (592 genes), MGMT promoter methylation (MGMT-m) fragment analysis and IHC at Caris Life Sciences. Microsatellite instability (MSI) was test by NGS, FA/IHC. The GC:AT transition rate was calculated as the prevalence of G:A and C:T changes seen in each tumor and > 80% was regarded as high transition(TR-H). TMB values were compared using Wilcoxon Rank Sum. TMB-H was defined as the top quartile of all TMB values (TMB>9). **Results:** TMB in the 3129 gliomas ranged from 0 to 372 mutations/MB (mean: 8.5, median: 6). TMB-H was observed in 31% of glioblastomas, 16% of astrocytomas (astro) (22% of grade III, 7% of grade I/II) and 22% of oligodendrogliomas (oligo) (32% of grade III and 15% of grade I/II). MGMT-m (58% vs. 47%; p=0.0001), pathogenic (p) or likely p (lp) EGFR (14% vs 10%, p=0.004) and PIK3CA mutations (13% vs. 9%, p=0.002), as well as p/lp in 30 other genes were more prevalent in TMB-H cases (p<0.01). In the 613 TMB-H tumors, TR-H was seen in 12% (73) and was strongly associated with increased TMB (median TMB 52 in TR-H vs. 9 in TR-L,) and MSI-H (7.3% vs. 1.1%), both p<0.0001. Tumors with both TR-H and MSI-H had a mTMB of 114 vs. 49 in TR-H /MSS tumors. MSI-H and TR-L tumors had an mTMB of 23 vs. 9 in MSS /TR-L tumors (p<0.0001). All 5 POLE-MT tumors had TMB of >100 (median 264) and TR-L; 4 of the 5 were also MSI-H. PDL1 IHC had no correlation with TMB, MSI or transition rates. In 89 paired samples taken >150 days apart (regardless of intervening treatment), acquisition of TMB-H was seen in 11 pairs: 8 glioblastomas, 2 grade II/III astro and 2 oligo. In the paired tumors that acquired TMB-H status compared to those that did not, a significantly higher prevalence of MGMT-m (82% vs. 37%, p=0.008) and IDH mutation (64% vs. 19%, p=0.004) were seen. 10 of the 11 recurrent tumors with acquisition of TMB-H had TR-H while none in the other 78 pairs. **Conclusions:** TMB varies significantly in gliomas and associates with POLE, TR-H and MSI-H, but not with an increase of PD-L1. POLE-mutated tumors had the highest TMB levels. TR-H, an indicator of alkylator-induced phenotype, is associated with a higher TMB than MSI-H, however, TR-H may synergize with MSI-H to further increase TMB. Tumors with an IDH mutation and MGMT-m are more prevalent in tumors with high TMB gain. Further understanding of molecular and immune profile of the TMB-H may facilitate more individualized treatment planning. Research Sponsor: None.

2550 Poster Session (Board #41), Fri, 8:00 AM-11:00 AM

Escalation portion of phase II study to evaluate the safety, pharmacokinetics, and clinical activity of the PI3K/mTOR inhibitor paxalisib (GDC-0084) in glioblastoma (GBM) with unmethylated O6-methylguanine-methyltransferase (MGMT) promotor status. *First Author: Patrick Y. Wen, Dana-Farber Cancer Institute, Boston, MA*

Background: Paxalisib (previously GDC-0084) is a potent, oral, selective, brain-penetrant, small molecule inhibitor of class I phosphoinositide 3-kinase and mammalian target of rapamycin. The PI3K pathway is upregulated in ~85% of GBM cases and paxalisib has shown efficacy in preclinical models. A phase I study (NCT01547546) investigated paxalisib dosed once daily in 47 patients with recurrent high-grade gliomas and established a maximum tolerated dose (MTD) of 45mg once daily. The current phase II study aims to explore the safety, tolerability, and clinical activity of paxalisib in newly diagnosed GBM and an unmethylated MGMT promotor following surgery and temozolomide chemoradiation per Stupp regimen. **Methods:** Part 1 of this study is an open-label, dose-escalation phase to assess the safety, tolerability and MTD. Dose-escalation started at 60mg and progressed in 15mg increments using a 3+3 design. Part 2 is an expansion cohort recruiting 20 patients randomized to administration in fed or fasted states at the MTD. **Results:** Part 1 is complete and reported here. Nine patients were recruited and an MTD of 60mg was determined. DLTs were hyperglycemia and oral mucositis. AEs were generally reversible and consistent with the PI3K inhibitor class with the most common events were rash, oral mucositis, and fatigue. PK at the MTD was broadly consistent with the data published for the phase 1 study. For eight response-evaluable patients in Part I the median progression-free survival (PFS) was 8.4 months, and 25% of patients remained progression free after 15 months of follow-up. Part 2 is ongoing. **Conclusions:** A higher MTD of 60mg was identified in newly diagnosed GBM with unmethylated MGMT promotor status than the 45mg MTD previously identified in recurrent high-grade glioma. An encouraging PFS signal is described in this poor-prognosis, unmethylated MGMT patient population. Clinical trial information: NCT03522298. Research Sponsor: Kazia Therapeutics Limited.

2551 Poster Session (Board #42), Fri, 8:00 AM-11:00 AM

Tumor treating fields effects on the blood-brain barrier in vitro and in vivo. *First Author: Ellaine Salvador, University of Wuerzburg, Department of Anesthesia and Critical Care, Division Molecular Medicine, Wuerzburg, Germany*

Background: The greatest hurdle, which even potent and effective drugs targeting central nervous system (CNS) tumors and other disorders face, is the blood brain barrier (BBB). The inability to cross the tight regulatory mechanism renders these drugs futile. Of late, administration of tumor treating fields (TTFields) as part of a combined treatment modality for glioblastoma demonstrated increased overall patient survival. Still, the effects of TTFields on the BBB have not yet been investigated. Here, we report the potential of TTFields application to open up the BBB. **Methods:** Murine brain endothelial cells were treated with 100-300 kHz TTFields for 24-96 h. Cells were also allowed to recover from 24-96 h after treatment. Subsequently, changes in cell morphology, integrity, and permeability were observed via staining of intercellular junction proteins (IJP) as well as transendothelial electrical resistance (TEER) and permeability assays. In vivo, rats were treated with 100 kHz TTFields or heat for 72 h after which they were IV injected with Evan´s Blue (EB)/ TRITC-dextran (TD) which was later quantified from the brain. Rat brain cryosections were also stained for IJPs as well as immunoglobulin G (IgG) to assess vessel structure. Finally, serial dynamic contrast-enhanced (DCE) MRI with gadolinium (Gd) contrast agent was performed pre- and post- TTFields. **Results:** Upon TTFields application, IJPs such as claudin-5 were delocalized from the cell membrane to the cytoplasm with maximal effects at 100 kHz. In addition, BBB integrity was significantly reduced and permeability for 4 kDa molecules was significantly increased. Cell morphology recovery was first observed at 48 h post-treatment and completely restored to normal after 96 h, indicating a reversibility of the TTFields effect on the BBB. In addition, EB and TD permeated the rat brain post-TTFields treatment. Brain cryosections displayed IJPs delocalization as well as IgG accumulation in the brain parenchyma. Confirming these observations, increased Gd in the brain was shown by DCE-MRI post-TTFields application. A reversion to normal conditions was detected 96 h after end of treatment, which was demonstrated by no difference in contrast enhancement between control and treated rats. **Conclusions:** TTFields application both in vitro and in vivo points towards its ability to transiently open the BBB. This presents TTFields as a novel aid for drug delivery geared towards treatment of CNS tumors and other related diseases. Hence, it is indicative of the possibility of an enhanced and more effective combinatorial therapeutic strategy. Research Sponsor: Novocure Ltd.

2552 Poster Session (Board #43), Fri, 8:00 AM-11:00 AM

Genome-wide methylation analysis in long-term survivors of glioblastoma (GBM). *First Author: Justin Chau, University of Iowa Hospitals and Clinics, Iowa City, IA*

Background: Identification of tumor characteristics that may be associated with survival in patients with glioblastoma (GBM) has been largely characterized by IDH mutations and MGMT promoter methylation status. However, these genetic changes and other currently available data are not sufficient to explain the longevity experienced by a subset of long-term survivors (LTS) - patients surviving longer than 3 years past diagnosis. **Methods:** The study identified GBM patients established and treated at University of Iowa Holden Comprehensive Cancer Center from 2007-2017 whose disease recurred after initial resection. Patients were categorized LTS if they survived > = 3 years beyond initial definitive resection; short-term survivors (STS) if less than 3 years. Pathologic specimens at initial and repeat resection underwent genome wide methylation analysis using the Infinium EPIC microarray system. Data were analyzed to identify genes that exhibited differentially methylated CpG regions. **Results:** Resection specimens from GBM survivors were compared to those of STS. A total of 29 samples were analyzed and compared (15 LTS and 14 STS samples). Multidimensional scaling plots identified significant differences in genomic constitution between LTS and STS specimens. Granular analysis yielded 89 differentially methylated regions significantly associated with long-term survival (adjusted $p < 0.05$). *PTPRN2* ($p = 0.000376$), *PTPN11* ($p = 1.38E-05$), and *PAX6* ($p = 0.000671$) were found to exhibit numerous differentially methylated CpG sites between MGMT-methylated vs. unmethylated specimens. Further notable, higher levels of differentially methylated CpG shores and open-seas regions on chromosome 12 were associated with long-term survival ($p = 1.89E-08$). **Conclusions:** Our study identified multiple significant epigenetic differences that, functionally or consequentially, may be associated with extended survival in GBM patients. The implication that CpG shores, rather than islands, are associated with long-term survival raises further intriguing questions regarding the depth of epigenetic complexity in this disease. More immediately, the surprising association of multiple protein phosphatases with LTS in our study may hint at the class' previously unspecified, yet integral, role in delaying disease progression and identify new, novel avenues for therapy. Research Sponsor: U.S. National Institutes of Health.

2553 Poster Session (Board #44), Fri, 8:00 AM-11:00 AM

Lymphocyte-activation gene 3 (LAG-3) expression in the inflammatory microenvironment of glioma. *First Author: Maximilian Mair, Department of Medicine I, Division of Oncology, Medical University of Vienna, Vienna, Austria*

Background: The blockade of lymphocyte-activation gene 3 (LAG-3), an inhibitory receptor on tumor-infiltrating lymphocytes, is currently under investigation in many extracranial tumor entities. **Methods:** 54 patients with diffuse glioma were included: 35 patients with glioblastoma (GBM, median age at diagnosis: 61 years) as well as 14 with WHO grade II and 5 with WHO grade III glioma (lower-grade glioma, LGG, median age at diagnosis: 45 years). Isocitrate dehydrogenase 1/2 mutations (IDH-mt) were present in 17/54 patients and 37/54 patients had IDH wildtype (IDH-wt) tumors. LAG-3 expression on tumor-infiltrating lymphocytes (TILs) was analyzed by immunohistochemistry (monoclonal anti-LAG-3 antibody, clone 17B4, LSBio Inc.). **Results:** LAG-3^+ TILs could be observed in 5/54 (9.3%) samples, while $CD3^+$ TILs were present in 32/54 (59.3%) and $CD8^+$ TILs in 24/54 (44.4%) samples. Only IDH-wt glioma presented with LAG-3^+ TILs ($p = 0.168$). Samples with LAG-3^+ TILs presented with a numerical trend towards higher presence of $CD3^+$ (5/27 $CD3^+$ vs. 0/22 $CD3^-$, $p = 0.072$) and $CD8^+$ TILs (4/24 $CD8^+$ vs. 1/30 $CD8^-$, $p = 0.159$). 4/7 (57.1%) samples presenting with PD-1^+ TILs also presented with LAG-3^+ TILs ($p = 0.001$). Furthermore, glioma samples with $LAG3^+$ TILs presented with higher expression of PD-L1 (median: 1% vs. 0%; $p = 0.166$). There was no difference in overall survival (OS) according to LAG-3^+ TIL infiltration (median OS in LAG-3^+: 21.7 months vs. LAG-3^-: 41.4 months, $p > 0.05$). **Conclusions:** LAG-3^+ TILs are rarely observed in IDH-wt and absent in IDH-mt glioma. Gliomas with an active inflammatory microenvironment present more frequently with $LAG3^+$ TILs. The diverse composition of the inflammatory microenvironment and particular inflammatory subgroups should be considered in future clinical trials on immune-modulating therapies in glioma. Research Sponsor: Medical University of Vienna, Pharmaceutical/Biotech Company.

2554 Poster Session (Board #45), Fri, 8:00 AM-11:00 AM

Clinical, radiological, and genomic features of BRAF V600E-mutated adult glioblastoma. *First Author: Mary Jane Lim-Fat, Dana-Farber Cancer Institute, Boston, MA*

Background: Although uncommon, detection of a BRAF V600E mutation in adult patients with glioblastoma has become relevant given the increased availability of NGS and encouraging therapeutic activity of BRAF/MEK inhibitors. The clinical course, radiological characteristics and genetic mutations in this patient population has, however, not been well described. **Methods:** Adult patients treated at Dana-Farber Cancer Institute or Massachusetts General Hospital with glioblastoma diagnosed from 2013-2019 and an identified BRAF V600E mutation on immunohistochemistry staining or institutional NGS platform were included. Patient demographics, treatments and outcomes were collected retrospectively. Molecular diagnostics (Oncopanel or SNaPSHOT) and cytogenetics (array CGH) were reviewed for relevant mutations or copy number variants (CNV). Qualitative MRI data was analyzed using Visually Accessible Rembrandt Images (VASARI) feature set. Response assessment was performed using the RANO criteria. **Results:** Nineteen glioblastoma patients had a BRAF V600E mutation (16 on NGS and 19 on IHC). The median age at diagnosis was 41 (22-69) years; 13/19 were female, 12/19 were Caucasian. Only 1/19 had an IDH mutation; 10 of the 17 with known methylation status had MGMT unmethylated tumors. The most frequent mutations on NGS or CNV on array-CGH were TERT (12/16), CDKN2A (10/16), EGFR (7/16), PIK3R1 (6/16) and CKDN2B (6/16). Most tumors were well circumscribed (12/19) and all were contrast-enhancing on MRI. While no patient had clear leptomeningeal involvement at diagnosis, 11/19 eventually developed subependymal or leptomeningeal dissemination. Six patients were treated with BRAF/MEK inhibition following progression after standard of care therapy, with 3/6 patients showing partial response and 2 showing stable disease as their best response. PFS after BRAF/MEK inhibition ranged from 1.9 to 19 months. Grade 1 skin rash was present in 1 patient, but no other adverse events were reported. Median OS for the patients with confirmed deaths (15/19) was 22.6 (14.5 – 39.0) months. **Conclusions:** Compared to the general glioblastoma population, adult patients with BRAF V600E mutations are younger, more frequently female, and have a higher median OS despite a much higher incidence of leptomeningeal dissemination. Outcome following BRAF/MEK targeted therapy was encouraging. Understanding the natural history and features of these tumors may help better screen patients for BRAF/MEK inhibition and identify novel therapeutic strategies. Research Sponsor: None.

2555 Poster Session (Board #46), Fri, 8:00 AM-11:00 AM

Proteomic profiling to identify therapeutics targets in glioblastoma (GBM). *First Author: Sheeno P. Thyparambil, OncoPlex Diagnostics, Culver City, MD*

Background: Glioblastoma (GBM) is an aggressive primary brain tumor with poor prognosis. Treatment at diagnosis is largely confined to surgery, radiation and temozolomide (TMZ) with median progression-free survival (PFS) of 7 months and median overall survival (mOS) of 15 months. GBM tumors recur in most cases and in patients with recurrent GBM, the mOS is 6.2 months. The lack of effective therapies underscores the importance of exploring other agents. We propose that quantitating therapy-associated protein biomarkers can improve treatment personalization for GBM. **Methods:** 97 FFPE GBM tissues were microdissected and solubilized for mass spectrometry-based proteomic analysis of therapy-associated protein biomarkers in our CLIA certified lab. We quantified protein levels of MGMT, hENT1, RRM1, TOPO1 and EGFR/TUBB3 (antibody target and payload resistance markers, respectively, for anti-EGFR ADCs) simultaneously. The multiplexed assay also quantified additional 24 clinically relevant proteins. **Results:** 43/57 patients were predicted to respond to TMZ based on undetectable levels of MGMT, confirming wide utility of this agent. 42/97(43%) patients were predicted to have gemcitabine sensitivity based on high expression of the response marker (hENT1 > 100 amol/ug) and low expression of the resistance marker (RRM1 < 700 amol/ug). 11/97(11%) patients expressed TOPO1 > 1350 amol/ug (75^{th} percentile of all indications tested by author's laboratory), suggesting likely response to irinotecan and topotecan. EGFR expression ranged from < 100 amol/ug to > 25000 amol/ug, including overexpression (> 1500 amol/ug) in 22%(21/97) of cases. While expression of EGFR(81/97, 84%) suggested likely response to anti-EGFR ADC, concurrent expression of TUBB3(78/81) may indicate resistance to several known payloads, such as taxanes and MMAE. Conjugation with another payload that targets sensitivity marker TOPO1 (68% expression) is a likely option. Proteomic analysis also revealed detectable levels of multiple RTKs (FGFR(4), AXL(20), IGF1R(10), MET overexpression(1), and HER2 overexpression(2)), indicating potential response to RTK inhibitors. Exploratory investigation in tumor vs TME using proteomics and metabolomics is ongoing. **Conclusions:** In this population of GBM patients, proteomic analysis identified protein targets of multiple approved and investigational therapies. Gemcitabine, which crosses the blood-brain barrier, may be considered as a salvage option after TMZ failure. Proteomic quantitation of EGFR and TUBB3 may improve patient selection for EGFR-targeting ADCs. Research Sponsor: OncoPlex Diagnosis (mProbe).

2556 Poster Session (Board #47), Fri, 8:00 AM-11:00 AM

Ibrutinib-based combination therapy exhibited therapeutic benefit in newly diagnosed primary central nervous system lymphoma. *First Author: Feili Chen, Guangdong Provincial People's Hospital, Guangzhou, China*

Background: Ibrutinib has shown single-agent activity in relapse/refractory (R/R) primary central nervous system lymphoma (PCNSL), and the high dose methotrexate (HD-MTX) has been the backbone of treatment of de-novo PCNSLs. Combination therapy of HD-MTX and ibrutinib has recently shown activity in R/R PCNSLs. **Methods:** Eleven newly diagnosed PCNSL patients who underwent combination therapy of HD-MTX and ibrutinib were analyzed for treatment response and safety profile. HD-MTX was given at 3.5 g/m2 every 2 weeks for a total of 8 doses. Ibrutinib was held on days of HD-MTX infusion until HD-MTX clearance. Single-agent daily ibrutinib was administered continuously after completion of induction therapy until disease progression, intolerable toxicity, or death. Patients' clinicopathologic characteristics were retrospectively reviewed and genomic traits were further analyzed. **Results:** Nine out of 11 patients have completed the induction phase of ibrutinib-based combination therapy and received ibrutinib maintenance in addition to two patients whose disease progressed during the therapy. An objective response rate (ORR) of 82% (9/11) was observed, including 7 patients with complete response (CR, 64%) and 2 patients with partial response (PR, 18%). The median progression-free survival (PFS) was 7.4 months while the median overall survival (OS) was not reached. The combination therapy of HD-MTX and ibrutinib was well tolerated and has acceptable safety. In addition, the presence of ctDNA in cerebrospinal fluid (CSF) samples closely correlated with tumor response. Sustained tumor responses were associated with the clearance of ctDNA from the CSF. **Conclusions:** Combination of ibrutinib and HD-MTX has acceptable safety and has demonstrated anti-tumor activity in newly diagnosed de-novo PCNSL patients. The detection of ctDNA in CSF is feasible for monitoring tumor burden in PCNSL patients. Research Sponsor: None.

2557 Poster Session (Board #48), Fri, 8:00 AM-11:00 AM

Clinical, radiologic & prognostic profile of IDH wild type diffuse astrocytic glioma with molecular features of glioblastoma. *First Author: Oluwatosin Akintola, MGH/DFCI/BWH/HMS, Boston*

Background: In 2018, The Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy (cIMPACT-NOW) recommended that IDH-wildtype diffuse astrocytic glioma Grade II/III with either EGFR amplification, combined whole chromosome 7 gain and whole chromosome 10 loss (+7/−10), or TERT promoter mutation should receive an integrated histological and molecular grade classification: Diffuse astrocytic glioma, IDH-wildtype with molecular features of glioblastoma, WHO grade IV. The natural history, radiologic characteristics and standard management for these patients has not been well described. They are typically excluded from clinical trials for WHO Grade IV gliomas. **Methods:** Adults diagnosed at Massachusetts General Hospital with IDH wildtype diffuse astrocytoma and EGFR amplification or TERT promoter mutation from 2011-2019 were identified. Demographics, functional status, radiologic features, MGMT promoter methylation status, time to progression, and overall survival were collected retrospectively. Qualitative MRI data was analyzed using the VASARI feature set. Response assessment was performed using the RANO criteria. **Results:** 50 patients were identified (table). 37/50 patients received standard Stupp protocol, 2/50 received hypofractionated radiotherapy with temozolomide, 6/50 received radiotherapy alone, and 1 patient received a MEK inhibitor. None were enrolled in clinical trials at diagnosis. mPFS was 10 months in the 47/50 with confirmed progression and mOS in the patients with confirmed deaths (40/50) was 17.5 months (4-47). 9/50 patients are alive with survival ranging 6-52 months. **Conclusions:** Outcomes for patients with molecularly defined GBM were variable. Analysis of the cohort to characterize factors that led to the observed variability is in progress. More studies on molecularly defined glioblastomas are required to better understand their behavior and to provide guidance for their inclusion or exclusion in clinical trials. Research Sponsor: None.

Demographics & clinical characteristics.	
(n=50)	
Age (y)	
Median	61.5
Range	35-85
Gender	
Male	28(56%)
Female	22(44%)
KPS	
Median	90
Range	60-100
Radiologic Features	
Non-Enhancing	20(40%)
Mild Enhancement	20(40%)
Marked Enhancement	10(20%)
Necrosis	9(18%)
Multifocal	18(36%)
Extent of Resection	
Gross Total	4(8%)
Subtotal	21(42%)
Biopsy	25(50%)
WHO Grade	
Grade III	42(84%)
Grade II	8(16%)
Molecular Diagnostics	
pTERT Mutant	31(62%)
EGFR Amplified	22(44%)
pTERTmut+EGFR amp	6(12%)
MGMT Status	
Positive	7(14%)
Negative	26(52%)
Untested	17(34%)

2558 Poster Session (Board #49), Fri, 8:00 AM-11:00 AM

Targeting glioblastoma with novel immunocytokines. *First Author: Patrick Roth, University Hospital Zürich, Zürich, Switzerland*

Background: There is an urgent need for novel treatment options for patients with glioblastoma, the most frequent malignant primary brain tumor. In contrast to other types of cancer, immunotherapeutic approaches have so far not been successful against glioblastoma. Converting the glioma microenvironment from a "cold" and immunosuppressive status into a more "hot" and immunopermissive phenotype may allow for clinically meaningful anti-tumor immune responses. **Methods:** We explored the activity of novel immunocytokines based on the L19 antibody, specific to a tumor-associated epitope of extracellular fibronectin, for the targeted delivery of three pro-inflammatory cytokines (IL-2, IL-12, TNF) to the microenvironment of gliomas. Following an extensive preclinical assessment in 2 orthotopic immunocompetent mouse glioma models, we used a fully-human L19-hTNF fusion protein to treat human patients with recurrent glioblastoma. **Results:** Intravenous administration of L19-mIL12 or L19-mTNF prolonged survival and cured a proportion of tumor-bearing mice while no effect was seen with L19-IL2. When L19-mIL12 or L19-mTNF were administered to glioma-bearing $RAG^{-/-}$ mice, no therapeutic activity was observed which suggests adaptive immunity as an underlying mechanism. On a mechanistic level, both immunocytokines induced the infiltration of the tumor site with lymphocytes and promoted the expression of pro-inflammatory cytokines in the tumor microenvironment. In addition, L19-mTNF induced tumor necrosis. Based on these preclinical findings, we initiated a phase I/II clinical trial with a fully-human L19-hTNF fusion protein for patients with isocitrate dehydrogenase (IDH1R132H) wildtype WHO Grade III or IV glioma at first relapse (NCT03779230). Treatment was safe and well tolerated in the first three glioblastoma patients. Administration of L19-hTNF resulted in reduced regional blood perfusion in the tumor region and was associated with more necrotic areas within the tumor as well as an increased number of tumor-infiltrating CD4 and CD8 T cells. **Conclusions:** The data obtained with the comprehensive preclinical characterization and subsequent clinical translation form the basis for future studies with immunocytokines as novel treatment option for patients with malignant brain tumors. Clinical trial information: NCT03779230. Research Sponsor: Philogen, Swiss National Sience Foundation.

2559 Poster Session (Board #50), Fri, 8:00 AM-11:00 AM

Evaluation of glioblastoma tumor microenvironment after treatment with pembrolizumab. *First Author: Nazanin Majd, MD Anderson Cancer Center, Houston, TX*

Background: Neoadjuvant pembrolizumab improved outcome of patients with recurrent Glioblastoma (GBM) in two early phase clinical trials. However, several large phase II/III studies in patients with newly diagnosed and recurrent GBM failed to demonstrate a therapeutic benefit of anti-PD-1 therapy. Therefore, identification of biomarkers of response is crucial for appropriate patient selection and further clinical development of anti-PD-1 therapy. We reported the outcome of our window-of-opportunity clinical trial of neoadjuvant pembrolizumab in 15 patients with recurrent GBM, demonstrating rare CD8+ T cells and abundant of CD68+ macrophages in GBM tissue after 3 weeks of anti-PD-1 treatment (NCT02337686). In the current study, we compared tumor infiltrating lymphocyte (TIL) and PD-L1 scores, known biomarkers of response to anti-PD-1 therapy in other cancers, in pre-trial vs. on-trial tumor tissue and associated these markers with survival. **Methods:** We determined TIL score (morphological assessment of the presence or absence of TILs, 0-3) and PD-L1 H score (defined as [1*1+ %]+[2*2+ %]+[3*3+ %], 0-200) and correlated these with survival. The Wilcoxon signed rank test was used to compare levels of PD-L1 H or TIL scores between pre-trial and on-trial specimens. The Cox proportional hazards models were used to assess associations between correlative markers and progression free survival or overall survival (OS). **Results:** The on-trial TIL level (median: 3) was significantly higher than the pre-trial TIL level (median: 1) ($p = 0.031$). However the difference between pre-trial and on-trial PD-L1 levels was not statistically significant ($p > 0.9$). Patients whose on-trial PD-L1 H score was ≥ 3 trended toward a longer OS than those with a PD-L1 H score < 3 (HR [95% CI] = 0.225 [0.043, 1.183]) ($p = 0.0782$). **Conclusions:** Although GBM tissue lacks abundant T cells, treatment with pembrolizumab increases trafficking of T cells to the tumor microenvironment, which is necessary but not sufficient to induce an effector T-cell response. Elevated PD-L1 expression may be a biomarker of response to anti-PD1 therapy in GBM, which needs confirmation in larger studies. Further genomic, transcriptomic, and methylation profiling of the pre-trial and on-trial tissues is ongoing. Clinical trial information: NCT02337686. Research Sponsor: Merck.

2560 Poster Session (Board #51), Fri, 8:00 AM-11:00 AM

A pilot study of levetiracetam as a sensitizer of temozolomide for newly diagnosed glioblastoma: A prospective, open-label, phase II study (KBTS-1601 study). *First Author: Chae-Yong Kim, Seoul Natl Univ Bundang Hosp, Seoul, South Korea*

Background: We evaluated the survival benefit of levetiracetam as a chemosensitizer of temozolomide for patients with newly diagnosed glioblastoma. **Methods:** This was an open-label, multicenter, phase II study (NCT02815410**)**. Eligible patients were aged 18 years or older and had newly diagnosed glioblastoma with an ECOG performance status of 0-2. All patients received radiotherapy with concurrent temozolomide (75 mg/m^2/day) followed by adjuvant temozolomide (150-200 mg/m^2/day for 5 days during six 28-day cycles). The first dose of levetiracetam was given just after the surgery at 250mg orally twice a day and increased up to 500mg twice a day prior to radiation. This prospective study was designed to test whether levetiracetam in conjunction with temozolomide improved survival. The historical control group was based on data from a study by Gwak et al. for Korean patients with newly diagnosed glioblastoma with a median overall survival(OS) of 17.5 months and a median progression-free survival (PFS) of 10.1 months. **Results:** Forty-six patients were enrolled between August 2016 and January 2019. The median follow-up duration was 24.9 months (range, 7.9-35.5). All patients completed standard radiation therapy with temozolomide, and 39 (84.8%) patients completed six cycles of adjuvant temozolomide. Median overall survival (OS) was 30.0 months, and median PFS was 15.0 months. OS at 6, 12, and 24 months was 100%, 91.3%, and 60.7%, respectively. PFS at 6, 12, and 24 months was 93.2%, 65.3%, and 22.6%, respectively. **Conclusions:** Addition of levetiracetam during concurrent and adjuvant temozolomide along with radiotherapy in patients with newly diagnosed glioblastoma may result in improved outcomes compared to historical data and merits further study. Clinical trial information: NCT02815410. Research Sponsor: Korean local company fund.

2561 Poster Session (Board #52), Fri, 8:00 AM-11:00 AM

Amide proton transfer MRI can accurately stratify gliomas according to their IDH mutation and 1p/19q co-deletion status. *First Author: Sotirios Bisdas, University College London, London, United Kingdom*

Background: Amide proton transfer (APT) MRI provides sensitive metrics at the amides and amines offsets from the water resonance and has been shown in small cohorts to differentiate low from high grade gliomas with better diagnostic performance than diffusion- and perfusion-weighted MRI. The purpose of our study was to assess APT-MRI performance to stratify gliomas according to their IDH mutation and 1p/19q status. **Methods:** Forty-five patients with primary gliomas and diffuse astrocytomas (26 WHO grade II, 11 WHO grade III, 8 WHO grade IV) underwent prospectively multiparametric MRI with APT imaging at 3T scanner. The molecular classification identified 9 patients with IDH-wildtype, 1p/19q retained and 36 with IDH-mutant (22 had 1p/19q-retained, 14 had 1p/19q-codeleted). Tumour segmentations were manually created and the masks were superimposed on the calculated magnetisation transfer ratio asymmetry (MTR_{asym}) spectra and proton transfer ratio APT maps. Individual and group analysis was conducted to analyse the statistical differences between quantitative imaging parameters for the IDH mutation and 1p/19q codeletion statuses. **Results:** The MTR_{asym} spectra showed a clear difference between IDH-wildtype and IDH-mutant gliomas, with the IDH-mutant gliomas presenting a stronger contribution in the amines ($p < 0.001$). In IDH-mutant 1p/19q-retained and IDH-mutant 1p/19q-codeleted, the MTR_{asym} spectra showed similarities in shape with higher intensity (approx. 60%) for the IDH-mutant 1p/19q-retained gliomas over the entire spectrum indicating an increased content in amines and amides in IDH-mutant 1p/19q-retained ($p < 0.01$). Notably, the latter entities showed higher amides levels than the IDH-wildtype gliomas ($p < 0.03$). **Conclusions:** APT-MRI shows a remarkable potential to disentangle the protein metabolism in gliomas, to link metabolic patterns to the IDH and 1p/19q status and hence provide robust surrogate biomarkers for non-invasive histomolecular classification with potential use as treatment monitoring tools. Research Sponsor: Biomedical Research Council, National Institutes of Health Research.

2562 Poster Session (Board #53), Fri, 8:00 AM-11:00 AM

Role of high-dose chemotherapy with autologous stem cell transplantation for primary central nervous system lymphoma: A systematic review. *First Author: Shaha Nabeel, Zucker School of Medicine/Northwell Health at Mather, Port Jefferson, NY*

Background: High dose chemotherapy (HDCT) followed by autologous stem cell transplant (ASCT) has shown to overcome intrinsic chemo-resistance and improve disease control in Primary Central Nervous System Lymphoma (PCNSL). Our study reviews the treatment outcome in PCNSL with sequential HDCT and ASCT. **Methods:** 8/34 studies were finalized after systematic search of PubMed, Cochrane, and Clinicaltrials.gov for treatment of PCNSL with HDCT followed by ASCT. **Results:** 251/288 patients were evaluated. Mean age was 55.5 years. 227 underwent HDCT-ASCT. 174 were newly diagnosed (ND) and 77 had relapsed refractory (R/R) PCNSL. ND patients showed superior outcomes in terms of progression free survival and overall survival. Combinations of High dose Rituximab, Busulfan and Cyclophosphamide significantly improved survival outcomes in RR patients. Significant toxicities mainly included pancytopenias and opportunistic. **Conclusions:** Primary CNS lymphoma treated with HDCT followed by ASCT has shown promising outcomes and has set a benchmark for future studies. Research Sponsor: None.

Treatment efficacy with HDCT and ASCT in PCNSL.

Author, Year, Phase.	n/N	Median Age (y)	Regimen IC+HDCT-ASCT	ND Vs RR	PFS at x years	OS at x years	CR
Kasenda, et al. 2017, II	39/39	57	RTCy+CMT-ASCT	RR	46% at 2y	56.4 % at 2y	56.4%
Illerhaus, et al. 2016, II	79/81	56	MRTCy+ RCT-ASCT	ND	78.5% at 1y	92% at 1 y	77.2%
Yi-Bin Chen, et al. 2015, II	18/29	58	RCy+RBCp-ASCT	RR	100% at 2y	100% at 2y	n/a
Omuro, et al. 2015, II	26/32	57	RMPV+TBCp-ASCT	ND	81% at 2 y	81% at 2 y	n/a
Alimohamed, et al. 2012, Prospective	21/27	56	TBCp-ASCT	ND	44% at 5y	44% at 5y	n/a
Illerhaus, et al. 2006, II	23/30	54	MCyT+TC-ASCT	ND	n/a	87% at 5 y	65%
Abrey, et al. 2003, Prospective	25/28	53	MCy+CECyMe-ASCT	ND	20% at 2.3y	55% at 2.3y	n/a
Soussain, et al. 2001, II	20/22	53	TBCp+CyEM-ASCT	RR	n/a	*P 63.7 at 3 y	80%

***P probability of overall survival.**

Abbreviations: IC: Induction Chemotherapy, HDCT: High dose chemotherapy, ASCT: Autologous Stem Cell Transplant, R: Rituximab, T: Thiotepa, Cy: Cytarabine, C: Carmustine, M: Methotrexate, P: Procarbazine, B: Busulfan, Cp: Cyclophosphamide, V: Vincristine, E: Etoposide, Me: Melphalan, N: Number of patients enrolled, n: Evaluable patients, ND: newly diagnosed, RR: relapsed/refractory, PFS: progression free survival, OS: overall survival, CR: Complete remission, n/a: not available, y: years

2563 Poster Session (Board #54), Fri, 8:00 AM-11:00 AM

Clinical experience of ONC201 in patients with recurrent H3 K27M-mutant spinal cord glioma. *First Author: Sylvia Christine Kurz, NYU Langone Health, New York, NY*

Background: High-grade gliomas of the spinal cord are a rare and understudied entity, representing $< 5\%$ of all spinal cord tumors. Reported median survival times range from 10-16 months. Up to 53% of tumors harbor the H3 K27M mutation, which is associated with an unfavorable prognosis. Postsurgical treatment often includes radiation $\pm$ temozolomide, although the role of chemotherapy has not been conclusively established. At recurrence, there are no effective therapies and most clinical studies exclude patients with spinal cord tumors. We report our clinical experience with ONC201, a small molecule DRD2 antagonist and caseinolytic protease P agonist, in patients with recurrent H3 K27M-mutant diffuse gliomas of the spinal cord (scDG). **Methods:** Adults and children with recurrent H3 K27M-mutant scDG received ONC201 in two Phase II clinical trials enrolling adult recurrent H3 K27M-mutant glioma patients (NCT02525692; NCT03295396) and in one Phase I clinical trial enrolling pediatric patients (NCT03416530). Adult patients received ONC201 at the RP2D dose of 625 mg weekly and pediatric patients received the RP2D of 625 mg weekly, scaled by body weight. All patients began ONC201 as a single agent until disease progression. Five patients continued ONC201 combined with bevacizumab beyond progression. **Results:** As of January 15, 2020, 12 evaluable patients (adult n = 8, pediatric n = 4) received ONC201. The median age was 20.9 (range: 7-72) years. The median follow-up time for the single agent ONC201 group was 5.4 (range 1.3-9.7) months while that of the combination group is 7.4 (range 6.2-25.1) months. The median number of ONC201 doses was 10 (range: 5-39) for the ONC201 single agent group and 34 (range: 21-100) for the combination group. Five of 7 patients remain alive in the ONC201 single agent group while 3 of 5 patients remain alive in the combination group. Three patients in the ONC201 single agent group and 2 patients in the combination group continue on treatment. There were no drug-related toxicities requiring dose reduction or discontinuation. **Conclusions:** Treatment with ONC201 alone or combined with bevacizumab is well tolerated in patients with recurrent H3 K27M-mutant scDG and a subset of patients experiences prolonged survival that exceeds historical outcomes. Clinical trial information: NCT02525692; NCT03295396; NCT03416530. Research Sponsor: NCI.

2564 Poster Session (Board #55), Fri, 8:00 AM-11:00 AM

Survival of subjects with recurrent glioblastoma receiving intratumoral administration of controlled IL-12 with limited exposure to dexamethasone. *First Author: Rimas Vincas Lukas, Northwestern Memorial Hospital, Chicago, IL*

Background: Interleukin-12 (IL-12) results in anti-tumor responses in preclinical models but requires tightly controlled production to achieve safety and elicit immune system activation to realize efficacy. A phase 1 "main study" (NCT02026271) enrolled subjects with Grade III or IV gliomas who at the time of resection received intratumoral administration of a replication-deficient adenovirus expressing IL-12 under control of a transcriptional switch (Ad-RTS-hIL-12, Ad) regulated by veledimex (V), referred to as "Controlled IL-12". It was anticipated that dexamethasone (dex), a lymphocytotoxic corticosteroid used to control edema, might diminish response to immunotherapies. We report updated findings from a substudy of subjects who were dex-free during the 4 weeks prior to Ad administration. **Methods:** Multicenter, phase 1 substudy (NCT03679754) that assesses safety and tolerability of Controlled IL-12 by local injection (Day 0, time of resection) of Ad (2 x 10^{11} viral particles) + V (20 mg PO QD x15 doses, Days 0-14) in subjects that were bevacizumab naïve and not receiving dex 4 weeks prior to Ad. **Results:** 36 subjects were treated. Of the 36, a majority received low-dose corticosteroids ($\leq$ 20 mg dex total during V) as compared with the main study (75% vs 40%). More subjects in the substudy as compared with the main study had multifocal vs. unifocal disease (39% vs 7%). The safety profile was similar for both. Adverse reactions were mild to moderate and were manageable and reversable upon withholding V. Activation of the switch in both the main study and substudy (V 20 mg; n = 51) resulted in increased mean peak values (Day 0-28) of serum IL-12 (25.8 vs. 20.4 pg/mL) and IFN-g (57.0 vs. 39.5 pg/mL). Initial median overall survival (mOS) (unifocal, $\leq$ 20 mg dex cumulative, n = 20) was 16.2 (8.9, 18.5) mons (mean follow-up 12.3 mons) (Neuro Oncol 2019; 21 [suppl_6]: vi5). mOS including the impact of dex and key subject characteristics from the two studies (n = 51) will be updated and tumor response data will be provided. **Conclusions:** Monotherapy with Controlled IL-12 resulted in sustained increase in serum recombinant IL-12 and downstream endogenous IFN-g. There is evidence of immune-mediated anti-tumor effects which is associated with increased mOS as compared with historical controls. Follow up will investigate the adverse impact of dex, as well as the effect of additional subject characteristics (*e.g.*, unifocal vs. multifocal disease) on mOS. Clinical trial information: NCT03679754. Research Sponsor: Ziopharm Oncology Inc.

2565 Poster Session (Board #56), Fri, 8:00 AM-11:00 AM

Molecular predictors of response to selinexor in recurrent glioblastoma (GBM). *First Author: Christopher James Walker, Karyopharm Therapeutics Inc, Newton, MA*

Background: The nuclear export protein exportin 1 (XPO1) is overexpressed in many cancers, including GBM. Selinexor is an inhibitor of XPO1 that crosses the blood-brain-barrier and targets cancer cells by sequestering tumor suppressor proteins and oncoprotein mRNAs in the cell nucleus, inducing cancer cell apoptosis. Selinexor is FDA approved for treatment of patients (pts) with refractory multiple myeloma and is under evaluation for GBM. **Methods:** We previously reported encouraging results from a phase II clinical trial of selinexor for molecularly unselected pts with recurrent GBM (ASCO 2019). On available pre-treatment archival tumor tissue from 57 cases, we performed DNA exome and RNA transcriptome sequencing to use both gene mutations and expressions for exploring molecular correlates of response in selinexor treated pts, in a hypothesis generating, post-hoc, exploratory analysis. Pts with inadequate drug exposure were excluded ($<$ 21 days or $<$ 3 doses). We compared OS and PFS between mutated and wild-type patients for genes mutated in at least 5 cases. RNAseq data were used to infer differential protein activities between patients with selinexor sensitive disease (defined as best response of partial or complete response, n = 7) vs. resistant disease (defined as progressive disease as best response, n = 23). **Results:** Two mutated genes were associated with longer survival in selinexor treated pts: *DOCK8* (n = 7; progression free survival [PFS], P = 0.013, hazard ratio [HR] = 3.75 [1.32-10.62]; overall survival, P = 0.009, HR = 15.39 [2.00-118.34]) and *PDX1* (n = 5, PFS, P = 0.014, HR = 4.468 [1.361-14.670]). Other commonly mutated genes in glioma, including *IDH1* (n = 9) were observed but not associated with survival. Protein activities inferred from RNA sequencing data were also correlated with response to selinexor. In a machine learning model, ZC3H12A (also called MCPIP-1), a negative regulator of inflammation; RAB43, a member of the RAS family that binds GTP and regulates vesicle trafficking, and SOCS3, a suppressor of cytokine signaling that can antagonize JAK/STAT signaling and repress innate immunity, predicted clinical benefit from selinexor (area under the ROC curve from leave one out cross validation = 0.89, permutation test P $<$ 0.04). **Conclusions:** *DOCK8* and *PDX1* mutations were favorable prognostic factors in selinexor treated pts. Activity of three proteins (ZC3H12A, RAB43, and SOCS3) predicted clinical benefit from selinexor. Further studies with more pts are required to validate our findings. ClinicalTrials.gov: NCT01986348 Research Sponsor: Karyopharm Therapeutics.

2566 Poster Session (Board #57), Fri, 8:00 AM-11:00 AM

Phase I trial of D2C7 immunotoxin (D2C7-IT) administered intratumorally via convection-enhanced delivery (CED) for recurrent malignant glioma (MG). *First Author: Annick Desjardins, Duke University Medical Center, Durham, NC*

Background: D2C7-IT is a recombinant immunotoxin comprised of a dual-specific antibody fragment targeting EGFRwt and EGFRvIII and a genetically engineered form of the *Pseudomonas* exotoxin, PE38-KDEL. We report the results of a phase I trial evaluating D2C7-IT delivered intratumorally by CED. **Methods:** Eligible patients were adults with recurrent supratentorial WHO grade III or IV MG; solitary tumor; $\geq$4 weeks after chemotherapy, bevacizumab or study drug; adequate organ function; and KPS$>$70%. Two patients per dose level (DL) were to enroll in the dose escalation portion (dose range: 40ng/mL to 23,354ng/mL). **Results:** From May 2015 to May 2018, 43 patients enrolled on study. Observed dose limiting toxicities include: grade 4 seizure (n=1) on DL3, grade 3 confusion and pyramidal tract syndrome (n=1) on DL13, and grade 4 cerebral edema (n=1) and grade 3 dysphasia (n=1) on DL17. Grade 3 or higher adverse events possibly related to D2C7-IT include: seizure (grade 4, n=2; grade 3, n=3), cerebral edema (grade 4, n=1), hydrocephalus (grade 3, n=5), headache (grade 3, n=4), hemiparesis (grade 3, n=4), dysphasia (grade 3, n=3), lymphopenia (grade 3, n=4), thromboembolic event (grade 3, n=3); and one each of grade 3 elevated ALT, urinary tract infection, fall, wound complication, generalized muscle weakness, confusion, encephalopathy, and somnolence. As of February 2020, four patients remain alive, with three patients demonstrating persistent radiographic partial response more than 54, 34 and 28 months after a single infusion of D2C7-IT. **Conclusions:** Dose level 13 (6,920ng/mL) was selected as the optimal phase II dose. Accrual in a dose expansion phase II trial is ongoing, and we are initiating a combination trial of D2C7-IT with checkpoint inhibitior. Clinical trial information: NCT02303678. Research Sponsor: U.S. National Institutes of Health.

2568 Poster Session (Board #59), Fri, 8:00 AM-11:00 AM

Intratumoral drug distribution of adavosertib in patients with glioblastoma: Interim results of phase I study. *First Author: Carlos G Romo, Johns Hopkins University School of Medicine, Baltimore, MD*

Background: Wee1 is a key regulator of the G2/M checkpoint and is frequently overexpressed in glioblastoma (GB). Adavosertib is a first-in-class oral, small molecule inhibitor of Wee1 that acts primarily as a DNA damage sensitizer. A phase I clinical trial was conducted to evaluate its safety and establish the recommended phase II dosing. Studies were undertaken to evaluate whether potentially therapeutic concentrations of the drug are achieved in recurrent tumor and adjacent non-enhancing brain regions with presumed intact blood-brain barrier (BBB). **Methods:** Twelve patients received five daily doses of adavosertib pre-operatively at either the maximum tolerated dose (MTD) for concurrent radiation or adjuvant temozolomide. Tissue from contrast enhancing (CE) and non-enhancing (NE) brain regions was obtained for analysis during surgical resection. A second stage is being conducted using microdialysis (MD) to facilitate continuous sampling of extracellular fluid (ECF) and measuring free drug concentrations in: normal-appearing brain, contrast enhancing tumor, and a peritumoral T2 hyperintense area. The concentration of total adavosertib in plasma and tissue homogenates and free drug in ECF were determined by validated LC/MS/MS methods. **Results:** Geometric mean concentrations of adavosertib after a 200 mg dose were 644 ng/mL and 119 ng/mL in CE and NE tissue specimens, respectively (6 patients). At the 425 mg dose, the mean concentrations were 3,576 ng/mL in CE tissue and 885 ng/mL in NE tissue (6 patients). MD was performed in 2 patients. Samples from functional MD catheters were collected from NE brain in patient no. 1 and from two NE areas and a FLAIR hyperintense region in patient no. 2, with the following results in the table. **Conclusions:** The total drug concentration in tissue samples was notably lower in regions of the brain with a relatively intact BBB as compared to contrast enhancing tissue. Concentrations of adavosertib measured by MD vary markedly depending on catheter location. Free drug levels in ECF within brain with a functional BBB, although considerably lower than total drug levels in tissue, were 2-10 times below the previously reported IC_{50} for antiproliferative activity against sensitive GB cell lines (127 ng/mL). Whether or not the target of the drug is effectively inhibited at these concentrations remains to be demonstrated. Clinical trial information: NCT01849146. Research Sponsor: U.S. National Institutes of Health.

Parameter	Pt. 1 Plasma	Pt. 1 NE brain	Pt. 2 Plasma	Pt. 2 NE brain	Pt. 2 NE brain	Pt. 2 T2
$C_{max\ (ng/mL)}$	641	22.5	511	47.9	66.5	12.6
$t_{1/2}$ (h)	10.7	10	12.6	8.4	7.9	11.3
AUC_{24}	6,917	430	5,450	665	936	182
AUC_{ECF}/AUC_p		0.062		0.12	0.17	0.033

2569 Poster Session (Board #60), Fri, 8:00 AM-11:00 AM

Superior therapy response predictions for patients with low-grade glioma (LGG) using Cellworks Singula: MyCare-009-04. *First Author: Manmeet Singh Ahluwalia, Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center, Neurological Institute, Taussig Cancer Institute and Cleveland Clinic, Cleveland, OH*

Background: Despite using cytogenetic and molecular-risk stratification and precision medicine, the current overall outcome of LGG patients remains relatively poor. Therapy selection is often based on information considering only a single aberration and ignoring other patient-specific omics data which could potentially enable more effective treatments. The Cellworks Singula report predicts response for physician prescribed therapies (PPT) using the novel Cellworks Omics Biology Model (CBM) to simulate downstream molecular effects of cell signaling, drugs, and radiation on patient-specific *in silico* diseased cells. We test the hypothesis that Singula is a superior predictor of progression-free survival (PFS) and overall survival (OS) compared to PPT. **Methods:** Singula's ability to predict response was evaluated in an independent, randomly selected, retrospective cohort of 137 LGG patients aged 14 to 73 years treated with PPT. Patient omics data was available from TCGA. Singula uses PubMed to generate protein interaction network activated and inactivated disease pathways. We simulated the PPT for each patient and calculated the quantitative drug effect on a composite LGG disease inhibition score based on specific phenotypes while blinded to clinical response. Univariate and multivariate proportional hazards (PH) regression analyses were performed to determine if Singula provides predictive information for PFS and OS, respectively, above and beyond age and PPT. **Results:** In univariate analyses, Singula was a significant predictor of both PFS (HR = 3.587, $p < 0.0001$) and OS (HR = 3.044, p = 0.0007). In multivariate PH regression analyses, Singula (HR = 3.707, $p < 0.0001$) remained an independent predictor of PFS after adjustment for PPT (p = 0.3821) and patient age (p = 0.0020). Singula (HR = 2.970, p = 0.0013) was also a significant independent predictor of OS after adjustment for PPT (p = 0.0540) and patient age ($p < 0.0001$). Results indicate that Singula is a superior predictor of both PFS and OS compared to PPT. Singula provided alternative standard of care therapy selections for all 34 disease progressors. **Conclusions:** Singula is a superior predictor of PFS and OS in LGG patients compared to PPT. Singula can correctly identify non-responders to PPT and provide alternative therapy selections. Research Sponsor: None.

2570 Poster Session (Board #61), Fri, 8:00 AM-11:00 AM

Postoperative radiation therapy (PORT) impact on clinical outcomes of resected atypical meningioma: A meta-analysis. *First Author: Kevin M. Gallagher, Feist-Weiller Cancer Center at LSUHSC-Shreveport, Overton Brooks VAMC, Shreveport, LA*

Background: Although meningiomas are among the most prevalent types of brain tumors, atypical meningiomas (AM) account for around 4% of all meningiomas. AMs tend to be more aggressive with relatively higher rates of recurrence and mortality. Gross total resection (GTR) has been the standard of care when possible. However, GTR itself is not always enough to prevent recurrence of AMs. The role of PORT remains controversial in AM as the comparative studies to support its use have provided conflicting results. The purpose of this meta-analysis is to evaluate the impact of PORT on clinical outcomes in resected AMs. **Methods:** A review of the medical literature was conducted using online databases. Inclusion criteria consisted of (i) AM diagnosis, (ii) English language, (iii) Simpson graded resections, and (iv) comparative studies reporting recurrence rates (RcR), Progression Free Survival (PFS), and Overall Survival (OS) with hazard ratios (HR) or Kaplan-Meier curves. A meta-analysis was conducted using an inverse variance method with random-effects model. **Results:** Twenty-two comparative studies with a total of 5,129 patients were included and analyzed. When GTR was attained, PORT was associated with improved RcR (HR = 0.72, 95%CI: 0.59-0.86) and PFS (HR = 0.77, 95%CI:0.65-0.90), but not OS (HR = 0.93, 95%CI:0.83-1.04). When subtotal resection (STR) was attained, PORT was associated with improved PFS (HR = 0.35, 95%CI:0.26-0.48) as well as OS (HR = 0.70, 95%CI:0.54-0.89). **Conclusions:** This is the first meta-analysis to show that PORT is associated with PFS benefit in AMs with GTR and STR. Moreover, PORT significantly improved OS of AMs that underwent STR but had no impact on OS when GTR was achieved. In the absence of randomized clinical trials, this meta-analysis represents the most compelling data supporting the use of PORT in this patient population. Research Sponsor: None.

TPS2572 Poster Session (Board #63), Fri, 8:00 AM-11:00 AM

Phase I/II study of T-DM1 alone versus T-DM1 and metronomic temozolomide in secondary prevention of HER2-positive breast cancer brain metastases following stereotactic radiosurgery. *First Author: Alexandra Dos Santos Zimmer, Women's Malignancies Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD*

Background: We demonstrated that low doses of temozolomide (TMZ) administered in a prophylactic, metronomic fashion significantly prevented development of brain metastases in murine models of breast cancer. Based on these findings, we developed a secondary-prevention clinical trial. **Methods:** Phase I is a standard 3+3 design: T-DM1 3.6mg/kg IV every 21 days plus TMZ 30, 40 or 50 mg/m2 daily, to identify the maximum tolerated dose (MTD) of the combination, and is completing accrual, with 9 patients accrued, currently on the third and last dose level. Phase II will randomize patients to T-DM1 3.6mg/kg versus T-DM1 3.6mg/kg plus TMZ at recommended phase 2 dose (RP2D), to evaluate if addition of TMZ improves the recurrence-free incidence from distant new brain metastases at one year from 50% to 65%. Patients will undergo radiology guided lumbar puncture at baseline and after 6 weeks of treatment (C3D1) for correlative studies, brain MRI, systemic restaging CTs, and questionnaires for evaluation of symptoms and quality of life. Eligibility: HER2+ breast cancer with brain metastases (up to 10 lesions), treated with SRS and/or resection $\leq$12 weeks before enrollment, no leptomeningeal metastases, no previous WBRT, ECOG $\leq$2 and adequate organ and marrow function. Biomarkers, including cell free DNA from CSF, serum and tumor block, exosomal DNA, serum markers for neuroinflammation, and patient reported outcomes, will be analyzed in an exploratory fashion. Target accrual: up to 18 patients in phase I and 98 in phase II. Clinical trial information: NCT03190967. Research Sponsor: U.S. National Institutes of Health.

TPS2573 Poster Session (Board #64), Fri, 8:00 AM-11:00 AM

Alliance A071701: Genomically guided treatment trial in brain metastases. *First Author: Priscilla Kaliopi Brastianos, Massachusetts General Hospital and Harvard Medical School, Boston, MA*

Background: Brain metastases, most commonly derived from melanoma, lung and breast cancers, are the most common brain tumor, with approximately 200,000 cases diagnosed annually in the United States. Median survival is on the order of months. For patients with clinically symptomatic brain metastases, approximately half succumb due to intracranial progression. In preclinical work, we demonstrated that brain metastases and primary tumors are often genetically distinct with frequent alterations in the CDK and PI3K pathway (Brastianos, Carter et al. Cancer Discovery 2015). **Methods:** We are currently accruing to a prospective multi-arm phase II study of CDK, PI3K/mTOR, and NTRK/ROS1 inhibitors in patients with brain metastases harboring alterations associated with sensitivity to these inhibitors (abemaciclib, paxalisib and entrectinib), respectively. Patients with new, recurrent or progressive brain metastases are eligible for this trial. Previously obtained tissue from brain metastases and extracranial sites (primary or extracranial metastases) are screened for the presence of these alterations, and if present in both tumor sites, patients will receive the appropriate corresponding targeted treatment. Screening is carried out with the SNaPshot NGS assay, which is a fully validated clinical test designed and developed at the MGH Center for Integrated Diagnostics. The primary endpoint of response rate (RR) in the central nervous system as per RANO criteria will be evaluated separately for each inhibitor, stratified by histology within each arm. There will be 21 evaluable patients assigned to each of the CDK and PI3K inhibitor and tumor type cohorts (breast, lung and other) and 10 patients assigned to the NTRK/ROS1 inhibitor cohort (lung) for a total of 136 evaluable patients. Although current systemic therapy for brain metastases is often ineffective, we hypothesize that targeted therapies will demonstrate efficacy in patients harboring the appropriate mutations. This study represents a novel individualized therapeutic approach in brain metastases, a disease with a critical need for effective therapy. Support: U10CA180821, U10CA180882, https://acknowledgments.alliancefound.org; Genentech, Kazia Therapeutics Limited, Eli Lilly; Clinical trial information: NCT03994796. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company, U.S. National Institutes of Health.

TPS2574 **Poster Session (Board #65), Fri, 8:00 AM-11:00 AM**

INDIGO: A global, randomized, double-blind, phase III study of vorasidenib (VOR; AG-881) vs placebo in patients (pts) with residual or recurrent grade II glioma with an isocitrate dehydrogenase 1/2 (IDH1/2) mutation. *First Author: Ingo K. Mellinghoff, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Low-grade gliomas (LGGs; WHO grade II) are incurable and ultimately progress to high-grade gliomas. The current treatment options consist of surgery followed by observation ("watch and wait") for pts with lower risk for disease progression or post-operative chemo-radiotherapy (high-risk population). There are no approved targeted therapies. *IDH1* and *IDH2* mutations (m*IDH1/2*) occur in approximately 70% and 4% of LGGs, respectively, and promote tumorigenesis via neomorphic production of D-2-hydroxyglutarate (2-HG). VOR, an oral, potent, reversible, brain-penetrant inhibitor of mIDH1/2, was evaluated in 76 pts with glioma in two phase 1 studies (dose escalation and perioperative) and was associated with a favorable safety profile at doses of $<$ 100 mg daily. Preliminary clinical activity was observed in non-enhancing glioma pts in both studies, most recently with an objective response rate (ORR) of 30.8% at 50 mg QD in the perioperative study and $>$ 90% 2-HG suppression at this dose level relative to untreated control samples (Mellinghoff et al., J Clin Oncol 2019). **Methods:** Approximately 366 pts will be randomized 1:1 to VOR (50 mg QD) or matched placebo and stratified by 1p19q status (intact vs codeleted). Key eligibility criteria include: age $\geq$12 years; grade 2 oligodendroglioma or astrocytoma (per WHO 2016 criteria) not in need of immediate treatment and without high-risk features; centrally confirmed m*IDH1/2* status; $\geq$1 prior surgery for glioma within the previous 5 years but no other anticancer therapy; Karnofsky performance status $\geq$80%; and centrally confirmed measurable, non-enhancing disease evaluable by magnetic resonance imaging. Crossover from placebo to the VOR arm is permitted upon centrally confirmed radiographic progression per RANO-LGG criteria. Primary endpoint is progression-free survival assessed by independent review. Secondary endpoints include safety and tolerability, tumor growth rate assessed by volume, time to next intervention, ORR, overall survival, quality of life assessed by the Functional Assessment of Cancer Therapy–Brain questionnaire, and plasma pharmacokinetics. Exploratory endpoints include seizure activity and neuro-cognitive function. Clinical data will be reviewed regularly throughout the study by an independent data monitoring committee. The study is currently enrolling pts in the US, with additional countries planned (NCT04164901). Clinical trial information: NCT04164901. Research Sponsor: Agios Pharmaceuticals, Inc.

TPS2575 **Poster Session (Board #66), Fri, 8:00 AM-11:00 AM**

A phase II/III randomized, blinded study of tozuleristide for fluorescence imaging detection during neurosurgical resection of pediatric primary central nervous system (CNS) tumors: PNOC012 (Pacific Pediatric Neuro-oncology Consortium). *First Author: Sarah Leary, Seattle Children's Hospital, Seattle, WA*

Background: Tozuleristide (also known as BLZ-100 or Tumor Paint) is a fluorescent imaging drug designed to specifically label and accumulate in tumor tissue, thus enabling more precise surgical tumor resection intraoperatively. Tozuleristide achieves tumor targeting through the peptide portion of the molecule, a modified chlorotoxin peptide, and its imaging properties from a coupled near-infrared fluorescent dye, an indocyanine green. Tozuleristide has been studied in 4 Phase 1 studies, including a trial in pediatric brain cancer subjects. No tozuleristide SAEs or dose limiting toxicity were observed in the 97 subjects treated in the Phase 1 program at doses up to 30 mg in adults or 17.3 mg/m^2 in pediatrics (Hansen S et al, WMIC 2018, P196). Eighty percent of pediatric subjects receiving tozuleristide had tumors considered fluorescence positive, including high and low grade glioma, ependymoma, and medulloblastoma. **Methods:** This study randomizes subjects in a 1:10 ratio to standard of care or tozuleristide arms. The primary efficacy objectives and endpoints are based on equivocal regions of tissue encountered in surgery. Prior to fluorescence assessment, the surgeon assesses the suspected nature of the tissue (more likely tumor/less likely tumor). Tissue specimens of equivocal regions are collected for blinded central pathology assessment. Sensitivity and specificity of the surgeon's designation, fluorescence assessment, and ratios of surgeon to fluorescence assessments comprise the primary efficacy analyses. Tozuleristide is given as an IV bolus dose of 15 mg/m^2 to pediatric subjects 1 to 36 hours prior to surgery. Subjects must have a MRI documented lesion consistent with a CNS tumor for which resection is planned. Measures of safety include adverse events, laboratory measures of hematology, liver and kidney function and changes in vital signs and ECGs. Pharmacokinetic blood samples are collected up to 3 hr post dose. Fluorescence imaging is assessed during surgery using an investigational "Canvas System" imaging device attached to a surgical microscope. Collected pathology specimens will also be subjected to further genetic, molecular and pathology studies, including fluorescence assessment of frozen tissue sections. SAEs and patient reported outcomes are collected for 3 months. The SMC for the study last reviewed the data for this study in July 2019 and recommended the trial continue as planned. Clinical trial information: NCT03579602. Research Sponsor: Blaze Bioscience Inc, Other Foundation.

TPS2576 **Poster Session (Board #67), Fri, 8:00 AM-11:00 AM**

A first-in-human phase I single-agent dose-escalation, food effect and dose expansion study of oral ONC206 in recurrent and rare primary central nervous system neoplasms. *First Author: Brett James Theeler, Walter Reed National Military Medical Center, Bethesda, MD*

Background: Blockade of the dopamine receptor D2 (DRD2) has emerged as a therapeutic target in neuro-oncology. ONC201, a first-generation imipridone that antagonizes DRD2, has demonstrated clinical activity in Diffuse Midline Gliomas, H3K27M-mutant (DMGs). Treatment options beyond surgical resection and radiation therapy are limited for most recurrent and rare primary CNS neoplasms. DRD2 blockade holds promise as a therapeutic target in multiple primary CNS cancers. ONC206 is a next generation imipridone and a chemical analog of ONC201 that possesses favorable drug properties such as oral bioavailability, robust stability, and blood-brain barrier penetrance. ONC206 exhibits enhanced allosteric inhibition of DRD2 and nanomolar affinity/potency as a DRD2 antagonist with complete antagonism and specificity for DRD2. ONC206 demonstrated broad spectrum anti-cancer efficacy in vitro across most solid tumor types tested in a panel of $>$ 1000 human cancer cell lines with nervous system tumors emerging as most responsive. In addition to its broad-spectrum activity in vitro, ONC206 efficacy has been demonstrated in xenograft mouse models. **Methods:** This is an open label, dose escalation, and food effect Phase I study of ONC206at the National Cancer Institute, Neuro-Oncology Branch. Adult patients 18 years and older with recurrent, primary CNS neoplasms will initially be accrued to the dose escalation portion of the study and evaluated for toxicity. Eligible diseases include recurrent glioblastoma, WHO Grade 2 and 3 infiltrating glial neoplasms, and rare primary CNS neoplasms in the NCI-CONNECT program: DMGs, ependymomas, medulloblastomas, and other rare CNS tumor types. The primary endpoint is to determine DLT during the first cycle (28 days). Dose escalation will proceed according to a standard 3+3 design. Both once weekly and more frequent dosing of ONC206 will be explored in the dose escalation scheme. After the MTD is established, food effect will be determined in a dedicated cohort using a balanced, single-dose, two-arm, two-period crossover design. Secondary endpoints will include objective response rate by RANO criteria, overall and progression-free survival, and disease control rate. Exploratory analysis of DRD2 and DRD5 expression, DRD2 dimerization, expression of MYC and N-MYC in tumor tissue in relation to clinical outcomes will also be performed. Research Sponsor: Oncoceutics.

TPS2577 **Poster Session (Board #68), Fri, 8:00 AM-11:00 AM**

BMX-HGG: Phase II trial of newly diagnosed high-grade glioma treated with concurrent radiation therapy, temozolomide, and BMX-001. *First Author: Katherine B. Peters, Duke University Medical Center, Durham, NC*

Background: Patients diagnosed with malignant high-grade gliomas (WHO grade III-IV) experience significant morbidity and mortality associated with these cancers. While the mainstay of therapy for patients with newly diagnosed high-grade glioma is surgery followed by concurrent chemotherapy and radiation therapy (RT), the outcomes remain very poor. BMX-001 (MnTnBuOE-2-PyP^{5+}) is a metalloporphyrin with differential action in response to radiation therapy and chemotherapy-induced oxidative stress. Early preclinical studies demonstrated BMX-001's ability to act as a radioprotectant to healthy tissue such as a central nervous white matter and as a radiosensitizer to cancer cells, in particular, human glioblastoma xenografts. We evaluated the safety of BMX-001 in combination with concurrent RT and temozolomide (TMZ) in a phase I study of newly diagnosed high-grade glioma patients, and we found that BMX-001 is safe and well-tolerated in this population. The maximum tolerated dose of BMX-001 during concurrent RT and TMZ was determined to be 28 mg delivered subcutaneously (SC) followed by 16 biweekly SC doses at 14 mg (Peters et al., Neuro-Oncology 2018). **Methods:** For this multi-site, open-label, phase II study (NCT02655601), we will randomize approximately 160 patients 1:1 to concurrent RT and TMZ with BMX-001 versus concurrent RT and TMZ alone. Key eligibility criteria include newly diagnosed histologically confirmed high-grade glioma (WHO III-IV), 18 $\geq$ years, and Karnofsky performance status $\geq$ 70%. The primary endpoint is overall survival. Secondary endpoints include cognitive performance as assessed by standardized cognitive testing, bone marrow protection, safety and tolerability, progression-free survival, overall tumor response rate, and plasma pharmacokinetics. Exploratory endpoints are health-related quality of life (as assessed by Functional Assessment of Cancer Therapy–Brain, Functional Assessment of Cancer Therapy-Cognition, and Functional Assessment of Chronic Illness Therapy-Fatigue), qualitative hair loss, and white matter integrity (as measured by MRI diffusion tensor/susceptibility imaging). Since November 2018, this phase II study has enrolled 64 of 160 high-grade glioma patients at six sites with future sites planned to be implemented. Clinical trial information: NCT02655601. Research Sponsor: BioMimetix.

TPS2578 **Poster Session (Board #69), Fri, 8:00 AM-11:00 AM**

IPAX-1: Phase I/II study of ^{131}I-iodo-phenylalanine combined with external radiation therapy as treatment for patients with glioblastoma multiforme. *First Author: Josef Pichler, Kepler University Hospital, Linz, Austria*

Background: Many tumor types, including glioblastoma multiforme (GBM), overexpress the L-type amino transporter 1 (LAT-1). ^{131}I-iodo-phenylalanine (^{131}I-IPA) is a small-molecule amino acid derivative taken up by LAT-1 with designated orphan status in the United States and European Union for the treatment of GBM. In preclinical research, combining ^{131}I-IPA with external radiation therapy (XRT) yielded additive cytotoxic effects (Israel *et al. Nucl Med Biol* 2011). Tumor accumulation of ^{131}I-IPA was shown in a proof-of-principle study (Baum *et al. Nucl Med Mol Imaging* 2011) and confirmed with single dosing of 2–7 GBq ^{131}I-IPA in combination with XRT in patients with recurrent GBM (Verburg *et al. Nuklearmedizin* 2013). The ^{131}I-IPA + XRT as Treatment for Patients with Glioblastoma Multiforme (IPAX-1) study evaluates the safety, tolerability, dosing schedule, and preliminary efficacy of ^{131}I-IPA in combination with second-line XRT in patients with recurrent GBM. **Methods:** IPAX-1 is a multi-center, open-label, phase 1/2, dose-finding study recruiting patients with previously confirmed histological diagnosis of GBM and evidence of first recurrence. Other key inclusion criteria are history of GBM standard therapy, at least 6 months since end of first-line XRT, pathologically increased amino acid tumor uptake shown by molecular imaging, and current indication for repeat radiation. Participants receive intravenous ^{131}I-IPA either as a single fraction (1f) followed by XRT, or as three equal fractions (3f) at weekly intervals followed by XRT commencing between the first and second ^{131}I-IPA administration. The 1f regimen (n = 5) evaluates single administration of 2 GBq ^{131}I-IPA. The 3f regimen is used to assess dose escalation, starting with 2 GBq (3 $\times$ 0.66 GBq; n = 5) and increasing in 2 GBq increments (n = 3 per activity level). The highest total dose planned is 8 GBq. XRT delivery is in 18 fractions (2 Gy each) on consecutive working days over 4 weeks. The study's primary aim is to assess the safety and tolerability of ^{131}I-IPA + XRT. Secondary objectives include evaluating the maximum tolerated dose of ^{131}I-IPA, feasibility of fractionated administration, radiation absorbed dose to tumor and biodistribution; and exploring the antineoplastic effect of combination therapy. IPAX-1 enrollments began in July 2019; the study will enroll up to 44 patients and is currently recruiting at five sites in Europe and Australia. Clinical trial information: NCT03849105. Research Sponsor: Telix International Pty Ltd.

TPS2579 **Poster Session (Board #70), Fri, 8:00 AM-11:00 AM**

GBM AGILE: A global, phase II/III adaptive platform trial to evaluate multiple regimens in newly diagnosed and recurrent glioblastoma. *First Author: Meredith Becker Buxton, UC San Francisco, San Francisco, CA*

Background: Glioblastoma (GBM) is an aggressive brain tumor with few effective therapies and is invariably fatal. Developing new therapies for patients with GBM requires focused interaction between industry, academia, nonprofits, patient advocacy, and health authorities, and novel approaches to clinical trials. Industry is wary of developing drugs for GBM due to the high failure rate and high cost of drug development. GBM Adaptive Global Innovative Learning Environment (GBM AGILE) Trial was designed by over 130 global key opinion leaders in consultation with health authorities to provide an optimal mechanism for phase II/III development in GBM. The Sponsor of GBM AGILE is the Global Coalition for Adaptive Research (GCAR), a nonprofit organization. GCAR's mission is to speed the discovery and development of treatments for patients with rare and deadly diseases by serving as sponsor of innovative trials. **Methods:** GBM AGILE is an international, seamless phase II/III platform trial designed to evaluate multiple therapies in newly diagnosed and recurrent GBM. Its goals are to identify effective therapies for GBM and match effective therapies with patient subtypes, with data generated to support regulatory filing for new drug applications. Bayesian response adaptive randomization is used within subtypes of the disease to assign participants to investigational arms based on their performance. The primary endpoint is overall survival. The trial is being conducted under a master Investigational New Drug Application/Clinical Trial Agreement and Master Protocol, allowing multiple drugs/drug combinations from different pharmaceutical companies to be evaluated simultaneously and/or over time. The plan is to add experimental therapies as new information is identified and remove therapies as they complete their individual evaluation against a common control. GBM AGILE received IND approval from the FDA in April 2019, enrolling its first patient in June 2019. Site activation is ongoing in the US, with approximately 40 US planned. The trial received CTA approval from Health Canada in January 2020. Expansion to Europe, China, and Australia is also underway. Clinical trial information: NCT03970447. Research Sponsor: Global Coalition for Adaptive Research, Pharmaceutical/Biotech Company.

TPS2580 **Poster Session (Board #71), Fri, 8:00 AM-11:00 AM**

Phase III TRIDENT trial: Radiation and temozolomide +/- tumor treating fields in newly diagnosed glioblastoma. *First Author: Wenyin Shi, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA*

Background: Tumor treating fields (TTFields) is a non-invasive, regional antimitotic treatment approved as a standard of care for glioblastoma (GBM). In the EF-14 phase III trial, TTFields (200 kHz) plus temozolomide (TMZ) significantly increased the survival of patients with newly diagnosed GBM (ndGBM) without increase in systemic toxicity. TTFields-related AEs were mainly skin AEs. In preclinical models, TTFields increase the therapeutic effects of radiation therapy (RT). A pilot study showed that TTFields concomitant with RT and TMZ is well tolerated. The benefit of concomitant TTFields with RT and TMZ will be tested in this phase III TRIDENT randomized trial. **Methods:** TRIDENT is an international phase III randomized trial comparing standard RT with TMZ vs the triple combination of RT plus TMZ with concomitant TTFields. RT is delivered through the TTFields arrays. Patients in both arms will receive maintenance TTFields with TMZ. TTFields (200 KHz) will be delivered $>$18 hours/day using Optune. Patients will continue TTFields treatment until second recurrence. Patients with pathologically confirmed newly ndGBM, $\geq$ 18 years, KPS $\geq$ 70, either sex, post-surgery or biopsy, who are amenable for RT/TMZ therapy will be enrolled. Patients will be stratified by extent of resection and MGMT promoter methylation status. The primary endpoint is overall survival (OS). Secondary end points include: progression free survival (PFS; RANO), 1- and 2-year survival rates, overall radiological response (ORR; RANO), progression-free survival (PFS2, PFS6, PFS12); severity and frequency of AEs (CTCAE V5.0); pathological changes in resected GBM tumors post treatment; quality of life (EORTC QLQ-C30); and correlation of OS to TTFields compliance. The hypothesis is that concomitant TTFields with radiation and TMZ will significantly improve OS as compared to radiation and TMZ alone. The sample size is 950, with 475 in each arm to detect a HR $<$0.8 with a 5% type I error. Survival will be measured from the time of randomization until date of death. At the time of analysis, patients who are lost to follow-up or still on protocol follow-up will be censored at the last date known to be alive. Research Sponsor: Novocure.

TPS2581 **Poster Session (Board #72), Fri, 8:00 AM-11:00 AM**

Phase II study of pembrolizumab plus SurVaxM for glioblastoma at first recurrence. *First Author: Manmeet Singh Ahluwalia, Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center, Neurological Institute, Taussig Cancer Institute and Cleveland Clinic, Cleveland, OH*

Background: Glioblastoma is the most common primary malignant brain tumor with median survival of approximately 15-16 months. Following first recurrence, progression free survival at six months ~15%. There is no therapy in recurrent glioblastoma associated with any survival benefit and there is an urgent need for better therapeutic options. Immunotherapy is one promising option for patients with cancer. This is being explored in glioblastoma and a number of forms of active specific vaccination and immune checkpoint based approaches have been devised and are being investigated in glioblastoma. **Methods:** Pembrolizumab is a potent humanized immunoglobulin G4 (IgG4) monoclonal antibody (mAb) with high specificity of binding to the programmed cell death 1 (PD-1) receptor. Survivin is a 16.5 kDa intracellular protein that belongs to the inhibitor of apoptosis protein (IAP) family. SurVaxM is a 15 amino acid antigenic peptide that targets surviving capable of binding several human MHC class I molecules. Primary Objective is to assess clinical activity of Pembrolizumab and SurVaxM in patients with recurrent glioblastoma using progression free survival at 6 months (PFS-6) as determined using RANO criteria. Secondary Objective(s) includes safety and tolerability of combination, response rates, progression free survival and overall survival. Exploratory Objective include measuring cellular and humoral immune responses during concurrent administration of Pembrolizumab and SurVaxM. This is a phase II study of two arms in patients with recurrent glioblastoma. Arm A is patients with first recurrence of glioblastoma who have failed prior chemotherapy and radiation but have not received any immunotherapy. Arm B is an exploratory arm of glioblastoma patients who have failed prior anti-PD1 therapy. This clinical trial will enroll 41 patients with glioblastoma at first recurrence (bevacizumab naïve) in arm 1.This will include a 6-patient toxicity/safety run-in. There will an exploratory cohort of 10 patients who have failed prior PD1 blockade for a total of 51 patients in 2 arms. Key inclusion criteria include diagnosis of glioblastoma, Age $\geq$18 years old, Previous first line treatment with at least radiotherapy with or without temozolomide and Documented first recurrence of GBM and Karnofsky performance status of 70 and normal organ function. Key exclusion criteria include more than one recurrence of GBM, presence of extracranial metastatic or leptomeningeal disease, patients with $>$ 1 cm midline shift on imaging. Patients must not require $>$ 10 mg daily of prednisone equivalent. Clinical trial information: NCT04013672. Research Sponsor: Merck, Pharmaceutical/Biotech Company.

3000 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Pilot study on outcome and antitumor efficacy of an autologous cancer cell vaccine applied in patients with advanced solid tumors. *First Author: Eglys Gonzalez Marcano, UniFontis, Sickte, Germany*

Background: In the last decade cancer immunotherapy has emerged as the most promising anti-tumor approach. The most commonly used immunotherapies are vaccines and checkpoint inhibitors. An autologous cell vaccine is made with the patient's own tumor cells processed in vitro, which may elicit a cytotoxic T-lymphocytic immune response against tumor cells antigens, resulting in tumor cell death. We performed a pilot study to evaluate the clinical relevance and general outcome of an autologous vaccine as a treatment in different types of cancer. **Methods:** A total of 31 patients (n=31) with advanced solid tumors and the lack of standard treatments were treated with an immunotherapy protocol consisting of 6 intradermal doses of the vaccine, given the first two doses at day 1 and 2, and the rest every two weeks. All patients signed an informed consent form. Response evaluation was assessed by PET/CT identified as metric (iRECIST) response and in some cases tumor markers where available. **Results:** Out of 31 patients treated, 2 patients suffered from pancreatic cancer, 2 from sarcoma, 1 from lung cancer, 13 from breast cancer, 2 from ovarian cancer, 1 from prostate cancer, 1 from cholangiocarcinoma, 4 from colorectal cancer, 1 from non-Hodgkin lymphoma, 1 from gastric cancer, 1 from laryngeal and hypopharyngeal cancer, 1 from fallopian tube cancer, 1 from peritoneal cancer. Side effects related to the therapy were rare including light redness in the area of injection and in one case inflammation of the tumor area. 26 patients were evaluated for metric response and 5 for tumor marker response assessment. For tumor marker follow up 9.6 % had a SD of $>$ 3 month and 6.5 % a PD. For metric follow up 12.9 % had a CR, 6.5 % a PR, 25.8 % a SD of $>$ 3 month and 38.7 % a PD. **Conclusions:** This study have confirmed an anti-tumor response in the majority of patients treated, with none to very low side effects and a good quality of life during the treatment. To obtain more detailed and significant data on the efficacy of this therapy, a further controlled clinical phase study should be performed. Research Sponsor: None.

3001 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Oral DNA vaccination targeting VEGFR2 combined with anti-PDL1 avelumab in patients with progressive glioblastoma: Safety run-in results—NCT03750071. *First Author: Wolfgang Wick, National Center for Tumor Diseases (NCT), UKHD and German Cancer Research Center (DKFZ), Heidelberg, Germany*

Background: VEGFR2 overexpression in glioblastoma serves as a target for VEGFR2 primed T cells using VXM01 DNA vaccine encoding for VEGFR2. VXM01 is delivered in a bacterial Ty21a carrier suitable for oral administration. A previous phase I/II study in 14 patients with progressive glioblastoma showed that detection of VEGFR2 specific T cells as well as altered intra-tumoral immunity is correlated with prolonged overall survival, one partial response was reported with VXM01 alone. Three patients received nivolumab in addition to VXM01, which resulted in one complete and one partial clinical response. Based on these findings, a trial combining VXM01 and avelumab was designed. **Methods:** A multicentre, open-label phase I/II study (*EudraCT* 2017-003076-31) in progressive glioblastoma includes 30 patients (24 non-resectable, 6 resectable) previously treated with temozolomide/radiotherapy. VXM01 is administered on day 1, 3, 5, 7 followed by boostings q4w. Avelumab 800mg is given intravenously q2w. Treatment continues up to week 48 followed by a 2 year observation period. The safety run-in phase of dose groups treated with VXM01 10^6 or 10^7 CFU plus avelumab was completed with 9 patients. Safety evaluation by the Data Safety Monitoring Board was performed after 3 and 9 patients treated for at least 5 weeks. Endpoints include safety and tolerability, objective response rate (ORR), clinical response using immune-response assessment in Neurooncology criteria (iRANO), and immunological assays like ELISpot, FACS, TCR-sequencing and tumor stainings. **Results:** No treatment-related toxicities were observed. Three partial responses with tumor reductions of 58, 81 and 95% to baseline were reported in 9 patients according to iRANO. Two of these patients are progression-free $>$ 6 months. Significant VEGFR2 specific T cell responses were measured in several patients, and pre-existing intra-tumoral T cells are positively associated with the effectiveness of the immunotherapy combination. **Conclusions:** VXM01 in combination with avelumab was safe and produces detectable peripheral VEGFR-2 specific immune responses. Three patients had an objective response. Clinical trial information: NCT03750071. Research Sponsor: Vaximm Gmbh.

3002 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A phase I combination study of vigil and atezolizumab in recurrent/refractory advanced-stage ovarian cancer: Efficacy assessment in BRCA1/2-wt patients. *First Author: Rodney Paul Rocconi, University of South Alabama, Mobile, AL*

Background: Recent studies have shown poor clinical outcomes and limited survival advantage to checkpoint inhibitors (CIs) in advanced stage ovarian cancer (OvC). Vigil is a personalized precision vaccine constructed from autologous tumor tissue transfected with a DNA plasmid encoding GM-CSF and bi-shRNA-furin thereby creating TGFβ expression control and enhancing immune activation. Phase 1 and 2 trials in OvC demonstrate safety, functional immune activation and clinical response benefit. Combining Vigil with CIs may broaden responsiveness of immunotherapy in OvC. **Methods:** This is a randomized, 3-part safety Phase 1 study of Vigil in combination with Atezolizumab in recurrent OvC patients. Part 2 is a randomized, intra-patient crossover study of Vigil first (VF) or Atezolizumab first (AF) for two cycles followed by sequence of the combination of the two agents. Vigil (1×10^6 or 1×10^7 cells/ml) or Atezolizumab (1200mg) were administered 1x every 21 days each cycle until progression or untoward adverse event. We now report the preliminary results of part 2 of the study. **Results:** Twenty-one patients were randomized (1:1) to VF (n = 11) or AF (n = 10), groups were similar in demographics. Grade 3/4 toxic events occurred in 17% of AF patients compared to 3% in VF patients. Median OS of VF patients (n = 11) was not reached vs. AF (n = 10) 10.8 months suggested modest advantage to VF (HR 0.33, one-sided p 0.097). However, the subset analysis of BRCA1/2 wild type (wt) demonstrated more significant overall survival benefit in VF (n = 7) median OS not reached vs. AF (n = 7) 5.2 months (HR 0.12, one-sided p 0.015). **Conclusions:** The combination of Vigil immunotherapy and checkpoint inhibitor atezolizumab in recurrent OvC demonstrated safety and suggest a lower toxicity profile and a significant OS advantage in recurrent *BRCA1/2*-wt OvC patients treated with Vigil first followed by the combination of Vigil and Atezolizumab. Clinical trial information: NCT03073525. Research Sponsor: None.

Group	N (VF/AF)	1-year OS rate (VF/AF)	Median OS (months) (VF/AF)	HR	p-value
ITT	21 (11/10)	90.9% vs 49.2%	NR vs 10.8	0.33 (95% CI: 0.064,1.7)	0.097
BRCA1/2-wt	14 (7/7)	100% vs 22.9%	NR vs 5.2	0.12 (95% CI: 0.018, 0.81)	0.015

3003 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Safety and tolerability of MEDI0562 in combination with durvalumab or tremelimumab in patients with advanced solid tumors. *First Author: Jonathan Wade Goldman, David Geffen School of Medicine, UCLA, Santa Monica, CA*

Background: We report safety and tolerability of MEDI0562, a humanized $IgG1_\kappa$ OX40 monoclonal antibody (mAb), in combination with durvalumab (durva; anti-PD-L1 mAb) or tremelimumab (treme; anti-CTLA-4 mAb) in patients (pts) with previously treated advanced solid tumors. **Methods:** In this phase 1, open-label study (NCT02705482), adult pts received escalating doses of MEDI0562 (2.25, 7.5 or 22.5 mg/kg) every 2 wks (Q2W) in combination with durva (1500 mg/kg) or treme (75 or 225 mg/kg) Q4W, until confirmed disease progression or unacceptable toxicity. Tumor assessments were performed Q8W with immune-related Response Evaluation Criteria in Solid Tumors. **Results:** In total, 27 and 31 pts received MEDI0562 + durva or treme, across 5 dose combination cohorts (3 + 3 design), with a maximum tolerated dose of 7.5 mg MEDI0652 + 1500 mg durva and maximum administered dose of 10 mg MEDI0562 + 225 mg treme. Median duration of exposure was 12.0 (range 2.0–80.9) and 8.0 (range 2.0–42.0) wks, respectively. Two (22.5 mg MEDI10562 + durva) and 3 (2.25 mg MEDI0652 + 225 mg treme, 22.5 mg MEDI0562 + 75 and 225 mg treme) dose limiting toxicities were observed. For MEDI0562 + durva and MEDI0562 + treme groups respectively, treatment-emergent adverse events (TEAEs) were reported in 96.3% and 100% of pts; most common TEAEs were fatigue (55.6%) and pruritus (45.2%), Gr 3/4 TEAEs occurred in 74.1% and 67.7%; and MEDI0562-related AEs were reported in 20 (74.1%) and 24 (77.4%) pts. Six TEAEs in each group led to MEDI0562 discontinuation (22.2% and 19.4%, respectively), 2 led to death (renal failure [7.5 mg MEDI0562 + durva], multiple organ dysfunction syndrome [22.5 mg MEDI0562 + 225 mg treme]). Three response evaluable pts had PR (11.5% [7.5 and 22.5 mg MEDI0562 + durva, n = 26]). Median overall survival was 17.4 and 11.9 mos for MEDI0562 + durva and MEDI0562 + treme, with stable disease seen in 9 pts from each group, 34.6% vs 29.0%, respectively. Serum exposure of MEDI0562 increased dose proportionally. Post treatment serum antidrug antibody (ADA) was detected in 20 pts from MEDI0562 + durva and MEDI0562 + treme (74.1% and 71.4%, respectively). The impact of ADA on MEDI0562 pharmacokinetics was seen at all doses. Mean percentage of Ki67+CD4+ and Ki67+CD8+ memory T cells increased, while mean percentage of OX40+CD4+ memory T cells decreased following the first dose of MEDI0562 + durva or treme. **Conclusions:** The safety profile of MEDI0562 in combination with durva or treme was similar between groups. Clinical activity was observed with MEDI0562 + durva in pts with advanced solid tumors. Clinical trial information: NCT02705482. Research Sponsor: AstraZeneca.

3004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A phase I, first-in-human, open-label, dose-escalation study of MGD013, a bispecific DART molecule binding PD-1 and LAG-3, in patients with unresectable or metastatic neoplasms. *First Author: Jason J. Luke, University of Pittsburgh, Hillman Cancer Center, Pittsburgh, PA*

Background: MGD013 is an investigational, first-in-class, Fc-bearing bispecific tetravalent DART molecule designed to bind PD-1 and LAG-3 and sustain/restore the function of exhausted T cells. MGD013 demonstrates ligand blocking properties consistent with anti-PD-1 and anti-LAG-3 benchmark molecules, and improves T cell responses beyond that observed with benchmark or component antibodies alone or in combination. **Methods:** This study characterizes the safety, tolerability, dose-limiting toxicities, maximum tolerated dose (MTD), PK/PD, and antitumor activity of MGD013 in patients (pts) with advanced solid and hematologic malignancies. Sequential single-pt cohorts were treated with escalating flat doses of MGD013 (1-1200 mg IV every 2 weeks), followed by a 3+3 design. Tumor-specific expansion cohorts are being treated at the recommended Phase 2 dose of 600 mg. **Results:** At data-cutoff, 50 pts (46% checkpoint-experienced) were treated in Dose Escalation, and 157 pts (32% checkpoint-experienced) in Cohort Expansion. No MTD was defined. Treatment-related adverse events (TRAEs) occurred in 146/207 (70.5%) pts, most commonly fatigue (19%) and nausea (11%). The rate of Grade $\geq$ 3 TRAEs was 23.2%. Immune-related AEs were consistent with events observed with anti-PD-1 antibodies. Mean half-life was 11 days; peripheral blood flow cytometry analyses confirmed full and sustained on-target binding during treatment at doses $\geq$ 120 mg. Among 41 response-evaluable [RE] dose escalation pts, 3 confirmed partial responses [cPRs] (triple negative breast cancer [TNBC], mesothelioma, gastric cancer) per RECIST 1.1 were observed, while 21 pts had stable disease [SD]. Among select expansion cohorts, PRs have been observed in epithelial ovarian cancer (n=2; both cPRs, and 7 with SD among 15 RE pts) and TNBC (n=2; 1 cPR, 1 unconfirmed PR [uPR], and 5 with SD among 14 RE pts). In a cohort of pts with HER2+ tumors treated with MGD013 in combination with margetuximab (investigational anti-HER-2 antibody), 3 PRs have been observed (breast [n=2], colorectal [n=1]; 1 cPR, 2 uPRs) and 2 pts with SD among 6 RE pts. Objective responses have been observed in several pts after prior anti-PD-1 therapy. Investigations into potential correlative biomarkers including LAG-3 and PD-1 are ongoing. **Conclusions:** MGD013, a novel molecule designed to coordinately block PD-1 and LAG-3, has demonstrated an acceptable safety profile and encouraging early evidence of anti-tumor activity. Clinical trial information: NCT03219268. Research Sponsor: MacroGenics, Inc.

3005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

PROCLAIM-CX-072: Analysis of patients with advanced solid tumors receiving long-term treatment with CX-072, a PD-L1 probody therapeutic, as a single agent or in combination with ipilimumab. *First Author: Fiona Thistlethwaite, The Christie NHS Foundation Trust and University of Manchester, Manchester, United Kingdom*

Background: Monotherapy with immune checkpoint inhibitors (ICIs) has demonstrated efficacy in many cancers. Combining ICIs PD-L1 + CTLA-4 enhanced efficacy but worsened toxicity vs monotherapy; therefore, CTLA-4 dose modifications are often needed, despite a dose-response effect having been shown for efficacy. CX-072 is an investigational PD-L1 PROBODY therapeutic that is preferentially activated in the tumor microenvironment (TME); localized activation may reduce immune-related AEs (irAEs). PROCLAIM-CX-072-001 identified 10 mg/kg Q2W (Mono10) as the recommended monotherapy dose. Here we provide data for Mono10 and for dose escalation of CX-072 in combination with IPI (Combo), with a focus on long-term ($\geq$6 mo) therapy. **Methods:** Mono10 was evaluated in multiple tumor types. Combo doses evaluated were CX-072 0.3–10 mg/kg and IPI 3–10 mg/kg Q3W. Patients (pts) with $\geq$6 mo treatment duration ($\geq$6M-TD) were compared to those with $<$ 6 mo of treatment ($<$ 6M-TD) as of November 30, 2019. **Results:** Disease control rates (DCR = CR+PR+SD) were 41% for Mono10 (n = 47 of 114; 10 PRs) and 37% for Combo (n = 10 of 27; 1CR + 4 PRs (1CR and 3PRs at 3 mg/kg IPI [IPI3]). Additional results are shown in the table. No treatment-related adverse events (TRAEs) led to death. The most common reason for discontinuation (dc) in all groups was disease progression. **Conclusions:** CX-072 monotherapy demonstrated durable responses consistent with activation of the PROBODY therapeutic in the TME. The safety profile supports the tolerability of CX-072 as monotherapy and when combined with IPI3. CX-072 + IPI3 demonstrated activity in heavily pretreated pts with various tumors. The safety profile of the combination of CX-072 with IPI3 compares favorably to historical data (grade $\geq$3 TRAEs 55% and leading to dc in 36%; Larkin J, et al. *N Engl J Med.* 2015;373:23-34). CX-072 + IPI3 is being explored in a phase 2 study in 2L melanoma Clinical trial information: NCT03993379. Research Sponsor: CytomX Therapeutics, Inc.

	Mono10 < 6M-TD (n = 86)	Mono10 ≥6M-TD (n = 28)	Combo < 6M-TD (n = 21)	Combo ≥6M-TD (n = 6)
Median follow-up (wk)	14.5	46.4	13.0	83.6
Median age (y)/no. prior treatments	60/2	60/2	56/3	55/4
PD-L1+ expression (%)	42	54	24	17
ECOG PS 0 (%)	33	57	43	33
Grade ≥3 TRAEs (%)	9	14	33	33
G3+ irAEs (%)	3	0	29	0
Treatment related serious AEs (%)	5	7	33	17
TRAEs leading to dc (%)	2	0	19	0

3006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Durvalumab and tremelimumab in combination with FOLFOX in patients with RAS-mutated, microsatellite-stable, previously untreated metastatic colorectal cancer (MCRC): Results of the first intermediate analysis of the phase Ib/II MEDETREME trial. *First Author: François Ghiringhelli, Department of Medical Oncology, Center GF Leclerc, Dijon, France, Dijon, France*

Background: Single agent PD-1/L1 inhibition are not effective in metastatic colorectal cancer (MCRC) with microsatellite stable tumors. However, signal of efficacy was shown using combo therapy of anti-PD-L1 and anti CTLA-4 in multitreated patients. FOLFOX regimen could induced immunogenic cell death and elimination of myeloid derived suppressor cells (MDSCs) thus leading to a potential positive effect on antitumor immune response. **Methods:** This is a single arm exploratory investigator-initiated trial planned to include 57 pts to receive mFOLFOX6 (6cycles) in combination with durvalumab (150mg/q2W) and tremelimumab (75mg/q4W). After 6 cycles of chemotherapy, patients are treated with durvalumab untils progression. Primary endpoint is 6 months' progression-free survival rate. Secondary endpoints are response rate, tolerability and translational research evaluating tissue and blood immune parameter. Upon Simon's design an efficacy intermediate analysis was planned after the 16th patient has passed 6 months. **Results:** As of 1st of January 2020 the 55/57 pts were enrolled and treated with the MEDETREME regimen at 8 French sites. The intermediate efficacy analysis was conducted on the 1st of January after a median of 13.4 months of treatment. The following adverse events were noted: asthenia (81.25%), neuropathy (87.5%), diarrhea (56.25%) and neutropenia (62.5%). Notable grade 3/4 (CTC AE 4.03) include asthenia (18.75%) diarrhea (12.5%) neutropenia (50%) and elevated blood pressure (25%). Most of adverse events were related to chemotherapy. It has been noted one cytolysis grade 3, one thyroid dysfunction grade 3 and one hypophysitis grade 3 related to immunotherapy. Median PFS was not reached. Progression free survival at 6 months was observed in 10/16 pts (62,5%) given 5 CR, 5 PR and 4 SD. Updated translational data will be presented at the meeting. **Conclusions:** The interim safety analysis has supported safety and efficacy of the MEDITREME regimen in first- line MCRC. Finally, results will be presented after maturation of follow up. Clinical trial information: NCT03202758. Research Sponsor: Astra-Zeneca.

3007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Association of LRP1B pathogenic genomic alterations with favorable outcomes with immune checkpoint inhibitors across multiple tumor types. *First Author: Landon Carter Brown, Duke Cancer Institute, Durham, NC*

Background: Low-density lipoprotein receptor-related protein 1b (LRP1b) is a putative tumor suppressor and one of the most frequently altered genes in cancer. Our prior single-center work suggested that *LRP1B* alterations may enrich for responses to immune checkpoint inhibitors (ICI) in solid tumors including prostate cancer; however, validation of these findings is needed. **Methods:** We conducted a multicenter, retrospective analysis of patients with *LRP1B* alterations (on tissue-based next-generation sequencing panels) treated with ICI at Duke, Johns Hopkins (JHU), and University of Michigan (UM). The primary objective was to assess the association between objective response rate (ORR) to ICI and pathogenic *LRP1B* alterations, defined as deletions or truncating alterations, when compared with *LRP1B* variants of undetermined significance (VUS), defined as missense mutations not predicted to be pathogenic in COSMIC. Missense changes with a COSCMIC FATHMM score of $>$ 0.8 were categorized separately as likely pathogenic. Summary statistics, ORR, progression free survival (PFS), and overall survival (OS) were calculated. **Results:** 101 patients (44 Duke, 35 JHU, 22 UM) with *LRP1B* alterations were treated with ICI. Median age was 61 (range 32-82). The most common tumor types by alteration (pathogenic or likely pathogenic/VUS%) were lung (33/47%), GI (17/13%), prostate (11/7%), sarcoma (2/9%), melanoma (11/0%), and others (26/24%). 93% of patients received single-agent PD-(L)1 inhibition. The ORR for patients with either pathogenic/likely pathogenic alterations, or VUS alterations was 57% and 18%, respectively. After excluding MSI-high or TMB-high ($>$ 10 mut/Mb) tumors, ORR was 14/25 (56%) and 6/36 (17%), respectively. Pathogenic or likely pathogenic *LRP1B* alterations were associated with longer PFS (HR 0.39, 95% CI 0.24-0.63) and OS (HR 0.58, 95% CI 0.36-0.95). **Conclusions:** This multicenter study shows impressive and durable objective response rates to ICI for patients harboring pathogenic *LRP1B* alterations when compared to those with *LRP1B* VUS, independent of TMB/MSI status. Further mechanistic insights and prospective validation studies are warranted. Research Sponsor: None.

	Pathogenic or likely pathogenic (n = 46)	VUS (n = 55)
CR n, (%)	1 (2%)	2 (4%)
PR n, (%)	25 (54%)	8 (15%)
SD n, (%)	11 (24%)	16 (29%)
PD n, (%)	8 (17%)	24 (44%)
NE n, (%)	1 (2%)	5 (9%)
Median PFS (95% CI)	14.1 mo (6.4-26.3)	3.4 mo (2.8-4.8)
Median OS (95% CI)	23.0 mo (11.0-27.3)	8.9 mo (8.0-18.0)
TMB-high n, (%)	23 (50%)	19 (35%)
MSI-high/MSI available n, (%)	5/45 (11%)	1/43 (2%)

3008 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Correlation of pathogenic POLE mutations with clinical benefit to immune checkpoint inhibitor therapy. *First Author: Benjamin Garmezy, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Mutations in DNA polymerase epsilon (*POLE*) may induce DNA replication errors, increasing neoantigen load and potentially enhancing clinical benefit to immune checkpoint inhibitors (ICI). We present a clinicopathologic analysis of patients (pts) with advanced cancers harboring *POLE* mutations and their response to ICI therapy at MD Anderson Cancer Center. **Methods:** We used targeted exome sequencing via CLIA-certified next generation sequencing assays to identify pts with *POLE*-aberrant tumors and their co-occurring mutations. The pathogenicity of each *POLE* mutation was annotated utilizing InterVar and ClinVar databases. Chi-square analysis was performed. **Results:** Tumors from 12,947 pts were analyzed and 448 (3.5%) pts had a mutation or copy number variation in *POLE* (3.5%), comparable to the TCGA PanCancer Atlas (4.0%). Clinical data were available for 293 pts; the most common cancers were colorectal (14.7%), non-small cell lung (13.7%), cholangiocarcinoma (13.3%) and melanoma (10.2%). There were 267 unique co-mutations, including *KRAS* (23.0%), *ARID1A* (21.5%), *BRCA2* (18.7%), *ATM* (18.4%), *CDKN2A* (17.5%), *BRAF* (15.3%), *EGFR* (15.3%), *ATRX* (12.6%), *CREBBP* (11.7%), *APC* (11.3%), *ATR* (11.0%), *BRCA1* (11.0%) and *CDK12* (10.4%). *POLE* variants were annotated in all pts: pathogenic/likely pathogenic (n = 34, 11.6%), benign/likely benign (61, 20.8%), and variant of unknown significance (198, 67.6%). 104 (35.8%) of 293 pts with *POLE* mutations received PD-1/L1 inhibitors as monotherapy or in combination. 93 (88.4%) of 104 pts were evaluable for response: Radiological CR 4.3% (n = 4), PR 26.9% (n = 25), SD 22.6% (n = 21), PD 46.2% (n = 43), for a clinical benefit rate (CR + PR + SD) of 53.8%. Pathogenic status of *POLE* mutation was associated with clinical benefit to PD-1/L1 inhibitors ($p = 0.04$). TMB ($p = 0.44$), PD-L1 ($p = 0.11$), and MSI ($p = 0.66$) status were not associated with pathogenic status. MSI-H status was not over-represented in pts with ICI clinical benefit ($p = 0.36$). **Conclusions:** Pathogenic *POLE* mutations were associated with clinical benefit to ICI therapy. Further studies are warranted to validate *POLE* mutations as a predictive biomarker. Multiple co-occurring DNA damage response mutations were found, which may contribute to ICI clinical benefit. Research Sponsor: None.

3010 Poster Discussion Session; Displayed in Poster Session (Board #74), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Combined PD-1 inhibition (Pembrolizumab) and CCR5 inhibition (Maraviroc) for the treatment of refractory microsatellite stable (MSS) metastatic colorectal cancer (mCRC): First results of the PICCASSO phase I trial. *First Author: Georg Martin Haag, Department of Medical Oncology, National Center for Tumor Diseases, University Hospital Heidelberg, Heidelberg, Germany*

Background: Checkpoint inhibition using PD-1/PD-L1 inhibitors does not show clinically relevant activity in MSS/pMMR (Mismatch Repair Proficient) colorectal cancer. Previous work showed that inhibition of CCR5 (C-C chemokine receptor type 5) leads to a macrophage re-polarization towards M1 macrophages within the tumor microenvironment which directly affects immune cell infiltrates. The current phase I trial explores a combined modification of the innate immune system (by CCR 5 blockade) and the adaptive immune system (by PD-1 inhibition) in the treatment of MSS CRC. **Methods:** 20 patients with metastatic MSS/pMMR colorectal cancer with failure of fluoropyrimidines, oxaliplatin, irinotecan, VEGF antibodies and EGFR antibodies (in ras WT patients) received pembrolizumab 200 mg q21d and maraviroc 300 mg bid cont. for 8 cycles, followed by pembrolizumab monotherapy for a maximum of 24 additional cycles. Imaging was performed every nine weeks (RECIST and irRECIST criteria). Primary endpoint was the feasibility rate (rate of patients receiving the protocol treatment during the core treatment without special event: treatment-related Grade $\geq$ 3 immune-related abnormalities, treatment-related Grade $\geq$ 4 AEs or any toxicity-related premature withdrawal of treatment). Secondary endpoints included safety/toxicity, ORR, PFS and OS. **Results:** 20 patients were enrolled. The median number of applied cycles was 3.5 for pembrolizumab and 3.5 for maraviroc. Two patients completed the core treatment period with pembrolizumab and started maintenance treatment. The feasibility rate was 94.7% (90% CI 77.4 to 99.7%), with one patient experiencing a special event. Except this grade 4 event (hyperglycemia) no $\geq$ 3 treatment-related toxicities were observed. According to irRECIST criteria one patient showed a partial response and one a stable disease as best response, resulting in an irDCR of 10.5%. Median PFS according to irRECIST was 2 months (CI 95%, 2 to 3), median OS 9 months (CI 95%, 6 to 20). **Conclusions:** Therapy with pembrolizumab and maraviroc was feasible and showed a beneficial toxicity pattern. Clinical activity in MSS CRC patients was limited, however prolonged disease stabilizations were observed in single patients and overall survival was higher than expected in this heavily pretreated population. Clinical trial information: NCT03274804. Research Sponsor: Merck Sharp & Dohme.

3011 Poster Discussion Session; Displayed in Poster Session (Board #75), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Interim subgroup analysis for response by PD-L1 status of CLASSICAL-Lung, a phase Ib/II study of pepinemab (VX15/2503) in combination with avelumab in advanced NSCLC. *First Author: Michael Rahman Shafique, Department of Thoracic Oncology, Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Antibody blockade of semaphorin 4D (SEMA4D, CD100) promotes tumoral dendritic cell and CD8+ T cell infiltration and reduces function and recruitment of immunosuppressive myeloid cells. Importantly, these mechanisms to overcome immune exclusion and suppression have been shown to complement immune checkpoint therapies in preclinical models. Pepinemab is an IgG4 humanized monoclonal antibody targeting semaphorin 4D. The CLASSICAL-Lung clinical trial tests the combination of pepinemab with avelumab to couple T cell activation via checkpoint inhibition with beneficial modifications of the immune microenvironment via pepinemab. **Methods:** This phase 1b/2, single arm, first-in-human study is designed to evaluate the safety, tolerability and efficacy of pepinemab with avelumab in 62 patients (pts) with advanced (stage IIIB/IV) non-small cell lung cancer (NSCLC), including immunotherapy-naïve (ION) pts and pts whose tumors progressed following immunotherapy (IOF). **Results:** Among 21 evaluable ION pts, 5 experienced partial response (PR), 3 pts had clinical benefit $\geq$ 1 year, and the disease control rate (DCR) is 81%. Pts enrolled in this study were observed to have lower PD-L1 expression relative to prior single agent studies (likely due to approval of pembrolizumab for first line therapy). We, therefore, performed subgroup analysis for response by PD-L1 status. The objective tumor response (ORR) in the PD-L1 negative and low population ($<$ 80% TPS by Dako 73-10 assay) appears to be approximately 2-2.5 fold greater with combination therapy than with historical single agent immune checkpoint controls. Notably, 97% of pts who experienced PR or SD were reported to have tumors with negative or low PD-L1 expression. Among 29 evaluable IOF pts, the combination resulted in 59% DCR, including 2 PR and 7 patients with durable clinical benefit of $\geq$ 23 weeks. Biomarker analysis of pre- and on-treatment biopsies confirmed increased $CD8^+$ T cell density correlating with response. Surprisingly, analysis of myeloid-derived suppressor cells (MDSCs) revealed a relative paucity of these cells in pretreatment NSCLC biopsies as compared to other cancer indications such as HNSCC. **Conclusions:** This trial is nearing completion with only 5 of 62 subjects remaining on study. Preliminary data suggest the combination is well tolerated and shows signs of increased antitumor activity, particularly in PD-L1 negative or low tumors. Updated clinical response data and immunophenotypic analyses will be presented. Clinical trial information: NCT03268057. Research Sponsor: Vaccinex, (Rochester, NY), and from Merck KGaA as part of the alliance between Merck KGaA, (Darmstadt, Germany) and Pfizer, Inc, (New York, NY, USA).

3012 Poster Discussion Session; Displayed in Poster Session (Board #76), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Long-term follow-up of anti-CD19 CAR T-cell therapy for B-cell lymphoma and chronic lymphocytic leukemia. *First Author: Kathryn Cappell, National Institute of Health, Bethesda, MD*

Background: T cells expressing anti-CD19 chimeric antigen receptors (CARs) can cause complete remissions of relapsed lymphoma. We conducted the first clinical trial of anti-CD19 CAR T cells to show responses against lymphoma. This CAR was later developed as axicabtagene ciloleucel. Here, we aimed to assess the long-term durability of remissions and the long-term adverse effects after anti-CD19 CAR T-cell therapy. **Methods:** Between 2009 and 2015, we treated 43 patients with anti-CD19 CAR T cells preceded by conditioning chemotherapy of cyclophosphamide plus fludarabine (NCT00924326). Three patients were re-treated for a total of 46 CAR T-cell treatments. Twenty-eight patients had aggressive lymphoma (diffuse large B-cell lymphoma or primary mediastinal B cell lymphoma), eight patients had low-grade lymphoma (five with follicular lymphoma and 1 each with splenic marginal zone lymphoma, mantle cell lymphoma, and unspecified low-grade non-Hodgkin lymphoma), and seven patients had chronic lymphocytic leukemia (CLL). Patients were treated in three cohorts that differed in the CAR T-cell production process and conditioning chemotherapy dose. **Results:** Of the 43 treated patients, 63% had chemotherapy-refractory lymphoma. Patients had received a median of 4 previous lines of therapy. The median CAR^+ T cell dose per kilogram was 2X10^6. The overall remission rate was 76% with 54% complete remissions (CR) and 22% partial remissions (PR). Patients with CR had higher median peak blood CAR levels (86 CAR^+ cells/μL) than those who did not have CR (16 CAR^+ cells/μL, $P = 0.0041$). Long-term adverse effects were rare except for B-cell depletion and hypogammaglobulinemia, which both improved over time. **Conclusions:** This is the longest follow-up study of patients who received anti-CD19 CAR T cells. Anti-CD19 CAR T cells cause highly durable remissions of relapsed B-cell lymphoma and CLL, and long-term adverse effects of anti-CD19 CAR T cells were rare and usually mild. Clinical trial information: NCT00924326. Research Sponsor: U.S. National Institutes of Health.

	All Patients	Aggressive lymphoma (n = 28)	Low-grade lymphoma (n = 10)	CLL (n = 8)
Median CAR^+ T cell dose per kg	2 X 10^6	2 X 10^6	3 X 10^6	3.5 X 10^6
Chemotherapy refractory (%)	63%	89%	20%	25%
Median prior lines of therapy (Range)	4 (1 to 12)	4 (2 to 12)	4 (1 to 7)	4 (1 to 7)
Overall Response (%)	76%	68%	90%	88%
Complete Response (%)	54%	50%	60%	63%
Median duration of complete response in months (Range)	58 (6 to 113)	50 (6 to 83)	60 (19 to 113)	70 (18 to 99)
Median event-free survival 45 evaluable treatments	60 (1-114)	15 (1 to 85)	66 (1-114)	41 (5-101)

3013 Poster Discussion Session; Displayed in Poster Session (Board #77), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Safety and efficacy results of GC027: The first-in-human, universal CAR-T cell therapy for adult relapsed/refractory T-cell acute lymphoblastic leukemia (r/r T-ALL). *First Author: Xinxin Wang, Gracell Biotechnologies Co., Ltd., Shanghai, China*

Background: Patients with r/r T-ALL usually have high relapse and mortality rates. Due to shared common surface antigen and potential contamination by malignant cells, development of autologous CAR-T therapies for r/r T-ALL has been lagged, regardless of the costly and lengthy process of autologous CAR-T production. Through targeting CD7, a common T cell antigen highly expressed in >95% T-ALL samples, universal CAR-T product GC027 has been developed using lentivirus and CRISPR/Cas9 system with demonstrated anti-leukemia ability in a murine xenograft model. **Methods:** Preliminary safety, anti-leukemic activity and expansion kinetics of GC027 are being evaluated in a single-arm, open-label, multi-center, prospective study for treating adult patients with r/r T-ALL. To date, a total of 5 patients (age 19-38 yrs, median 24 yrs) were enrolled with marrow tumor load 4-80.2% (median prior lines 5). All 5 pts have received a 6-day enhanced preconditioning chemotherapy followed by a single infusion of GC027. No patient was bridged to HSCT. Adverse events, disease response, and expansion kinetics were evaluated in this study. **Results:** As of Feb. 6, 2020, 5 pts had received a single dose of GC027, including 1 at $0.6x10^7$/kg, 3 at $1x10^7$/kg, 1 at $1.5x10^7$/kg. 3 pts achieved MRD negative complete responses (MRD- CR) at D28 evaluation and remained MRD- at follow-up re-evaluations (161, D118, 61, respectively) without bridging to HSCT. 1 pt just achieved D28 MRD- CR at time of submission. 1 pt achieved MRD+ CR at D14, but his disease progressed at D29 and deceased due to relapse. In all 4 pts with MRD- CR, peak expansions of GC027 in peripheral blood were observed between week 1-2, analyzed by flow cytometry and Q-PCR. Grade 3 cytokine release syndrome (CRS) occurred in 4 pts and Grade 4 CRS occurred in 1 pt (ASBMT Consensus Grading). CRS symptoms were manageable and resolved after treatment and supportive care. None developed neurotoxicity or GvHD. One had prolonged cytopenia due to fungal infection and required antifungal therapy. **Conclusions:** With a single infusion of GC027, 80% of the patients had robust CAR-T cell expansion and achieved persistent MRD- CR without using any biologics as part of the preconditioning therapy or bridging to HSCT. The first-in-human, universal CAR-T therapy for r/r T-ALL, GC027 has demonstrated superior clinical efficacy and induced deep response in patients with acceptable safety profile. The trial enrollment is ongoing and updated data will be presented at the meeting. Clinical trial information: ChiCTR1900025311. Research Sponsor: Gracell Biotechnologies Co., Ltd.

3014 Poster Discussion Session; Displayed in Poster Session (Board #78), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Feasibility and preliminary safety and efficacy of first-in-human intraperitoneal delivery of MCY-M11, anti-human-mesothelin CAR mRNA transfected into peripheral blood mononuclear cells, for ovarian cancer and malignant peritoneal mesothelioma. *First Author: Christina M. Annunziata, Women's Malignancies Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD*

Background: MCY-M11 is a mesothelin-targeting chimeric antigen receptor (CAR) therapy made by a non-viral, mRNA-based platform, for rapid (< 1 day) CAR manufacturing. We are conducting a phase I dose escalation trial in ovarian cancer and malignant peritoneal mesothelioma (MPM) (NCT03608618). **Methods:** MCY-M11 are fresh, non-expanded, autologous peripheral blood mononuclear cells (PBMCs) transfected by flow electroporation with mRNA encoding a human anti-mesothelin CAR. Following a 3+3 design, patients are treated in dose level (DL) escalating cohorts (DL1 1.0×10^7, DL2 5.0×10^7, DL3 1.0×10^8, DL4 5.0×10^8 cells/dose), in one cycle of weekly x 3 doses, intraperitoneal (ip) without preconditioning chemotherapy. **Results:** By January 2020, CP-M11-101 study successfully completed DL1 and DL2 without safety concerns. Based on 11 patients treated in DL1, DL2 and DL3, ip infusion of MCY-M11 is safe and well tolerated. No infusion-related adverse events and no dose limiting toxicities (DLTs) have occurred. No neurotoxicity has been observed. Most reported treatment-related adverse events have been Grades 1-2 per NCI CTCAE. One patient in DL3 presented with G2 pericarditis, fever and transient neutropenia clinically assessed as related SAEs, that resolved without further complications. These events were assessed as on-target off-tumor effects and possibly G1 cytokine release syndrome (CRS). Two unrelated SAEs (G2 confusion in a patient in DL2; G3 enterocutaneous fistula in a patient in DL3) were reported. These 2 patients have been replaced as they did not complete the evaluation period (3 weekly infusions and the DLT 43 day follow up). There have been no treatment-related discontinuations or deaths. Three patients in DL2 showed stable disease (SD) by RECIST 1.1 at the end of the DLT period. Of them, 1 completed the study and did not participate in additional follow up, 1 remained in SD 6 months, and 1 remained in SD 2 months. In DL3, 1 patient remains in SD at 2 months, and evaluation is pending for the other 2 patients. Enrollment is ongoing. **Conclusions:** Feasibility of 1-day manufacturing of MCY-M11 for ip delivery is demonstrated. Treatment has been safe. Initial SD observed in DL2 and DL3 with one-cycle infusions is encouraging and supports exploration of additional strategies such as the addition of preconditioning chemotherapy and multiple cycles to increase efficacy. Clinical trial information: NCT03608618. Research Sponsor: MaxCyte Inc.

3015 Poster Discussion Session; Displayed in Poster Session (Board #79), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Early safety from a phase I, multicenter, open-label clinical trial of talimogene laherparepvec (T-VEC) injected (inj) into liver tumors in combination with pembrolizumab (pem). *First Author: J. Randolph Hecht, David Geffen School of Medicine, University of California, Los Angeles, CA*

Background: T-VEC is a genetically modified, oncolytic HSV-1 designed to selectively replicate within tumors and produce GM-CSF to enhance systemic antitumor immunity. The safety and efficacy of T-VEC in treatment of advanced melanoma has been demonstrated as monotherapy and in combination with checkpoint inhibitors (Andtbacka *JCO* 2015, Chesney *JCO* 2017, Ribas *Cell* 2017). T-VEC has also demonstrated tolerable safety for intrahepatic inj (Hecht *JCO* 2018). This phase 1b, multicenter, open-label, dose escalation study (NCT02509507) evaluates the safety of intrahepatic inj of T-VEC in combination with intravenous (IV) pem in patients (pts) with hepatocellular carcinoma (HCC) or liver metastases (mets). **Methods:** The primary objective is to assess the maximum tolerated concentration (MTC) of T-VEC inj into liver tumors based on the incidence of dose-limiting toxicities (DLTs). DLT rate was evaluated with the mTPI up-and-down design. Eligible pts were ≥ 18 years, had progressive HCC or breast cancer, colorectal cancer, gastroesophageal cancer, melanoma, non-small cell lung cancer, or renal cell cancer liver mets, with measurable liver tumors suitable for inj. This dose escalation study comprised 2 groups: A (non-HCC) and B (HCC). T-VEC was given initially at 10^6 plaque-forming units (PFU)/mL followed by up to 4 mL of 10^7 PFU/mL (cohort 5) or 10^8 PFU/mL (cohort 6) every 21 (±3) days (Q21D). Inj volume was based on lesion size. Pem (200 mg) was given IV Q21D. **Results:** Here we report on three cohorts: A5 (10^7 PFU/mL T-VEC + pem), A6 (10^8 PFU/mL T-VEC + pem), and B5 (10^7 PFU/mL T-VEC + pem). Twenty-nine pts were treated: 7 in A5, 17 in A6, 5 in B5. Median age was 61 years (range: 30, 76). Median number of inj was 4 and median treatment duration was 88 days. One DLT of cholestatic hepatitis was observed out of 6 DLT evaluable pts in cohort A5. No DLTs were observed in cohort A6 and B5. MTC was 10^8 PFU/mL in non-HCC patients; exploration of MTC in the HCC population is ongoing. Treatment-emergent adverse events (TEAEs) were consistent across cohorts. The most common treatment-emergent treatment-related adverse events (TETRAE) were pyrexia (79.3%), chills (37.9%), and nausea (37.9%). Eight pts (27.6%) had grade 3/4 TEAEs: 2pts (6.9%) related to the combination therapy and the rest not related to treatment. No fatal AEs were observed. **Conclusions:** T-VEC intrahepatic inj in combination with IV pem at standard doses has thus far been demonstrated as feasible and tolerable to continue further investigation. Clinical trial information: NCT02509507. Research Sponsor: Amgen Inc.

3016 Poster Discussion Session; Displayed in Poster Session (Board #80), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Pharmacodynamic, safety, and efficacy results of a phase I/II trial of intratumoral INT230-6 alone (IT-01) or in combination with pembrolizumab (PEM) (Keynote A10) in patients with advanced solid tumors. *First Author: Jacob Stephen Thomas, USC Norris Comprehensive Cancer Center, Los Angeles, CA*

Background: INT230-6 is comprised of cisplatin (CIS), vinblastine (VIN) and an amphiphilic penetration enhancer which facilitates dispersion throughout tumors and diffusion into cancer cells when given IT. Preclinical experiments show strong synergy with a PD1 antibody. **Methods:** Solid tumors pts that progressed on standard treatment were enrolled. INT230-6 dose was set by tumor volume, injected Q2weeks x 5. Escalation occurred by increasing number of tumors injected, loading per tumor, and total dose. In another arm, PEM (200mg IV Q3weeks) was combined with INT230-6. Patients were monitored for safety weekly while on INT230-6. Blood and tumors were assessed for PK and PD. **Results:** 46 pts (17 unique cancer types) were enrolled in the monotherapy arm and 4 pts in the PEM combo arm with a median of 3 prior treatments. Doses from 0.3 ml up to-160 ml of INT230-6 (80 mg CIS and 16mg of VIN) were injected. PK results indicate 95% of the drugs are retained in the tumor when compared to historical IV dosing. No dose limiting toxicity was reported. Two pts experienced drug-related SAE's of tumor pain. The most frequent treatment-related AEs were: pain at injected site (48%), fatigue (40%) and nausea (33%). Most AE's were grade 1 and 2, 17% were grade 3, and none ≥ grade 4. Several injected and non-injected tumors had > 30% decreases in diameter. Assessments revealed substantial reductions in tumor volume (> 50%). Stable pts had a median increase of 50% in circulating CD4 and CD8 T-cells, while PD subjects showed decreases in circulating T-cells ($p < 0.05$). Dose-response suggests that monotherapy subjects receiving > 50% of tumors injected at dose/tumor volume ratio of > 1:4 (target dosing), predicts for prolonged SD with 88%(7/8) having SD ≥ 4mo, correlating with reduced tumor viability on IHC, and increase in tumor-infiltrating lymphocytes (TIL's). **Conclusions:** Proof of concept was demonstrated that INT230-6 delivers high drug doses into the tumor without systemic exposure and typical cytotoxic AEs. Systemic and local immune activation was observed. INT230-6 was safe and well tolerated in > 175 deep tumor injections with tumor burden reduction in injected and non-injected tumors (an abscopal effect). Patients who received target dosing often had prolonged disease control post treatment. Updated safety, response and biomarker data from the monotherapy and PEM combo arm will be presented. Clinical trial information: 03058289. Research Sponsor: Intensity Therapeutics.

3017 Poster Discussion Session; Displayed in Poster Session (Board #81), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase I/II study to evaluate systemic durvalumab + intraperitoneal (IP) ONCOS-102 in patients with peritoneal disease who have epithelial ovarian (OC) or metastatic colorectal cancer (CRC): Interim phase I clinical and translational results. *First Author: Dmitriy Zamarin, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Metastasis to the peritoneal cavity is associated with end-stage disease in many cancers, including OC and CRC, both of which exhibit poor responses to checkpoint inhibitors. Locoregional treatment with oncolytic viruses may be used to improve the efficacy of checkpoint inhibitors at both treated and distant tumor sites. This study evaluates the combination of IP-administered ONCOS-102, an oncolytic adenovirus encoding for granulocyte macrophage colony stimulating factor (GMCSF), with systemic durvalumab, an anti PD-L1 antibody, in patients with peritoneal disease who have histologically confirmed OC or metastatic CRC and have failed prior standard therapies. **Methods:** This ongoing Phase 1/2, open-label study (NCT02963831) evaluates safety and antitumor/biologic activity of durvalumab (1500 mg IV, every 4 weeks x 12) + ONCOS-102 (IP, weekly x 6); cyclophosphamide is given pre first ONCOS-102 dose. Phase 1 uses a 3+3 design to evaluate the ONCOS-102 dose (1 or 3 x 10^{11} VP) to be given with durvalumab. Phase 2 evaluates the activity of the combination using Simon's 2-stage MINIMAX design. Safety, response rate by RECIST 1.1, and immunological effects in tumors were evaluated for Phase 1; the current abstract reports on the phase 1 results. **Results:** Enrollment opened 7 Sep 2017; data cutoff, 1 Nov 2019. There were 17 patients treated in Phase 1: 8 CRC, 9 ovarian; 94% female; median age, 56 [37-77] years; ECOG PS0, 47%; ECOG PS1, 53%. There were no DLTs. Grade 3 treatment-related AEs included hypokalemia (n = 2); anemia, myocarditis, increased GGT, and influenza like illness (n = 1 each). There were 4 deaths due to PD. One patient had durable confirmed partial response and remains on treatment $>$ 1 year; 4 patients had stable disease as best overall response. Two patients remained on treatment at data cutoff. Analysis of pre- and on-treatment tumor biopsies revealed changes in the tumor-infiltrating immune cells and PD-L1 expression, including an increase in tumor-infiltrating CD8 T cells in 5 of 11 evaluable patients. **Conclusions:** Combination of durvalumab and IP ONCOS-102 was safe, and no DLTs were observed. Preliminary analyses demonstrate evidence of biologic and clinical activity. Phase 2 enrollment is ongoing. Clinical trial information: NCT02963831. Research Sponsor: Ludwig Institute for Cancer Research, Cancer Research Institute, Pharmaceutical/Biotech Company.

3018 Poster Discussion Session; Displayed in Poster Session (Board #82), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Impact of radiotherapy on risk of adverse events in patients receiving immunotherapy: A U.S. Food and Drug Administration pooled analysis. *First Author: Mitchell Steven Anscher, U.S. Food and Drug Administration, Silver Spring, MD*

Background: Immune checkpoint inhibitors (ICIs) are widely used in the treatment of multiple advanced malignancies. Radiotherapy (RT) has been used in combination with ICIs to activate tumor-specific T cell responses, and RT also promotes non-specific acute and chronic inflammatory responses both locally and systemically. More than 50% of patients receive RT at some point during their course of cancer therapy, and relatively little information is available pertaining to the impact of RT, if any, on the risk of adverse events (AEs) in patients receiving ICIs. **Methods:** Pooled data from prospective trials of ICIs submitted to the FDA in initial or supplemental BLAs or NDAs through 12/2019 were included (N=66). Trials from applications that were withdrawn or not approved were not included. Patients were subdivided by whether or not radiotherapy was administered at any time during the course of their cancer treatment. AEs common to both ICI treatment and RT were identified to focus on the following reactions: neutropenia, thrombocytopenia, colitis, hepatitis, pneumonitis, and myocarditis. Descriptive statistics were used to examine AEs associated with the use of radiation and ICIs. **Results:** A total of 25,836 patients were identified, of which 9087 (35%) received RT and 16,749 (65%) did not. Radiation was associated with similar rates of AEs overall with numerically higher hematologic toxicities and pneumonitis and numerically lower colitis, hepatitis and myocarditis (Table). Patients receiving RT were more likely to experience Grade 3-5 hematologic toxicities compared to those not receiving RT. **Conclusions:** To our knowledge, this is the largest report of AE risk associated with the use of radiation and ICIs. Our results show that the incidence of hematologic toxicity and pneumonitis in patients receiving RT may be slightly higher. Analysis to determine comparability of baseline demographic characteristics, comprehensive AE profile, and timing of RT is underway. Research Sponsor: None.

Description of toxicity in patients treated with ICI with or without RT.

	Incidence -risk All Grades (%)		Grades 3-4 (%)		Grade 5 (%)	
Toxicity	**RT (n=9,087)**	**No RT (n=16,749)**	**RT**	**No RT**	**RT**	**No RT**
Neutropenia	8.4	5.8	6.0	3.9	0	0
Thrombocytopenia	6.9	3.8	3.6	1.4	0	0.01
Pneumonitis	5.0	3.1	1.0	0.9	0.13	0.11
Colitis	2.0	3.0	1.2	1.7	0	0.01
Hepatitis	0.6	0.9	0.4	0.7	0	0.02
Myocarditis	0.03	0.06	0.01	0.05	0.02	0.02

3020 Poster Discussion Session; Displayed in Poster Session (Board #84), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The preliminary efficacy and safety data of KN046 in patients failed on prior immune checkpoint inhibitors therapy. *First Author: Hongyun Zhao, Department of Medical Oncology, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Sun Yat-sen University, Guangzhou, China*

Background: KN046 is a bispecific antibody that blocks PD-L1 and CTLA-4 by interaction with PD1 and CD80/CD86. KN046-CHN-001 (NCT03529526) is a, dose escalation and expansion phase Ia/Ib clinical trial in China. Here we reported safety, tolerability and preliminary efficacy in patients failed on prior immune checkpoint inhibiters (ICIs) treatment. **Methods:** Patients progressed on ICIs (including but not limited to antibodies targeting PD-1, PD-L1, OX40, et al) with pathologically confirmed solid tumor, ECOG 0-1, measurable lesion per RECIST v1.1, no immune-related adverse events (IRAEs) led to ICIs discontinuation, were enrolled and received intravenous KN046 treatment across four dose levels including 3.0 mg/kg (n = 3) and 5.0 mg/kg (n = 20) Q2W; and 5.0 mg/kg (n = 4), 300.0 mg flat dose (n = 2) Q3W. Safety and tolerability were assessed per NCI-CTCAE v5.0. Treatment-emergent AEs (TEAEs) and IRAEs were decided by investigators. Efficacy was evaluated by investigators per RECIST 1.1 every 6 weeks. **Results:** Twenty-nine who progressed on prior ICIs therapy were enrolled (25anti-PD-1 antibody; 3 anti-OX40 antibody; and 1 anti-CD137 antibody) and were included in the current analysis. Among 29 patients, 19 were nasopharyngeal cancer (NPC) and 9 were non-small cell lung cancer (NSCLC). The median duration of the exposure of KN046 was 12 weeks (range 2 to 40). Eleven patients remained on the treatment and 18 discontinued due to disease progression (n = 13), AE (n = 1), death (n = 1) and others (n = 3). Twenty-six (89.7%) patients experienced TRAEs of all grades and 2 (6.9%) experienced grade$\geq$3 TRAEs (1 grade 3 anemia and 1 grade 3 infusion-related reaction). The most common ($\geq$10%) TRAEs were pruritus (8, 27.6%), rash (8, 27.6%), asthenia (6, 20.7%), fatigue (6, 20.7%), pyrexia (5, 17.2%), infusion related reaction (4, 13.8%), alanine aminotransferase elevation (3, 10.3%) and white blood cell count elevation (3, 10.3%). Eleven (37.9%) patients experienced irAEs (with no grade$\geq$3). Objective responses were occurred in 3 (12.0%, 25 evaluable) patients, disease control rate was 52.0% (10 stable disease). Median progression free survival was 2.69 (95%CI 1.31,5.52) months. Median overall survival was not reached. PFS rates for 3 and 6 Months were 41.0% (95%CI 18.5, 62.5) and 21.9% (95%CI 4.6, 47.3). OS rates for 6 and 9 months were88% (95%CI 57.2, 97.1) and 58.7% (95%CI 8.3, 89.2), respectively. **Conclusions:** Overall, KN046 showed a favorable safety profile and promising clinical benefit in advanced solid tumor patients who failed on prior ICIs therapy. Clinical trial information: NCT03529526. Research Sponsor: Alphamab (Australia) Co Pty Ltd.

3021 Poster Session (Board #85), Fri, 8:00 AM-11:00 AM

Envafolimab (KN035) in advanced tumors with mismatch-repair deficiency. *First Author: Lin Shen, Peking University Cancer Hospital & Institute, Beijing, China*

Background: KN035 is a novel fusion protein of humanized anti-PD-L1 single domain antibody and human IgG1 Fc formulated for subcutaneous injection. This open-label phase II study evaluated the safety and antitumor activity of KN035 in patients with advanced microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) cancer. **Methods:** The study included patients aged $\geq$18 years with previously treated MSI-H/dMMR colorectal cancer (CRC) or other advanced solid tumors. MSI-H/dMMR status was assessed centrally for CRC and gastric cancer (GC) and locally for other tumors. KN035 was administered at 150 mg once weekly until progression, unacceptable toxicity, or withdrawal. Tumor assessments were every 8 weeks. The primary endpoint was the objective response rate per RECIST v1.1 by independent radiology review. The primary efficacy population (PEP) included patients with CRC who failed fluoropyrimidine (F), oxaliplatin (O), and irinotecan (I) plus those with advanced GC who had failed at least one prior systemic treatment. This was a planned interim analysis performed after the first 50 patients in the PEP had at least two on-study tumor assessments (PEP_i). **Results:** As of December 17, 2019, 103 patients with MSI-H/dMMR advanced cancers were enrolled at 25 centers in China. The PEP_i included 39 patients with CRC and 11 with GC, with a median follow-up of 7.5 months. The overall population included 65 patients with CRC (24 had prior therapy with F and O or I), 18 with GC, and 20 with other tumors, with a median follow-up of 6.7 months. The confirmed objective response rate was 30% (95% CI: 17.9%, 44.6%) in the PEP_i, 54.2% (95% CI: 32.8%, 74.4%) in the CRC patients who had prior therapy with F and O or I, and 34.0% (95% CI: 24.9%, 44.0%) in the overall population. Of patients who had an objective response at the interim analysis, 80% of those in the PEPi, 84.6% of CRC patients who had prior therapy with F and O or I, and 85.7% of those in the overall population were still responding at the time of data cutoff. Median progression-free survival was 6.6 months in both the PEP_i and the overall population. Median overall survival was not reached in either population. Fourteen (13.6%) patients had grade 3–4 treatment-related adverse events. No grade 5 treatment-related adverse events, pneumonitis, or colitis were reported. Local injection-site reactions, all grade 1 or 2, were reported in nine patients. **Conclusions:** Envafolimab demonstrated durable antitumor activity with a manageable safety profile in patients with previously treated advanced MSI-H/dMMR cancer. Clinical trial information: NCT03667170. Research Sponsor: 3D Medicines (Sichuan) Co. Ltd.

3022 Poster Session (Board #86), Fri, 8:00 AM-11:00 AM

Tumor microenvironment associated with increased pretreatment density of activated PD-1+ LAG-3+/− TIM-3− CD8+ T cells facilitates clinical response to axicabtagene ciloleucel (axi-cel) in patients (pts) with large B-cell lymphoma. *First Author: Jerome Galon, HalioDx, Marseille, France*

Background: Axi-cel is a US and EU-approved autologous anti-CD19 chimeric antigen receptor (CAR) T cell therapy for pts with relapsed/refractory large B cell lymphoma after ≥ 2 prior therapies. In ZUMA-1 (NCT02348216), the objective response rate was 83% (58% complete response rate; Locke et al. *Lancet Oncol*. 2019). T cell-related biology (Immunosign 21; Immunoscore) measured pretreatment in the tumor microenvironment (TME) was associated with response to axi-cel (Rossi et al. AACR 2018. #LB-016; Rossi et al. AACR 2019. #CT153). This expanded analysis characterized the pretreatment TME immune contexture and examined associations between immune cell subsets and response. **Methods:** In ZUMA-1, pts received axi-cel at a target dose of 2.0×10^6 CAR T cells/kg. Archival pretreatment tumor biopsy samples were analyzed by multiplex immunohistochemistry (Brightplex). Two panels were developed and applied to assess T cell (CD3, CD8, FoxP3, PD-1, LAG-3, TIM-3) and myeloid cell (CD11b, CD14, CD15, LOX1, S100A9, CD68) subsets (n = 14 total). The association between T cell and myeloid cell subset density, prespecified immune scores (Immunosign 21; Immunoscore), and objective response was evaluated. T test values were based on Brightplex analysis. **Results:** Pretreatment tumor biopsy samples from 18 pts were analyzed (14 objective responders and 4 nonresponders). The pretreatment TME comprised all major myeloid and T cell subsets, with diverse distribution across samples analyzed. The median TME density of monocytes (CD11b+ CD15− CD14+; 1215 cells/mm^2) and macrophages (CD68+; 530 cells/mm^2) was greater than that of the total CD8+ T cell subset (312 cells/mm^2). The pretreatment Immunosign 21 and Immunoscore scores associated positively with the density of all major T cell subsets and some myeloid subsets. The density of activated CD8+ T cells (PD-1+ LAG-3+/− TIM-3−) was most significantly associated with clinical response versus other T cell subsets. The density of nonactivated CD8+ T cells (PD-1− LAG-3− TIM-3−) and exhausted CD8+ T cells (PD-1+ LAG-3+ TIM-3+) were not significantly associated with response. Additional characterization of the immune contexture and correlative analysis of cell subsets will be presented. **Conclusions:** These results suggest that a TME associated with increased density of activated PD-1+ LAG-3+/− TIM-3− CD8+ T cells, measurable pretreatment, facilitates clinical response in pts post–axi-cel. Research Sponsor: Kite, a Gilead Company.

3023 Poster Session (Board #87), Fri, 8:00 AM-11:00 AM

Product characteristics and pharmacological profile of KTE-X19 in patients (pts) with relapsed/refractory (R/R) mantle cell lymphoma (MCL) in the phase II registrational ZUMA-2 trial. *First Author: Michael Wang, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: ZUMA-2 is a Phase 2 study evaluating KTE-X19, an autologous anti-CD19 CAR T cell therapy, in pts with R/R MCL (1 – 5 prior therapies, including a BTK inhibitor). In the primary efficacy analysis of ZUMA-2 (N = 60), the objective response rate was 93% (67% complete responses) and was generally comparable among high risk pts (Wang et al. ASH 2019 #754). CAR T cell levels in blood were associated with objective response (including minimal residual disease [MRD] negativity) and toxicity. Here, we describe a comparative analysis of KTE-X19 pharmacology profile in higher vs lower risk pts in ZUMA-2. **Methods:** Product attributes, CAR T cell and serum cytokine levels in blood, and their associations with clinical outcomes, were analyzed using previously described methods (Locke et al. *Mol Ther* 2017). MRD (10^{-5} sensitivity) was assessed by next-generation sequencing. Pharmacology data are reported for all 68 pts treated with KTE-X19 (2×10^6 cells/kg). **Results:** Manufactured KTE-X19 products showed a slight bias to CD8 and effector memory/effector phenotype. Median CD4/CD8 ratio was 0.7 (range, 0.04 – 3.7); T cell phenotypes included naive (median, 24.5%; range, 0.3 – 80.7), central memory (median, 12.8%; range, 2.3 – 51.6), effector memory (median, 24.5% (range, 0.8 – 70.3) and effector (median, 28.7%; range, 2.8 – 65.2). MRD negative (n = 24/29) vs positive pts (n = 5/29) at 1 mo post KTE-X19 had increased median cytokine levels, including IL-15, IL-2, IFN-γ, IL-10, and IL-6, peaking in serum within 7 days post treatment. Pts who were MRD negative by 1 mo post treatment also had increased median peak levels of Granzyme B and soluble PD-L1. Six pts developed Grade 4 neurologic events (NE), including 1 cerebral edema case; 3 had concurrent Grade 4 cytokine release syndrome. These pts had higher peak cytokine levels vs pts without Grade 4 NE, with lack of reversion to baseline by Day 28 of serum IL-6 and sVCAM-1. Peak CAR T cell in blood and serum cytokine levels were generally comparable in higher vs lower risk pts defined as *TP53* mutated (n = 6/36) vs unmutated (n = 30/36), or high vs low Ki-67 proliferation index (PI; ≥ 30% [n = 40/49] and < 30% [n = 9/49]), consistent with the comparable clinical efficacy of KTE-X19 in these subgroups. **Conclusions:** PD profile of KTE-X19 associated with efficacy (MRD status at 1 mo) and treatment-related NE. In contrast to approved therapies, KTE-X19 showed comparable pharmacology and clinical outcomes in pts with higher vs lower risk MCL defined by *TP53* mutation or Ki-67 PI. Clinical trial information: NCT02601313. Research Sponsor: Kite, a Gilead Company.

3024 Poster Session (Board #88), Fri, 8:00 AM-11:00 AM

Assessing readmission after axicabtagene ciloleucel immunotherapy. *First Author: Paula Perkins, Fred Hutchinson Cancer Research Center, Seattle, WA*

Background: Axicabtagene ciloleucel (axi-cel) is an FDA approved CD19 targeted CAR-T for patients (pts) with diffuse-large-B cell lymphoma (DLBCL) after 2 lines of treatment. Pts are monitored inpatient for minimum 7 days after CAR-T infusion but remain at risk of complications after discharge that can lead to readmission. We report our institutional experience on the rate and etiology of readmissions after initial discharge. **Methods:** In this retrospective study, readmission was defined as an inpatient stay greater than 48 hours while under the auspice of the Immunotherapy service. Cytokine release syndrome (CRS) and neurotoxicity (NT) were graded based on the Lee and CTC v.4 criteria, respectively. Logistic regression models were used to study the association between clinical factors and readmission. **Results:** 44 pts received axi-cel. Median age was 62 (25-79). 33 pts (75%) had primary refractory disease and 14 (30%) had prior transplant. Pts had median 3 lines (2 -9) of treatment before axi-cel. Median time from most recent treatment to leukapheresis was 10 weeks (0.5-109). 22 pts (48%) received bridging therapy between leukapheresis and lymphodepletion (LD). Median duration of initial planned admission was 7.5 days (6-16). Incidence of CRS was 88% (all grades) and 12% (grade 3/4). Median time to start of CRS was 3 days (0-13). Incidence of NT was 61% (all grades) and 16% (grade 3/4) and median time to NT was 6 days (3-14). 6 pts (14%) were readmitted after initial hospitalization (1 had 2 readmissions). Median day of readmission was 13 (9-25). Median duration of subsequent hospitalization was 5 days (2-31). Reasons for readmission were: infection (2), CRS (2), GI bleed (1), progressive disease (PD) (1) and NT (1). 4 of 6 pts had no CRS or NT before readmission. 2 of the 4 were readmitted on days 9 and 13 for NT. The other 2 pts were readmitted for infection and GI bleed. 1 pt had grade 2 CRS and grade 2 NT during first admission and was readmitted on day 25 for PD. Last pt had grade 2 CRS and grade 3 NT during first admission with discharge day 13, readmission day 14 through day 17 with recurrent NT and second readmission day 30 for infection. 3 of 6 pts had ICU admissions during second admissions. There was no association between pre- and post- CAR-T variables and risk of readmission in multivariable models. **Conclusions:** Readmissions after discharge from initial planned hospitalization for axi-cel are not uncommon. This data supports our current policy of close monitoring until at least a month after CAR-T therapy and supports the requirement of a full-time caregiver until discharge from the Immunotherapy service. Research Sponsor: None.

3026 Poster Session (Board #90), Fri, 8:00 AM-11:00 AM

First-in-human clinical trial of the autologous CD7-CART for relapsed/refractory ACUTE lymphoblastic leukemia/lymphoma. *First Author: Mingzhi Zhang, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China*

Background: CD7 represents a potential target for T-cell acute lymphoblastic leukemia/lymphoma (T-ALL/T-LBL). We developed CD7 nanobody derived chimeric antigen receptor T-cells (CD7-CART), and established a non-gene editing strategy by anchoring CD7 in the ER and/or Golgi to overcome the CART fratricide. **Methods:** This single-arm, open-label, phase I study is to investigate CD7-CART cell manufacturing feasibility without contamination of malignant T cells, and the safety and efficacy of the CART on patients with CD7 positive relapsed/refractory T-ALL/T-LBL. 3 subjects, identified as both CD4 and CD8 negative T-ALL or T-LBL were enrolled. CART cells were manufactured by using CD4+/CD8+ sorted T cells from leukapheresis. All patients (Pts) were pretreated with Flu/Cy prior to CART infusion. 1x10^6/kg CART cells were given to case 2 and 3, while 1.5x10^6/kg to case 1. **Results:** Case 1 was diagnosed as refractory ALL with myeloid differentiation, who had received intensive chemotherapy and allogeneic hematopoietic stem cell microtransplantation. Case 2 was diagnosed as ALL (T/B mixed type) but relapsed with CNS involvement, and received radiotherapy in addition to intensive chemotherapy. Prior to CART infusion, case 2 had no abnormal B cells but 17.69% of abnormal early T cellsfrom BM. Case 3 had stage VI of T-LBL, which recurred after multi-cycle chemotherapy of BFM-90 regimen and autologous SCT. After CART treatment, no neurotoxicity was observed in all pts. Case 1 had grade 3 CRSwhile case 2 and 3 had grade 1, although increased IL-6 was detected in all pts. Significant CART expansion and persistence were observed in case 2 and 3, and MRD negative CR was confirmed on day 28 in both pts. The number of generalized lymphadenopathy, lymph node size, and the degree of metabolism were all significantly reduced in case 3. Case 1 had only moderate CART expansion, but abnormal early T cells from BM decreased from 70.03% to 19.57% on day 30. After CART infusion, the number of peripheral abnormal T cells became either undetectable in case 2 and 3, or significantly decreased in case 1. Interestingly, CART had unsustained effect on normal T cells in all pts. As of Feb-10-2020, case 1 has 5 months of OS, including 3 months of PFS. Case 2 and 3 has reached 2 and 1 months of PFS and is still in remission. **Conclusions:** CD7-CART cells can be manufactured without contamination of malignant T cells. CD7-CART therapy is well-tolerated and has great therapeutic potential for relapsed/refractory CD7 positive T cell malignancies. Clinical trial information: NCT04004637. Research Sponsor: National Key R&D Program of China (2016YFC1303403).

3027 Poster Session (Board #91), Fri, 8:00 AM-11:00 AM

Successful tumor-infiltrating lymphocyte (TIL) growth from uveal melanoma (UM) using a three-signal (3.0) method. *First Author: Meredith Pelster, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Metastatic UM is a rare cancer with poor response rates to systemic therapy. Adoptive transfer of patient-specific TIL may represent the best strategy for treatment. TIL are harvested from primary or metastatic tumors and initially expanded in culture with high dose IL-2 prior to undergoing rapid expansion protocol and therapeutic administration. Here, we report improved rates of initial expansion using a previously described TIL 3.0 method which utilizes dual agonistic antibodies to TCR and 4-1BB (Urelumab) for stimulation, respectively, with high dose IL-2, compared to the traditional method. **Methods:** Between 2006 and 2019, patients were consented for TIL harvest from either primary or metastatic UM tumors. Demographics, clinical features, and outcomes of the TIL initial expansion were collected. Success rates, number of cells expanded, and days in culture for the two methods were analyzed using partially overlapping samples t-tests and z-tests. **Results:** There were 85 harvests and expansions from 76 patients using the traditional method and 32 expansions from 30 patients using TIL 3.0. Initial TIL expansion was successful in 97% of TIL 3.0 harvests compared to 35% for the traditional method ($p < 0.001$). More TIL were expanded with TIL 3.0 compared to the traditional method (291.3 million cells vs. 88.6 million cells, $p < 0.001$), and fewer days were required in culture (18.5 vs. 29.0, $p < 0.001$). Both primary UM harvests and metastatic harvests were more successful with TIL 3.0 (90% vs. 12% for primary, $p < 0.001$, and 100% vs. 42% for metastatic, $p < 0.001$). **Conclusions:** Expansion of UM tumors via the TIL 3.0 method led to successful growth in 97% of harvests. Therapeutic administration to patients with TIL 3.0 is under active investigation. Research Sponsor: U.S. National Institutes of Health, Other Government Agency.

	Traditional (n=85)	TIL 3.0 (n=32)
Age, years, median (range)	54.0 (28-68)	58.5 (28-72)
Gender		
Male, n (%)	45 (59%)	17 (57%)
Female, n (%)	31 (41%)	13 (43%)
TIL source		
Primary UM, n	25	10
Metastatic UM, n	60	22
Primary UM features		
Largest basal diameter, mm, median (range)	13.9 (8.5-20.5)	13.4 (10.0-18.1)
Apical dimension, mm, median (range)	8.9 (3.8-14.6)	8.9 (2.3-14.6)
Gene expression profile	5 (20%)	3 (30%)
Class 1A, n (%)	5 (20%)	0 (0%)
Class 1B, n (%)	9 (36%)	5 (50%)
Class 2, n (%)	6 (24%)	2 (20%)
Unknown, n (%)		
Metastatic harvest location		
Liver, n (%)	18 (30%)	7 (32%)
Lung, n (%)	6 (10%)	3 (14%)
Skin/soft tissue, n (%)	30 (50%)	10 (45%)
Other, n (%)	6 (10%)	2 (9%)

3028 Poster Session (Board #92), Fri, 8:00 AM-11:00 AM

Association of lymphocyte to monocyte ratio with clinical response and survival in patients with relapsed, aggressive non-Hodgkin lymphoma treated with axicabtagene ciloleucel CAR-T. *First Author: Abdullah S. Al Saleh, Mayo Clinic, Rochester, MN*

Background: Chimeric antigen receptor T-cell (CAR-T) therapy induces complete remission (CR) in 30-40% of patients with non-Hodgkin lymphoma (NHL). However, for patients who do not achieve CR as their first response, predictors for achieving CR as best response can guide management between careful observation or early intervention. Increased absolute lymphocyte count to absolute monocyte count ratio (ALC/AMC) predicts better response rates and survival in NHL patients receiving chemotherapy and/or autologous stem cell transplant. We evaluated the prognostic impact of ALC/AMC in CAR-T therapy for NHL. **Methods:** This was a retrospective review of patients who received CAR-T for NHL from June 2016-August 2019. ALC/AMC was assessed at the start of lymphodepletion (LD) chemotherapy. The receiver operator curve (ROC) was used to determine the best cutoff for ALC/AMC in predicting CR at 3 months. Event-free survival (EFS) was defined from time of CAR-T infusion to relapse or death, whichever occurred first. Overall survival (OS) was defined from time of infusion to death of any cause. **Results:** Forty-seven patients received axicabtagene ciloleucel, with a median follow-up of 14 months. By ROC, ALC/AMC > 0.8 before LD chemotherapy was predictive of achieving CR at 3 months. Baseline characteristics were similar between the high (n = 30) and low (n = 17) ALC/AMC groups. Patients with an ALC/AMC > 0.8 at the time of LD chemotherapy were more likely to achieve CR at 3 months (46% vs. 12%, p = 0.01), 6 months (52% vs. 0%, $p < 0.0005$), and 12 months (42% vs. 0%, p = 0.01). Correspondingly, the EFS and OS were significantly shorter in patients with ALC/AMC$\leq$0.8 vs. those > 0.8 (median EFS: 2 vs. 13 months, $P < 0.0001$) and (median OS: 15 months vs. not reached, P = 0.03), respectively. Association between ALC/AMC ratio and EFS and OS remained consistent in multivariate Cox models after adjusting for other prognostic variables, including abnormal lactate dehydrogenase and increased ferritin level at infusion day. **Conclusions:** ALC/AMC > 0.8 before lymphodepletion chemotherapy is a strong predictor for complete remission as well as improved event-free and overall survival for axicabtagene ciloleucel in NHL. Research Sponsor: None.

3029 Poster Session (Board #93), Fri, 8:00 AM-11:00 AM

A prospective phase I trial of dendritic cell-based cryoimmunotherapy in metastatic castration-resistant prostate cancer. *First Author: Liv Cecilie Vestrheim Thomsen, Centre for Cancer Biomarkers, University of Bergen, Bergen, Norway*

Background: Dendritic cell (DC)-based cryoimmunotherapy (CryoIT) was used to treat metastatic castration-resistant prostate cancer in a Phase I clinical trial. Primary objective was safety of treatment. Secondarily, clinical, radiological and immunological treatment responses were investigated. **Methods:** In 18 patients cryoablation by a freeze-thaw process under general anesthesia was performed, followed by intratumoral autologous immature DC injection. In the last 9 patients checkpoint inhibition of either CTLA-4 or PD-1 was added. Subjects had minimum 46 weeks follow-up. Adverse events (AEs) and blood analyses were registered at all visits. Disease progression was determined by three imaging modalities according to (i)RECISTv1.1 and progression-free survival (PFS) by Kaplan-Meier method. Circulating tumor cells (CTC/7.5 mL, CellSearch) and ultradeep T-cell receptor (TCR) b-chain sequences (TCRSafe) were enumerated. Patients were separated by CTC into none (n=10), 1-4 (n=4) and $\geq$ 5 (n=4). Health related quality of life (HRQoL) measured by EORTC-QLQ C30 questionnaire were answered at inclusion, and 10, 22 and 46 weeks post CryoIT. Scores were calculated according to the EORTC manual. **Results:** Subjects progressing within 22 weeks had higher PSA (p=0.03). AE profile of the total cohort (n=18) was comparable with interim reports (n=13); of 20 possible DC-related AEs one was severe (urinary retention) and 19 mild-to-moderate, and spread independent of treatment regime. Maximum tolerated dose of DC was not reached. By 46 weeks, imaging showed 6 patients partial response or stable disease. Median PFS was 150 days in total cohort. Pretreatment CTC counts $\geq$5 indicated higher progression rates and recurring CTC. Ultradeep TCR-sequencing showed more prevalent and higher expressed (>5-fold) new TCR clonotypes at 2-6 weeks in men without progression. Participants reported high and stable HRQoL scores throughout the study. However, presence of CTC was associated with worse HRQoL scores at week 10 (p=0.031) and 22 (p=0.005). **Conclusions:** DC treatment seems safe and well tolerated, also combined with checkpoint inhibitors. Effect is indicated in subjects with moderate pre-treatment PSA levels. Immune responses are suggested by higher number of novel TCR clonotypes in men with non-progressive disease. Clinical trial information: NCT02423928. Research Sponsor: Alden Cancer Therapy II, Centre for Cancer Biomarkers CCBIO, University of Bergen, Bergen, Norway.

3030 Poster Session (Board #94), Fri, 8:00 AM-11:00 AM

Ongoing, first-in-human, phase I dose escalation study of the investigational CD47-blocker TTI-622 in patients with advanced relapsed or refractory lymphoma. *First Author: Krish Patel, Swedish Cancer Institute, Seattle, WA*

Background: CD47 is an immune checkpoint that binds signal regulatory protein alpha (SIRPα) and delivers a "do not eat" signal to suppress macrophage phagocytosis. Cancer cells frequently overexpress CD47 to escape immune surveillance. TTI-622 is a fusion protein consisting of the CD47-binding domain of human SIRPα linked to the Fc region of human IgG4. TTI-622 acts as a decoy receptor, preventing CD47 from delivering its inhibitory signal and enabling macrophage activation and anti-cancer activity via pro-phagocytic signals present on cancer cells. Unlike many CD47-blocking antibodies, TTI-622 does not bind to human erythrocytes and thus may not cause anemia in patients. **Methods:** In phase 1A, patients with advanced relapsed or refractory lymphoma received IV TTI-622 once per week with dose increased based on traditional 3+3 escalation. Dosing was on a mg/kg basis with the third and subsequent weekly doses approximately 2-fold higher than the first 2 doses (e.g., 0.05, 0.05, and 0.1 mg/kg for weeks 1, 2 and 3). Blood samples were obtained for PK analysis and assessment of CD47 receptor occupancy (RO) on peripheral T cells. **Results:** At data cut-off, 19 patients (11 M, 8 F) of median age 62 years (range, 24-86) with the following lymphomas: DLBCL 10; HL 6; and TCL, MCL and FL, 1 each, with a median of 3 prior therapies (range, 1-8) were enrolled. No DLTs have been observed in 5 dose levels (0.05 to 4.0 mg/kg). Grade $\geq$3 related neutropenia occurred in 2 patients; other related AEs occurring in 2 patients each included abdominal pain, fatigue, and nausea; no patients experienced a related SAE. Acute, post-dose platelet decreases occurred transiently and generally were Grade 1- 2; no related Grade $\geq$3 thrombocytopenia or anemia AEs have been observed. Preliminary PK data indicate a dose-proportional increase in exposure and a T1/2 of approximately 4-5 days following repeat infusions (Week 6). Preliminary biomarker data reveal approximately 60% RO at the end of the first infusion of 2 mg/kg and more sustained 24-hour RO at 1 and 2 mg/kg vs $\leq$ 0.8 mg/kg. To date, 1 patient with stage 4 non-GCB DLBCL (5 prior therapies) initially achieved PR by Wk 8 and CR by Wk 36, with response ongoing. **Conclusions:** TTI-622 is well tolerated at doses up to 4 mg/kg per week. Preliminary data indicate dose-dependent increases in PK exposure and target engagement with 1 DLBCL patient having achieved a durable, ongoing CR. Dose escalation is ongoing and additional safety, PK, biomarker and response data will be available at the time of meeting presentation. Clinical trial information: NCT03530683. Research Sponsor: Trillium Therapeutics Inc.

3031 Poster Session (Board #95), Fri, 8:00 AM-11:00 AM

Modulation of inhibitory signals in CAR T cells leads to improved activity against glioblastoma. *First Author: Khaled Sanber, Center for Cell and Gene Therapy, Department of Medicine, Baylor College of Medicine, Houston, TX*

Background: Early clinical trials have demonstrated the safety of chimeric antigen receptor (CAR) T cells targeting glioblastoma (GBM), however, their efficacy remains limited by multiple obstacles including the immunosuppressive tumor microenvironment. Adoptively transferred CAR T cells remain susceptible to inhibition via the engagement of co-inhibitory receptors on their surface such as PD1, BTLA, CTLA4 and LAG3. The subsequent recruitment of Src homology region 2 containing protein tyrosine phosphatase 2 (SHP2) by these receptors to the immune synapse may represent a common mechanism of T cell inhibition, as SHP2 can de-phosphorylate key signaling molecules that mediate T cell activation (including CD28 and CD3ζ). We hypothesized that SHP2 deletion will simultaneously offset the effects of multiple co-inhibitory receptors, thereby improving the anti-tumor activity of CAR T cells. **Methods:** Electroporation of sgRNA/Cas9 ribonucleoprotein complexes into human T cells was used to knockout (KO) SHP2. Retroviral vector transduction was used to express a clinically-utilized second generation CAR (with a CD28 endodomain) targeting HER2. The phenotype of wild-type (WT) and $SHP2^{KO}$ CAR T cells was evaluated with mass cytometry and flow cytometry. Their anti-tumor function was tested *in vitro* using the xCELLigence assay (an impedance-based cytotoxicity assay), and *in vivo,* in an orthotopic xenograft mouse model of GBM. **Results:** Efficient and reproducible depletion of the SHP2 protein in human T cells was verified using western blotting. The Inference of CRISPR Efficiency (ICE) Assay confirmed efficient editing of the PTPN11 gene encoding SHP2. An anti-HER2 CAR was efficiently expressed in the $SHP2^{KO}$ T cells. SHP2 deletion did not significantly affect CAR T cell expansion, proliferation or baseline phenotype. However, following co-culture with HER2+ LN229-GBM cells, the CD8+ central memory (CCR7+ CD45RA-) and effector memory (CCR7- CD45RA-) subsets were enriched to a greater extent in the $SHP2^{KO}$ CAR T cells. The pattern of cytokine co-expression varied between donors in a single-cell analysis comparing $SHP2^{KO}$ to WT CAR T cells after encountering LN229 cells. Functionally, $SHP2^{KO}$ CAR T cells derived from the majority of healthy donor and patient peripheral blood eliminated LN229 cells more rapidly *in vitro.* In an orthotopic mouse model of GBM, $SHP2^{KO}$ CAR T cells showed better early control of established LN229 xenografts and improved survival in comparison to WT CAR T cells. **Conclusions:** SHP2 deletion in CD28ζ.CAR T cells improves their anti-tumor activity. Research Sponsor: Stand Up to Cancer, Other Foundation.

3032 Poster Session (Board #96), Fri, 8:00 AM-11:00 AM

CYAD-101: An innovative non-gene edited allogeneic CAR-T for solid tumor cancer therapy. *First Author: Hans Prenen, University Hospital Antwerp, Edegem, Belgium*

Background: In contrast to autologous CAR-T cell therapies, allogeneic donor-derived CAR-T cells can be banked and used in a timely fashion overcoming the critical time delay of just in time autologous cell manufacture. CYAD-101 is an allogeneic CAR-T that uses a non-gene edited peptide-based technology (TIM) to control graft versus host disease (GvHD) combined with a NKG2D-based CAR. Pre-clinical studies confirmed that CYAD-101 maintained CAR-directed anti-tumor activity in the absence of the induction of GvHD. Clinical grade CYAD-101 cells were produced for the phase 1 alloSHRINK trial (NCT03692429). **Methods:** A bank of clinical grade CYAD-101 cells was generated through two production runs using a single donor apheresis. Together, the bank generated > 53 billion CYAD-101 cells suitable for the entire dose escalation segment and short expansion phase of the trial (15 patients in total). Both runs showed high consistency with the CYAD-101 product generated composed mainly of $CD4^+$ T cells (>85%) with a transduction level of > 92%, low relative expression of CD69/CD25 and largely absent expression levels of PD-1/LAG-3. The CYAD-101 cells were predominantly (>80%) $CD45RA^-$/ $CD62L^-$/ $CD27^-$ suggestive of an effector memory T cell population. **Results:** Upon co-culture with target K562 cells, CYAD-101 readily produced IFN-γ that was blocked by a NKG2D blocking antibody confirming specificity of the CAR. CYAD-101 cells showed in vitro cytotoxicity against tumor cells and produced an array of Th1 (IFN-γ, IL-2 and TGF-β) and Th2 (IL-4, IL-5) cytokines. Importantly, minimal IFN-γ was produced upon TCR stimulation while stimulation with a non-TCR mitogen (PMA + ionomycin) lead to high levels of IFN-γ. Together, these data show that clinical grade CYAD-101 cells were able to functionally respond through the CAR but showed minimal TCR-driven activation. Fifteen refractory metastatic CRC patients who had previously failed at least one line of oxaliplatin—containing therapy were treated with three doses of CYAD-101 cells given on Day 3 of three successive FOLFOX chemotherapy cycles. Updated clinical results continue to demonstrate an encouraging clinical activity (2 patients with partial response and 9 with stable disease) and the absence of GvHD in the context of CYAD-101 cell engraftment. **Conclusions:** These early clinical results demonstrate the safety and tolerability of a non-gene edited predominantly $CD4^+$ CAR-T therapeutic approach. The initial observations of clinical activity in metastatic CRC patients warrants the continued development of this therapy. Clinical trial information: NCT03692429. Research Sponsor: Celyad SA.

3034 Poster Session (Board #98), Fri, 8:00 AM-11:00 AM

Safety and efficacy of optimized tandem CD19/CD20 CAR-engineered T cells in patients with relapsed/refractory non-Hodgkin lymphoma. *First Author: Yajing Zhang, Chinese PLA General Hospital, Beijing, China*

Background: Chimeric antigen receptor T (CAR T) cells targeting CD19 have been used to achieve breakthroughs in the treatment of hematological malignancies, however, a high recurrence rate is the main obstacle to durable remission following CAR T cell therapy. **Methods:** As an open-label and single-arm phase I/IIa trial (ClinicalTrials.gov number, NCT03097770), we screened 99 patients with r/r B-NHL—including DLBCL, PMBCL, CLL/SLL, MCL, TFL and FL—according to the 2008 WHO Classification of Tumors of Hematopoietic and Lymphoid Tissue, and a total of 87 patients received an infusion of one dose tandem CD19/CD20 CAR-engineered T cells on day 0 in the range of 0.5×10^6-10×10^6 cells per kilogram of body weight after conditioning chemotherapy. The primary objective was to evaluate the safety and tolerability of CAR T cells. Efficacy, progression-free survival (PFS) and overall survival (OS) were evaluated as secondary objectives. Our clinical trials is registered with ClinicalTrials.gov, NCT03097770. Safety was assessed by CTCAE Version 5.0, and clinical response by PET-CT referred to standard international criteria. The trial remains open, and recruitment to extension cohorts with alternative endpoints is underway. **Results:** Between May 11, 2017, and Jan 31, 2020, 99 patients were enrolled and 87 received tandem CD19/CD20 CAR-engineered T cells across phases I/IIa. As of the cutoff date, 74 assessable patients were followed up for a median of 13.5 months (IQR 33.2 - 3.3), 62 (84%) had an objective response, and 55 (74%) had a complete response. The median progression-free survival and overall survival were all not reached. Cytokine release syndrome (CRS) occurred in 62 patients (71%), with 61% grade 1 or 2 and 10% grade 3 or more. CAR-T-cell-related encephalopathy syndrome (CRES) of grade 3 occurred in 2 patients (2%) . Three treatment-related deaths (2 in pulmonary infection and 1 in deposition of CART cells in pulmonary alveoli). **Conclusions:** In this study, optimized tandem CD19/CD20 CAR-engineered T cells induced a potent and durable anti-tumour response with controllable CRS and CRES. Clinical trial information: NCT03097770. Research Sponsor: National Natural Science Foundation of China.

3035 Poster Session (Board #99), Fri, 8:00 AM-11:00 AM

Efficacy of SCRI-CAR19x22 T cell product in B-ALL and persistence of anti-CD22 activity. *First Author: Rebecca Alice Gardner, Seattle Children's Hospital, Seattle, WA*

Background: Loss of CD19 expression is a major cause of limited durable B-ALL remission following CD19 CAR T cells, which might be overcome by utilization of dual CD19xCD22 CAR T cell targeting. **Methods:** A Phase I trial (NCT03330691) of SCRI-CAR19x22 was developed using dual transduction of lentiviral vectors encoding for either a CD19- or CD22-specific CAR T cell construct, both with 4-1BB co-stimulation. Manufacturing was performed in a closed G-Rex system with IL-7, IL-15 and IL-21. After lymphodepletion, CAR T cells were infused at 1 or 3 X 10^6 CAR T cells/kg dose levels. Leukemic response and CAR T cell persistence were evaluated by flow cytometry. **Results:** Products were successfully manufactured in all 28 enrolled subjects with 7.92 average days in culture (range of 7-11 days) and consisted of an average CD8:CD4 ratio of 3.09 (range 0.19 to 8.9). The cellular product CAR composition was 29% CD19, 31% CD22 and 39% CD19 and CD22 targeting. 13 subjects had prior exposure to CD19 or CD22 targeting therapies with diverse expression of CD19 and CD22 on the leukemic blasts. No dose limiting toxicities occurred in the 27 infused subjects. The recommended phase 2 dose is 3 x 10^6 CAR+ cells/kg. CRS was present in 80% of subjects, with 85% of CRS being grade 2 or less, and a peak grade of 3 (n = 3). Mild neurotoxicity occurred in 38%, with a single grade 3 event. 84.6% obtained a CR, of which 95% were MRD negative. Of the 4 subjects who did not achieved a CR, 2 had a pre-existing CD19 negative population and one had previously received CAR T cells and rejected SCRI-CAR19x22. There have been 4 relapses with varying CD19 and CD22 expression as follows: 1 CD19-CD22-, 1 CD19+CD22+, and 2 CD19-CD22+. The in vivo engraftment of CAR T cells peaked most frequently between day +7 and +14 and was predominated by the CD19 CAR+ T cells. **Conclusions:** We demonstrate manufacturing feasibility and safety of SCRI-CAR19x22. While initial efficacy is demonstrated, CD22 activity is poor due to limited expansion of the CD22 CAR-containing components and subjects with pre-existing CD19 negative leukemia fared poorly. Development of a revised CD22 CAR that exhibits a reduction tonic signaling is underway, with plans to explore the new construct in the context of a dual-targeting CD19xCD22 CAR T cell product. Clinical trial information: NCT03330691. Research Sponsor: Philanthropy.

3036 Poster Session (Board #100), Fri, 8:00 AM-11:00 AM

In vitro and in vivo characterization of MDNA11: A long-acting "beta-only" IL-2 superkine in syngeneic mice tumor models and nonhuman primates. *First Author: Moutih Rafei, Université de Montréal, Montréal, QC, Canada*

Background: Use of IL-2 (Proleukin) remains limited due to its short half-life, toxicity, and its ability to preferentially activate Tregs resulting in unwanted immune suppression. Approaches to reduce binding to CD25 (IL2α), such as pegylation techniques, also results in reduced affinity to CD122 (IL2β). To bypass these limitations, we engineered MDNA11, an IL-2 Superkine containing core mutations to diminish binding to CD25 while increasing affinity to CD122. To increase half-life, MDNA11 was fused to an albumin scaffold, which is known to allow accumulation at the tumor site. **Methods:** MDNA11 was evaluated using *in vitro* and *in vivo* studies that included: IL-2 signaling in human PBMCs, Biacore binding analyses, PK studies in mice, and efficacy studies in syngeneic tumor models with or without immune checkpoint inhibitors (ICIs). In addition, dose-range finding studies in cynomolgus monkeys (NHP) were performed to characterize the safety and PK/PD profiles of MDNA11. **Results:** MDNA11 displayed enhanced STAT5 signaling in human NK and naïve CD8 T-cells with diminished Treg activity. In mice, the terminal half-life of MDNA11 was 24-fold longer than IL-2. As a result, MDNA11 triggered effective tumor growth control, as monotherapy or in combination with ICI, in multiple tumor models in spite of q1wk dosing for two weeks. MDNA11 administration to mice with pre-established CT26 colon cancer resulted in tumor-free animals and induced strong memory response and protection against subsequent re-challenges. MDNA11 also inhibited the growth of B16F10 melanomas, which translated into a durable increase in tumor infiltrating CD8 T-cells. When tested in NHP, MDNA11 led to increased circulating CD8 T-cells lasting for almost 14 days with limited effects on Tregs and eosinophils (the latter being a source of IL-5 causing vascular leak syndrome). High doses resulted in mild side effects that were transient and reversible even following repeated dosing. **Conclusions:** The long-acting MDNA11 Superkine has superior potency over IL-2 at activating naïve CD8 T-cells and NK cells, while exhibiting diminished Treg activation. This molecule potently inhibited tumor growth and induced durable regression and long-term memory response. Studies in NHP showed prolonged proliferation of immune effector cells lasting almost two weeks post-MDNA11 administration. The sum of these data underscores the potency of MDNA11 to trigger the host's immune response to control or eradicate established tumors. Research Sponsor: Medicenna Therapeutics.

3037 Poster Session (Board #101), Fri, 8:00 AM-11:00 AM

A randomized phase I/IIa study to evaluate the safety and efficacy of SNK01 (non-genetically modified autologous natural killer cells with enhanced cytotoxicity) plus pembrolizumab in patients with stage IV non-small cell lung cancer. *First Author: Eo Jin Kim, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea*

Background: Despite the increased promise of checkpoint inhibitors in the treatment of lung cancer, the overall response rate is approximately 30% with up to 30% moderate to severe side effects. Natural killer (NK) cells have recently been implicated in antitumor response to immune checkpoint inhibitors. SNK01 is a novel non-genetically modified autologous natural killer cell therapy with enhanced cytotoxicity which has been found to have tumoricidal effects against several lung cancer cell lines. **Methods:** 18 patients with Stage IV NSCLC (PD-L1+, EGFR-, ALK-) who all failed prior frontline platinum-based therapy were randomized 2:1 to Pembrolizumab every three weeks +/- 6 weekly infusions of SNK01 at either 2×10^9 or 4×10^9 cells per infusion. Primary endpoint is safety and secondary endpoints are objective response rate (ORR), progression-free survival (PFS), overall survival (OS), time to progression (TPP), and quality of life (QoL). **Results:** 14 patients have been enrolled up to date and 9 have completed treatment. Median age is 69 (52-73). Two patients discontinued treatment prior to receiving their first dose of SNK01 due to Grade 3 toxicity to Pembrolizumab. Three patients have completed therapy with Pembrolizumab alone and all had progressive disease. Three patients have completed Pembrolizumab with 2×10^9 SNK01 and three patients have completed Pembrolizumab with 4×10^9 SNK01. Of patients receiving full combination therapy, there have been no adverse events or any reported toxicity while overall QoL has been improved. The week 9 overall response rate in the combination group is 66% using iRECIST (3/6 cPR, 1/6 PR). All remaining planned patients are currently being enrolled and a full update will be presented. **Conclusions:** These preliminary results demonstrate that combination therapy with Pembrolizumab and SNK01 is very safe and even appears to reduce checkpoint associated toxicity while increasing overall tumor response compared to Pembrolizumab monotherapy alone in Stage IV NSCLC patients who have failed prior platinum-based treatment. Research Sponsor: NKMAX.

3038 Poster Session (Board #102), Fri, 8:00 AM-11:00 AM

Phase I study of CRISPR-engineered CAR-T cells with PD-1 inactivation in treating mesothelin-positive solid tumors. *First Author: Zhenguang Wang, Molecular & Immunological Department, Bio-therapeutic Department, Chinese PLA General Hospital, Beijing, China*

Background: Our previous phase I study with MPTK-CAR-T (mesothelin-directed 28ζ CAR-T cells with PD-1 and TCR disruption by CRISPR-Cas9 system) demonstrated feasibility and safety of CRISPR-mediated PD-1 inactivation in CAR-T cells, and suggested the natural TCR is beneficial for the proliferation of CAR-T cells in solid tumors. Based on these observations, we initiated a pilot dose escalation study to investigate mesothelin-directed CAR-T cells with only PD-1 disruption by CRISPR (termed as GC008t) in patients with mesothelin-positive advanced solid tumors (NCT03747965). **Methods:** On the data cut-off date (Jan 20, 2020), nine patients (6 pancreatic cancers, 2 ovarian cancers, 1 colorectal cancer) were treated (5 received ≥12 numbers of therapy), three in cohort 1 ($0.1\text{-}0.2 \times 10^7$/kg), four in cohort 2 ($0.5\text{-}1.0 \times 10^7$/kg), two in cohort 3 ($2.5\text{-}5 \times 10^7$/kg). Eight of the 9 patients received lymphodepletion regimen of cyclophosphamide and nab-paclitaxel with or without gemcitabine. Four of the 9 patients received repeat infusions of GC008t per protocol. **Results:** Comparable proliferation capacity was observed *in vitro* between the MPTK-CAR-T and the GC008t products. The mean PD-1 surface expression in cell products was 0.5% (range, 0.2%-0.9%). GC008t infusions were well tolerated with no observed on-target/off-tumor toxicity, autoimmune activity. Only two patients in cohort 3 developed grade 1 CRS with fever and rash. Circulating GC008t expanded with a peak at day 7-14 and became undetectable by qPCR beyond 1 month. The mean peak levels of circulating CAR-T cells between GC008t and MPTK-CAR-T at similar dose level were not statistically significant. Failure of GC008t engraftment after repeat infusion was observed in 2 out of 4 patients. The best response of the 7 evaluable patients was stable disease in 4 and partial response in 2 patients (dosed $\geq 1 \times 10^7$/kg) with PFS of 80 and 160 days. **Conclusions:** Phase I trial of GC008t further establishes that genetic inactivation of PD-1 in CAR-T cells by CRISPR is feasible and safe. The expansion and persistence of CAR-T cells with PD-1 disruption is not improved significantly even in the setting of natural TCR and lymphodepletion. Future endeavors are needed to improve the clinical efficacy of CAR-T therapy in the treatment of solid tumor. Clinical trial information: NCT03747965. Research Sponsor: National Natural Science Foundation of China;National Key Research and Development Program of China;Strategic Priority Research Program of the Chinese Academy of Sciences.

3039 Poster Session (Board #103), Fri, 8:00 AM-11:00 AM

Safety and efficacy of chimeric antigen receptor T cells modified to target mesothelin and express PD-1 antibodies in patients with relapsed/refractory solid cancers in a phase I trial. *First Author: Juemin Fang, Shanghai Tenth People's Hospital, Tongji University, Shanghai, China*

Background: The limitations of chimeric antigen receptor T cells (CAR-T) in solid tumors are immunosuppressive tumor microenvironment and difficult infiltration to tumor. In order to reduce on-target off-tumor toxicities and circumvent the immune-suppressive tumor microenvironment(TME), we modified autologous CAR-T to be specific for mesothelin (MSLN) on cancer cells and secrete PD-1 antibodies (aPD1-MSLN-CAR T cells). Here, we report the safety and efficacy of aPD1-MSLN-CAR T cells in 10 patients with relapsed/refractory solid cancers in this single-arm, open-label, first-in-human phase I pilot study (ClinicalTrial.gov: NCT03615313). **Methods:** aPD1-MSLN-CAR T cells were prepared from peripheral blood mononuclear cells and engineered using PiggyBac Transposon System to target MSLN and secrete PD-1 antibodies. 10 patients with mesothelin positive relapsed/refractory solid cancers after failure to standard therapies were treated with aPD1-MSLN-CAR T cells for two or more cycles until disease progression or intolerable toxicity. The dose escalation of CAR T cells was designed to be 5×10^6/kg, 5×10^7/kg, and 1×10^8/kg, respectively. Adverse events were evaluated according to CTCAE-V4.03 and clinical response was assessed by RECIST 1.1. CAR expression was analyzed using quantitative real-time polymerase chain reaction. PD-1 antibodies were detected by ELISA. Serum IL-2, IL-4, IL-6, IL-10, IFN-γ and TNF-α were measured using flow cytometry. **Results:** The most common adverse events were mild fatigue and fever. Abdominal pain was also observed in 1 patient. Grade 1 and 2 cytokine release syndromes were observed without neurologic symptoms in 10 patients. After aPD1-MSLN-mRNA-CAR T cells treatment, 2 patients (20%) achieved partial response (PR), 4 (40%) remained stable (SD), and the rest 4 (40%) patients developed disease progression (PD). The median PFS was 97 days [95% CI (13, 180)] estimated by Kaplan-Meier method. **Conclusions:** These findings lend support that the combination of modified CAR T cells targeting MSLN with PD1 inhibition for solid tumors is safe. Modified CAR-T cells expressing PD-1 antibodies maybe an option to improve CAR-T efficacy as a result of refined TME. Clinical trial information: NCT03615313. Research Sponsor: Funding from Shanghai Tenth People's Hospital.

Characteristics and clinical responses.

Characteristics	NO.
Mean Age, years	54.5 (39, 67) years
Male/ Female	2/8
Ovarian cancer	6
Rectal cancer	2
Gallbladder cancer	2
PR	2(20%)
SD	4(40%)
PD	4(40%)
PFS, days	97 [95% CI (13, 180)]

3040 Poster Session (Board #104), Fri, 8:00 AM-11:00 AM

Final results of controlled IL-12 monotherapy in adults with grade III or IV gliomas. *First Author: E. Antonio Chiocca, Brigham and Women's Hospital, Boston, MA*

Background: Interleukin-12 (IL-12), a master regulator of the immune system, results in anti-tumor responses in preclinical models, but safe use requires tightly controlled production. This phase 1 trial (NCT02026271) is the first to evaluate the safety and tolerability of Ad-RTS-hIL-12 (Ad) under transcriptional control with veledimex (V) in adults with grade III or IV gliomas. **Methods:** Multicenter, phase 1, open-label, 3 + 3 dose escalation study of Ad (a single intratumoral injection, 2×10^{11} viral particles, Day 0) with oral V dosing (Days 0 to 14) of 10, 20, 30, and 40 mg in subjects with rGBM. **Results:** 38 subjects were treated (resection group: V 10 mg (n = 6); 20 mg (n = 15); 30 mg (n = 4); 40 mg (n = 6); and, stereotactic group: V 20 mg, n = 7). The adverse event profile of Ad+ V, was predictable and controllable, with the main adverse reactions (ARs) being mild to moderate. All ARs were manageable and reversible upon withholding V. We observed increased peak (mean ± SEM) serum recombinant IL-12 and downstream endogenous IFN-g: V 10mg 21.4 ± 11.7 pg/mL and 14.6 ± 7.1 pg/mL; V 20 mg 25.8 ± 7.1 pg/mL and 57.0 ± 26.5 pg/mL; V 30 mg 65.7 ± 45.5 pg/mL and 60.7 ± 50.0 pg/mL; V 40mg 108.8 ± 41.0 pg/mL and 167.5 ± 70.9 pg/mL, V 20mg (stereotactic) 25.1 ± 7.2 pg/mL and 69.8 ± 48.5 pg/mL, respectively. In the V 20 mg cohort, there was an increase in tumor-associated T cells ($CD3^+CD8^+$%) from pre-Ad (mean ± SEM) 0.6 ± 0.4 to biopsy (~5 mons) 6.3 ± 5.0 and production of IFN-g 97.2 ± 85.3 pg/g (n = 2). Median overall survival (mOS) in the V 20 mg cohort (resection, n = 15) was 12.7 mons (mean follow-up, 13.1 mons). Subjects with unifocal disease (n = 6) who received low-dose (≤ 20mg total) dexamethasone during active dosing (Days 0-14) had an mOS of 17.8 mons. Tumor response data will be presented. **Conclusions:** Results of Controlled IL-12 in rGBM are promising, with V-dependent and proportional increases in IL-12 and IFN-g resulting in immune activation, with a favorable safety profile and encouraging survival. The 20 mg V dose is the recommended phase 2 *dose*. Controlled IL-12 is being evaluated in a monotherapy substudy (n = 36, V 20 mg) and two combination studies with immune checkpoint inhibitors for rGBM. Clinical trial information: NCT02026271. Research Sponsor: Ziopharm Oncology.

3041 Poster Session (Board #105), Fri, 8:00 AM-11:00 AM

Selective targeting of HER2-overexpressing solid tumors with a next-generation CAR-T cell therapy. *First Author: Jenny Mu, Arcellx, Inc., Gaithersburg, MD*

Background: Conventional chimeric antigen receptor T cell (CAR-T) therapies have achieved limited clinical success in the treatment of solid tumors, in part due to the challenges of identifying tumor antigen(s) that are uniquely expressed on tumor cells. The dearth of such targets requires that current CAR-T therapies be re-engineered to preferentially target tumor cells thereby mitigating potential on-target off-tumor toxicity to normal cells. Herein we describe a novel cell therapy platform comprising Antigen Receptor Complex T (ARC-T) cells that are readily activated, silenced, and reprogrammed *in vivo* by administration of a novel tumor-targeting soluble protein antigen-receptor X-linker (sparX). The formation of the ARC-T, sparX, and tumor complex is required for the ARC-T to kill the tumor. Because ARC-T activity is entirely dependent on the dose of sparX administered, therapeutic doses of sparX may be defined that preferentially target cells over-expressing a target antigen and thus limit coincident kill of normal cells expressing lower levels of target antigen. **Methods:** We have created a library of sparX that bind different cell surface antigens, including HER2. The HER2 sparX was tested as both monovalent and bivalent constructs *in vitro* by assessing ARC-T cell activation, cytokine release and target cell cytotoxicity. *In vivo* efficacy models utilized NSG mice and incorporated tumor volume measurements and histopathologic assessments to evaluate tumor clearance. **Results:** *In vitro* studies demonstrate that co-culture of ARC-T cells, sparX-HER2 and HER2-expressing target cells drives T cell activation, expansion, cytokine secretion and cytotoxicity of target cells in a dose-dependent manner. Furthermore, by affinity tuning the HER2 binding domain and bivalent formatting of sparX-HER2, we achieved selective killing of HER2-overexpressing breast cancer cells with minimal effect on cells expressing HER2 levels representative of normal tissues. *In vivo* proof-of-principal studies with ARC-T/sparX-HER2 similarly demonstrate complete eradication of HER2-overexpressing solid tumor cells. **Conclusions:** These results demonstrate that a single intravenous dose of ARC-T cells can traffic to a solid tumor site and induce tumor eradication upon systemic administration and co-localization of tumor-targeting sparX in a mouse model. Bivalent formatting of sparX-HER2 further enabled ARC-T sensitivity to target antigen density to avoid the on-target off-tumor toxicity that has hindered conventional monovalent CAR-T treatments. Research Sponsor: Arcellx, Inc.

3043 Poster Session (Board #107), Fri, 8:00 AM-11:00 AM

Correlating immune toxicity, blood cell counts, and overall survival in cancer patients receiving immune therapy. *First Author: Rong Lu, UT Southwestern Medical Center, Dallas, TX*

Background: Baseline circulating white blood cell differential counts have been proposed as possible markers of response to Immune therapy (ICI) and immune toxicity (irAE), but have not been validated for clinical practice. **Methods:** 214 patients with various cancers receiving ICI had clinical lab results and overall/organ specific irAE analyzed. Absolute lymphocyte (ALC), eosinophil (AEC) and neutrophil (ANC) counts <7 days of starting and 3-12 weeks after ICI were correlated with survival and development of irAE. The association between overall irAE and cell count changes was evaluated using multivariate logistic regression, adjusting for patients' age, gender, race, and including all 3 types of cell count changes in one model. The association between overall survival and cell counts changes was tested using multivariate Cox proportional hazard model, adjusting for age, gender, race, and overall irAE (yes/no). **Results:** The combination of MEDIAN rise or fall in ALC, ANC and AEC after ICI combined with development of irAE was associated with altered overall survival (OS). Higher statistically significant (p=<0.05) OS was seen in patients with AEC↑/irAE+(n=94; median OS 14.9 months), ANC↓/irAE+(60; 17.9 mo), ALC↑/irAE+(65; 11.5 mo), ALC↓/irAE+(92; 12.2 mo). Lower OS was seen with ANC↑/irAE-(21; 5.4 mo), ALC↑/irAE-(9; 5.8 mo), ALC↓/irAE-(24; 6.1 mo). All these relationships were unchanged if patients were grouped into ANY rise during the 3-12 weeks rather than median. After multivariable adjustment for age/sex/race there was statistically significant association between higher baseline ALC and development of any irAE (p=0.05) and grade ≥2 irAE (p=0.02). No association was seen between overall toxicities and ANC or AEC. Organ-specific irAE's with statistically significant associations included pneumonitis:↓AEC (p=0.05), hepatitis:↓ANC (p=0.05), hypothyroidism:↓ANC (p=0.02), colitis:↑ALC (p=0.02). Skin rash, hypophysitis and adrenalitis were not associated with any cell count changes. **Conclusions:** In patients with cancer receiving immune therapy, the predictive value of serial monitoring in ALC, AEC and ANC is greatly enhanced by the addition of irAE detection. irAEs appear to be a greater predictor of survival than changes in blood counts. In contrast to prior reports we found ANC/ALC/AEC in isolation were less reliable in predicting improved survival. Lack of standardized methods of assessing irAE's confound identifying strong associations with clinical lab-derived cell counts. Research Sponsor: None.

3044 Poster Session (Board #108), Fri, 8:00 AM-11:00 AM

Association of reinvigoration of circulating anti-telomerase CD4 Th1 response in cancer patients with anti-PD-1 response. *First Author: Emeline Orillard, University Hospital Jean Minjoz, Besançon, France*

Background: Increasing evidence highlights the crucial roles played by CD4+ Th1 cells in cancer immunity and immunotherapy (Spitzer et al., Cell 2017, Borst et al., Nat rev Immunol 2018). Here, we investigate the relevance of circulating CD4 Th1 response against shared tumor-associated antigens (TAA) in cancer patients treated by anti-PD-1 immunotherapy. **Methods:** A total of 46 advanced cancer patients (pts) including 32 pts with non-small cell lung cancer (NSCLC), 14 pts with melanoma, were enrolled (ITHER trial NCT02840058). Patients were treated with anti-PD-1 therapy as standard of care (26 pts with nivolumab and 20 pts with pembrolizumab). Peripheral blood mononuclear cells were collected before and after treatment at 1 and 3 months. The presence of circulating TAA-specific Th1 response was measured by IFNy ELISPOT assay using a mixture of 15mer peptides derived from telomerase (TERT) (Laheurte et al., Oncoimmunology 2016 and Br J C 2019). **Results:** At the baseline, the anti-TERT Th1 response was observed in 37% of pts. After anti-PD-1 therapy, *de novo* induction and/or amplification of pre-existing anti-TERT Th1 response was found in 26 % of pts (12/46). Whereas, a decrease of this response was documented in 15% of pts (7/46).The presence of anti-TERT Th1 response in peripheral blood during anti-PD-1 treatment was associated with a prolonged progression free-survival (PFS) as compared to the immune non responder pts (14.4 vs 2.6 months respectively, p = 0.006, HR 0.39 [0.2;0.76]). Similar observation was made for the overall survival (OS) (22.3 vs 12.3 months respectively, p = 0.04 HR 0.45 [0.21;0.96]). Notably, *de novo* reinvigoration of peripheral anti-TERT Th1 response after anti-PD-1 therapy was associated with a better clinical outcome as compared to the group of pts with decreased immune response after treatment (Median OS not reached vs 5.8 months). In contrast, no association with anti-PD-1 response was observed neither with circulating anti-NY-ESO-1 or with anti-viral Th1 response, concurrently measured in these patients. **Conclusions:** The reinvigoration of circulating CD4 Th1 against telomerase in patients treated by anti-PD-1 is associated with a better clinical outcome. These results underline the potential interest of monitoring circulating antitumor CD4 Th1 response for immune checkpoint inhibitors management. Research Sponsor: None.

3045 Poster Session (Board #109), Fri, 8:00 AM-11:00 AM

Novel biomarker panel based on cellular and soluble checkpoint proteins for PD-1/PD-L1 blockade treatment efficacy. *First Author: Hiroki Nagai, Valley Hospital, Paramus, NJ*

Background: Although anti-PD-1/PD-L1 therapy has become one of the standard treatments for advanced cancers, its low treatment efficacy (10-30%) has remained a major issue. We sought to perform a detailed immune profiling of cells and soluble proteins in order to characterize key regulators and signaling molecules and identify therapeutic targets and biomarkers that may improve treatment efficacy and diagnosis. **Methods:** This observational study enrolled 49 advanced cancer patients treated with PD-1/PD-L1 blockade monotherapy. Treatment response was assessed by RECIST 1.1. PBMC and plasma samples were collected at baseline and every 6 weeks following initial treatment. Immune profiling of PBMC was done by multi-parametric flow cytometer, and t-SNE analysis was used to identify key immune subtypes. Soluble proteins were evaluated by LUMINEX assays. Cut-off values were determined by ROC curve analysis. **Results:** Three unique subtypes of immune cells were identified. The population of $CD11c^{+}HLA\text{-}DR^{low}CD80^{+}CD86^{-}$ $CD274^{+}$ cells (regDC) at baseline was significantly higher in patients with progressive disease (PD, n=28) than in patients showing clinical benefit (non-PD, n=21; p=0.030). The higher regDC population also correlated with higher levels of IL-8, IL-10, CXCL1, CXCL5, and CXCL11 in plasma. The population of $CD4^{+}CD25^{+}CD62L^{+}$ T cells (Treg) was also higher in PD patients ($p<0.001$). A unique subtype of $CD4^{+}CD28^{-}$ T cell, however, was higher in non-PD patients ($p<0.001$). For the soluble proteins, the levels of sLAG-3 and sGITR in plasma correlated with better clinical outcome in low regDC patients (p=0.004 and 0.044, respectively). The combined biomarker panel (cellular and protein markers) yields high sensitivity (90.5 %) and specificity (82.1 %) for predicting treatment efficacy. Disease control rate (DCR) and median progression free survival (PFS) are shown in the Table. **Conclusions:** To our knowledge, this pilot study is the first to detect three immune cell subtypes, regDC, Treg and $CD4^{+}CD28^{-}$ cells, associated with clinical outcome in the treatment of PD-1/PD-L1 blockade. Profiling of immune cell subtypes and soluble immune checkpoint proteins can serve to identify therapeutic targets and biomarkers for treatment efficacy. We will report the data with further enrollment. Research Sponsor: None.

	DCR (%)	p value	PFS (days)	p value
High/low regDC	13.3 /55.9	0.011	74 vs 178	0.010
High/low Treg	13.7 /85.0	<0.001	69 vs 407	<0.001
High/low $CD4^{+}CD28^{-}$ T cell	81.3 /24.2	<0.001	561 vs 74	<0.001
Our model outcome favorable/unfavorable	79.2 /8.0	<0.001	500 vs 67	<0.001

3046 Poster Session (Board #110), Fri, 8:00 AM-11:00 AM

Plasma next-generation sequencing (NGS) in advanced non-small cell lung cancer (aNSCLC) patients (pts) treated with immune checkpoint inhibitors (ICIs): Impact of *STK11* and *TP53* mutations on outcome. *First Author: Alberto Pavan, Medical Oncology 2, Istituto Oncologico Veneto IOV-IRCCS, Padua, Italy*

Background: ICIs revolutionized aNSCLC treatment. The next challenge lays on the search for predictive markers. Detection of multiple tumor-related genetic alterations through NGS in cell free DNA is a promising tool, provided the limited availability of tumor tissue in most cases. **Methods:** Between January 2017 and October 2019, aNSCLC pts consecutively referring to our Institution were prospectively screened with plasma NGS while included in two clinical trials: VISION (NCT02864992) and MAGIC trial, an observational study. In VISION trial NGS was performed in plasma (Guardant360 test) and tissue (Oncomine Focus Assay). In MAGIC Myriapod NGS-IL 56G Assay was used. Aim of the study was to evaluate the impact of *STK11*, *KRAS* and *TP53* mutations (muts) on outcome of ICI-treated pts, with overall survival (OS) as primary endpoint. A control group of pts not receiving ICIs was also analyzed. **Results:** A total of 235 NSCLC pts were enrolled and received ICIs. 93 pts were analyzed in plasma at the time of beginning ICIs: median OS was 18.9 m (95% CI: 13.7-24.1) and median immune-related progression free disease (irPFS) 3.8 m (95% CI: 2.5-5.1). 49 (52.7%), 22 (23.7%) and 8 (8.6%) pts carried *TP53*, *KRAS* and *STK11* pathogenic alterations, respectively. *STK11* mutated pts showed a trend for worse OS compared with wildtype counterpart (14.9 m, 95% CI: 6.5-23.3, *versus* 20.3, 95% CI: 13.4-27.2, p = 0.192) *KRAS* muts had no impact on outcome. Pts with *TP53* or *STK11/KRAS* co-mut (n = 3) had worse OS (12.3 m, 95% CI: 9.2-15.4; HR = 3, 95% CI: 1.6-5.8, p = 0.001 and 5.9 m, 95% CI: 1.4-7.6; HR = 2.9, 95% CI: 1.4-6.3, p = 0.007) and worse irPFS (2.8 m, 95% CI: 1.7-3.9, HR = 1.8 95% CI: 1.1-3.1, p = 0.03 and 1.2 m, 95% CI: 0.9-1.5, HR = 2.2 95% CI: 1.2-4.1, p = 0.01). Number of muts negatively impacts pts' OS (HR = 1.2, 95% CI: 1.1-1.3, p = 0.02) and was higher among *TP53* mutated pts ($p <$ 0.001, Mann-Whitney test). In multivariate analysis, *TP53* and *STK11/KRAS* retained significance. A control group of pts not receiving ICIs was analyzed (n = 101): median OS was 16.8 m (95% CI: 13-20.6). Nor *STK11* (n = 10), nor *STK11/KRAS* (n = 6) had impact on OS (HR = 1.8, 95% CI: 0.7-4.7, p = 0.267 and 1.4, 95% CI: 0.7-3.0, p = 0.293) while the presence of *TP53* muts (n = 41) was associated with shorter OS (11.4 m, 95% CI: 7.3-15.5; HR = 2.2, 95% CI: 1.2-4.2, p = 0.009). **Conclusions:** NGS performed in plasma might be used to detect predictive markers. *TP53* muts in plasma at baseline had prognostic value, while *STK11/KRAS* muts were associated with worse outcome to ICIs. Research Sponsor: None.

3047 Poster Session (Board #111), Fri, 8:00 AM-11:00 AM

Changes in lymphocyte/monocyte ratio, prognostic marker to predict overall survival in patients with advanced cancer treated with immune checkpoint inhibitor. *First Author: Sandip H. Patel, The Ohio State University Comprehensive Cancer Center, Department of Internal Medicine, Division of Medical Oncology, Columbus, OH*

Background: Immunosuppressive factors within the tumor microenvironment (TME) pose a barrier to response to treatment with immune checkpoint inhibitors (ICI). Monocytes alter the TME to promote cancer progression through local immune suppression and angiogenesis. Peripheral blood lymphocyte-to-monocyte ratio (LMR) may reflect the interaction between host immunity, represented by lymphocytes, and the tumor microenvironment, represented by monocytes. A low LMR in the peripheral blood may serve as a surrogate biomarker and has been associated with poor prognosis in various cancers; however, its role has not been well defined in the era of treatment with ICI. **Methods:** We retrospectively evaluated 1034 patients with advanced cancer treated with ICI from 2011 to 2017. We calculated LMR as ratio of absolute lymphocyte/monocyte counts at baseline and median of 21 days after first cycle of ICI (on-treatment LMR) and considered low if < 2. Overall survival (OS) was calculated from the initiation of ICI to date of death or censored at last follow-up. Median OS with 95% confidence intervals (CI) was estimated using the Kaplan-Meier method. Log rank test was used for group comparison. **Results:** 536 pts (52%) with LMR $<$ 2 at baseline had shorted median OS compared to 498 (48%) with LMR$\geq$2 (median OS 8.4 months vs 17.8 months, $p < 0.001$). Of 1034 pts with baseline LMR, 837 had follow up LMR evaluable. In patients with baseline and on-treatment LMR, those with baseline LMR < 2, who had on treatment LMR $\geq$2, had OS of 16.8 months (95% CI 10.3-23.5) compared to median OS 8.0 months (95% CI 6-9.4) for patients with on treatment LMR < 2 after first cycle of ICI, $p < 0.001$. Patients with baseline LMR$\geq$2, who had on treatment LMR $\geq$ 2, had median OS of 23 months (95% CI 19.7-28.9), but median OS was 9.4 months (95% CI 7.1-11.1) for patients with on-treatment LMR < 2 after first cycle of ICI, $p < 0.001$. **Conclusions:** We observed a statistically significant association between not only baseline LMR but also change in LMR from baseline after first cycle of ICI and overall survival in cancer patients treated with ICI. The role of LMR at baseline and on-treatment LMR should be evaluated in further studies incorporating known additional prognostic factors for ICI therapy. Research Sponsor: None.

LMR ratio (Baseline)	LMR ratio (After first cycle of Immunotherapy)	Number of Patients (%)	Median Overall Survival (Month) and 95% CI	p value
< 2		536 (52%)	8.7 (7.4-9.9)	< 0.001
	< 2	341	8 (6-9.4)	<
	≥2	90	16.8 (10.3-23.5)	0.001
≥2		498 (48%)	17.8 (15.7-21.6)	
	< 2	108	9.4 (7.1-11.1)	<
	≥2	298	23 (19.7-28.9)	0.001

3048 Poster Session (Board #112), Fri, 8:00 AM-11:00 AM

Neutrophil-lymphocyte score: A novel prognostic scoring system that utilized the dynamic change of neutrophil, lymphocyte, and albumin and its comparison to other indices. *First Author: Songzhu Zhao, Center for Biostatistics, The Ohio State University, Columbus, OH*

Background: Indications for immune checkpoint inhibitor (ICI) in cancer care are expanding rapidly. There is increasing need for accurate decision tool to better guide treatment. We have constructed a new prognostic scoring system, neutrophil-lymphocyte score (NRS), based on the nonlinear dynamic change of neutrophil to lymphocyte ratio (NLR) in relation to survival over the first cycle of ICI treatment. We compared this novel system to existing indices such as NLR, lymphocyte to monocyte ratio (LMR), platelet to lymphocyte ratio (PLR), Advanced Lung Cancer Inflammation Index (ALI), and Systemic Immune-inflammation Index (SII). **Methods:** This is a retrospective analysis of 837 patients at Ohio State University from 2011-18. Neutrophil (ANC), lymphocyte (ALC), platelet (plt), monocyte (AMC), albumin (alb), and body mass index (BMI) were collected at baseline. Repeat labs were collected at cycle 2. NLR = ANC/ALC, ALI = BMI x alb / NLR, LMR = ALC/AMC, SII = platelet x NLR, PLR = plt/ALC. NLR Ratio = baseline NLR / repeat NLR. Based on the association between NLR and the overall survival, we assigned 1 point (p) for baseline NLR < 0.7, 6p for 0.7 to < 2, 5p for 2 to < 3, 4 p for 3 to < 4, 3 for 4 to 5, 2p for 5 to < 9, and 1p for $\geq$9. We also assigned 1p for NLR ratio < 0.6, 2p for 0.6 to < 0.8, 3p for 0.8 to < 1.2, 5p for 1.25 to < 1.4, 3p for 1.4 to < 1.6, and 2p for $\geq$1.6. NLS = sum of these 2 scores . NLS_A = NLS*alb. Time-dependent receiver operator characteristic (ROC) curves with integrated time-dependent area under the curve (TD AUC) values were used to evaluate the predictive accuracy of each index for survival. **Results:** For baseline and repeat values, all indices were statistically significant ($P < 0.001$) in predicting survival. Baseline integrated TD AUC were: ALI 0.704, NLR 0.692, SII 0.663, LMR 0.645, and PLR 0.612. All of the repeat indices at cycle 2 had higher prognostic value than their baseline counterparts. Integrated TD AUC for indices at cycle 2 were: ALI 0.740 (with baseline BMI), NLR 0.729, SII 0.694, LMR 0.671, and PLR 0.652. NLS_A was a composite score based on the dynamic change of NLR from cycle 1 to 2 and the treatment alb with integrated TD-AUC at 0.754. **Conclusions:** Indices constructed from ANC, ALC, AMC, Plt, alb, and BMI can be obtained inexpensively and provide great prognostic value for pts on ICI. We have constructed a novel scoring system (NLS_A) and demonstrated its improvement over the current prognostic indices. Studies with a larger cohort are needed to further improve and validate this system. Research Sponsor: Research support provided by the REDCap project and The Ohio State University Center for Clinical and Translational Science grant support (National Center for Advancing Translational Sciences, Grant UL1TR002733). Dr. Owen is a Paul Calabresi Scholar suppo.

3049 Poster Session (Board #113), Fri, 8:00 AM-11:00 AM

Clinical value of noninvasive biomarkers reflecting a collagen-rich stroma in metastatic melanoma patients treated with anti-PD1 therapy. *First Author: Christina Jensen, Biomarkers & Research, Nordic Bioscience, Herlev, Denmark*

Background: Poor response to anti-PD1/PD-L1 remains a clinical challenge in a subgroup of patients with metastatic melanoma. Recent evidence strongly suggests that these poor responses are associated with TGF-β signaling and CD8+ T-cell excluded tumors characterized by a collagen-rich peritumoral stroma that blocks the interaction between T cells and tumor cells. In the pursuit of identifying non-invasive biomarkers associated with a T-cell excluded phenotype and predict resistance/response to immune checkpoint inhibitor therapy, we evaluated the association between blood-based biomarkers measuring type III collagen formation and cross-linking and survival outcomes in metastatic melanoma patients treated with anti-PD1 therapy. **Methods:** 107 patients with metastatic melanoma who started anti-PD1 monotherapy between May 2016 – March 2019 entered in a prospective real-life study (nivolumab n = 62, pembrolizumab n = 45). Type III collagen formation (PRO-C3) and type III collagen formation and cross-linking (PC3X) were measured with ELISAs in pre-treatment serum. Biomarker levels were associated to Disease Control Rate (according to RECIST v.1.1) by Mann-Whitney test and correlated to survival outcomes by Kaplan-Meier and Cox regression analyses. **Results:** PRO-C3 was significantly elevated in patients with progressive disease compared to the combined group of patients with complete response, partial response and stable disease (p = 0.046). High PRO-C3 and PC3X ($> 75^{th}$ percentile) prior to treatment were significantly associated with poor overall survival (PRO-C3: HR = 2.4, p = 0.008; PC3X: HR = 2.2, p = 0.019) and progression free survival (PRO-C3: HR = 1.91, p = 0.016; PC3X: HR = 1.94, p = 0.013). The median overall survival was 417 and 511 days in biomarker high patients compared to 1269 and 1269 days in biomarker low patients, for PRO-C3 and PC3X, respectively. **Conclusions:** Biomarkers quantified in a pre-treatment liquid biopsy reflecting excessive collagen formation and cross-linking were associated with poor response and survival outcomes in metastatic melanoma patients treated with anti-PD1 therapy. This supports an association between collagen formation and resistance to anti-PD1 therapy. Furthermore, if validated, these non-invasive collagen biomarkers may have potential for guiding patient stratification for immune checkpoint inhibitor therapy and combination therapies. Clinical trial information: NTR7015. Research Sponsor: The Danish Research Foundation, Erasmus Medical Center.

3050 Poster Session (Board #114), Fri, 8:00 AM-11:00 AM

TCR clonality and Treg frequency as predictors of outcome in stage III NSCLC treated with durvalumab. *First Author: Sally CM Lau, Princess Margaret Cancer Center, University Health Network, Toronto, ON, Canada*

Background: Novel blood-based biomarkers evaluating T-cell receptor (TCR) clonality as well as the frequency/activation of immune populations hold significant potential for predicting response and elucidating the biology of anti-tumor immunity in stage 3 NSCLC treated with durvalumab. In this study, we sought to characterize clinical and immunologic predictors of durable response to therapy with a specific focus on TCR clonality and peripheral immune populations. **Methods:** Stage 3 NSCLC patients undergoing chemoradiation (CRT) and durvalumab were prospectively recruited and underwent baseline and serial blood collections. TCR repertoire analysis was performed on cfDNA using hybrid-capture TCR sequencing and TCR diversity estimated using Shannon's entropy index. Viably preserved peripheral blood mononuclear cells (PBMC) were analyzed by high-dimensional flow cytometry using validated panels to evaluate T/B/NK-cell, Treg and myeloid populations. Correlations between cell populations were examined using linear and cox regression. **Results:** 134 stage 3 NSCLC patients who received durvalumab had a median PFS was 15.4 months, with worse PFS in patients with PD-L1 1-49% (HR 2.4, p = 0.03) and PD-L1 $<$ 1% (HR 2.6, p = 0.03). Smoking and *EGFR/ALK* mutations were not predictors of PFS. Immune profiling was performed in a pilot of 19 patients. Baseline TCR diversity did not associate with clinical factors or outcome. However, lack of clonal expansion after CRT indicated by a higher Shannon's index was significantly associated with increased frequency of Tregs after durvalumab ($p < 0.05$). In turn, this elevation in Tregs was associated with significantly reduced PFS in *EGFR/ALK* wt patients (p = 0.03) and a trend towards reduced PFS in the overall cohort (HR 5.2, p = 0.1). **Conclusions:** Clonal expansion of T cells after CRT may influence the likelihood of an anti-tumor immune response following PD-L1 blockade in stage 3 NSCLC. Similarly, expansion of peripheral Treg populations is associated with increased likelihood of disease recurrence. Further characterization of TCR clonality, minimal residual disease and T cell subpopulations using serially collected blood is ongoing. Research Sponsor: This study is performed under the auspice of the LIBERATE study, which is an institutional liquid biopsy program at the University Health Network supported by the BMO Financial Group Chair in Precision Cancer Genomics (Chair held by Dr. Lillian Siu), Ontario Institute of Cancer Research, Tumor Genomics Laboratory Grant.

3051 Poster Session (Board #115), Fri, 8:00 AM-11:00 AM

Sequential monitoring of circulating stromal cells from blood is predictive of progression in NSCLC patients undergoing anti-PD-L1 therapy after definitive chemoradiation therapy. *First Author: Daniel Adams, Creatv MicroTech, Inc., Monmouth Junction, NJ*

Background: Cancer Associated Macrophage-Like cells (CAMLs) are a recently described circulating stromal cell common in the peripheral blood of patients with solid tumors. In non-small cell lung carcinoma (NSCLC), patients with CAMLs ≥50μm after completion of chemoradiation therapy (CRT) have been shown to have worse progression free survival (PFS). However, with the recent addition of anti-PD-L1 therapies in conjunction with CRT as standard of care, it has never yet to be evaluated whether CAMLs remain predictive for monitoring progression in NSCLC patients post anti-PD-L1 therapy. **Methods:** A 2 year single blind prospective study was undertaken to test the relationship of ≥50μm CAMLs to PFS based on imaging in lung patients before and after induction of CRT and PD-L1. We recruited 104 patients with pathologically confirmed unresectable NSCLC Stage II (n = 14), Stage III (n = 83), Stage IV (n = 3), and locally recurrent disease (n = 4). Baseline (BL) blood samples were taken prior to start of therapy. A second time point blood sample (T1) was taken at the end of radiotherapy (~40 days). A third time blood sample (T2) was taken after induction of anti-PD-L1 therapy (e.g. Imfinizi, Keytruda, etc.). Blood was filtered by CellSieve filtration and CAMLs were quantified. Analysis by CAML size of $<$ 49 μm or ≥50 μm was used to evaluate PFS hazard ratios (HRs) by censored univariate & multivariate analysis. **Results:** CAMLs were found in 87% of samples averaging 2.9 CAMLs/7.5mL sample. At BL, CAMLs ≥50 μm had similar PFS to patients with $<$ 50 μm CAMLs (HR = 1.1 95%CI 0.6-1.95 p = 0.8661). However, after CRT (T1), patients with CAML size ≥50 μm had worse PFS (HR = 3.2, 95%CI 1.8-5.8 p = 0.0002). After induction of anti-PD-L1 therapy (T2), patients with ≥50 μm CAMLs also had worse PFS (HR = 2.8 95%CI 1.5-5.4 p = 0.0037). CAML size at BL was not accurate at predicting progression within 24 months; however ≥50 μm CAMLs after CRT or after 1 cycle of anti-PDL1 therapy was 71% accurate at predicting progression of disease. **Conclusions:** Our data suggests that in NSCLC, ≥50 μm CAMLs after completion of CRT or appearing after induction of anti-PD-L1 therapy appears to predict progressive disease. If validated, additional studies are needed to determine if CAMLs can serve as a significantly prognostic blood based marker for predicting survival in NSCLC patients early in the treatment regime. Research Sponsor: U.S. National Institutes of Health.

3052 Poster Session (Board #116), Fri, 8:00 AM-11:00 AM

Tumor methylation patterns to measure tumor fraction in cell-free DNA. *First Author: Colin Melton, GRAIL, Inc, Menlo Park, CA*

Background: Cell-free DNA (cfDNA) tumor fraction (TF), the proportion of tumor molecules in a cfDNA sample, is a direct measurement of signal for cfDNA cancer applications. The Circulating Cell-free Genome Atlas study (CCGA; NCT02889978) is a prospective, multi-center, observational, case-control study designed to support development of a methylation-based, multi-cancer detection test in which a classifier is trained to distinguish cancer from non-cancer. Here we leveraged CCGA data to examine the relationship between cfDNA containing tumor DNA methylation patterns, TF, and cancer classification performance. **Methods:** The CCGA classifier was trained on whole-genome bisulfite sequencing (WGBS) and targeted methylation (TM) sequencing data to detect cancer versus non-cancer. 822 samples had biopsy WGBS performed; of those, 231 also had cfDNA targeted methylation (TM) and cfDNA whole-genome sequencing (WGS). Biopsy WGBS identified somatic single nucleotide variants (SNV) and methylation variants (MV; defined as methylation patterns in sequenced DNA fragments observed commonly in biopsy but rarely [$<$ 1/10,000] in the cfDNA of non-cancer controls [n = 898]). Observed tumor fragment counts (SNV in WGS; MV in TM), were modeled as a Poisson process with rate dependent on TF. TF and classifier limits of detection (LOD) were each assessed using Bayesian logistic regression. **Results:** Across biopsy samples, a median of 2,635 MV was distributed across the genome, with a median of 86.8% shared with ≥1 participant, and a median of 69.3% targeted by the TM assay. TF LOD from MV was 0.00050 (95% credible interval [CI]: 0.00041 - 0.00061); MV and SNV estimates were concordant (Spearman's Rho: 0.820). MV TF estimates explained classifier performance (Spearman's Rho: 0.856) and allowed determination of the classifier LOD (0.00082 [95% CI: 0.00057 - 0.00115]). **Conclusions:** These data demonstrate the existence of methylation patterns in tumor-derived cfDNA fragments that are rarely found in individuals without cancer; their abundance directly measured TF, and was a major factor influencing classification performance. Finally, the low classifier LOD (~0.1%) motivates further clinical development of a methylation-based assay for cancer detection. Clinical trial information: NCT02889978. Research Sponsor: GRAIL.

3053 Poster Session (Board #117), Fri, 8:00 AM-11:00 AM

Rechallenging with immune checkpoint inhibition after a treatment-limiting immune-related adverse event. *First Author: Richard Lee O'Neal, University of Kentucky, Markey Cancer Center, Greenville, KY*

Background: Immune checkpoint inhibition (ICI) with cytotoxic T-lymphocyte antigen 4 (CTLA-4), programmed death 1 (PD-1), or programmed death ligand-1 (PD-L1) blockade can be associated with the development of immune related adverse events (irAE), many of which can be treatment-limiting. Due to an absence of randomized controlled trials, the current approach in regards to ICI discontinuation versus rechallenging remains controversial. **Methods:** We assessed all patients who had received ICI at a single academic institution from 5/2015 to 1/2019, identifying those who had delays in their treatment. Retrospective chart review was performed to determine type of ICI, type and grade of irAE, treatment of irAE, and recurrence and grades of irAE if ICI was resumed, as well as to assess overall survival (OS). **Results:** 562 patients received ICI (lung cancer [232, 41%], melanoma [66, 12%], kidney cancer [43, 8%], bladder cancer [27, 5%], and other cancers [194, 34.5%]) from 5/2015 – 1/2019. Of these, 121 (22%) had a treatment-limiting irAE (most commonly dermatitis [24%], colitis [17%], pneumonitis [14%], and hepatitis [12%]). Of the patients who had ICI held, 80/121 (66%) were eventually rechallenged, while 41/121 (34%) discontinued permanently. When rechallenged with ICI, 47/80 (59%) had no further treatment-limiting irAEs, 16/80 (20%) had a recurrence of the same irAE, and 17/80 (21%) developed a different irAE. Of those who were rechallenged, only 17/80 (21%) ultimately had to discontinue because of a second irAE. At a median follow up time of 12.1 months, median OS was not reached in those patients who experienced a treatment limiting irAE and was 8.1 months in those who did not (hazard ratio [HR] for death, 0.33; 95% CI 0.23 – 0.48; $p < 0.001$). At 12 months from initiation of ICI, 77.0% of patients who had a treatment-limiting irAE were alive, compared to 39.6% of those who did not have an event. Restarting ICI after a treatment-limiting irAE was not associated with a change in OS (HR 0.66 [95% CI 0.27 – 1.66], p = 0.38). **Conclusions:** Patients who discontinued ICI secondary to irAEs had relatively low rates of recurrent toxicity when rechallenged with treatment. These patients were just as likely to develop a new toxicity as a recurrence of the original irAE, and relatively few had to discontinue permanently. Development of a treatment-limiting irAE was associated with improved OS compared to those who did not. This study suggests that rechallenging with ICI may be safe in selected patients, though this did not have an impact on OS. Research Sponsor: None.

3054 Poster Session (Board #118), Fri, 8:00 AM-11:00 AM

An open-label, phase I trial of BI 754091 alone and in combination with BI 754111 in Asian patients (pts) with advanced solid tumors. *First Author: Yoon-Koo Kang, Asan Medical Center, Seoul, South Korea*

Background: Dual blockade of immune checkpoint molecules, PD-1 and LAG-3, may enhance the anti-tumor response versus PD-1 blockade alone. This Phase I trial investigated BI 754091, an anti-PD-1 antibody, as monotherapy and in combination with BI 754111, an anti-LAG-3 antibody, in Asian pts with advanced solid tumors. **Methods:** This trial comprised 3 parts. Parts 1 and 2 (dose escalation) were in pts with unresectable/metastatic solid tumors. In Part 1, pts received BI 754091 240 mg intravenously (iv), every 3 weeks (q3w); in Part 2, pts received BI 754091 240 mg in combination with BI 754111 (400 mg, 600 mg or 800 mg iv, q3w). Dose escalation was guided by a Bayesian logistic regression model, with overdose control. The primary endpoint in Parts 1 and 2 was maximum tolerated dose (MTD) of BI 754091 alone or in combination with BI 754111, based on dose-limiting toxicities (DLTs) in Cycle 1. In Part 3, BI 754091 240 mg plus BI 754111 600 mg q3w was assessed in 4 expansion cohorts. Cohorts A–C included pts with: A) gastric/esophagogastric junction cancer; B) esophageal cancer; C) hepatocellular cancer; all had received ≥1 line of prior systemic therapy and no prior anti-PD-(L)1 therapy. Cohort D included pts who had received prior anti-PD-(L)1 therapy for the tumor types in Cohorts A–C. The primary endpoint in Part 3 was objective response (confirmed complete response or partial response [PR] per RECIST 1.1). **Results:** In Part 1, 6 pts received BI 754091 240 mg. In Part 2, 9 pts received BI 754091 240 mg plus BI 754111 (400 mg/600 mg/800 mg; n = 3 per cohort). No DLTs were reported in Parts 1 and 2. In Part 3, 121 pts were treated (97 [80%] male, median age 61 years [range 23–80]); Cohorts A/B/C/D included 33/33/20/35 pts. All-grade adverse events (AEs) and treatment-related AEs (TRAEs) were experienced by 96 (79%) and 47 (39%) pts, respectively. The most commonly reported AEs (all/≥G3) were pyrexia (21%/0%), decreased appetite (17%/2%), anemia (11%/6%), and nausea (9%/0%). 36 (30%) pts reported immune-related AEs, most commonly hypothyroidism, in 7 (6%) pts. Confirmed PR was observed in 6 pts (5%; Cohort A/B, n = 4/2) and 35 (29%) pts had stable disease (Cohort A/B/C/D, n = 9/11/10/5). **Conclusions:** MTD was not reached for BI 754091 monotherapy or for BI 754091 in combination with BI 754111. The recommended dose for the combination was determined as BI 754091 240 mg plus BI 754111 600 mg q3w. Treatment was well tolerated and consistent with that observed in the global trial. Preliminary anti-tumor activity was seen. Clinical trial information: NCT03433898. Research Sponsor: Boehringer Ingelheim.

3055 Poster Session (Board #119), Fri, 8:00 AM-11:00 AM

Evolving development of PD-1 therapy: Cetrelimab (JNJ-63723283) from monotherapy to combination with erdafitinib. *First Author: Victor Moreno, START Madrid-FJD, Fundación Jiménez Díaz University Hospital, Madrid, Spain*

Background: Cetrelimab (CET) is an investigational checkpoint inhibitor (CI). In part 1 of a first-in-human (FIH) trial (LUC1001; NCT02908906), pts with advanced solid tumors with ≥1 prior treatment received CET 80–800 mg Q2W or 480 mg Q4W. Response rates and safety profiles were similar to other CIs. Based on preclinical and clinical data, a phase 1/2 study (NORSE; NCT03473743) of CET + erdafitinib (ERD) in metastatic urothelial carcinoma (mUC) + FGFR alterations (alt) was initiated and is ongoing. **Methods:** In LUC1001 Part 2, pts with nonsmall cell lung cancer (NSCLC), melanoma (MEL), or MSI-H/dMMR colorectal cancer (CRC) received CET IV 240 q2w. Overall response rates (ORR = % complete response + partial response [PR] confirmed) were assessed as per RECIST v1.1. Adverse events (AEs) were assessed for all patients receiving CET IV 240 q2w in parts 1 and 2. **Results:** As of July 1, 2019, 122 pts with NSCLC (n=30); MEL (n=50); or CRC (n= 42) had been treated in Part 2. Median age ranged from 58 to 64 yrs (overall range, 23–86 yrs). Duration of treatment was 8.1 mos (range, 0.0-24.7) for NSCLC; 5.5 mos (range, 0.0-25.0) for MEL; and for 3.0 mos (0.0-16.1) for CRC. ORR was 37% in NSCLC; 53% in PD-L1+ NSCLC (≥50% by IHC), 28% in MEL; 32% in non-uveal MEL, 14% in CRC and 24% in centrally confirmed MSI-high CRC. In all CET IV 240 q2w treated pts in the FIH study (N= 162), treatment-related grade ≥3 and serious AEs were reported in 15% and 12% of pts, respectively. All grade and grade ≥3 immune-related (ir) AEs were reported in 41% and 8% of pts, respectively Most common ir AE: hypothyroidism (8%), asthenia (6%), diarrhea (4%), rash (4%), hyperthyroidism (4%), dyspnea (3%), pruritis (3%) and pneumonitis (3%). There was 1 treatment-related death due to myasthenia gravis. In the phase 1 combination study (NORSE), pts with mUC + FGFR alt (n=17) received fixed-dose CET IV 240 q2w + ERD 6mg, 8 mg or 8mg + up titration (UpT) to 9 mg to establish the RP2D for the combination as CET + ERD 8mg + UpT. In the RP2D group (n=10), 60% had treatment-related grade ≥3 AEs. ORR (all confirmed PR) was 50% in the all treated response-evaluable group (n=16). **Conclusions:** CET is a CI with efficacy and safety profiles in advanced solid tumors similar to approved CIs. In NORSE phase 1, CET+ERD demonstrated antitumor activity in mUC with an acceptable safety profile. NORSE phase 2 is evaluating this combination as first-line therapy in pts with mUC with FGFR alt. References: Rutkowski, et al J Clin Oncol.2019; 37 (8 suppl): 31-31. Moreno, et al. ASCO-GU Genitourinary Cancers Symposium. February 13-15, 2020. San Francisco, CA. Clinical trial information: NCT02908906 and NCT03473743. Research Sponsor: Janssen Research and Development.

3056 Poster Session (Board #120), Fri, 8:00 AM-11:00 AM

A phase I study of ALX148, a CD47 blocker, in combination with standard anticancer antibodies and chemotherapy regimens in patients with advanced malignancy. *First Author: Laura Quan Man Chow, University of Washington, Seattle, WA*

Background: CD47 is a myeloid checkpoint upregulated by tumor cells to evade the host immune response. ALX148 (A) is a fusion protein comprised of a high affinity CD47 blocker linked to an inactive immunoglobulin Fc region. ALX148 enhances innate and adaptive immune responses against cancer and has previously been shown to be well tolerated in combination with the checkpoint inhibitor (CPI), pembrolizumab (P), and trastuzumab (T) in a range of solid tumors (ASCO 2019 #2514). ALX148 safety and activity in combination with T or P and standard chemotherapy regimens are reported in patients (pts) including head and neck squamous cell cancer (HNSCC) and HER2 positive gastric/gastroesophageal cancer (GC). **Methods:** Pts with advanced malignancy were administered AP or AT. Patients with ≥2L HNSCC progressed on platinum therapy received AP, while those with untreated advanced disease received AP+5FU (FU)+platinum. Pts with ≥2L GC progressed on T+FU+platinum received AT +/- ramucirumab (ram)+paclitaxel (pac). Safety, response, pharmacokinetic and pharmacodynamic (PD) markers were assessed. Data are reported as of 21, Jan. 2020. **Results:** Patients received AP (n=52); AP+FU+platinum (n=1); AT (n=30); or AT+ram+pac (n=3) as of data cutoff. Eighty-two pts experienced any adverse event (AE). Fifty-seven pts administered AP or AT regimens reported mostly low grade ALX148 treatment related (TR) AEs, the most common being fatigue (18%), AST increase (11%), platelets decreased (10%), ALT increase (8.5%), anemia (8.5%), and pruritus (8.5%). Pts receiving AP+FU+platinum or AT+ram+pac reported no TRAEs as of data cutoff. Anticancer activity was observed in response-evaluable pts. AP: HNSCC CPI-naïve (n=10) 40% ORR, mPFS 4.6 [95% CI:0.5; 7.5], mOS not reached with 14.4m median follow-up; AP: HNSCC CPI-experienced (n=10) 0% ORR, mPFS 2.0 [95% CI:0.9;3.6], mOS 7.4 [95% CI:3.1;NC]; and AT: GC (n=20) 20% ORR, mPFS 2.2 [95% CI:1.9;5.4], mOS 8.1 [95% CI:3.4;12.8]. Full peripheral CD47 target occupancy and increased infiltrating immune cells in tumor biopsies were seen. Exploratory analysis of biomarkers associated with response is ongoing. **Conclusions:** Initial data suggests ALX148 demonstrates excellent tolerability in combination with anti cancer antibodies and standard chemotherapy. Clinical activity in pts with advanced CPI naïve HNSCC (including PD-L1 negative) and GC compares favorably with historic controls. Final data from AP and AT cohorts and initial data from chemotherapy combination cohorts will be presented. Clinical trial information: NCT03013218. Research Sponsor: ALX Oncology Inc.

3058 Poster Session (Board #122), Fri, 8:00 AM-11:00 AM

Anti-CTLA-4 probody BMS-986249 alone or in combination with nivolumab in patients with advanced cancers: Initial phase I results. *First Author: Martin Gutierrez, Hackensack University Medical Center, Hackensack, NJ*

Background: Blockade of the CTLA-4 pathway with ipilimumab (IPI) ± nivolumab (NIVO; anti–PD-1) is an effective treatment for a variety of cancers. To optimize the risk-benefit profile of CTLA-4–directed therapy, a Probody therapeutic technology platform (Pb-Tx, CytomX Therapeutics) was used to generate BMS-986249, a peptide-masked version of IPI that is unmasked by tumor-associated proteases. Pb-Tx may localize CTLA-4 activity to the tumor, minimize systemic toxicity, and allow for higher doses of anti–CTLA-4 ± anti-PD-1. In preclinical studies, BMS-986249, given at similar doses, showed comparable intratumoral and reduced peripheral pharmacodynamic activity relative to IPI (Engelhardt, AACR 2020). Here, we present the initial results of the first-in-human phase 1/2 study of BMS-986249 ± NIVO in pts with advanced (adv) cancers (NCT03369223). **Methods:** During dose escalation, pts received BMS-986249 at or above the approved doses of the parent molecule using a Q4W or Q8W dosing schedule as monotherapy (240–2400 mg Q4W or 1600 mg Q8W; ≈ 3–30 mg/kg vs approved 3 mg/kg Q3W IPI) or in combination (240–1200 mg Q4W or 800 mg Q8W) + NIVO 480 mg Q4W. Safety and pharmacokinetics (PK) were evaluated. Efficacy is being assessed in the dose-expansion phase. **Results:** As of December 7, 2019, 82 anti–CTLA-4 naive pts with various adv cancers received BMS-986249 ± NIVO (mono, n = 39; combo, n = 43). Median age 60 (25–78) y; 95% pts had prior systemic therapy. TRAEs occurred in 59% of pts (Gr 3/4, 23%) with mono and 74% of pts (Gr 3/4, 30%) with combo. Diarrhea was the most common any-Gr TRAE (mono, 23%; combo, 21%) and Gr 3/4 TRAE (mono, 15%; combo, 7%). Rates of Gr 3/4 TRAEs increased with higher doses of BMS-986249 but were substantially reduced with Q8W schedule (eg, 800 mg Q4W, 18%; 1600 mg Q4W, 60%; 1600 mg Q8W, 9%). Most TRAEs resolved, no Gr 5 TRAEs occurred. The peptide-masked intact probody accounted for most (73%) of the systemic BMS-986249-related species; elimination of the probody indicated involvement of both catabolism and cleavage processes. **Conclusions:** BMS-986249 ± NIVO displayed a clinically manageable safety profile, allowing assessment of comparably higher BMS-986249 dose intensity (240-1200 mg; ≈ 3-15 mg/kg) + NIVO (480 mg Q4W, full dose) than that tested with IPI + NIVO. The types of TRAEs were consistent with CTLA-4 blockade, and the overall data align with the proposed Pb-Tx mechanism of action. The preclinical and clinical data support the ongoing randomized BMS-986249 + NIVO expansion in pts with adv melanoma, in addition to other adv tumors. Clinical trial information: NCT03369223. Research Sponsor: Bristol-Myers Squibb.

3059 Poster Session (Board #123), Fri, 8:00 AM-11:00 AM

Phase Ib clinical study of CBP501, cisplatin, and nivolumab administered every three weeks in patients with advanced refractory tumors: Efficacy in dose-escalation and expansion cohorts. *First Author: Marc Ryan Matrana, Ochsner Cancer Institute, New Orleans, LA*

Background: CBP501 is a 12-amino acid G2 checkpoint abrogator and calmodulin-modulating peptide that increases platinum influx into tumor cells and induces tumor immunogenic cell death. CBP501 also suppresses platinum-induced release of cytokines by macrophages, lowers cancer stem cell populations, and reduces migration, invasion, and epithelial-mesenchymal transition of tumor cells. We report safety and efficacy outcomes from dose-escalation and expansion cohorts of a Phase Ib study of CBP501 combined with cisplatin and nivolumab (NCT03113188). **Methods:** An open-label Phase I trial was conducted using a 3+3 design: CBP501 and cisplatin were dosed simultaneously by 1h infusion Q3W at 4 different combined dose levels (CBP501: 16 or 25 mg/m^2; cisplatin: 60 or 75 mg/m^2) in the dose-escalation cohort. Nivolumab (240 mg) was dosed on the same day as a 1h infusion following CBP501/cisplatin. CBP501 and cisplatin were fixed at 25 and 60 mg/m^2, respectively, in the expansion cohort. Eligible patients had pathologically confirmed, locally advanced or metastatic solid tumors, age ≥18 years, ECOG PS 0-1, life expectancy > 3 months. The dose-expansion cohort had pretreated metastatic exocrine pancreatic cancer or microsatellite stable colorectal cancer (CRC). Scans were performed every 6 weeks while on study, then every 3 months. **Results:** The most common related adverse events (AEs) were infusion-related reaction (rash, itching, hives; n = 32/37 [Gr 1, n = 4; Gr 2, n = 28]; 86%) and anemia (n = 19/37 [Gr 1/2, n = 10; Gr 3, n = 9]; 51%). There were no additional safety signals other than those known for each agent. At January 9, 2020 (interim analysis), efficacy was evaluable in 17/19 patients in the dose-escalation cohort. Unconfirmed partial response was seen in 18% (3/17; 1 pancreatic, 1 colorectal, 1 cholangiocarcinoma), with > 3 months stable disease (SD) in 41% (7/17), disease control in 41% (7/17), and > 8 months overall survival (OS) in 53% (9/17). In the expansion cohort, efficacy was evaluable in 8/13 patients with pancreatic cancer: > 4 months SD was 50% (4/8), median progression-free survival 4.2 months, and median OS 5.9 months (6/8 ≥3rd line). The CRC cohort median OS for all CRC patients (n = 10) including the dose-escalation cohort (n = 5) was 17.5 months (10/10 ≥3rd line). **Conclusions:** The triple-drug combination is reasonably tolerable with preliminary signs of efficacy in refractory solid tumors, including those in which cisplatin and nivolumab have limited single-agent activity. Clinical trial information: NCT03113188. Research Sponsor: CanBas Co., Ltd.

3060 Poster Session (Board #124), Fri, 8:00 AM-11:00 AM

Characteristics and outcomes of real-world (RW) patients (pts) with microsatellite instability-high (MSI-H) solid tumors treated with pembrolizumab monotherapy (P) after FDA approval. *First Author: Tamara Snow, Flatiron Health, New York, NY*

Background: The first tumor-agnostic, biomarker-based FDA approval in oncology was P in May 2017 for pts with MSI-H or mismatch repair (MMR) deficient tumors. 1 yr overall survival (OS) was >70% for colorectal cancer (CRC) and >60% for non-CRC in P-treated MSI-H clinical trial pts (Le 2019; Marabelle 2019). As tumor-agnostic therapies are a new paradigm, it is important to assess their use and effectiveness in routine clinical practice. We examined characteristics and outcomes of RW pts with MSI-H solid tumors who received P after May 2017. **Methods:** Pts with MSI-H solid tumors who received P after May 2017 were selected from the Flatiron Health-Foundation Medicine (FH-FMI) clinico-genomic database, a nationwide de-identified EHR-derived database linked to comprehensive genomic profiling (CGP) data. Pts with 2+ visits in the FH network from 01/2011-09/2019 with CGP prior to P use were included. Clinical characteristics were assessed at first P use. Time to treatment discontinuation (TTD) and OS from first P use were estimated with Kaplan-Meier analyses of all pts and the largest tumor types. **Results:** 33,395 pts had a solid tumor tested for MSI by CGP, of which 557 (1.7%) were MSI-H (median age 68 yrs; 34% male). 129 MSI-H pts across 33 tumor types received first P after May 2017. CRC (N=36) and Endometrial cancer (N=39) were most common. 52 pts (40%) had a concurrent MMR alteration (MLH1, MSH2, MSH6 or PMS2); median TMB was 32.2 mut/mb (IQR 20.9-47.5). Median number of therapies prior to P was 1; median time from CGP to first P use was 3 mos. Table shows OS and TTD. **Conclusions:** In this RW study, P use was observed across 33 MSI-H tumor types. Median OS exceeded 1 yr across all pts and in CRC, Endometrial, and Other cohorts. 1 yr OS rate was consistent with P trial outcomes. Further study should evaluate whether effectiveness differs across diseases, MSI testing method, or other genomic attributes to improve treatment selection. Research Sponsor: Flatiron health Inc.

OS and TTD in P-treated, pantumor MSI-H pts.

	N	Median TTD, mos [95% CI]	Median OS, mos [95% CI]	N at risk at 12-mos	12-mos OS, % [95% CI]
All Pts	129	5.5 [4.1-7.6]	NR [14.6-NR]	38	62.7 [53.3-73.7]
CRC	36	4.5 [2.8-9.2]	NR [12.9-NR]	9	71.8 [55.0-93.7]
Endometrial	39	6.2 [3.0-11.0]	NR [11.0-NR]	13	58.4 [42.9-79.5]
Other*	54	6.1 [2.8-8.2]	17.3 [9.9-NR]	16	60.3 [46.7-78.0]

*Tumors included (largest to smallest N): Gastric, Occult/Unknown Primary, Prostate, Esophageal/Gastroesophageal Junction, Breast, Hepatobiliary, Small Intestine, Non-Small Cell Lung, Pancreatic, Ovarian

3061 Poster Session (Board #125), Fri, 8:00 AM-11:00 AM

A first-in-human phase I study in patients with advanced and/or refractory solid malignancies to evaluate the safety of ATOR-1015, a CTLA-4 x OX40 bispecific antibody. *First Author: Jeffrey Yachnin, Karolinska Institutet, Stockholm, Sweden*

Background: ATOR-1015 is a human CTLA-4 x OX40 targeting IgG1 bispecific antibody developed to be a next generation CTLA-4 antibody with enhanced immune activation and tumor-directed activity for improved efficacy and reduced toxicity. **Methods:** The primary objective of the study is to determine the maximum tolerated dose (MTD) and/or the recommended phase 2 dose (RP2D) in patients with advanced solid malignancies. Safety and tolerability of ATOR-1015 are assessed by adverse events (AEs), vital signs, ECG, laboratory evaluations and physical examinations. Secondary objectives include pharmacokinetics (PK), immunogenicity and clinical efficacy. Clinical efficacy is assessed using Response Evaluation Criteria in Solid Tumors for immune-based therapeutics (iRECIST). The study is designed with single patient cohorts for doses below 100 mg followed by a modified 3+3 design (NCT03782467). Intra-patient dose escalation is allowed. ATOR-1015 is administered intravenously every other week as a single agent until confirmed progressive disease, unacceptable toxicity or withdrawal of consent. **Results:** From March 2019 to February 2020, 15 patients have been exposed to ATOR-1015. The median age of the patients is 52 years (range 40-72). The following cancer types have been included: colorectal cancer (n=8), uveal melanoma (n=2), pancreatic cancer (n=2), ovarian cancer (n=2), and cholangiocarcinoma (n=1). Patients received a median of 6 prior lines of therapy (range 3-16). Dose levels from 0.043 mg to 200 mg have been evaluated and declared safe. Dose escalation is ongoing, and 400 mg is under evaluation. The median time on study was 8 weeks (range 2.1-34.3). Four patients are on study and eleven patients have discontinued treatment. Reasons for discontinuation include clinical deterioration (n=7), death due to disease progression (n=2), confirmed disease progression (n=1) and investigator´s decision (n=1). Six of the 15 patients experienced drug-related AEs which were grade 2 or less. Infusion-related reactions (IRR) were reported in four patients. One of those four also had abdominal pain and mediastinal burning sensation. The IRR symptoms were predominantly rash. One patient had vitiligo, and one had rash. No dose-limiting toxicities have occurred. Preliminary PK data show dose-proportional kinetics up to 200 mg. **Conclusions:** The dosing of ATOR-1015 has been safe and well-tolerated up to 200 mg. Dose escalation continues and the current dose level under evaluation is 400 mg. Clinical trial information: NCT03782467. Research Sponsor: Alligator Bioscience AB.

3062 Poster Session (Board #126), Fri, 8:00 AM-11:00 AM

Phase Ia dose escalation of IBI318, a first-in-class bispecific anti-PD-1/PD-L1, in patients with advanced tumors. *First Author: Rui-hua Xu, Sun Yat-sen University Cancer Centre, Guangzhou, China*

Background: With the proven success of PD-1 and PD-L1 monoclonal antibodies, exploiting antibody based immune checkpoint strategies has potential to reduce disease burden and improve patient survival outcome. IBI318, as a first-in-class anti-PD-1/PD-L1 bispecific antibody, could provide more potent anti-tumor activity and more durable response. Here we report preliminary results from an ongoing phase 1a/1b study of IBI318 in advanced tumors. **Methods:** In the dose escalation of Phase 1a, patients with advanced and/or refractory solid tumors or hematological malignancies were enrolled to receive IBI318. Dose escalation was from 0.3 mg to 600 mg (8 cohorts) via an accelerated titration followed by a modified toxicity probability interval-2 design with a 28-day dose-limiting toxicity (DLT) observation period. Patients without DLT will receive IBI318 every two week (Q2W). Tumor assessments were performed every 6 weeks. **Results:** As of Jan 10, 2020, 15 pts who had failed at least one line of treatment had been enrolled (1 pt each in 0.3 mg, 1 mg, 3 mg and 10 mg; 3 pts in 30 mg; 3 pts in 100 mg, 3 pts in 300 mg and 2 pts in 600 mg) for dose escalation and received at least 1 dose of treatment. Median duration of treatment was 6.1 (range: 2.1-24.7) weeks. IBI318 had been well tolerated with no DLT from 0.3mg to 300mg group. 11 of 15 pts had treatment related AEs (TRAEs) and the most common (≥10%) TRAEs were pyrexia (20.0%, G1/2) and infusion-related reaction (20.0%, G1/2). 1 patient in 300 mg had an immune-related AE (G2 arthritis). No ≥G3 TRAE had been observed. 12 pts had at least one on-study tumor assessment. 3 of 9 pts receiving dose level ≥10mg had achieved partial response (1 confirmed, 1 pending confirmation and the other PD after the first PR scan). A total of 10 pts discontinued treatment due to disease progression (8) and AE (2, G4 lung infection and G4 upper gastrointestinal hemorrhage, both were not related to treatment). **Conclusions:** IBI318 has shown an acceptable safety profile. Preliminary efficacy results are promising in advanced cancer patients. The study is currently ongoing at dose level of 600 mg Q2W. Clinical trial information: NCT03875157. Research Sponsor: Innovent Biologics, Inc.

3063 Poster Session (Board #127), Fri, 8:00 AM-11:00 AM

Safety of BI 754111, an anti-LAG-3 monoclonal antibody (mAb), in combination with BI 754091, an anti-PD-1 mAb, in patients with advanced solid tumors. *First Author: Melissa Lynne Johnson, Sarah Cannon Research Institute, Nashville, TN*

Background: LAG-3, an immune checkpoint receptor involved in T-cell regulation, is frequently co-expressed with PD-1. LAG-3 and PD-1 signaling contributes to immune cell exhaustion and reduces the immune response to tumor cells. Dual inhibition of PD-1 and LAG-3 may reactivate the T-cell response better than blockade of either individual pathway. Here, we report combined safety data from 4 trials investigating BI 754111, an anti-LAG-3 mAb, in combination with BI 754091, an anti-PD-1 mAb, in patients with advanced solid tumors. **Methods:** Data from 2 phase I dose-escalation/expansion trials, 1 phase I imaging trial, and 1 phase II trial were included. Eligible patients had advanced and/or metastatic solid tumors with measurable disease and an Eastern Cooperative Oncology Group performance status ≤1. Patients received BI 754111 (intravenously [iv], 4–800 mg) in combination with BI 754091 (iv, 240 mg fixed dose) every 3 weeks (q3w). Patients remained on treatment until progressive disease or unacceptable toxicity. In each trial, safety was assessed by incidence and severity of adverse events (AEs), and graded according to Common Terminology Criteria for AEs, version 5. **Results:** Overall, 321 patients were treated with BI 754111 in combination with BI 754091 (200 [62%] male; median age, 63 years [range 18–88]). Median treatment exposure was 85 days (range 9–625). Of these patients, 282 (87.9%) had any AE (G≥3 in 99 [30.8%]). 285 patients received the 600 mg recommended phase II dose of BI 754111 plus BI 754091 240 mg q3w. Median treatment exposure in these patients was 74 days (range, 8–590). The table shows the 3 most common AEs and 4 most common immune-related AEs, and their frequency. 21 (7.4%) patients had AEs leading to study drug discontinuation, most commonly infusion-related reactions (IRRs) in 6 (2.1%) patients. Serious AEs (all-cause) occurred in 77 patients (27.0%), most commonly pleural effusion in 6 (2.1%) and deep vein thrombosis in 4 (1.4%) patients. 2 patients (0.7%) experienced an AE resulting in death (cardiac tamponade and acute kidney injury, both related to underlying diseases). **Conclusions:** The combination of BI 754111 and BI 754091 had a manageable safety profile, similar to other checkpoint inhibitors. Clinical trial information: NCT03156114, NCT03433898, NCT03697304, NCT03780725. Research Sponsor: Boehringer Ingelheim.

N (%)	All grades (N = 285)	Grade ≥3 (N = 285)
Any AEs	**247 (86.7)**	**88 (30.9)**
Fatigue	65 (22.8)	4 (1.4)
Pyrexia	53 (18.6)	1 (0.4)
Nausea	47 (16.5)	2 (0.7)
Any immune-related AEs	**60 (21.1)**	**16 (5.6)**
IRRs	14 (4.9)	3 (1.1)
Hypothyroidism	9 (3.2)	0
Rash maculopapular	7 (2.5)	2 (0.7)
Hyperthyroidism	7 (2.5)	1 (0.4)

3064 Poster Session (Board #128), Fri, 8:00 AM-11:00 AM

Results of a first-in-human phase I study of SRF231, a fully human, high-affinity anti-CD47 antibody. *First Author: Amita Patnaik, START, San Antonio, TX*

Background: CD47 is a transmembrane protein that acts as a "Don't Eat Me" signal to evade immune recognition. It is overexpressed in multiple cancer subtypes and is associated with poor prognosis. SRF231 is an investigational, fully human, high-affinity CD47-targeting antibody that delivers an activating signal to myeloid cells and displays favorable preclinical characteristics regarding its receptor occupancy/tumor exposure/efficacy relationship. **Methods:** In a Phase 1 study, SRF231-101 (NCT03512340), patients with advanced solid and hematologic malignancies who had failed standard therapy were enrolled in dose escalation cohorts (accelerated single-patient followed by standard 3+3) to establish the preliminary safety of SRF231 as a monotherapy and identify a dose and schedule suitable for expansion. In addition to collection of safety data, clinical outcomes were evaluated based on Response Evaluation Criteria in Solid Tumors (RECIST v1.1) and SRF231 pharmacokinetic (PK) and pharmacodynamic (receptor occupancy) analyses were performed. **Results:** As of January 11, 2020, a total of 46 patients were enrolled, 25 in every-3-week intravenous (IV) dosing schedules and 21 in weekly IV dosing schedules. Weekly dosing schedules also explored the use of a 1.0 mg/kg initiation dose. Other than one patient with recurrent follicular lymphoma, all patients had recurrent/refractory solid tumors. The most common treatment emergent adverse events across dosing schedules were low-grade fatigue (43%), headache (35%), and pyrexia (30%). On every-3-week dosing schedules, 2 dose-limiting toxicities (DLTs) were observed: Grade 3 febrile neutropenia and Grade 3 hemolysis, both at a 12.0 mg/kg dose level. On weekly dosing schedules, 3 DLTs were observed: Grade 4 thrombocytopenia (6.0 mg/kg), Grade 4 amylase and lipase increased (4.0 mg/kg with initiation dose), and Grade 3 fatigue (4.0 mg/kg). The maximum tolerated dose was 9.0 mg/kg on an every-3-week and 4.0 mg/kg on a weekly schedule. Receptor occupancy was maintained at > 90% throughout the dosing period with a 4.0 mg/kg weekly dose schedule. Out of 37 patients who were response evaluable by RECIST, there were no complete or partial responders, although prolonged stable disease has been observed. **Conclusions:** Preliminary data from a Phase 1 study of SRF231, an anti-CD47 antibody, demonstrate that SRF231 may be administered safely and doses of 4.0 mg/kg weekly maintain > 90% receptor occupancy throughout the dosing period. Updated safety data, clinical outcomes, and PK/pharmacodynamic data will be presented. Clinical trial information: NCT03512340. Research Sponsor: Surface Oncology, Inc. Cambridge, MA, USA.

3065 Poster Session (Board #129), Fri, 8:00 AM-11:00 AM

A phase Ib study of TQ-B2450 plus anlotinib in patients with advanced solid tumor. *First Author: Ying Cheng, Jilin Cancer Hospital, Changchun, China*

Background: Anlotinib, an antiangiogenic multi-target tyrosine kinase inhibitor, significantly improved clinical outcomes in solid tumors. TQ-B2450 is an engineered anti-programmed death-ligand 1 antibody. This onging phase 1b study aimed to assess the safety and effect of TQ-B2450 plus anlotinib in advanced solid tumors. **Methods:** This phase 1b study, which included a dose-escalating phase and an expansion phase, enrolled patients with advanced solid tumor who failed in or had no standard treatment between June 2019 and January 2020.Eligible patients were firstly assigned into sequential dose-escalating cohorts including 10mg and 12mg anlotinib plus TQ-B2450 following the conventional 3+3 design. If the starting dose of 10mg anlotinib led to ≥2 dose-limiting toxicities (DLTs), 8mg anlotinib would be administered. After the dose-escalating phase, eligible patients were enrolled into the expansion cohort. The primary outcomes were safety and objective response rate. **Results:** In the dose-escalating phase, three eligible patients received 10mg anlotinib plus TQ-B2450 had no DLTs in the first cycle, neither did three patients with 12mg anlotinib plus TQ-B2450. Then the expansion phase started, sixteen patients received 12mg anlotinib plus TQ-B2450. Finally, a total of 22 patients were included (6 small cell lung cancers [SCLC], 8 non-small cell lung cancers [NSCLC], 2 colorectal cancers, 2 breast cancers, 2 ovarian cancers, 1 thymic carcinoma and 1 cervical cancer). Ten ≥3 grade adverse events were observed (Table). Seventeen patients underwent at least once effect evaluation. One SCLC patient with 10mg anlotinib plus TQ-B2450 had confirmed partial responses (PR). Four patients with 12mg anlotinib plus TQ-B2450 had unconfirmed PR (2 SCLC and 2 NSCLC). And 9 patients had stable disease, 3 patients had progression disease. **Conclusions:** 12mg anlotinib plus TQ-B2450 showed an acceptable safety profile and promising response in advanced solid tumors. Clinical trial information: NCT03897283. Research Sponsor: None.

The ≥3 grade adverse events.

≥3 grade adverse events	10mg anlotinib plus TQ-B2450, n=3	12mg anlotinib plus TQ-B2450, n=19
Hypertriglyceridemia	1	4
Dyspnea	1	
Pericardial effusion	1	
Oropharyngeal and gingival pain		1
Decreased lymphocyte count	1	
Elevation of γ-glutamyltransferase	1	

3066 Poster Session (Board #130), Fri, 8:00 AM-11:00 AM

Assessing the effect of immunosuppressive agents for immune-related adverse event management on tumor response. *First Author: Pankti Reid, University of Chicago, Chicago, IL*

Background: High grade immune-related adverse events (irAEs) to cancer immune checkpoint inhibitors (ICI) require considerable immunosuppression (IS) with high-dose steroids and steroid-sparing IS (SSIS) for steroid-dependent cases. T lymphocyte-specific IS has generally been avoided or used with significant caution due to the fear that these agents may negatively impact ICI efficacy. We sought to determine whether T cell-specific IS agents, such as calcineurin inhibitors (CNIs), have an adverse effect on tumor control when compared to other immunomodulatory drugs (IMDs). **Methods:** We retrospectively analyzed clinical annotations of adult patients treated with ICIs for malignancy from 1/1/2000-12/31/2019, highlighting patients who were managed with SSIS, specifically those most commonly used for autoimmune disease therapy. Topical IS use was excluded. Patients were categorized as tumor responders or non-responders, and irAEs were graded according to National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE). Progression-free survival (PFS) was assessed via Kaplan-Meier curve. **Results:** 1331 unique individuals were prescribed ≥1 ICIs, with 526 prescribed systemic steroids (39.5%) and 90 (6.8%) patients prescribed SSIS agents, 25 patients with >1 SSIS: mycophenolate (39), methotrexate (26), leflunomide (5), azathioprine (3), rituximab (24), tocilizumab (3), infliximab (8), etanercept (1), adalimumab (1), golimumab (1) and CNIs (18): cyclosporine, tacrolimus. IMDs hydroxychloroquine (6) and sulfasalazine (5) were also prescribed. The objective response rate was 50.0% in the CNI group compared to 45.5% in the IMD cohort and 45.4% in the irAE group (CTCAE grade matched) with steroids alone without any SSIS. Median PFS were compared between CNI cohort (5.4 months, range 1.3-34 months) to IMD (1.1 months, range 0.4-6.4, p=0.02) and steroid alone (2.4 months, range 0.69-17.7, p=0.48). Multiple regression analysis identified irAE presence as an independent correlates to tumor response (p=0.02). **Conclusions:** T cell-specific IS should not be excluded from irAE treatment algorithm as we observed that PFS was comparable to immunomodulators and similar efficacy was observed compared to steroids alone. Rapid identification and management of irAEs can help mitigate morbidity but there are virtually no reliable clinical trials to guide irAE management with SSIS. These findings support the need for larger, prospective evaluation of immunosuppression use for high grade irAE therapy. Research Sponsor: None.

3067 Poster Session (Board #131), Fri, 8:00 AM-11:00 AM

Fecal microbiota transplantation (FMT) for immune checkpoint inhibitor induced–colitis (IMC) refractory to immunosuppressive therapy. *First Author: Yinghong Wang, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: ICIs are efficacious treatment for several advanced malignancies. IMC can limit their use, and can be refractory to medical treatment (immunosuppression) with significant morbidity. Gut microbiome alteration affects IMC development. We sought FMT as a novel therapy for IMC refractory to immunosuppressive therapy. **Methods:** 15 patients who received FMT for IMC after failure of immunosuppressive therapy were included (6/2017-1/2020). FMT was performed via colonoscopy with healthy donor's stool. **Results:** Median age was 55 years with 67% males. 5 patients received PD(L)-1, one CTLA-4 and 9 on combination. Majority had genitourinary cancers followed by melanoma. Median time from ICI to IMC was 75 days. 14 patients had grade 3-4 diarrhea and 9 had grade 3-4 colitis. Endoscopy showed mucosal inflammation in 12 patients and normal mucosa in 3 patients. IMC was refractory to 2-3 doses of infliximab or vedolizumab after corticosteroids prior to FMT. Median time from IMC onset to FMT was 75 days. 13 patients received one . 11 patients achieved clinical response within 10 days of FMT (7-14). Symptom remission was maintained for a median follow-up of 13 months. 6 patients resumed non ICI cancer treatments after FMT. 4 patients had persistent symptoms; 2 continued on vedolizumab, 1 had total colectomy, and 1 transferred to hospice. 4-8 weeks after FMT, endoscopic remission was achieved in 64% of the 11 patients who responded to FMT. No adverse events were reported. **Conclusions:** FMT treatment was successful in 73% of patients with for IMC refractory to immunosuppressive therapy. Controlled clinical trials are warranted to confirm our conclusion. Research Sponsor: None.

Characteristics of FMT (n = 15).

Characteristic	Data (N=15)
Median days from IMC onset to FMT (IQR)	75 (58-127)
Median time from FMT to symptom improvement– days (IQR)	10 (7-14)
Resumed cancer treatment after FMT—no (%)	6 (40)
Symptom improvement after FMT—no (%)	11 (73)
Endoscopic remission achieved—no (%)	7 (64)
Histology remission achieved—no (%)	5 (45)

3068 Poster Session (Board #132), Fri, 8:00 AM-11:00 AM

Circulating tumor DNA dynamics as prognostic and predictive biomarkers of response to pembrolizumab in patients with virally-related tumors (VRT) treated within the INSPIRE study. *First Author: Marc Oliva Bernal, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: We previously showed a correlation between circulating tumor DNA (ctDNA) dynamics and response to pembrolizumab in a cohort of mixed tumors treated in the INSPIRE study (Yang et al, ESMO 2019). We investigated the prognostic and predictive value of ctDNA dynamics in patients (pts) with VRT. **Methods:** Pts with VRT (HPV+ squamous cell carcinoma (SCC), EBER+ nasopharyngeal carcinoma (NPC) and MCPyV+ Merkel carcinoma (MC)) and a control cohort of non-VRT (HPV- head and neck SCC) treated with single-agent pembrolizumab were selected for the analysis. ctDNA was assayed at baseline and start of cycle 3 using a pt-specific amplicon-based NGS assay (Signatera). Samples were considered ctDNA positive if ≥2 of 16 pt-specific targets met the qualifying confidence score threshold. Whole exome sequencing (WES) performed in baseline tumor tissue; presence of HPV, EBV and MCPyV in tumor determined through bioinformatic analysis of WES data (VirusFinder, *PMID23717618*). Changes in tumor size (mm) and response data using RECIST 1.1 were collected. Progression-free survival (PFS) and overall survival (OS) were estimated by Kaplan-Meier method. **Results:** Twenty pts with VRT (HPV+ head and neck = 8, cervical = 2 and anal = 2 SCC; EBER+NPC = 2; MC = 6) and 11 pts with non-VRT were included. Median follow-up: 11 months (0,5-11). Treatment response: VRT 6 responders (CR + PR + SD > 18weeks) and 14 non-responders (SD < 18 weeks + PD); non-VRT 3 responders and 8 non-responders. Median OS and PFS for all pts were 10.61 and 3.2 months, respectively. No differences in PFS (p = 0.60) nor OS (p = 0.66) were observed among responders between VRT and non-VRT. Among non-responders, VRT had significantly higher OS but not PFS when compared to non-VRT (HR 0.30, p = 0.01 and HR 0.82 p = 0.62, respectively). VRT had quantitatively higher ctDNA at baseline vs non-VRT (Mean 7.9 vs 0.4 ng, p < 0.001). ΔctDNA (Change in ctDNA between baseline and cycle 3) strongly correlated with changes in tumor measurements and response by RECIST 1.1 (Spearman Rho = 0.75) and was associated with survival regardless of viral status (Table). **Conclusions:** ΔctDNA strongly correlated with changes in tumor response and survival in both VRT and non-VRT. Higher baseline ctDNA was found in VRT. Correlation with circulating viral DNA and radiomics analyses is on-going. Research Sponsor: None.

Variable	HR[1] for PFS	p-value	HR[1] for OS	p-value
VRT vs non-VRT	1.1	0.8	0.6	0.3
ΔctDNA continuous	1.6[2]	**0.01**	1.5[2]	**0.03**
ΔctDNA up vs. down	4.1	**0.003**	4.1	**0.007**

1. Hazard Ratio. 2. Per unit increase in ΔctDNA

3069 Poster Session (Board #133), Fri, 8:00 AM-11:00 AM

Using autoantibody signatures to predict immunotherapy discontinuation in melanoma patients. *First Author: Iman Osman, The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York, NY*

Background: Immune checkpoint inhibitors (ICIs), e.g., ipilimumab (IPI) and/or nivolumab (NIVO), produce durable survival benefit in a substantial proportion of melanoma patients but can also induce severe immune-related adverse events (irAEs) requiring treatment discontinuation. There is no biomarker to predict irAEs in ICI-treated melanoma patients. Given the similar clinical manifestation between irAEs and autoimmune disorders, we hypothesized that a subset of patients possess a subclinical baseline predisposition to developing irAEs that is characterized by specific autoantibodies (autoAbs). **Methods:** Pre-treatment melanoma patient sera from the CheckMate-238 Phase III trial of adjuvant IPI vs. NIVO were used for autoAb profiling with HuProt proteomic arrays (CDI Labs). The outcome of interest is to predict toxicity events that caused treatment discontinuation. For each treatment arm, we allocated patients to training and testing datasets in a 3:1 ratio. We calculated the area under the curve (AUC) of the receiver operating characteristic curve to select a probability threshold, which was applied to the testing dataset to assess accuracy, sensitivity, and specificity. Functional enrichment among autoAb protein targets was assessed using Metascape. **Results:** There were 707 irAEs among 597 patients (IPI = 423, NIVO = 174), of which 355 required treatment discontinuation (IPI = 287, NIVO = 68). In the training sets, we identified a 170 autoAbs signature consisting of 102 autoAbs for IPI treatment and 68 autoAbs for NIVO treatment. In the independent testing set, the signatures showed AUC of 0.85 (0.78, 0.92), 82% sensitivity, 78% specificity, and overall accuracy of 81% to predict IPI discontinuation, and AUC of 0.87 (0.74, 0.99), 75% sensitivity, 97% specificity, and overall accuracy of 88% to predict NIVO discontinuation. Enrichment of nuclear lumen-associated protein targets was identified among autoAb signatures that predict IPI or NIVO discontinuation. **Conclusions:** The identified signature within a large Phase III trial cohort highlights the potential utility of pre-treatment autoAbs for prediction of patients at high risk of developing irAEs in the adjuvant setting necessitating treatment termination. We are currently validating and refining toxicity-associated autoAb signatures with the goal of developing a Clinical Laboratory Improvement Amendments (CLIA)-certified assay to enable clinicians to optimize immunotherapy delivery and patient selection. Research Sponsor: P50 CA225450 NYU Melanoma SPORE, P30 CA016087: Cancer Center Support Grant; R01CA231295.

3070 Poster Session (Board #134), Fri, 8:00 AM-11:00 AM

Spatial analysis of tumor immune microenvironment (TIME) in patients treated with Bintrafusp alfa. *First Author: Houssein Abdul Sater, National Cancer Institute, Genitourinary Malignancies Branch, Bethesda, MD*

Background: Bintrafusp alfa is a first-in-class bifunctional fusion protein composed of the extracellular domain of TGF-βRII receptor (TGF-β "trap") fused to a human IgG1 mAb blocking PD-L1. In preclinical models, bintrafusp alfa treatment promoted CD8+ T cell and NK cell activation, and both immune cell (IC) populations were required for optimal bintrafusp alfa mediated tumor control. However, the effect of bintrafusp alfa on TIME in humans has not been reported. **Methods:** In this unplanned interim analysis of a biomarker expansion cohort (NCT 02517398), patients (pts) with advanced non-small cell lung cancer (NSCLC) underwent paired biopsies (bx) before and on treatment with bintrafusp alfa (~ 50 days apart). The objective was to evaluate frequency and localization of tumor infiltrated ICs by IHC. Out of 12 pts, 7 had matched (Pre vs Post) tumor-containing specimens sufficient for multiplex immunofluorescence (MxIF) analysis of TIME. Four pts were excluded as Post bx histology for 3/12 [2 PR (partial response), 1 SD (stable disease)] was negative for tumor (necrosis or fibrosis) and 1/12 did not have a Post bx performed. **Results:** TIME study shows CD8 T cell infiltrates were increased in Post compared to Pre bx (median 161 vs 62/mm^2; interquartile range [IQR] 65–396/mm^2 vs 31–135/mm^2; p = 0·04). While M2 macrophages were also increased (median 800 vs 367/mm^2; IQR 776–1131/mm^2 vs 171–831/mm^2; p = 0·04), the ratio of M1/M2 was reversed in pts with SD (↑) compared to pts with PD (↓). Other ICs such as CD4, T-regs, NK cells and M1 macrophages were not changed. On average compared to baseline, M2 macrophages were > 2 fold closer to every other IC in pts with PD, but > 2 fold further from any IC in pts with SD. Tregs were relatively closer to other IC in PD pts. Linear Discriminant Analysis was also performed and results indicate that differential IC densities (mainly M1 macrophages and CD4 T cells) do perform as classifiers between long (> 5 months) and short (< 5 months) term responses. **Conclusions:** This study suggests that bintrafusp alfa not only can enhance intratumoral effector IC infiltrates (CD8) but also has a modulating effect on the spatial distribution of both M1/M2 macrophages within the NSCLC TIME. The differential proximity of M2 macrophages to other IC infiltrates and changes in M1/M2 ratios in association with response suggests that an M1/M2 macrophage balance is directly involved in response and/or resistance to bintrafusp alfa. Given the limited number of patients in this cohort, we intend to study effects of bintrafusp alfa in a larger cohort of patients. Clinical trial information: 02517398. Research Sponsor: None.

3071 Poster Session (Board #135), Fri, 8:00 AM-11:00 AM

Preliminary dose escalation results from a phase I/II, first-in-human study of MGC018 (anti-B7-H3 antibody-drug conjugate) in patients with advanced solid tumors. *First Author: John D. Powderly, Carolina BioOncology Institute, Huntersville, NC*

Background: Antibody-drug conjugates (ADCs) are cancer agents that have a cytotoxic payload linked to a monoclonal antibody (mAb) that target cancer cells. ADCs offer increased cytotoxic activity while reducing normal tissue exposure. B7-H3 is expressed on multiple solid tumors with limited normal tissue expression. MGC018 is an investigational ADC with a duocarmycin payload linked to an anti-B7-H3 mAb. It is hypothesized that MGC018 has activity against B7-H3 expressing tumors with an acceptable safety profile. **Methods:** This study evaluates safety, dose-limiting toxicities (DLT), and maximum tolerated dose (MTD) of MGC018 in a dose escalation 3+3+3 design. In addition, pharmacokinetics, immunogenicity, and tumor response using RECIST v1.1 are evaluated. Cohort expansion will enroll at the MTD to assess safety and tumor response. **Results:** The study is enrolling Cohort 3 (6 total cohorts planned) in dose escalation. 20 patients (pts) were enrolled as of Feb 03, 2020. At least 1 treatment related adverse event (TRAE) occurred in 16 pts (80.0%). The most common TRAEs were neutropenia/decreased neutrophil count (35%); fatigue, lymphopenia/decreased lymphocyte count (30.0%); palmar plantar erythrodysaesthesia (PPE), skin hyperpigmentation (25.0%); pruritis, nausea, chills, infusion related reaction (20.0%); and vomiting, pyrexia, maculopapular rash (15.0%). Eleven pts (55.0%) experienced TRAEs ≥ Grade 3; events were decreased lymphocyte count/lymphopenia (n = 6), decreased neutrophil count/neutropenia (n = 3), PPE (n = 2), and maculopapular rash (n = 2). Three related serious adverse events occurred in 3 unique pts: pneumonitis in a pt with concurrent bacterial pneumonia, non-infectious gastroenteritis, and stasis dermatitis in a pt with chronic venous insufficiency. One DLT has occurred (Grade 4 neutropenia). No febrile neutropenia was observed. Target lesion decrease was noted in 1 pt each with small cell lung cancer (-6.3%), non-small cell lung cancer (-23.8%), and metastatic castrate-resistant prostate cancer (mCRPC) (-29.4%) with PSA change from 82.8 ng/ml to 57.1 ng/ml. One mCRPC pt with bone only disease had substantial improvement on bone scan and PSA decrease from 60 ng/ml to 4.7 ng/ml. **Conclusions:** Results to date demonstrate a manageable safety profile with early evidence of clinical activity. Continued dose escalation and clinical investigation of MGC018 is ongoing. Clinical trial information: NCT03729596. Research Sponsor: MacroGenics, Inc.

3073 Poster Session (Board #137), Fri, 8:00 AM-11:00 AM

A signal-seeking trial of olaparib and durvalumab in homologous repair-deficient tumors: A sub-study of the cancer molecular screening and therapeutics (MoST) program. *First Author: Anthony M. Joshua, Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada*

Background: Data on the utility of a PARP inhibitor in combination with a checkpoint inhibitor remain limited, particularly in the histology agnostic setting with homologous recombination deficiency (HRD). This study evaluated the clinical activity of the combination of olaparib and durvalumab with the primary study endpoint of progression-free survival (PFS) at 6 months (PFS6m). **Methods:** This was a phase II, single-arm, signal-seeking study of the MoST program. Patients were recruited into two cohorts based on HRD genes, agnostic to histology: (1) BRCA 1/2 deficient tumours, excluding breast, prostate, ovarian cancers, and (2) other HRD related genes. Molecular testing was performed using in-house and commercial panels on archival tumour tissue centrally adjudicated by a molecular tumour board. All patients were treated with olaparib 300mg bid for 1 month, followed by combination with durvalumab 1500mg q4 weekly for 13 cycles. Olaparib treatment was then continued until disease progression. **Results:** Between Nov 2017-Feb 2019, 48 patients were enrolled (16 to BRCA 1/2 cohort 1 and 32 to HRD related genes cohort 2). Most common tumour sites were bone/soft tissue (15%, N=7), pancreas (13%, N=6) and stomach (8%, N=4). Overall best response in cohort 1 was PR (25%, N=4) and SD 4 (25%, N=4), and cohort 2 was PR (6%, N=2) and SD (56%, N=18). Median PFS was 3.65m (Cohort 1) and 3.56m (Cohort 2) respectively. PFS6m was 35% (Cohort 1) and 38% (Cohort 2) respectively. PDL1 status was not predictive of olaparib and durvalumab benefit. The most common grade 3/4 adverse events were anemia (11%%, N=4), abdominal pain (9%, N=3), increased lipase (9%,N=3), increased amylase (9%, N=3), dyspnea (6%, N=2), Hyperglycemia dyspnea (6%, N=2), Pancreatitis dyspnea (6%, N=2) and hematuria (6%, N=2). **Conclusions:** Olaparib and durvalumab show promising activity in a histology agnostic setting, particularly in BRCA deficient tumours. Further research is needed to identify biomarkers that correlate with treatment benefit. Results from longer clinical follow-up and additional biomarker analyses will be presented. Clinical trial information: ACTRN12617001000392. Research Sponsor: Department of Health, Australia.

3074 Poster Session (Board #138), Fri, 8:00 AM-11:00 AM

Statin treatment improves response to anti-PD1 agents in patients with malignant pleural mesothelioma and non-small cell lung cancer. *First Author: Luca Cantini, Clinical Oncology, Polytechnic University of Marche, AOU Ospedali Riuniti, Ancona, Italy*

Background: After progression to standard chemotherapy, only a small proportion of malignant pleural mesothelioma (MPM) and non-small cell lung cancer (NSCLC) patients (pts) benefit from anti-programmed cell death (PD-1) treatment. Combination strategies might improve response. In pre-clinical models, statins showed vaccine adjuvant activities and synergized with anti-PD1 agents. In this multi-center study, we evaluated the impact of baseline statin treatment in MPM and NSCLC pts. **Methods:** We separately examined MPM and NSCLC pts treated with anti-PD1 monotherapy after progression to standard chemotherapy at two European academic institutions. As control cohort, MPM pts treated with first-line chemotherapy were also examined. Pts receiving statins at start of treatment were compared with those who did not. Objective response rate (ORR), progression-free survival (PFS) and overall survival (OS) were analyzed. **Results:** A total of 287 patients were examined. Twenty-seven out of 80 (34%) MPM and 36 out of 130 (20%) NSCLC pts received statins at start of anti-PD1 treatment. The most common statins were simvastatin, atorvastatin and rosuvastatin. In MPM pts, statin use was associated with improved ORR (22% versus 5%, $P = 0.05$), longer PFS (median 6.7 versus 2.4 months, hazard ratio (HR) 0.42, 95% confidence interval (CI) 0.23–0.77, $P < 0.01$), and longer OS (median not reached versus 6.0 months, HR 0.43, 95% CI 0.21–0.85, $P = 0.01$). In NSCLC pts, statin use was associated with improved ORR (40% versus 22%, $P = 0.04$), longer PFS (median 7.8 versus 3.6 months, HR 0.59, 95% CI 0.37–0.97.2, $P = 0.03$) but similar OS (median 13.1 versus 10.1 months, HR 0.79, 95% CI 0.49–1.28, $P = 0.30$). At multivariate analyses, after adjusting for ECOG performance status (PS) and histological subtype, the impact of statins remained significant for ORR, PFS and OS in MPM and for PFS in NSCLC. Conversely, no association between statin use and outcomes was found in 77 MPM pts treated with first-line chemotherapy. **Conclusions:** This study shows that statin use at start of anti-PD1 treatment improves response to anti-PD1 agents in MPM and NSCLC pts who progressed to standard chemotherapy in routine clinical practice. This association could not be found in MPM pts treated with first-line chemotherapy, thus suggesting a synergy between statins and anti-PD1 agents. Prospective studies are needed to confirm whether the combination of statin and anti-PD1 therapy could improve outcome in pts with poorly immunogenic thoracic malignancies. Research Sponsor: None.

3075 Poster Session (Board #139), Fri, 8:00 AM-11:00 AM

Interrogation of neoantigen-specific CD8 T cells in peripheral blood following PD-L1 blockade in patients with metastatic urothelial carcinoma (mUC). *First Author: Jeppe Sejerø Holm, Technical University of Denmark, Kgs. Lyngby, Denmark*

Background: Proliferation of CD8 T cells can be detected in the blood of cancer patients (pts) following a single dose of immune checkpoint blockade (ICB) and tends to be more robust in responding pts. Furthermore, tumor mutational burden (TMB) is seen to predict outcome to ICB across cancers. Mutation-derived neoepitopes presented on the tumor cell surface is believed to be recognized by T cells and are thus critical for tumor clearance. However, the capacity to mount a neoantigen T cell response and the kinetics in relation to ICB remain poorly understood. **Methods:** 24 pts with mUC were treated with atezolizumab (anti-PD-L1) 1200mg q3w on IMVigor 210 at MSKCC and included in here. Pt-specific neoepitopes were predicted based on whole-exome and RNA sequencing of pre-treatment archival tumors using the MuPeXI platform. Using DNA-barcode labelled pMHC multimers, we investigated CD8 T cell recognition of mutation-derived neoepitopes by screening pt PBMC samples pre- and post-treatment with atezolizumab (n = 85 PBMC samples). The kinetics of neoepitope-specific CD8 T cells were assessed for association with durable clinical benefit (DCB; defined as progression free survival $>$ 6 mo). **Results:** Neoepitope peptide libraries of between 200-587 peptides were generated per pt (mean = 260 peptides per pt). 31 out of a combined 56 possible pt HLA types across the cohort were utilized for T cell analyses (mean four HLAs per pt). MHC multimer-based screening of pt PBMCs revealed detection of neoepitope-specific CD8 T cells in 22 of 24 pts pre-treatment (range one to 14 neoepitope responses) and 21 of 22 pts post-treatment (up to 273 weeks after trial start; one to 19 neoepitope responses). There were large inter- and intra-patient variations of neoepitope-specific CD8 T cell responses during treatment with the largest increases occurring at the 3-wk, post-treatment initiation timepoint. We observed that pts with DCB tend to raise a broader neoantigen T cell response than patients without DCB. 38% of pts without DCB and 67% of pts with DCB exhibited an increase in neoepitope-specific CD8 T cell responses within 3 wks of treatment initiation. **Conclusions:** Using high-throughput screening, pt-specific neoepitope reactive CD8 T cells could be detected pre- and post-treatment in pts with mUC treated with atezolizumab. Phenotypic characterization of neoepitope reactive CD8 T cells is ongoing. These data may help elucidate the dynamics and characteristics of the T cells of highest relevance to the ICB-induced, anti-tumor immune response. Research Sponsor: Ludwig Grant, Other Foundation.

3076 Poster Session (Board #140), Fri, 8:00 AM-11:00 AM

Checkpoint inhibitor treatment-related cutaneous adverse events in skin of color patients at Memorial Sloan Kettering Cancer Center. *First Author: Amaris Geisler, CUNY School of Medicine, New York, NY*

Background: The advent of immune checkpoint inhibitors (CPIs) for the management of advanced malignancies has led to unintended consequences of nonspecific immune activation. Cutaneous immune related adverse events (irCAEs) are the most common and first to manifest, on average within 3.6 weeks of treatment initiation. irCAEs may require CPI treatment dose reduction or discontinuation and negatively impact patient quality of life. There is substantial variability in the reporting of these toxicities and inadequate reporting in skin of color patients (SOC), who are often underrepresented in oncology clinical trials. The purpose of this study is to characterize irCAEs in SOC cancer patients. **Methods:** A single center retrospective analysis of electronic medical records from 2009-2020 was conducted. SOC was defined as African American, Hispanic, Native American/Pacific Islander, or Asian. irCAEs were graded using the Common Terminology Criteria for Adverse Events (CTCAE) v5.0. **Results:** Of 1459 SOC patients that presented to our institution and received CPIs during the study period, 175 (12%) presented to dermatology for irCAEs [African American (56, 32%); Asian (98, 56%); Hispanic (20,11%); Native American (1, 0.5%)]. Patients' toxicities were stratified by CPI mechanism: anti-PD-1/L1 (139, 79%), combination of anti-PD-1/L1 plus anti-CTLA-4 (29, 17%), and anti-CTLA-4 therapy (7, 4%). Of 376 irCAEs, pruritus (62, 16%), xerosis (42, 11%), maculopapular rash (40, 11%), and cutaneous hyperpigmentation (36, 10%) were most frequently diagnosed. There were 86 (23%) grade 1, 93 (25%) grade 2, and 18 (5%) grade 3 events. Average time from CPI-treatment initiation to irCAE onset was 6.5 months (SD 7.9). Fifteen (9%) patients required CPI dose reduction or discontinuation due to skin toxicity. Topical corticosteroids (133, 76%) were the most frequently used treatment for all irCAEs. **Conclusions:** Our findings suggest that irCAEs occur frequently in SOC cancer patients. Furthermore, a 6.5-month delay in time to diagnosis highlights a need for increased surveillance of these cutaneous toxicities in darkly pigmented skin. Generally, SOC patients present unique diagnostic and management challenges due to differences in skin biology and propensity toward hyperpigmentation; however, in SOC *cancer* patients, the mechanisms of oncologic immunotherapy must be considered in developing successful treatment strategies and management of dermatologic health in this population. Research Sponsor: None.

3077 Poster Session (Board #141), Fri, 8:00 AM-11:00 AM

Novel blood-based biomarker predicting severe toxicity in melanoma anti-CTLA-4 immunotherapy treatment. *First Author: Vylyny Chat, New York University School of Medicine, New York, NY*

Background: Immune checkpoint inhibition (ICI) has improved clinical outcomes of metastatic melanoma (MM). However, 65-80% of treated patients experience immune-related adverse events (irAEs), urging for the availability of personalized and easy-access clinical biomarkers. We have previously shown that germline genetics related to host immunity affects ICI response and MM survival. In this study, we investigated if germline immune-related expression quantitative trait loci (ieQTLs) may predict ICI-induced irAEs in MM. **Methods:** Through a comprehensive interrogation of a healthy twin-cohort expression dataset (MuTHER), we identified 40 ieQTLs most significantly associated with the expression of 382 immune-related genes. These germline variants were genotyped using the MassARRAY system in anti-CTLA-4-treated MM patients, collected as part of a multi-institutional collaboration. Using multivariable logistic regression models, we tested the association of 40 ieQTLs with irAEs in a discovery cohort of 97 MM patients followed by a validation in additional cohort of 97 anti-CTLA-4 treated patients. **Results:** We found rs7036417 significantly associated with severe anti-CTLA-4 irAEs in the discovery (OR = 6.18; 95%CI = 1.61-23.74; p = 0.007) and validation (OR = 6.73, 95%CI = 1.42-31.86; p = 0.02) cohorts. Pooled analysis showed that carriers of two rs7036417 alternate alleles (TT) have a 6-fold increased risk of developing severe irAEs (OR = 6.11; 95% = 2.26-16.56;p = 0.0003). This association was not observed with ICI response or survival. The alternate allele of rs7036417 is associated with higher expression of *SYK* (spleen-associated tyrosine kinase), suggesting that elevated SYK contributes to developing severe irAEs. **Conclusions:** We report that rs7036417, an ieQTL in *SYK*, associates with an increased risk of severe irAEs, independent of ICI efficacy. *SYK* plays an important role in B-cell/T-cell expansion and increased pSYK has been reported in patients with rheumatoid arthritis or systemic lupus erythematosus. Based on our data, the over-expression of SYK likely explains the biological mechanisms of the association between rs7036417 and anti-CTLA4 irAEs. These findings propose a novel blood-based baseline biomarker stratifying the patients at increased risk of severe irAEs, with a clinical effect substantially surpassing those observed for currently available predictors. Our ongoing studies are currently investigating SYK eQTL as a novel target in toxicity-reducing therapies. Research Sponsor: U.S. National Institutes of Health.

3078 Poster Session (Board #142), Fri, 8:00 AM-11:00 AM

Success and failure of additional immunosuppressants in steroid-refractory pneumonitis related to immune checkpoint blockade. *First Author: Jason Beattie, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Severe immune related adverse events (irAEs) with immune checkpoint blockade are uncommon but can be fatal. Steroids are the most common initial treatment for most non-endocrine irAEs, but some patients are or become refractory to steroids. When steroids are not effective, there is limited data to guide management strategies, particularly in the context of pneumonitis. **Methods:** All patients at MSK treated with immune checkpoint blockade from 2013-2020 were queried for receipt of an immunosuppressant (e.g. TNF antagonists, mycophenolate mofetil, cyclophosphamide) beyond steroids. Patient records were then manually reviewed to identify patients who received such therapy for management of immunotherapy-related pneumonitis. **Results:** Among 5363 patients treated with immune checkpoint blockade, 364 (6.8%) received an additional immunosuppressant for an irAE, including 28 (0.5% of all patients treated) patients treated for pneumonitis. Most of these pneumonitis events (19/28, 68%) were grade 3 or higher. Agents used included mycophenolate mofetil (7/28; 25%), TNF antagonists (23/28; 82%), and cyclophosphamide (1/28; 3.5%); more than one medication was used in 3 patients (11%). The indications were primary non-response to steroids (n = 16, 57%) and recrudescence after initial response to steroids (n = 12, 43%). At 90 days from initiation of the additional immunosuppressant, 13/28 (46%) patients were alive with improvement or resolution of pneumonitis while 15/28 (54%) had died. Survival with resolution/improvement was more common in patients treated for recrudescence vs primary non-response (67% vs 25%, p = 0.05). **Conclusions:** Outcomes with additional immunosuppressants in the setting of steroid-refractory immune-related pneumonitis are poor, but resolution can occur in some cases. A deeper understanding of the mechanistic underpinnings of irAEs is needed to more effectively tailor immunosuppressant therapies, particularly in severe pneumonitis events. Research Sponsor: None.

3079 Poster Session (Board #143), Fri, 8:00 AM-11:00 AM

Preliminary results of sintilimab plus different dose of IBI305 (anti-VEGF monoclonal antibody) in patients with advanced hepatocellular carcinoma: A phase Ib study. *First Author: Wen Zhang, Department of Medical oncology, Cancer Hospital, CAMS, Beijing, China*

Background: The study aimed to evaluate the safety and efficacy of sintilimab, a PD-1 blockade, plus IBI305, a biosimilar candidate of bevacizumab, in patients (pts) with advanced hepatocellular carcinoma (HCC). **Methods:** Adults with histocytologically confirmed advanced or metastatic HCC were enrolled in this two-part study. Part 1 was dose escalation trial, with initial dose of sintilimab 200 mg plus IBI305 7.5 mg/kg, q3w (low-dose group). If tolerable, IBI305 was escalated to 15 mg/kg (high-dose group). In part 2 for extension, at least 20 pts were enrolled to each tolerable dose group. **Results:** As data cutoff (Jan. 7, 2020), 50 pts were enrolled, 29 in low-dose group and 21 in high-dose group. 41 patients were systemic treatment naïve. The median treatment cycle was 4 (range: 1-19) in low-dose group and 11 (range: 1-16) in high-dose group. Most TRAEs were G1-2 with the most common being hypertension (28.0%) and pyrexia (26.0%). Totally, the grade 3 or more TRAEs were occurred in 6 (12.0%) pts, including hypertension occurred in 2 (4%) pts. The objective response rate (ORR) per RECIST v1.1 was 24.1% (95%CI: 10.3 - 43.5) in low-dose group, and 33.3% (95% CI:13.3 - 59.0) in high-dose group. As with the cutoff date, the median PFS has not been reached and the 6-month PFS rates were 60.5% (95%CI 36.1, 78.0) and 75.8% (95% CI: 47.3, 90.2), respectively. **Conclusions:** The combination of sintilimab and IBI305 showed promising efficacy and favourable safety profile in advanced HCC in both low-dose and high-dose groups. The preliminary result of this study warrant further exploration of dose selection for anti-VEGF/VEGFR agent when combined with PD-1/PD-L1 antibody. Clinical trial information: NCT04072679. Research Sponsor: Innovent Biologics, Inc.

Antitumor activity in both groups.

	Sintilimab 200 mg + IBI305 7.5 mg/kg Total (N=29)	Sintilimab 200 mg + IBI305 15 mg/kg Total (N=21)
Number of subjects having at least one radiological assessment [a]	29	18
CR, n	0	0
PR, n	7*	6**
SD, n	15	9
PD, n	7	3
ORR (95%CI), %	24.1 (10.3 - 43.5)	33.3 (13.3 - 59.0)
DCR (95%CI), %	75.9 (56.5 - 89.7)	83.3 (58.6 - 96.4)

[a]: three subjects had no radiological assessment till data cutoff and were excluded from the table. Number of subjects having at least one radiological assessment is used for the denominator of percentage in this table. * Seven patients were confirmed by RECIST v1.1. ** Five patients were confirmed by RECIST v1.1.

3080 Poster Session (Board #144), Fri, 8:00 AM-11:00 AM

Influence of antibiotic therapy (ATB) on oncological outcomes of metastatic non-small cell lung cancer (mNSCLC) patients treated with chemo-immunotherapy (CIT). *First Author: James Clark, Department of Surgery & Cancer, Imperial College London,, London, United Kingdom*

Background: ATB exposure is proven to worsen response and survival in immunotherapy recipients. However, its influence on outcomes from CIT is currently undefined. **Methods:** We conducted a retrospective, multi-centre observational study including 77 mNSCLC patients who received pembrolizumab, pemetrexed and carboplatin CIT as first-line therapy for mNSCLC, between December 1, 2018 and January 1, 2020 in 3 academic referral centres in Europe and in the United States. We documented ATB exposure in the 30 days prior to CIT commencement (pATB) or concurrently (cATB) until CIT cessation. Outcome measures included overall (OS) and progression-free survival (PFS) calculated from commencement of CIT, and overall response rates (ORR) defined by Response Evaluation Criteria in Solid Tumors (v1.1). **Results:** We enrolled 77 patients, 41 of whom were female (n = 53%) with adenocarcinoma (n = 73, 95%), performance status (PS) 0-1 (n = 69, 90%) PD-L1 Tumour Proportion Score < 50 (n = 57, 74%). Median OS was 16.4 months (95%CI 8.4-24.4), median PFS was 6.7 months (95%CI 5.7-7.6). ORR was 48% including 1 complete (1%) and 36 partial responses (47%). Eleven patients (14%) received pATB, with penicillin/cephalosporins (p/c, n = 7, 63%) for <7 days (n = 10, 90%). Thirty-five patients (45%) received cATB with p/c (n = 11, 40%) for <7 days (n = 28, 80%). Most common indication for ATB was peri-procedure prophylaxis in pATB (n = 7, 63%) and suspected febrile neutropenia in cATB (n = 14, 40%). pATB ($p = 0.004$) but not cATB ($p = 0.85$) predicted for worse OS (19.6 vs 6.5 months, Hazard Ratio [HR] 2.9 95%CI 1.3-6.3). Neither pATB nor cATB predicted for PFS or ORR ($p > 0.05$). Multivariable analyses confirmed pATB (HR 2.3 95%CI 1.1-5.5, p = 0.05) to predict for OS independent of PD-L1 status, PS and cATB. pATB+/- groups were balanced with regards to age, gender, PS nor PD-L1 status ($p > 0.05$). **Conclusions:** Whilst cATB does not compromise outcome from CIT, this study reproduces the detrimental effects observed for pATB exposure in immunotherapy recipients. Mechanistic verification of the immune-biologic foundations underlying this association is urgently warranted. Research Sponsor: None.

3081 Poster Session (Board #145), Fri, 8:00 AM-11:00 AM

Targeting HER2 in combination with anti-PD-1 and chemotherapy confers a significant tumor shrinkage of gastric cancer: A multi-institutional phase Ib/II trial of first-line triplet regimen (pembrolizumab, trastuzumab, chemotherapy) for HER2-positive advanced gastric cancer (AGC). *First Author: Sun Young Rha, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea*

Background: Combining anti-PD-1 agent and trastuzumab has shown synergy in HER2 positive preclinical cancer models. We first report the result of a multi-institutional phase Ib/II trial of triple combination (pembrolizumab, trastuzumab, and chempotherapy) as first line therapy for HER2 positive AGC. (PANTHERA trial; NCT02901301). **Methods:** Pembrolizumab 200mg IV D1, Trastuzumab 6mg/kg (after 8mg/kg load) D1, Capecitabine 1000mg/m^2 bid D1-14, and Cisplatin 80mg/m^2 D1 every 3 weeks was selected as recommended phase II dose. The primary endpoint for phase II was ORR per RECIST v1.1. Secondary endpoints included PFS, OS, DoR, safety, and molecular analysis by targeted NGS. **Results:** Total of 43 patients were treated with median follow up of 16.1 months, and 11 pts remained on the treatment (treatment duration range: 1.4 to 24 months). There was significant tumor shrinkage of 95.3% with 54.6% median depth of response, with 76.7% ORR (CR 16.3%, PR 60.5%, conversion surgery 4.6%), and 97.7% DCR. Median PFS was 8.6 months (95% CI 7.2-22.0) and median OS was 18.4 months (95% CI 17.9-NA). Subsequent chemotherapy was given to 83.3% of 30 progressed pts. There were no MSI-H/dMMR or EBV-positive pts. PD-L1 status (57.1% of pts $\geq$ CPS 1 and 14.3% of pts $\geq$ CPS 10 among 35 pts), metastatic organ or baseline tumor burden was not related to the survival. Treatment-related AE ($\geq$G3) occurred in 32 pts (74.4%) including 17 pts (39.5%) with neutropenia G3-4. Immune-related AEs ($\geq$G3) occurred in 4 pts (10%). Ninety-six tumor tissues from 32 pts (paired tumor tissues from 25 pts) were analyzed with targeted NGS. TMB (median 12.7 mut/MB with range of 9.45-16.71) was not related to the PD-L1 expression or survival. **Conclusions:** First-line triplet regimen (Pembrolizumab, Trastuzumab, and Chemotherapy) confers a significant tumor shrinkage for HER2 positive AGC, regardless of PD-L1 status. Phase III Keynote-811 study (NCT03615326) is ongoing based on the protocol of this study. Clinical trial information: NCT02901301. Research Sponsor: MSD, Pharmaceutical/Biotech Company.

Response and survival of PANTHERA Trial (cut-off date: 12-31-2019).

Tumor Shrinkage rate	ORR	DCR	PFS	OS	DoR	6-months PFS
95.3%	76.7%	97.7%	8.6 months (95% CI 7.2-22.0)	18.4 months (95% CI 17.9-NA)	10.8 months (95% CI 7.2-NA)	76.7% (95% CI 65.1-90.5)

3082 Poster Session (Board #146), Fri, 8:00 AM-11:00 AM

Association of a STK11/KEAP1-mutation gene expression signature in lung adenocarcinoma with immune desertion in squamous cell carcinomas and mediation by NFE2L2 deregulation. *First Author: Damian Tobias Rieke, Department of Hematology and Oncology - Charité Universitätsmedizin Berlin, Berlin, Germany*

Background: KEAP1 and STK11 mutations are associated with resistance to immune checkpoint inhibition (ICI) in non-small cell lung cancer (NSCLC). Mechanisms are currently unknown. **Methods:** We examined mutation, methylation, copy number and gene expression data from the cancer genome atlas (TCGA) lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LSCC), head and neck squamous cell carcinoma (HNSCC) and cervical carcinoma (CESC) data sets as well as public single cell gene expression data from a HNSCC cohort. Pathway annotations were performed using gene set enrichment analysis. A previously published cohort of NSCLC patients treated with ICI was analyzed for the predictive value of NFE2L2 mutations on PFS. **Results:** Annotation of STK11 and KEAP1 mutant LUAD revealed identical gene set enrichment for mitochondrial metabolism and downregulation of the STING-pathway, immune checkpoints, and interferon signaling. A STK11/KEAP1-mutation derived gene expression signature was established in LUAD and found to be driven by NFE2L2-regulated genes. This gene expression signature was independently predictive of immune desertion in LSCC, CESC and HNSCC and associated with STING-pathway downregulation in single cell sequencing analyses in HNSCC. KEAP1 and STK11 mutations were less frequent in LSCC, CESC and HNSCC but NFE2L2 mutations were identified in 15, 6 and 5%, respectively. NFE2L2 mutant SCC exhibited upregulation of the 15-gene- signature as well as immune desertion. In NSCLC, NFE2L2 mutations were associated with significantly worse PFS with ICI. **Conclusions:** Alterations of KEAP1, STK11, NFE2L2 and other related genes are linked to NFE2L2 target gene upregulation and immune desertion in LUAD, CESC, LSCC and HNSCC alike. The NFE2L2 pathway should be investigated clinically as a putative negative predictive biomarker for ICI and a potential therapeutic target. Research Sponsor: None.

3083 Poster Session (Board #147), Fri, 8:00 AM-11:00 AM

Prevalence of human leukocyte antigen-B27 supertype in the context of positively charged neoepitopes and association with PD-L1 as an immune escape mechanism. *First Author: Charlene Marie Fares, Department of Medicine, Division of Hematology/Oncology, UCLA, Los Angeles, CA*

Background: Recent evidence suggests efficacy of immune checkpoint blockade may be influenced by human leukocyte antigen (HLA)-B. HLA-B27 supertype has an electronegative binding pocket which favorably binds and displays neoepitopes harboring positively charged amino acids (AAs). Based on immune surveillance, we postulate that B27 tumors that have favorable neoepitopes should face negative selective pressure, and B27 tumors with favorable neoepitopes that develop could be more likely to upregulate immune escape mechanisms. Here we evaluate the relationship between prevalence of B27 and positively charged neoepitopes and assess association between positively charged neoepitopes and expression of PD-L1. **Methods:** TCGA datasets from head and neck squamous cell (HNSC), lung squamous cell (LUSC), and melanoma (SKCM) patients were evaluated. HLA alleles were determined with OptiType and supertype was based on 2008 criteria. Nonsynonymous mutations were annotated with Ensembl VEP and VAtools. pVAC-Seq using NetMHCpan algorithm predicted neoepitopes 9 AAs in length. Favorable B27 neoepitopes were defined as those having new positively charged AA substitutions (H/K/R) from negative or uncharged wildtype AAs. RNA-seq data for the PD-L1 gene were normalized on transcripts per million and log2 transformed. Linear regression tests were performed between PD-L1 gene expression values and fraction of nonsynonymous mutations resulting in neoepitopes with new positively charged AAs in patients with B27. **Results:** Data from 497 HNSC, 494 LUSC, and 468 SKCM patients were analyzed. B27 was observed in 20.1%, 23.2%, and 26.5% of HNSC, LUSC, and SKCM patients, respectively, with a significant difference seen between HNSC and SKCM by chi-square test (χ^2 = 5.14, p = .023). Of new charged AAs resulting from nonsynonymous mutations, 76.3% in HNSC, 74.0% in LUSC, and 72.0% in SKCM were positively charged ($p < .05$ between all histologies, paired t-tests). In B27 patients, association between PD-L1 gene expression and fraction of neoepitopes with new positively charged AAs was seen in HNSC (r = 0.25 p = .036) and SKCM (r = 0.30 p = .007), but not LUSC (r = -0.12 p = .296). **Conclusions:** With increasing fraction of positively charged neoepitopes, a decrease in prevalence of B27 was observed, suggesting improved binding and immune elimination of tumors with favorable neoepitopes. In B27 tumors that develop despite having favorable neoepitopes, upregulation of PD-L1 could be a putative mechanism to evade immune detection. Research Sponsor: None.

3084 Poster Session (Board #148), Fri, 8:00 AM-11:00 AM

Rapid expansion of M-MDSCs and association with high levels of plasma TSLP and primary resistance to PD-1 inhibitors in metastatic NSCLC. *First Author: Sally CM Lau, Princess Margaret Cancer Center, University Health Network, Toronto, ON, Canada*

Background: Elevated frequency of peripheral myeloid cell populations has consistently been associated with poor response to immune checkpoint inhibitors (ICI) in metastatic non-small cell lung cancer (mNSCLC). The mechanisms underlying this relationship remains poorly understood. Thymic stromal lymphopoietin (TSLP), a cytokine involved in T-cell maturation, has been implicated in a complex feedback loop leading to tumor growth and expansion of myeloid populations. We hypothesized that TSLP levels directly correlate with the presence and expansion of myeloid derived suppressor cell (MDSC) populations and sought to explore their association with response to PD-1 inhibitors in mNSCLC. **Methods:** mNSCLC patients treated with ICIs underwent baseline and serial blood collection. Peripheral blood mononuclear cells (PBMC) were analyzed by high-dimensional flow cytometry using validated panels to evaluate T/B/NK-cell, Treg and myeloid populations. Plasma cytokines including TSLP were analyzed using ELISA and Luminex assays. Cox and logistic regressions were utilized to correlate biomarkers with progression-free survival (PFS), overall survival (OS) and radiographic response. **Results:** 30 mNSCLC patients treated with single-agent ICI were included in the analysis. TSLP level was significantly associated with expansion of monocytic(M)-MDSCs in response to ICI treatment (p=0.02). M-MDSC frequency after a median of 20 days of ICI treatment was significantly associated with progressive disease (PD), reduced PFS and OS (all $p<0.05$) whereas no correlation was seen with baseline M-MDSC frequency. Patients with a doubling of M-MDSCs (n=11) after treatment had a primary PD rate of 64% vs 24% (OR 7.0, p=0.04) and significantly worse median PFS (2.5 vs 7.8 months, HR 2.6 p=0.04). **Conclusions:** Early expansion of circulating M-MDSCs after treatment with PD-1 inhibitors is associated with elevated baseline TSLP levels and primary disease progression following ICI therapy in mNSCLC. These findings suggest that elevated TSLP and early expansion of myeloid populations may represent an important mechanism of primary resistance to PD-1 inhibitors in mNSCLC. Research Sponsor: None.

3085 Poster Session (Board #149), Fri, 8:00 AM-11:00 AM

A phase I/II study of GB1275, a first-in-class oral CD11b modulator, alone, and combined with pembrolizumab in specified advanced solid tumors or with chemotherapy in metastatic pancreatic cancer (KEYNOTE-A36). *First Author: Drew W. Rasco, START, San Antonio, TX*

Background: GB1275 is a first-in-class CD11b modulator that reduced myeloid-derived suppressor cells (MDSCs) and tumor associated macrophages (TAMs) at the tumor site, repolarized M2 immunosuppressive TAMs to an M1 phenotype, and increased tumor infiltration of activated CD8+ T cells in preclinical models. When combined with an anti-PD-1 antibody or chemotherapy, these immunomodulatory effects translated into potent anti-tumor effects and prolonged survival in orthotopic PDAC models [Panni RZ, et al. Sci Transl Med. 2019 Jul 3;11(499)]. This ongoing first-in-human study consists of dose escalation of GB1275 monotherapy (Regimen A), GB1275 + pembrolizumab (Regimen B), and GB1275 + nab-paclitaxel + gemcitabine (Regimen C), followed by Phase 2 expansion in newly diagnosed metastatic pancreatic, MSS colorectal, and PD-L1-positive gastric/GEJ cancers. Here we report interim results of the dose escalation portion of the trial. **Methods:** The dose escalation phase is based on a standard oncology phase 1, 3+3 design. Cohorts of 3 to 6 patients (pts) with histologically confirmed locally advanced/metastatic pancreatic, esophageal, gastric, MSS colorectal, prostate, or breast cancer were sequentially assigned to ascending dose levels of GB1275 taken orally twice daily (BID) in 1 of 3 regimens: Regimen A was initiated first; Regimen B commenced after completion of the first two cohorts of Regimen A, and Regimen C will be initiated when Regimen A is completed. Dose escalation was based on assessment of safety including dose-limiting toxicity (DLT). Serial blood and tumor samples were collected for pharmacokinetic (PK) and biomarker analyses. **Results:** As of January 21, 2020, 13 pts were treated, with 3 each in Regimen A (GB1275 100mg, 200 mg and 400 mg BID) dose levels and 4 in Regimen B with GB1275 100 mg BID + pembrolizumab. No DLTs have been reported. GB1275 treatment-related adverse events were reported in 5 pts; all were Grade 1 in severity. Preliminary PK analyses showed a mean elimination half-life of ~7 hours. Reduction in peripheral MDSCs was observed in the majority of pts with serial samples. Biomarker analysis in serial tumor tissue is ongoing. **Conclusions:** Preliminary data show minimal treatment-related toxicities with the studied regimens. PK data support BID dosing. Dose escalation is ongoing. Updated data will be presented. Clinical trial information: NCT04060342. Research Sponsor: Gossamer Bio, Inc.

3086 Poster Session (Board #150), Fri, 8:00 AM-11:00 AM

The spatial localization of CD163+ tumor-associated macrophages predicts prognosis and response to therapy in inflammatory breast cancer. *First Author: Christophe Van Berckelaer, Translational Cancer Research Unit, GZA Hospitals & CORE, University of Antwerp, Antwerp, Belgium*

Background: The mechanisms contributing to the aggressive biology of inflammatory breast cancer (IBC) are under investigation. A specific immune response seems to be an important driver, but the functional role of infiltrating immune cells in IBC remains unclear. Tumor-associated macrophages (TAMs) are associated with worse outcome, while CD8+ cytotoxic T cells demonstrate anti-tumor properties in breast cancer. In this study, we assessed spatial associations between CD163+ TAMs, CD8+ cells and cancer cells in IBC, using deep-learning and ecological statistics. **Methods:** We collected clinicopathological variables, evaluated PDL1-positivity (SP142, Ventana) and scored TILs according to the TIL working group guidelines on H&E slides for 144 IBC patients. Immunostainings for CD8 and CD163 (Hematoxylin-DAB) were done according to validated protocols. All slides were digitized, underwent virtual multiplexing and were evaluated in Visiopharm to quantify the number of DAB+ immune cells. Each immune cell was located using XY coordinates and spatial interactions were examined using a Morisita Horn Index (MHI). Tumor cell coordinates were collected using a deep-learning algorithm applied to the CD8-stained slide. This algorithm was trained in 18 images with more than 150.000 iterations (Deeplabv3+). **Results:** Complete pathological response (pCR) after neo-adjuvant chemotherapy was achieved by 30.6% (n= 30/98) of the patients with initially localized disease. Besides PDL1-postivity (*P*= .03), infiltration with CD8+ T cells (*P*= .02) and TAMs (*P*= .01) also predicted pCR. However, a likelihood ratio test showed no difference between a model using CD8+ cells, TAMs or TILs. Interestingly, the colocalization of CD163+ and CD8+ cells (MHI >0.83) was associated with pCR (*P*= .01) and remained significant in a multivariate model (OR: 3.18; 95% CI: 1.04 – 10.6; P= .05) including TIL score, PDL1-positivity and hormone receptor (HR) status. Furthermore, a shorter disease-free survival (DFS) was associated with HR-status, no pCR and the colocalization of TAMs near tumor cells (HR: 3.3; 95% CI: 1.6 – 7.1; P= .002) in a multivariate model. The density of TAMs was not associated with outcome. **Conclusions:** The impact of TAMs on clinical outcome appears to depend on the spatial arrangement. The number of TAMs solely was not associated with outcome, but patients with more TAMs in proximity of the tumor cells had a worse DFS. Surprisingly, the clustering of TAMs near CD8+ cells was associated with pCR independent of the number of TAMs or TILs. Research Sponsor: Research Foundation - Flanders (FWO).

3087 Poster Session (Board #151), Fri, 8:00 AM-11:00 AM

Discovery of a novel shared tumor antigen in human lung cancer. *First Author: Diane Tseng, Stanford University, Palo Alto, CA*

Background: While there has been much attention on mutation-associated neoantigens in tumors, there is less known about non-mutated tumor antigens that are shared across individuals. Understanding tumor-infiltrating T cell recognition of shared tumor antigens is important for understanding cancer immune recognition and escape, and may reveal novel targets for therapy. **Methods:** We have established a novel approach for discovering shared tumor antigens in human lung cancer. This approach involves identifying candidate T cell receptor (TCR) alpha/beta pairs that are predicted to exhibit specificity for shared tumor antigens in the context of a given human leukocyte antigen (HLA). We then screen the T cell receptor for binding to yeast display libraries of peptide-HLA. The Mark Davis lab at Stanford has previously developed an algorithm that groups T cell receptors into antigen specificity groups based on shared motifs within the TCR complementarity-determining region 3 (CDR3) sequences. Leveraging a dataset of over 700K CDR3 sequences from 178 HLA-typed non-small cell lung cancer (NSCLC) patients, we have found up to 4,300 antigen specificity groups after applying stringent cutoffs. We sequenced TCR alpha/beta pairs from 15 patients with lung adenocarcinoma (n = 4,705). **Results:** We identified an antigen specificity group enriched in tumor compared to adjacent uninvolved lungs. Antigen screening of the T cell receptor belonging to this specificity group using an A02 yeast display libraries led to the identification of a dominant peptide after four rounds of enrichment. We functionally validated that the peptide derived from the protein TMEM161A stimulated Jurkat cells expressing the TCR alpha/beta receptor of interest. We show that full-length TMEM161A protein is processed and presented into a peptide that stimulates primary T cells expressing the TCR alpha/beta receptor. We observe that a peptide from Epstein-Barr virus (EBV) protein LMP2 also stimulated the same TCR alpha/beta receptor. We have show that TMEM161A RNA and protein are overexpressed in human lung cancer compared to adjacent uninvolved lungs. **Conclusions:** We have demonstrated a novel approach toward antigen discovery and identified a shared tumor antigen TMEM161A in human lung cancer. Research Sponsor: Lung Cancer Research Foundation, Conquer Cancer Foundation of the American Society of Clinical Oncology, Ellie Guardino Cancer Foundation Award from the Stanford Cancer Institute.

3088 Poster Session (Board #152), Fri, 8:00 AM-11:00 AM

Effect of Kaiso on immune signaling of breast cancer exosomes. *First Author: Windy Marie Dean-Colomb, Lousiana State University School of Medicine, New Orleans, LA*

Background: Exosomes are communication vesicles that act as mediators of intracellular transfer of genetic information, an important role in intercommunication between tumor cells and immune cells. However, the mechanism underlining this cell-cell communication is not well understanding, particularly in African American breast cancer patients. Recently, our lab has demonstrated that Kaiso, a novel bi-modal transcription factor is highly expressed in African American breast cancer and notably, high Kaiso expression correlates with breast cancer aggressiveness and the disparity in survival outcomes of breast cancer patients of African American compared to European American patients. However, the differential expression and biological consequences of Kaiso in immune signaling of breast cancer exosomes has not been studied yet. Herein we demonstrate the biological role of Kaiso in immune signaling in breast cancer exosomes. **Methods:** In this study we utilized Nanostring immune profiling technology along with multiple *in vitro* and *in vivo* assays were used to study the role of Kaiso in breast cancer immune escape. **Results:** Nanostring pan cancer immune profiling demonstrated that European American breast cancer exosomes exhibited higher expression of TILs markers, T cell activation markers and $CD8^+$T Cells markers compared to African American ($p < 0.05$, FDR), while we observed an increase in the expression of the anti-phagocytic molecule CD47 in breast cancer patient exosomes of African American compared to European American patients. In addition to that CD47 and SIRP-α (Signal Regulatory Protein) are highly expressed in Kaiso-scrambled MDA-MB-231 cells (sh-Scr) and exosomes, whereas THBS1, which is a regulator of CD47 expression and is regarded as angiogenesis inhibitor is significantly increased in sh-Kaiso MDA-231 cells and exosomes. Additionally, we observed that Kaiso directly binds methylated sequences in the promoter region of CD47 and THBS1 by ChIP assay. Furthermore, in vivo sh-Kaiso cells injected into athymic mice exhibited delayed tumor formation after four weeks with smaller tumor size as compared to sh-SCR cells ($p < 0.05$), and we observed higher expression of THBS1 with lower expression of CD47 and SIRP-α molecules by IHC and exosomes isolated from *in vivo* tumors ($p < 0.05$), indicating that Kaiso is associated with macrophage mediated immune escape. **Conclusions:** These findings demonstrate the important role of kaiso in immune signaling through exosomes which may be related with more aggressive cancer phenotype in breast cancer, especially in African Americans. Research Sponsor: DOD.

3089 Poster Session (Board #153), Fri, 8:00 AM-11:00 AM

Immune profiling and clinical outcomes in patients treated with ramucirumab and pembrolizumab in phase I study JVDF. *First Author: Roy S. Herbst, Yale University, New Haven, CT*

Background: In Study JVDF (NCT02443324), we combined ramucirumab (VEGFR2 antagonist) and pembrolizumab (PD-1 antagonist) to simultaneously target the tumor microenvironment and immune checkpoints in patients with advanced non-small cell lung cancer (NSCLC), gastric or gastroesophageal junction adenocarcinoma (G/GEJ), urothelial carcinoma (UC) or biliary tract cancer (BTC). We reported that this combination was associated with increased antitumor activity in patients with PD-L1 positive tumors by immunohistochemistry (IHC) compared with PD-L1 negative tumors.1) Here we explore the association between baseline gene expression profiles and clinical outcomes. **Methods:** JVDF was a nonrandomized phase 1a/b trial that treated patients with intravenous ramucirumab at 8 mg/kg on days 1 and 8 (G/GEJ, BTC) or 10 mg/kg on day 1 (G/GEJ, NSCLC, UC) plus pembrolizumab (200 mg day 1) every 3 weeks.[1] Baseline tumor samples from 53 patients across 7 study cohorts were analyzed with the NanoString PanCancer Immune Profiling Panel for RNA expression and the DAKO PD-L1 IHC 22C3 pharmDx assay for PD-L1 protein expression. Clinical outcomes included progression-free survival (PFS), overall survival (OS), and objective response rate (ORR). **Results:** Across cohorts, PD-L1 gene expression was correlated with increased IFNγ gene expression and immune-related gene signatures (T effector, T cell-inflamed (TIS)), and trended with PD-L1 protein expression. Expression of immune checkpoint-related genes and myeloid-derived suppressor cell /regulatory T cell markers was increased in the NSCLC TPS$\geq$50% PD-L1 IHC subgroup (N=8), while no clear pattern of expression was observed in other cohorts. Higher T effector and TIS scores appeared associated with better survival and response in NSCLC cohorts (mean TIS: 1.21$\pm$0.80 in responders (N=7) vs -0.13$\pm$0.57 in non-responders (N=7); p=0.004), and a trend was observed in G/GEJ cohorts (mean TIS: -0.18$\pm$0.30 (N=5) vs -0.39$\pm$0.21 (N=13); p=0.207). Of note, partial responses and stable disease were also observed in NSCLC and G/GEJ patients with a low baseline inflammatory signature score. Additional analyses are ongoing and will be presented. **Conclusions:** Baseline PD-L1 gene and protein expression tends to correlate with immune-related gene expression, and an inflamed tumor microenvironment may be associated with better clinical outcomes with ramucirumab and pembrolizumab. However, interpretation is limited by lack of control arm and sample size.1) Herbst et al. Lancet Oncol. 2019 Aug; 20 (8): 1109-1123. Clinical trial information: NCT02443324. Research Sponsor: Eli Lilly and Company.

3090 Poster Session (Board #154), Fri, 8:00 AM-11:00 AM

Relationship of infusion duration to safety, efficacy, and pharmacodynamics (PD): Second part of a phase I-II study using VSV-IFNβ-NIS (VV1) oncolytic virus in patients with refractory solid tumors. *First Author: Jaime R. Merchan, University of Miami, Miami, FL*

Background: VV1 (Voyager V1) is derived from VSV, an RNA virus with low human seroprevalence, engineered to replicate selectively in and kill human cancer cells. In Part 1 of this study, we demonstrated the safety of intratumoral VV1 and dose-response, using serum IFNβ as a biomarker; we observed viral replication in tumor and concomitant lymphocyte/neutrophil trafficking (SITC 2018). 2 other studies suggested greater efficacy and higher IFNβ levels with IV administration. Longer infusion durations were reported to mitigate infusion reactions (IRRs) for another oncolytic. **Methods:** We studied 3 different infusion durations of VV1 monotherapy at the recommended phase 2 IV dose (1.7×10^{10} $TCID_{50}$) in patients with advanced solid tumors. Endpoints included safety, preliminary anti-tumor activity, viral titers, IFNβ PD and shedding. Patients received IV VV1 once on D1 and were monitored for DLT over 21 days with efficacy assessments every 6 weeks. IRRs were classified using Lee 2014 criteria for CRS as either constitutional symptoms only (G1) or involving hypotension (G2). **Results:** 18 patients were treated at 30, 60 and 180-minute durations (n = 7, 5 and 6, respectively). No DLTs, deaths or G3-4 related IRR AEs were observed. Most pts were female (67%), white (100%), with ECOG PS 0 (61%) and median 4 lines of prior systemic therapy (range 1-14) for colorectal (CRC; 56%), squamous cell carcinoma (11%), pheochromocytoma (11%), sarcoma (11%) or other (11%) cancers. The table shows results (number of patients) by infusion duration. **Conclusions:** There was no difference in safety between the 3 infusion durations, while efficacy and PD markers suggested better anti-tumor effect with 30-minute infusion. VV1 is safe for caregivers, with no viral shedding. Part 3 of this study will now treat CRC patients with VV1 in combination with a checkpoint inhibitor (avelumab). A 5-arm phase 2 basket study in combination with cemiplimab is proceeding with 30-minute infusions. Clinical trial information: NCT02923466. Research Sponsor: Vyriad.

Duration (mins)	N	IRR G1	IRR G2	Total IRRs	RECIST PR/SD	IFNβ > 150 pg/mL	Shedding
30	7	4	3	7	5	4	0
60	5	4	1	5	3	0	0
180	6	2	3	5	1	0	0

3091 Poster Session (Board #155), Fri, 8:00 AM-11:00 AM

Impact of relacorilant, a selective glucocorticoid receptor antagonist, on the immunosuppressive effects of endogenous cortisol. *First Author: Andrew Greenstein, Corcept Therapeutics, Menlo Park, CA*

Background: Cortisol, an endogenous glucocorticoid receptor (GR) agonist, controls a broad transcriptional program that affects T-cell activation, pro-inflammatory cytokine secretion, and immune cell trafficking. By selectively antagonizing GR, relacorilant may reverse the immunosuppressive effects of cortisol in solid tumor cancers. **Methods:** Immune cells and GR expression were assessed by IHC and calculated based on The Cancer Genome Atlas (TCGA) data. Human PBMCs were stimulated with αCD3+IL-12 +/- cortisol or cortisol + relacorilant. EG7 tumor-bearing mice were treated with anti-PD1 (RMP1-14) ip Q5D +/- relacorilant QD. Whole blood mRNA was measured via Nanostring, hematology was performed using standard complete blood count assays, and cytokines were assessed by immunoassays in study NCT02762981. **Results:** GR expression was observed in human tumor and immune cells. Its abundance was positively correlated with tumor infiltration of T_H2, Treg, and PDL1$^+$ cells ($P<$ .001) and negatively correlated with T_H1 cells ($P<$ .001). In PBMCs, cortisol inhibited, and relacorilant restored, CD8$^+$ T-cell activation ($P<$ .001) and pro-inflammatory cytokine secretion (TNFα $P=$ .006, IFNγ $P<$ .05). In the EG7 syngeneic model, relacorilant increased αPD1 efficacy ($P=$ .007) and decreased circulating IL-10 ($P<$ .002). In patients with advanced solid tumors, relacorilant + nab-paclitaxel systemically suppressed the expression of canonical GR-controlled genes (*ptgs2* $P<$ .001) and genes encoding candidate-immunomodulatory drug targets (*cxcl8*, *ptger4*, *ido1;* $P<$ .001). In a small subset of patients (n = 11), sustained clinical response was associated with increased T-cell count ($P=$ .06) and IFNγ ($P=$ .03), as well as decreased Tregs ($P=$ .06) and IL-10 ($P=$ .03). **Conclusions:** Evidence of T-cell activation by relacorilant was observed in PBMCs, syngeneic mouse tumors, and patients with sustained response in a Phase 1 study. This supports the hypothesis that relacorilant can reverse immune suppression by endogenous cortisol in solid tumor cancers. Clinical studies with immune checkpoint inhibitors and relacorilant are planned. Research Sponsor: Corcept Therapeutics.

3092 Poster Session (Board #156), Fri, 8:00 AM-11:00 AM

A phase I study of mRNA-2752, a lipid nanoparticle encapsulating mRNAs encoding human OX40L, IL-23, and IL-36γ, for intratumoral (iTu) injection alone and in combination with durvalumab. *First Author: Manish R. Patel, Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL*

Background: mRNA-2752 is a novel mRNA-based therapeutic agent encoding OX40L T cell co-stimulator, IL-23 and IL-36γ pro-inflammatory cytokines. Here we present findings from a first-in-human study of iTu mRNA-2752 in solid tumor patients as monotherapy or in combination with durvalumab (durva). At the time of presentation, data will encompass the monotherapy escalation MTD/RDE along with the supporting translational work, and the available data in combination. **Methods:** iTu mRNA-2752 was administered every 2 weeks for up to 7 doses as monotherapy or in combination with durva in patients with advanced solid malignancy or lymphoma. Biomarker analyses include measurement of IL-23, IL-36γ and pro-inflammatory cytokine proteins in pre- and post-treatment tumor biopsies and plasma. PD-L1 immunohistochemistry was used to further characterize baseline status and changes to the TME with treatment. **Results:** As of 20 December 2019, 23 solid tumor patients have been treated either with mRNA-2752 alone (n = 14) or in combination (n = 9) and has been well tolerated with no dose limiting toxicities or related grade 3/4 toxicities. Of the 17 patients evaluated per RECIST and iRECIST, 1 had a PR (iRECIST), 6 had SD, and 10 had PD. The patient with a PR (52% tumor reduction) received 0.5 mg mRNA-2752 with durva, and had aPD-1/L1 naïve squamous-cell bladder carcinoma. Tumor shrinkage was observed in an additional 5 patients in injected and/or uninjected lesions in both monotherapy and combination. Preliminary biomarker data showed increased IL-23 and IL-36γ protein expression after 6-24 hours, and increased levels of downstream cytokines IL-22 and IL-6, respectively. Pro-inflammatory cytokines (e.g. IFN-γ, TNF-α) were also significantly increased at 1 day and 1-week post-treatment. Significant increases in PD-L1 expression predominantly in tumor-associated immune cells were observed after first dose and persisted up to 29 days after treatment. **Conclusions:** iTu mRNA-2752 given as monotherapy and in combination with durva is tolerable at all dose levels studied, and administration can be associated with tumor shrinkage. Analyses of tumor and plasma biomarkers suggest a sustained immunomodulatory effect of treatment that includes elevated IFN-γ, TNF-α, and PD-L1 levels. These data support the ongoing testing of the mRNA-2752/durva combination in the dose escalation part of the study. Clinical trial information: NCT03739931. Research Sponsor: Moderna Tx. Inc.

3093 Poster Session (Board #157), Fri, 8:00 AM-11:00 AM

Clinical activity of MCLA-128 (zenocutuzumab), trastuzumab, and vinorelbine in HER2 amplified metastatic breast cancer (MBC) patients (pts) who had progressed on anti-HER2 ADCs. *First Author: Erika Paige Hamilton, Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN*

Background: MCLA-128 (zenocutuzumab), a HER3 pathway inhibitor, is a humanized bispecific full-length IgG1 antibody targeting both HER2 and HER3 with enhanced ADCC activity. The unique Dock & Block mechanism inhibits HER3 from interacting with its ligands and targets HER2 at a different epitope than trastuzumab, blocking HER2/HER3 dimerization and downstream PI3K/AKT/mTOR signaling. In MBC, HER3 overexpression and/or HER3 ligand upregulation are important drivers leading to trastuzumab resistance, indicating a role for MCLA-128. Preclinical activity was seen in HER2+ breast models when MCLA-128 was combined with trastuzumab. Furthermore, single agent MCLA-128 showed consistent antitumor activity in heavily pretreated HER2+ MBC pts. A phase 2, open-label study explored the MCLA-128/trastuzumab plus vinorelbine triplet in an MBC population. **Methods:** This open-label trial planned for up to 40 evaluable women with HER2+/amplified MBC progressing on up to 5 anti-HER2 lines including trastuzumab, pertuzumab and an anti-HER2 ADC. Pts received MCLA-128 (750 mg, 2h IV), trastuzumab (8 mg/kg loading, then 6 mg/kg) and vinorelbine (25 mg/m^2, D1 and 8), q3w. A safety run-in of MCLA-128 + trastuzumab ± chemotherapy was performed. Disease control rate (DCR; RECIST 1.1, per investigator), best overall response (BOR), overall response rate (ORR), safety, and PK are evaluated. Data cutoff was 14Nov2019. **Results:** 28 pts with a median 3 lines (range 2-5) of anti-HER2 therapy (metastatic setting) and 3 (range 1-6) metastatic sites, received a median of 5 (range 1-17) MCLA-128 cycles. Among 26 pts evaluable for efficacy, 20 patients had CR/PR/SD as BOR; DCR was 77% (90%CI: 60-89) with 1 confirmed CR and 4 PRs (2 unconfirmed). Common related AEs (all grades; G3-4) were neutropenia/neutrophil count decrease (61%; 46%), diarrhea (61%; 4%), asthenia/fatigue (46%; 0), nausea (29%; 0). No clinically significant LVEF decline was seen. At the end of cycle 1, mean trough levels of MCLA-128 was 19.1 μg/mL, and mean terminal half-life was 112 h (n = 8-11). Data on the primary endpoint, clinical benefit rate at 24 weeks, and biomarkers will be provided. **Conclusions:** The triplet MCLA-128-based combination is active in heavily pretreated pts with HER2+/amplified MBC. The regimen is safe and well tolerated with a manageable AE profile mostly related to the chemotherapy component. Clinical trial information: NCT03321981. Research Sponsor: Merus NV.

3094 Poster Session (Board #158), Fri, 8:00 AM-11:00 AM

A phase I, open-label, multicenter, single-dose escalation and multi-dose study of a monoclonal antibody targeting CEACAM1 in subjects with selected advanced or recurrent malignancies. *First Author: Roni Shapira, Chaim Sheba Medical Center, Tel Hashomer, Israel*

Background: The carcinomembryonic antigen cell adhesion molecule 1 (CEACAM1, CD66a) is a member of the CEA gene family. CEACAM1 interacts homophilically and heterophilically with CEACAM5, and is involved in various anti-proliferative activities. CEACAM1 is expressed on a variety of epithelial and hematological cells, including multiple types of cancer and activated lymphocytes. High CEACAM1 expression in some tumor types is known to be associated with poor disease prognosis. Recently it was demonstrated CEACAM1 is co-expressed on exhausted lymphocytes with other immune checkpoints such as TIM-3 and may regulate downstream activity. CM24 is a novel humanized α-CEACAM1-specific antibody with nM affinity to the N terminal domain of CEACAM1, which blocks intercellular CEACAM1 interactions. **Methods:** The primary objective was to test the safety and tolerability of CM24 in adult patients with advanced or recurrent cancer. Secondary objectives included assessment of CM24 PK and PD profiles, anti-tumor response and the recommended Phase 2 dose. Patient received IV infusion of CM24 at 7 dose levels ranging between 0.01 and 10 mg/kg in a cycle of 4 doses administered q2wks followed by a 6-week observation only period and additional 6 cycles. **Results:** 27 patients (median pretreatment of 4 prior regimens; range 2-8, 11 colorectal, 7 melanoma, 4 ovarian, 3 gastric, 2 NSCLC; 13 males, 14 females, mean age of 60 years), were included. Treatment with CM-24 was overall well-tolerated without DLTs up to 10 mg/kg. The most frequent AE was grade 1-3 increased alanine aminotransferase (7 subjects) and the most severe AE was grade 3/4 increase in gamma-glutamyltransferase (4 subjects). Drug-related AEs were observed in 63% of the subjects with grade 3-5 occurred in 3.7%. Eight subjects (29.6%) had stable disease as the best overall response. Median overall survival was 4 (3.4, 8.0) and 6.2 (2.7, 10.2) months for the 3 and 10 mg/kg doses, suggesting dose response. Cmax, AUC and t1/2 increased with increasing dose with the longest t1/2 of 11.2 days obtained at 10mg/kg. The average target occupancy of CM24 at 3mg/kg and 10mg/kg were 75% and 93%, respectively. **Conclusions:** PK and target-mediated drug disposition analysis suggest that doses higher than 10mg/kg are needed for target saturation at a q2 week regimen while a q3 week regimen is less optimal. A phase 1/2 clinical trial testing CM24 in combination with anti-PD-1 therapy in patients with NSCLC including assessment of CEACAM1 expression is warranted. Clinical trial information: NCT02346955. Research Sponsor: Merck Sharp & Dohme Corp.

3095 Poster Session (Board #159), Fri, 8:00 AM-11:00 AM

Gut microbiome to predict efficacy and immune-related toxicities in patients with advanced non-small cell lung cancer treated with anti-PD-1/PD-L1 antibody-based immunotherapy. *First Author: Taiki Hakozaki, Department of Thoracic Oncology and Respiratory Medicine, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan*

Background: The gut microbiome (GM) plays an important role in shaping systemic immune responses. Preclinical and clinical data suggest that GM influences anti-PD-1/PD-L1 or -CTLA-4 Antibody (Ab)-mediated anti-cancer responses. Furthermore, there is strong evidence that antibiotics (ATB) worsen clinical outcomes based on multiple retrospective and one prospective studies using immune checkpoint inhibitor (ICI). However, whether GM profiling, at baseline or post-ATB, could represent a biomarker of response in advanced non-small cell lung cancer (NSCLC) during ICI therapy remains unknown. **Methods:** We prospectively collected baseline (pre-ICI) fecal samples and clinical data Japanese patients (pts) with NSCLC treated with anti-PD-1/PD-L1 Abs in first or second-line therapy. We performed a 16S rRNA V3-V4 sequencing of gene amplicons of fecal microbes. Amplicon sequence variants were generated with dada2 R package. Diversity analysis was performed with phyloseq R. Differential abundance analysis was performed with both LEfSe and DESeq2 methods. Clinical endpoints were progression-free survival (PFS), overall survival (OS), objective response rate (ORR), and immune-related adverse events (irAE). **Results:** 70 fecal samples were analyzed. Median OS and PFS in all patients were 16.1 and 5.2 months, respectively. 16 pts (23%) were exposed to ATB 1 month prior to ICI initiation. Pts on ATB had lower α-diversity at baseline and underrepresentation of *Clostridiales* and *Ruminococcaceae UCG 13*. When analyzing ATB-free pts, lower α-diversity was observed in non-responders. In addition, *Ruminococcaceae UCG 13* was enriched in patients with OS $>$ 12 months, favorable ORR, and PFS $>$ 6 months. *Clostridiales* order was also enriched in patients with OS $>$ 12 months. Compositional GM differences were also observed between the patients who experienced clinically significant ($\geq$grade 2) irAE; *Lactobacillaceae* and *Raoultella* were enriched in pts who had no significant irAE. **Conclusions:** We demonstrated the negative influence of ATB on GM composition and identified differential bacteria repertoire in pts experiencing favorable clinical outcomes or low grade irAE. Our data pave the way to the development of diagnosis tools aimed at identifying gut dysbiosis to predict resistance or irAE during ICI for NSCLC. Research Sponsor: This work was supported by JSPS KAKENHI Grant Number JP19K16820.

3096 Poster Session (Board #160), Fri, 8:00 AM-11:00 AM

A phase I dose-escalation and expansion study of intratumoral CV8102 as single-agent or in combination with anti-PD-1 antibodies in patients with advanced solid tumors. *First Author: Thomas Eigentler, Department of Dermatology, University Hospital Tübingen, Tübingen, Germany*

Background: CV8102 is a non-coding, non-capped RNA that activates the innate (via TLR7/8, RIG-I) and adaptive immunity dose-dependently. CV8102 injected intratumorally (i.t.), as a single agent or combined with systemic anti-PD-1 antibody (Ab) led to tumor growth inhibition in animal models and showed synergism with PD-1 blockade. **Methods:** An open-label, cohort-based, dose escalation and expansion study in patients with advanced cutaneous melanoma (cMEL), cutaneous squamous cell carcinoma (cSCC), head and neck squamous cell carcinoma (hnSCC) or adenoid cystic carcinoma (ACC) is ongoing investigating i.t. CV8102 as single agent and in combination with anti-PD-1 antibodies. [NCT03291002]. **Results:** As of December 2019, 23 patients in the cohort A (single agent) and 13 patients in cohort C (combination with anti-PD-1 Ab) were exposed to at least one dose of CV8102 at dose levels of 25-600 μg (single agent) and 25-450 μg (combination). No dose limiting toxicities (DLTs) were observed within the first two weeks of study drug treatment. Most frequent TEAEs were G1/2 fatigue, fever, chills and headache. 4 (17%) patients (pts) in cohort A and 3 (23%) pts in cohort C experienced related G3 TEAEs that were manageable with supportive treatment (liver enzyme increases (3), abscess at injection site (1), hypertension (1), asymptomatic elevation of pancreatic enzymes (2)). In cohort A, 2 cMEL patients experienced an objective response according to RECIST 1.1 (1 CR in a PD-1 naïve pt and 1 PR in a PD-1 refractory pt) and 2 further pts (cMEL, hnSCC) showed SD with shrinkage of tumor lesions. **Conclusions:** CV8102 i.t. was well tolerated without dose limiting toxicities to date and showed evidence of single agent activity. Updated results on safety, efficacy and serum biomarkers will be presented. Clinical trial information: NCT03291002. Research Sponsor: CureVac AG.

3097 Poster Session (Board #161), Fri, 8:00 AM-11:00 AM

Immune activation in first-in-human anti-macrophage antibody (anti-Clever-1 mAb; FP-1305) phase I/II MATINS trial: Part I dose-escalation, safety, and efficacy results. *First Author: Petri Bono, Terveystalo Finland and University of Helsinki, Helsinki, Finland*

Background: The scavenger receptor CLEVER-1 mediates the clearance of "unwanted" self-components and is highly expressed on tumor associated macrophages (TAMs). CLEVER-1 expression is associated with immunotherapy resistance and poor survival in several cancers. Pre-clinical studies demonstrate that CLEVER-1 inhibition increases TAM pro-inflammatory cytokine secretion and antigen presentation reactivating CD8 T cell responses with robust anti-tumor activity. Targeting CLEVER-1 could therefore overcome the immunosuppressive tumor microenvironment and has led to the development of FP-1305, a humanized anti-CLEVER-1 IgG4-antibody. **Methods:** The MATINS (Macrophage Antibody To INhibit immune Suppression) trial is a multicenter first-in-human phase I/II study (NCT03733990) to assess the tolerability, safety and preliminary efficacy of FP-1305 in patients (pts) with advanced cancers including immunotherapy-refractory melanoma, cholangiocarcinoma, hepatocellular carcinoma, ovarian cancer, colorectal (CRC), and pancreatic ductal adenocarcinoma. Part 1 consisted of a dose escalation phase; 30 pts (median age 65, range 30-81) were enrolled to examine 5 dose levels (0.1, 0.3, 1.0, 3.0, 10 mg/kg), to determine the optimal dose of FP-1305 for Parts 2 and 3. Two-stage time-to-event continual reassessment method (TITE-CRM) was utilized for the dose escalation in Part 1. Pts received 1-8 cycles (median 3) of FP-1305 Q3w. FP-1305 was well tolerated without dose-limiting toxicities. A consistent increase in blood NK cells, CD8/CD4 T cell ratio, B cells and a decrease in regulatory T cells was demonstrated. FP-1305 dosing led to the activation ($CD25^+$) and Th1 skewing ($CXCR3^+$) of T cell populations including increase in effector CD8 T-cells with downregulation of several inhibitory immune checkpoint molecules (PD-1, PD-L1, CTLA-4, and LAG3). Increased circulating IFNγ levels were detected, with the highest levels in a heavily pretreated metastatic, microsatellite stable (MSS) colorectal cancer patient leading to a partial tumor response (-52%). FP-1305 is the first macrophage checkpoint inhibitor candidate promoting immune switch with promising tolerability and clinical anti-tumor activity. FP-1305 represents a novel treatment option to provoke immune response especially in non-inflamed tumors. Full safety, pharmacokinetic and efficacy results of MATINS trial (Part 1) will be presented for the first time in a final late breaking abstract. Clinical trial information: 2018-002732-24. Research Sponsor: Faron Pharmaceuticals.

3098 Poster Session (Board #162), Fri, 8:00 AM-11:00 AM

First-in-class microbial ecosystem therapeutics 4 (MET4) in metastatic solid cancer patients treated with immunotherapy: MET4-IO. *First Author: Daniel Vilarim Araujo, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Therapeutic augmentation of the intestinal microbiome to improve immunotherapy outcomes is an active area of investigation. Microbial Ecosystem Therapeutics (METs) are consortia of human-derived bacteria designed to be reproducible, scalable and safe alternatives to fecal transplant. MET4 is a first-in-class consortium of taxa associated with immune checkpoint inhibitor (ICI)-responsiveness. Here we describe preliminary results of MET4-IO, an interventional trial assessing the safety and ecological effects of MET4 in ICI recipients. **Methods:** MET4-IO is a randomized investigator-initiated trial, evaluating MET4 in solid cancer patients treated with ICI. MET4-IO involves 3 cohorts of 65 total patients: Group A, a safety cohort of 5 patients already on ICI; Group B, patients starting ICI, randomized 3:1 to receive MET4 or not; Group C, patients on ICI who experience radiological progression but not clinical deterioration, randomized 1:1 to receive MET4 or not. Stool and blood samples are collected at baseline and 4-5 additional time-points. For this interim analysis, 16S rRNA gene sequencing was performed on fecal specimens. Shannon diversity, relative abundance (RA), number and fold-change of MET4 taxa $>$ RA 0.01 were assessed and compared to controls. **Results:** As of January 26, 2020, 21 patients were enrolled (A = 5,B = 12,C = 4), and 15 (71%) received MET4. The mean age was 65.9 years, 40% were females, 52% had head and neck cancer and 19% melanoma. Sixteen patients (76%) were treated with an anti-PD1 agent as monotherapy and 5 with a combination of anti-PD1 and anti-CTLA4 antibodies. G3-4 toxicities (CTCAEv5.0) attributed to ICI were observed in 13% vs. 17% of MET4 exposed and control patients, respectively. Three patients (20%) experienced toxicities attributed to MET4, all grade 1 except G2 dyspepsia in 1 patient. A greater number of MET4-associated taxa were detectable in MET4 recipients than controls ($p < 0.01$), with a trend towards higher cumulative RA ($p = 0.10$). No significant change in Shannon diversity after MET4 was observed, however controls were more likely to lose diversity overtime than MET4 recipients ($p = 0.05$). Colonization with MET4 varied by recipient and by taxon. *Bifidobacterium*, *Collinsella* and *Enterococcus* were significantly more common and abundant in MET4 recipients than controls. **Conclusions:** In this cohort, MET4 treatment was safe and associated with higher MET4-associated taxa in recipients than controls. Further analyses including peripheral blood immunophenotyping are ongoing. Clinical trial information: NCT03686202. Research Sponsor: University Health Network, Pharmaceutical/Biotech Company.

3099 Poster Session (Board #163), Fri, 8:00 AM-11:00 AM

Open-label, phase I study evaluating feasibility and safety of subcutaneous IMP321 (LAG-3Ig fusion protein, eftilagimod alpha) combined with avelumab in advanced stage solid tumor entities: Results from stratum D of the INSIGHT platform trial. *First Author: Thorsten Oliver Goetze, University Cancer Center Frankfurt, Institut für Klinisch-Onkologische Forschung and IKF Klinische Krebsforschung GmbH am Krankenhaus Nordwest, Frankfurt, Germany*

Background: Stratum D of the INSIGHT study investigates the feasibility and safety of s.c. application of IMP321 (eftilagimod alpha) combined with the PD-L1 inhibitor avelumab in advanced stage solid tumors. The MHC class II agonist IMP321 activates antigen-presenting cells followed by CD8 T-cell activation. The addition of avelumab aims at enhancing activity by combining IMP321's activating effects on immune cells with the release of immune inhibitory effects caused by interruption of the PD-1/PD-L1 axis. **Methods:** This investigator-initiated phase I trial consists of four strata: intratumoral (A) or intraperitoneal IMP321 (B); s.c. IMP321 with SOC (C) or with PD-L1 inhibition (D). This abstract focuses on Stratum D. Patients (pts) receive 800mg avelumab i.v. q2w along with s.c. IMP321 injections (6mg IMP321 in cohort 1 and 30mg IMP321 in cohort 2). 12 pts are planned in stratum D: 6 pts in cohort 1 and 6 pts in cohort 2. Primary endpoint is safety. **Results:** So far, 8 pts have been enrolled (6 in cohort 1 and 2 in cohort 2). In 6 pts (cohort 1) treated for different tumor indications (gastric, gallbladder, colon cancer, pleural mesothelioma), no dose limiting toxicities occurred. 3 serious adverse events (SAEs) (1 acute kidney injury grade 5 in 1 pt, 2 preileus grade 3 in 1 pt) were reported, none of them was related to any of the study drugs. In total, 34 adverse events (AEs; grade 1-2, 21; grade 3, 12; no grade 4; grade 5, 1) have been documented in 5 pts. Most common grade 1-2 AEs were pain, nausea, and injection site reaction in 50%, 33%, and 17% of the pts. Most common grade 3 AEs were nausea/vomiting, preileus/ileus, and ascites in 33%, 33%, and 17% of the pts. One AE grade 5 (acute kidney injury) was reported. 4 AEs grade 1-2 were possibly or definitely related to IMP321 (injection site reaction 2x; fever; lipohypertrophy), 6 AEs grade 1-2 were possibly or definitely related to avelumab (nausea 2x; chills; fever; dyspnea; lipohypertrophy). All AEs grade 3-5 were unrelated to any of the study drugs. Of the 8 pts enrolled so far, 4 had disease progression (acc. to RECIST 1.1), 1 partial response, 1 stable disease with some extent of tumor shrinkage, and 2 have not had tumor assessment yet. **Conclusions:** Combination treatment with avelumab 800mg and IMP321 6mg is safe and well tolerated. Cohort 2 will be presented at the meeting. Clinical trial information: NCT03252938. Research Sponsor: Immutep.

3100 Poster Session (Board #164), Fri, 8:00 AM-11:00 AM

Initial results from a phase II study (TACTI-002) in metastatic non-small cell lung or head and neck carcinoma patients receiving eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab. *First Author: Enriqueta Felip, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain*

Background: Eftilagimod alpha (efti) is a soluble LAG-3 protein that binds to a subset of MHC class II molecules to mediate antigen presenting cell (APC) activation and then CD8 T-cell activation. The stimulation of the dendritic cell network and subsequent T cell recruitment with efti may lead to stronger anti-tumor responses than observed with pembrolizumab alone. We hereby report initial results of a phase II trial (NCT03625323). **Methods:** A predefined number of patients (pts) are recruited into this 3-cohort trial irrespective of PD-L1 expression; part A: 1st line, PD-X naïve NSCLC; part B: 2nd line, PD-X refractory NSCLC and part C: 2nd line PD-X naive HNSCC. The study has a Simon's 2-stage design, with objective response rate (ORR) as primary endpoint. Secondary endpoints include disease control rate, progression free and overall survival, PK, PD and immunogenicity. Additional pts (N2) will be recruited for each part if pre-specified thresholds for ORR are met. Up to 109 pts will be enrolled. Efti is administered as 30 mg subcutaneous injection every 2 wks for 8 cycles and then every 3 wks for 9 cycles with pembrolizumab (200 mg intravenous infusion every 3 wks for up to 2 yrs). The study was approved by ethic committees and institutional review boards. **Results:** Between 04 Mar 19 and 31 Jan 2020, 48 pts were enrolled and evaluated for safety and exposure. The median age was 66 yrs (range 48-84) and 73 % were male. The ECOG was 0 in 50 % and 1 in 50 % of pts, respectively. Pts received a median of 5 (7) and in total 311 (413) pembrolizumab (efti) administrations, respectively. Three pts (6.3 %) discontinued study treatment due to AEs. The most common ($>$ 10%) adverse events (AEs) being cough (31 %), asthenia (23 %), decreased appetite (19 %), fatigue (19 %), dyspnea (17 %), diarrhea (15 %) and constipation 13 %). From part A all pts (n = 17) were evaluated. Eight pts (47 %) had a partial response (iPR) and six (35 %) had stable disease according to iRECIST representing an ORR (DCR) of 47 % (82 %). irPRs were observed in all different PD-L1 groups ($<$ 1%; $\geq$ 1 % $\leq$49 %; $\geq$ 50 %). Ten (10; 59 %) pts are still on therapy (8+ months). In part C stage 1 15/18 pts are evaluable and six (40 %) had an iPR to date. **Conclusions:** Efti in combination with pembrolizumab is safe and shows encouraging antitumor activity in all comer PD-L1 1st line NSCLC and 2nd line HNSCC. Stage 2 has opened for both parts. Clinical trial information: NCT03625323. Research Sponsor: Immutep S.A.S.

3101 Poster Session (Board #165), Fri, 8:00 AM-11:00 AM

A phase I study to evaluate the T-cell engager AMV564 alone and in combination with pembrolizumab in subjects with advanced solid tumors. *First Author: Alexander Starodub, Riverside Peninsula Cancer Institute, Newport News, VA*

Background: Overcoming the immune-suppressive tumor environment induced by myeloid-derived suppressor cells (MDSC) is a major challenge in immune therapy. CD33 signaling in immature myeloid cells promotes expansion of MDSC and production of immune-suppressive factors. AMV564 is a bivalent, bispecific T-cell engager that binds CD3 and CD33. Preferential binding of AMV564 to areas of high CD33 density enables selective targeting of MDSC. Ex vivo data (Cheng 2017; *Blood*;130:51) and an ongoing clinical trial in acute myeloid leukemia (NCT03144245) demonstrate the ability of AMV564 to deplete MDSC while sparing monocytes and neutrophils. **Methods:** In this 3+3 dose escalation study, patients with advanced solid tumors receive AMV564 once daily via subcutaneous (SC) injection for 2 out of 3 wks per cycle, alone or in combination with pembrolizumab (200 mg every 3 wks). Key objectives are to evaluate AMV564 safety, identify a maximum tolerated or recommended phase 2 dose, and evaluate PK, immunophenotype of myeloid and T cell compartments, and preliminary efficacy. **Results:** Eleven patients have been enrolled: 8 monotherapy (3 at 15 mcg/d, 5 at 50 mcg/d) and 3 combination (5 mcg/d). Tumor types include ovarian (n = 2), small bowel, gastroesophageal junction, endometrial, rectal, penile, urothelial, squamous cell carcinoma (skin), appendiceal, and non-small cell lung. AMV564 was associated with grade (G) 1-2 injection site reactions and G1-2 fevers, which were manageable with acetaminophen and diphenhydramine, as well as G2 weight gain and G3 anemia. No dose-liming toxicity has been observed in any cohort. Three monotherapy patients (15 mcg/d) were evaluable for efficacy with $\geq$1 on-treatment scan; 2 had SD and 1 PD per RECIST 1.1 criteria. T cell activation, as shown by redistribution from the periphery (margination), was apparent in the first week of dosing for most patients. Compensatory myelopoiesis led to initial expansion of MDSC which were then depleted by AMV564. Increased cytotoxic T cell activation and T-helper (Th) 1 response was evidenced by increased T-bet positive CD4 and CD8 cells and controlled or decreased regulatory T cells. In some patients, effector memory CD8 cell populations (Tem and Temra) were expanded. **Conclusions:** AMV564 is safe and tolerable when administered SC at doses of 15 mcg/d alone and 5 mcg/d in combination with pembrolizumab. AMV564 depleted MDSC populations and altered T cell profiles consistent with activation of cytotoxic T cells and a Th1 response. Clinical trial information: NCT04128423. Research Sponsor: Amphivena Therapeutics.

3102 Poster Session (Board #166), Fri, 8:00 AM-11:00 AM

An increase in serum choline levels to predict progression-free survival (PFS) in patients (pts) with advanced cancers receiving pembrolizumab. *First Author: Geoffrey Alan Watson, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Recent work from our laboratory demonstrated that T cell-derived acetylcholine induces vasodilation and increases T cell migration to infected tissues in response to viral infection (Cox et al. Science 2019). Choline acetyltransferase catalyzes the production of acetylcholine from choline and acetyl-CoA, however acetylcholine is challenging to quantify due to its extremely short half-life while choline is stable. This study is the first reported attempt to correlate serum choline levels in patients (pts) with advanced solid tumors receiving pembrolizumab with treatment outcomes. **Methods:** Blood samples were collected pre-treatment in 106 pts treated with pembrolizumab 200 mg IV Q3W in the investigator-initiated INSPIRE study (NCT02644369). Of these, 81 pts had on-treatment blood samples collected at week 7 (pre-cycle 3). Serum choline was analyzed with an HPLC-tandem mass spectrometry assay. PD-L1 staining was performed in baseline tumor tissues using 22C3 antibody and scored using modified proportion score. Tumor mutational burden (TMB) was calculated based on number of nonsynonymous mutations detected using whole exome sequencing. Multivariable Cox models were used to assess the impact of choline on PFS and OS, while adjusting for cohort, PD-L1 expression and TMB. **Results:** This pan-cancer group of 106 pts (median age 55, 62% females) comprised of 5 cohorts: squamous cell carcinoma of the head and neck = 19 pts, triple negative breast cancer = 22, high grade serous ovarian cancer = 21, melanoma = 19, mixed solid tumors = 32. With a median follow-up of 11 months, the median PFS = 1.9 months and median OS = 13.9 months for the entire cohort. In univariable analysis adjusted by cohort, baseline serum choline levels in 106 pts did not correlate with PFS or OS. However, an increase in serum choline level at week 7 compared to pre-treatment (D choline) in 81 pts was significantly associated with a better PFS (aHR 0.49, 95% CI 0.28-0.85, p = 0.01), and a trend towards a better OS (aHR 0.57, 95% CI 0.32-1.03, p = 0.064). In multivariable analysis, D choline remains significantly associated with an improved PFS (p = 0.0087) after adjustment for cohort, PD-L1 and TMB. **Conclusions:** This is the first exploratory report of serum choline levels in pan-cancer pts receiving pembrolizumab. The association between improved PFS and D choline suggests a possible role for the cholingeric system in the regulation of antitumor immunity. Further nonclinical and clinical studies are required to validate this finding. Research Sponsor: Merck.

3103 Poster Session (Board #167), Fri, 8:00 AM-11:00 AM

Single vector multiplexed shRNA provides a non-gene edited strategy to concurrently knockdown the expression of multiple genes in CAR T cells. *First Author: David Edward Gilham, Celyad, Mont-Saint-Guibert, Belgium*

Background: Engineered T cells expressing chimeric antigen receptors (CAR) are now delivering clinically relevant results in patients with advanced hematological malignancies. One critical area for future development is to modulate gene expression thereby endowing the engineered T cell with specific desired features that enhance anti-tumor activity. **Methods:** Short-hairpin RNA (shRNA) were cloned individually or multiplexed within micro-RNA scaffolds that enabled the co-expression of the individual shRNA with a CAR and a selectable marker all driven by a PolII promoter within a single retroviral vector. Primary human T cells transduced with the CAR-shRNA vectors were selected, expanded in vitro, subjected to negative selection to eliminate any remaining TCR^+ cells and examined for target gene expression and functional activity. **Results:** A 500bp DNA fragment incorporating a shRNA-specific for CD3ζ cloned into a retroviral vectoreffectively knocked down expression of CD3ζ in transduced BCMA-specific CAR T cells. The consequent reduction of cell surface TCR expression resulted in minimal cytokine production upon TCR stimulation in vitro providing a potential allogeneic CAR T approach. These CAR T cells showed no demonstrable evidence of GvHD induction when infused in NSG mice yet maintained BCMA-specific CAR activity in KMS-11 and RPMI-8226 established myeloma models. Initial studies further confirmed that two shRNA could be expressed from a single retroviral vector to modulate the expression of multiple genes. Further engineering of the microRNA framework reduced the size of the transgene load to 394bp while enabling the expression of up to 4 shRNA within a single vector. shRNA specific for CD3ζ, beta-2-microglobulin, CD52 and diacylglycerol kinase alpha were engineered into the framework downstream of a CD19-CAR. Transduced Jurkat cells showed concurrent knockdown of the respective gene products at the mRNA and protein levels. **Conclusions:** A first-in-human clinical trial evaluating the first-generation single shRNA-vector in the context of a BCMA-targeting CAR as a non-gene edited approach to allogeneic CAR T cell therapy will be initiated in 2020. The proof of principle study here shows that multiple shRNAs are active within a single viral vector thereby avoiding the need for bespoke individual clinical reagents to target multiple genes. The multiplexed shRNA vector system is now in further development to explore whether this strategy can enhance the therapeutic potential of CAR T cells. Research Sponsor: Celyad SA.

3104 Poster Session (Board #168), Fri, 8:00 AM-11:00 AM

Combination therapy with DPX-Survivac, intermittent low-dose cyclophosphamide (CPA) and pembrolizumab for the treatment of advanced and metastatic solid tumors: Early safety and efficacy results from a phase II basket study. *First Author: Henry Jacob Conter, William Osler Health System, Brampton, ON, Canada*

Background: DPX-Survivac is a targeted T cell therapy against tumors expressing survivin. The robust and durable survivin specific T cells induced by DPX-Survivac have been shown to infiltrate tumors and are associated with clinical response in blood and solid tumors. In nonclinical studies, treatment with DPX-Survivac increases PD-L1 and PD-1 expression providing the rationale for combination with anti-PD1/L1. This study investigates if enhanced clinical benefits can be achieved in a subset of solid tumor indications with different response rates to pembrolizumab single agent therapy. **Methods:** Subjects with survivin-expressing advanced, recurrent HCC, NSCLC, bladder and MSI-H tumors are enrolled to single arm, non-randomized cohorts that each utilizes a Simon 2-stage design. The primary objectives are to determine the ORR by RECIST 1.1 and safety profile of treatment with DPX-Survivac/CPA and pembrolizumab. Secondary objectives are DoR, DCR, PFS, and OS as measured by iRECIST. Exploratory analyses will look at T cell kinetics and infiltration of the tumor along with extensive biomarker analyses to further support the mechanism of action of DPX-Survivac when combined with pembrolizumab. **Results:** Thirty subjects across HCC (N = 5), NSCLC (12), bladder (6) and MSI-H (7) tumors that express survivin were enrolled for this analysis. The median number of prior lines of therapies was 2 [0 to 10]; 16/30 previously received and progressed on or after CPI therapy. As of the data cutoff, 10 subjects had at least 1 on-treatment scan. Six of 10 subjects (60%) demonstrated target lesion regressions with 3 achieving PR by RECIST (2 bladder, 1 MSI-H [endometrial]) and 3 achieving SD (2 with prior CPI), all are ongoing. Twenty-one of 30 subjects remain on treatment. Nine subjects have discontinued treatment: 5 subjects due to early progression, 2 due to unrelated AEs, and 2 withdrew consent. Treatment has been well tolerated with no immune-related AEs and 2 related SAEs reported. The majority of AE have been grade 1-2 injection site reactions. DPX-Survivac treatment induced a robust survivin-specific T cell response and tumor immune infiltration which are being evaluated for potential correlation with clinical response. **Conclusions:** DPX-Survivac/CPA with pembrolizumab is well tolerated and shows early signs of clinical efficacy and disease control in advanced and metastatic solid tumors. Clinical trial information: NCT03836352. Research Sponsor: IMV Inc.

3105 Poster Session (Board #169), Fri, 8:00 AM-11:00 AM

A phase I, dose-escalation study of ADG106, a fully human anti-CD137 agonistic antibody, in subjects with advanced solid tumors or relapsed/refractory non-Hodgkin lymphoma. *First Author: Li Zhang, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: ADG106 is a fully human agonistic anti-CD137 monoclonal IgG4 antibody, targeting a unique epitope of CD137 with novel mechanism of actions for CD137 agonism, CD137 ligand antagonism and potent cross-linking *via* FcgRIIb. This phase 1 study was conducted to assess its safety, tolerability, pharmacokinetic (PK) profile, immunogenicity and preliminary efficacy. **Methods:** Eligible patients with age 18 to 75, ECOG ≤1, measurable lesion received intravenous infusion of ADG106 every 3 weeks for a maximum of 24 months. Accelerated titration was applied in 0.1mg/kg dose level and traditional Fibonacci 3+3 method was applied in 0.5, 1.5, 3.0, 5.0 and 10.0 mg/kg dose levels. A dose-expansion cohort will be started for dose levels that have been proved tolerable and with evidence of clinical or biological activity. **Results:** Data cutoff at Jan 17 2020, 15 patients [5 adenoid cystic carcinoma (ACC), 5 non-small cell lung cancer (NSCLC), 3 nasopharyngeal carcinoma, 1 malignant pleural mesothelioma and 1 follicular lymphoma] were enrolled and received treatment: 0.1mg/kg (n = 1), 0.5mg/kg (n = 3), 1.5mg/kg (n = 5), 3mg/kg (n = 3), and 5mg/kg (n = 3). Of these 15 patients, 6 with ongoing treatment, 9 discontinued (8 progression disease, 1 lack of clinical benefit). Medium treatment duration was 2 cycles (range 2-8). No dose limiting toxicities were observed. Seven (47%) patients experienced treatment-related AEs (TRAEs): rash (13%), pruritus (13%), nausea (7%), pyrexia (7%), hemoptysis (7%), mouth ulceration (7%), vomiting (7%), chest discomfort (7%), LDH increased (7%). All TRAEs were grade 1, no grade ≥3 occurred. One serious adverse event (anemia, not related) was observed. Pharmacokinetic analysis of ADG106 showed a half-life ranging from 5~10 days, with dose-dependent increase of systemic exposure. Treatment induced anti-drug antibodies were developed in 3 (20%) patients. No objective response was observed among the 14 evaluated patients. Disease control rate was 57% (8 stable disease), tumor shrinkage was observed in 3 (21%) patients (2 ACC, 1 NSCLC). **Conclusions:** ADG106 is safe and tolerable at doses up to 5 mg/kg in solid tumors and non-Hodgkin lymphoma. The dose expansion cohorts have started at selected doses. Clinical trial information: NCT03802955. Research Sponsor: None.

3106 Poster Session (Board #170), Fri, 8:00 AM-11:00 AM

Deep learning-based predictive imaging biomarker model for EGFR mutation status in non-small cell lung cancer from CT imaging. *First Author: Abhishek Mahajan, Tata Memorial Centre, Mumbai, India*

Background: Deep learning based radiogenomic (DLR) models present a promising performance in assisting lung cancer care. The purpose of this study was 1) To develop and validate DLR signatures to predict the EGFR mutation, 2) To assess the incremental value of these DLR signatures in comparison to the traditional clinical and semantic features. **Methods:** 223 patients were selected from two phase III randomized trials in patients with advanced non-squamous NSCLC with *EGFR*-sensitizing mutation and EGFR wild type who were planned to receive palliative therapy (trial 1: gefitinib or gefitinib plus pemetrexed and carboplatin and trial 2: pemetrexed maintenance and erlotinib maintenance). Our method is an end-to-end pipeline that requires only the manually selected tumour region in a CT image without precise tumour boundary segmentation or human-defined features. Two deep convolutional neural networks with 3D U-Net architectures are trained to segment lung masses and nodules from 3D regions of the CT image. The primary end point was EGFR prediction using Radiomics and DLR pipeline. We also compared the performance of combination of models in predicting the mutational status. **Results:** A total of 223 patients (mean age, 54.18 years; age range, 28–80 years) were included in this study. There were 121 (54.3%) patients with EGFR mutation and 102 (45.7%) patients who were EGFR wild type. On multivariate logistic regression analysis, Clinical variable and CT semantic features that were found to be significantly associated EGFR mutation were tumor stage, smoking status, pure solid texture, presence of non-tumor lobe nodule, and average enhancement. For predicting EGFR mutation, ROC curve plotted with clinical variables model, CT semantic variables model, Radiomics model, DLR model showed an AUC value of 0.70, 0.73, 0.94, 0.72 respectively. Clinical variables and semantic features were added to the radiomics predictive model and deep learning predictive model independently, showed further improvement in the accuracy for either model from AUC 0.94+/-0.02 to 0.96+/-0.02 and from AUC 0.72+/-0.02 to 0.82+/-0.04 respectively. **Conclusions:** The radiomics and DLR model by machine-learned information, extracted from CT images without precise manual segmentation, could predict EGFR mutation with very high accuracy. This AI based model can be used as non-invasive and easy-to-use surrogate imaging biomarker for EGFR mutation status prediction. Clinical trial information: CTRI/2018/10/022102. Research Sponsor: DBT-BIRAC research grant.

3107 Poster Session (Board #171), Fri, 8:00 AM-11:00 AM

GEN-009, a neoantigen vaccine containing ATLAS selected neoantigens, to generate broad sustained immunity against immunogenic tumor mutations and avoid inhibitory peptides. *First Author: Roger B. Cohen, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA*

Background: Tumor-specific neoantigens provide personalized targets for immunotherapy. Vaccines against epitopes predicted by *in silico* approaches very rarely induce $CD4^+$ and $CD8^+$ *ex vivo* T cell responses regardless of formulation. ATLAS selects neoantigens for vaccine inclusion using *ex vivo* screening of all patient-specific mutations to identify pre-existing $CD4^+$ or $CD8^+$ T cell responses and to exclude Inhibigens, which are inhibitory peptides that suppress immunity and accelerate tumor progression. The Inhibigen burden correlates with patient outcomes in observational studies and rapid tumor progression in mouse models. **Methods:** GEN-009-101 is a phase 1/2a study testing safety, immunogenicity and clinical activity in immune responsive tumors. After next-generation tumor sequencing and ATLAS testing of autologous leukocytes, up to 20 stimulatory synthetic long peptides adjuvanted with poly-ICLC comprise each personalized vaccine. Eight vaccinated patients have been followed for sustained immunological responses and clinical outcomes. **Results:** The 40 doses given across patients have induced only mild local discomfort and no DLT. Vaccination has generated immune responses against 99% of administered peptides, with both $CD8^+$ and $CD4^+$ responses in *ex vivo* fluorospot assays. To date, no patients have developed recurrent disease. Broad immunity develops as early as Day 29 and is sustained for over 12 months. Immune response against individual peptides is correlated with peptide concentration (OR = 1.26, $p \leq 0.0001$) but not with other classifiers such as GRAVY index (Grand Average of Hydropathy), tumor type, injection site or sex. The Inhibigen burden prior to treatment again correlates with disease progression. **Conclusions:** GEN-009 identifies tumor specific immune targets from the individual patient's tumor mutagens. Initial clinical data show that ATLAS antigen selection may be critical to the induction of broad, rapid and sustained immunity against tumor specific neoantigens. Clinical vaccination with PD-1 blockade is in process. Clinical trial information: NCT03633110. Research Sponsor: None.

		ATLAS Neoantigens		Post-vaccination Response		
Pt	Tumor type	Stimulatory	Inhibitory	*ex vivo* CD4/CD8	IVS CD4/CD8	Total Positive
1	NSCLC	6	0	10% / 40%	100% / 20%	100%
2	Urothelial	16	4	50% / 38%	63% / 50%	100%
3	Melanoma	199	41	6% / 38%	100%/100%	100%
4	Urothelial	18	1	100%/69%	85%/31%	100%
5	NSCLC	16	9	55% / 45%	100%/64%	100%
6	Urothelial	24	104	77%/15%	77%/62%	100%
7	Urothelial	14	4	38%/75%	88%/63%	100%
8	SCCHN	15	15	89%/11%	78%/33%	89%

3108 Poster Session (Board #172), Fri, 8:00 AM-11:00 AM

Evidence of intratumoral localization, activation, and immunomodulatory effect of CX-072, a probody therapeutic targeting PD-L1, in a phase I/II trial. *First Author: Susan Lyman, CytomX Therapeutics, Inc., South San Francisco, CA*

Background: PROBODY therapeutics (Pb-Tx) are masked antibodies designed to be selectively activated in the tumor microenvironment by tumor-associated proteases and to remain largely inactive in normal tissue. CX-072, a Pb-Tx directed against PD-L1, is designed to reduce the potential for immune-associated adverse events in normal tissues while maintaining anti-tumor activity. CX-072 is being investigated in PROCLAIM-CX-072 (NCT03013491), a first-in-human phase 1/2 trial. CX-072 is administered as monotherapy or in combination with ipilimumab to patients with metastatic or recurrent solid tumors or lymphomas for which approved PD-1/-L1–based therapy is not available. We present the updated results of a tissue-based biomarker program designed to assess activation, localization, and mechanism of action of CX-072 in patient tumors. **Methods:** Tumor biopsies were collected during the screening phase, and also 3–5 days after the first or third dose of 0.3–30 mg/kg CX-072. Tumor-associated protease activity was measured by tissue zymography. Intratumoral CX-072 activation was measured using capillary immunoelectrophoresis, and PD-L1 levels were measured by an ultrasensitive ELISA. Intratumoral CD8 expression was analyzed using immunohistochemistry. Intact and total CX-072 in plasma were measured by LC-MS/MS. **Results:** Twenty-six of 30 (87%) evaluable predose biopsies had detectable levels of relevant protease activity. Intratumoral activation of CX-072 was quantifiable in 3 of 8 (38%) biopsies from patients treated with CX-072 at 3 mg/kg and in 12 of 12 (100%) biopsies from patients treated with $\geq$10 mg/kg. In contrast, CX-072 remained predominantly in the intact form in circulation. The molar ratio of activated intratumoral CX-072 to total intratumoral PD-L1 ranged from ~14x to > 100x in patients dosed at 10 mg/kg, and the calculated tumor receptor occupancy for these patients was $\geq$99%, congruent with quantitative systems pharmacology model predictions. An increase in $CD8^+$ T cells and elevation of cytotoxic T-cell markers was observed in the tumors of 11 of 18 (61%) CX-072 monotherapy patients, consistent with inhibition of the PD-L1 pathway. **Conclusions:** These results demonstrate that the Pb-Tx CX-072 behaves as designed in patients. Clinical trial information: NCT03013491. Research Sponsor: CytomX Therapeutics, Inc.

3109 Poster Session (Board #173), Fri, 8:00 AM-11:00 AM

MR1 in combination with tumor mutational burden and PD-1/PD-L1 expression as a potentially novel clinical predictor for T cell exhaustion and immune checkpoint inhibitor response. *First Author: Mark Farha, University of Michigan Medical School, Ann Arbor, MI*

Background: Immune checkpoint inhibitors (ICIs) restore T cell function by reversing T cell exhaustion. Variable response to ICIs warrants the development of precise predictive biomarkers, which is challenging due to difficulty in capturing the interplay of factors involved with tumor cell immune recognition. High intratumoral expression of MR1, the MHC-I related protein basally expressed on cancer cells, may drive T cell exhaustion through presentation of cancer-specific antigens. Here, we construct a database to study the relationship between MR1, tumor mutational burden (TMB), the PD-1/PD-L1 axis and T cell exhaustion across 8,975 sequenced tumors and 27 cancer types. **Methods:** RNA Seq by expectation maximization (RSEM) values from the TCGA were collected and normalized along with expression data for markers of interest (Table). TMB was defined as the number of non-synonymous somatic mutations per sample. For each cancer, 5 cohorts were created based on ascending mean expression levels of MR1, PD-1, PD-L1, and increasing TMB. For each cancer, an "immunogenicity score" for these factors was computed, and its relationship with T cell exhaustion signatures was assessed via linear regression. Data is presented as adjusted R^2 and p-value. **Results:** While PD-1 and T cell exhaustion marker expression were correlated across cancers, the "immunogenicity score" (IS) correlated with exhaustion markers specifically in cancers with FDA-approved ICIs. Excluding MR1 from the score weakened the correlation with EOMES and TBET expression (Table). Each component of the score analyzed independently failed to show a statistically significant correlation for both EOMES and TBET expression. **Conclusions:** In this cross-cancer analysis, we support the hypothesis that presentation of metabolic intermediates in cancer cells via MR1 may drive T cell exhaustion. Also, the novel "immunogenicity score", which incorporates MR1 into standard biomarkers for response to ICIs may convey the global picture of cancer cell recognition by the immune system and warrants further investigation as a tool for predicting clinical response. Research Sponsor: None.

		IS		IS minus MR1		MR1		TMB		PD-L1		PD-1	
	Exhaustion Marker	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p	R^2	p
FDA-Approved ICI	EOMES	**0.24**	**0.05**	0.17	0.08	0.04	0.24	0.08	0.86	0.09	0.16	**0.29**	**0.03**
	TBET	**0.56**	**0.001**	0.32	0.02	0.13	0.12	0.08	0.97	**0.29**	**0.03**	**0.55**	**0.002**
Non-FDA approved ICI	EOMES	0.02	0.27	0.09	0.14	0.08	0.98	0.03	0.47	0.06	0.20	**0.58**	**0.001**
	TBET	0.11	0.12	0.16	0.08	0.07	0.75	0.04	0.49	0.14	0.10	**0.76**	**1.33x10^-5**

3110 Poster Session (Board #174), Fri, 8:00 AM-11:00 AM

SBT6050, a HER2-directed TLR8 therapeutic, as a systemically administered, tumor-targeted human myeloid cell agonist. *First Author: Heather Metz, Silverback Therapeutics, Seattle, WA*

Background: Solid tumors are replete with myeloid cells which, when activated, drive potent anti-tumor responses. Clinical development of systemically administered myeloid cell agonists, however, has been hindered by acute toxicities due to peripheral activation of the targeted cell types. Intratumoral administration, the route of delivery typically used for innate immune/myeloid cell agonists, is limited by tumor accessibility and a dependence on abscopal responses. A systemically delivered myeloid cell agonist with tumor-localized activity has the potential to overcome challenges encountered with other innate immune/myeloid cell agonists in clinical development. **Methods:** SBT6050 is a novel therapeutic comprised of a potent toll-like receptor (TLR) 8 agonist payload conjugated to a HER2-directed monoclonal antibody. Delivery of the payload into the endosome of human myeloid cells, where TLR8 resides, requires the co-engagement of HER2 on tumor cells and Fc gamma receptor on human myeloid cells. Thus, SBT6050 is designed for systemic delivery and tumor-targeted activation of human myeloid cells. **Results:** Studies with human immune cells show that SBT6050 potently induces, in a HER2-dependent manner, multiple anti-tumor immune activities due to its direct activation of myeloid cells and the subsequent induction of T and NK cell cytolytic activity. SBT6050 is designed to activate human myeloid cells only in the presence of HER2-positive tumor cells with moderate (2+ by IHC) or high (3+ by IHC) expression levels. Tumor-localized activity has been demonstrated in mouse models using a SBT6050 mouse surrogate. Systemic delivery results in robust single agent efficacy in multiple mouse tumor models, even those engineered to lack T cells, without accompanying peripheral cytokine production. Trastuzumab and SBT6050 bind to distinct epitopes on HER2 and enhanced activity is observed when the two agents are combined. **Conclusions:** SBT6050 is a systemically administered, tumor-targeted myeloid cell agonist that demonstrates single agent efficacy in multiple mouse tumor models without peripheral cytokine production. A first-in-human study with SBT6050 is expected to begin this year for patients with HER2-expressing solid tumors. Research Sponsor: Silverback Therapeutics.

3111 Poster Session (Board #175), Fri, 8:00 AM-11:00 AM

A pilot study of Bruton's tyrosine kinase inhibitor ibrutinib alone and in combination with PD-1 inhibitor nivolumab in patients with metastatic solid tumors. *First Author: Brooke Benner, Ohio State University Comprehensive Cancer Center, Columbus, OH*

Background: Myeloid-derived suppressor cells (MDSC) are expanded in cancer and promote immune suppression. We have shown that ibrutinib inhibits migration and immunosuppressive function of MDSC. Moreover, the combination of ibrutinib and a PD-L1 inhibitor has been found to have synergistic anti-tumor effects in a multiple solid tumor mouse models. Therefore, we conducted a pilot study testing the combination of ibrutinib and nivolumab in patients with metastatic solid tumors. **Methods:** Sixteen patients with advanced solid tumors were recruited to this trial. Ibrutinib was dosed as an oral single agent, starting 7 days prior to cycle 1 of nivolumab and given until cycle 1, day 8 of nivolumab. Nivolumab was administered intravenously on days 1 and 15 on 28-day cycles. Patients had blood samples collected prior to initiation of ibrutinib, day 1 of cycle 1, day 8 of cycle 1, day 1 of cycle 2, and at the time of disease progression. From these specimens, we measured circulating MDSC levels, other circulating immune subsets, T cell proliferation, and cytokines/chemokines levels. Circulating MDSC levels were measured by mass spectrometry. T cell function was evaluated by CFSE to monitor proliferating cells by dye dilution and cytokine/chemokine levels were measured with a U-PLEX assay. Data were analyzed using two-tailed, paired Student's *t*-tests to assess statistical significance. **Results:** An increase in circulating MDSC (22% to 28%; SD 9.158) levels was observed following 7 days of single-agent ibrutinib compared to baseline. However, in combination therapy, MDSC levels decreased (19%; SD 13.17) prior to cycle 2. Despite increasing levels of circulating MDSC, T cell function improved throughout the study. Furthermore, plasma levels of chemokines associated with MDSC recruitment and migration significantly decreased with ibrutinib treatment (IL-12, CCL2, CCL3, and CCL4). Of the 16 patients, four achieved a partial response and four achieved stable disease. Median progression free survival was 3.5 months and median overall survival was 11.5 months. **Conclusions:** The combination of ibrutinib and nivolumab was well tolerated, demonstrated early signs of immune modulation, and showed preliminary signs of promising clinical activity in patients with metastatic solid tumors. Clinical trial information: NCT03525925. Research Sponsor: Pelotonia IRP.

3112 Poster Session (Board #176), Fri, 8:00 AM-11:00 AM

A phase II, open-label study of tomivosertib (eFT508) added on to continued checkpoint inhibitor therapy in patients (pts) with insufficient response to single-agent treatment. *First Author: Anthony B. El-Khoueiry, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA*

Background: Despite the broad activity of checkpoint inhibitors across tumor types, primary or secondary resistance after initial response represents a major challenge. Tomivosertib (T), a potent and highly selective inhibitor of the immunosuppressive kinases MNK-1 and 2, blocks expression of checkpoint proteins PD-1, PD-L1, and LAG-3 as well as immunosuppressive cytokines IL-6 and IL-8. In preclinical models, T was shown to trigger an anti-tumor immune response and enhance the activity of checkpoint inhibitors in a T-cell dependent manner. In prior clinical studies, T had an acceptable safety profile as a single agent and in combination with anti-PD-L1 agent avelumab. **Methods:** Patients experiencing insufficient response (progression or stable disease for 12 weeks or more) to any FDA-approved checkpoint inhibitor in any approved indication were eligible. T at 200 mg oral (PO) BID was added to the existing checkpoint inhibitor until disease progression or unacceptable toxicity was noted. **Results:** 39 pts (23 male, 16 female) were enrolled across seven cancer types. Median age was 68 (range 42-85). Median prior therapies were 2 (range 1-6). The most common cancers were lung (N = 17), urothelial (N = 6), renal (N = 5) and head and neck (N = 5). 36 pts continued on anti PD-1 antibody (Pembrolizumab and Nivolumab, 18 each) and 3 on anti PD-L-1 antibody (Durvalumab 2, Atezolizumab 1) . The most common grade 3/4 treatment related adverse events occurring in more than 1 pt were alanine aminotransferase increase (2), blood creatine phosphokinase increase (2) and maculo-papular rash (2). 7 patients discontinued treatment (18%) due to adverse events attributable to either drug. Three partial responses (PR) per RECIST 1.1 were observed in pts with previous progression on checkpoint inhibitor therapy, one each in NSCLC (1/17), gastric (1/1) and renal cancer (1/5). 7 NSCLC pts (41%) were progression free for $\geq$ 24 weeks. All NSCLC patients entered the study with progression by RECIST 1.1 on single agent checkpoint inhibitor prior to adding T. **Conclusions:** The addition of T to existing checkpoint therapy was well tolerated and manifested clinical activity including objective responses in pts with progression on existing checkpoint inhibitor. A Progression Free Survival rate at 24 weeks of 41% was noted in NSCLC patients. Additional studies evaluating the addition of T to checkpoint inhibitor therapy after progression on anti PD-1 or PD-L-1 therapy are planned. Clinical trial information: NCT03616834. Research Sponsor: eFFECTOR Therapeutics.

3113 Poster Session (Board #177), Fri, 8:00 AM-11:00 AM

Characterization of NRG1 gene fusion events in solid tumors. *First Author: Sushma Jonna, Georgetown Lombardi Comprehensive Cancer Center, Washington, DC*

Background: *NRG1* fusions are actionable genomic alterations detected across tumor types. The *NRG1* gene encode for neuregulin, which serves as a ligand for ERBB3 and ERBB4 receptors and activates downstream signaling through the MAPK and PI3K pathways. Here, we update the detection of *NRG1* gene fusions across tumor types and further describe fusion characteristics. **Methods:** Samples submitted for clinical molecular profiling that included RNA-sequencing (Archer Dx or Caris MI transcriptome) were retrospectively analyzed for *NRG1* fusion events. All *NRG1* fusions with $\geq$ 3 junction reads were identified for manual review and for characterization of fusion class, intact functional domains, domain prediction, breakpoints, frame retention and co-occurring alterations by NGS. **Results:** A total of 82 *NRG1* fusion events (0.2% of 44,570) were identified. Among the fusions identified, the distribution across tumor types was as follows: non-small cell lung cancer (NSCLC, 54%), breast cancer (11%), ovarian cancer (7%), pancreatic cancer (7%), cholangiocarcinoma (6%), colorectal cancer (5%), and other (10%). Forty-two unique fusion partners were identified, the most common being *CD74* (23%), *ATP1B1* (9%), *SLC3A2* (7%), *RBPMS* (6%) and *SDC4* (4%). Almost half (47%) of all fusion events are expected to include the transmembrane domain contributed by the *NRG1* fusion partner. Lung and pancreatobilliary cancers had the highest rates of transmembrane domain retention from their fusion partners (63.6% and 54.5%, respectively). In all other tumor groups, most fusion partners lacked transmembrane domains. In 15% of cases, the chimeric transcripts are predicted to lead to increased expression of NRG1. The most commonly reported breakpoints in *NRG1* occur in exon 6 and exon 2. While fusions with the *NRG1* breakpoint at exon 2 retain the immunoglobulin (Ig) domain and all downstream portions (including EGF-like domain), those at exon 6 do not contain the Ig portion and result in shorter chimeric proteins. The breakpoints in all *CD74:NRG1* fusions, the most common fusions in NSCLC, occur at exon 5 or 6 and cause truncation of domains upstream of the EGF-like domain. In *ATP1B1:NRG1* fusions, the most common fusions in pancreatobilliary cancers, the breakpoints are at exon 1 or 2 and retain the Ig domain. **Conclusions:** *NRG1* fusion products are diverse across tumor types, but the significance of these variations is not clear. The biological and clinical implications of retaining certain domains of *NRG1* (such as the Ig domain) and of fusion partners warrants further investigation. Research Sponsor: None.

3114 Poster Session (Board #178), Fri, 8:00 AM-11:00 AM

An in vivo model to evaluate donor-dependent cytokine release in response to single-agent or combination immune-oncology therapies. *First Author: Kyle Draheim, The Jackson Laboratory, Sacramento, CA*

Background: Although immune-oncology therapies such as checkpoint inhibitor, bi-specific antibody and CAR-T cell therapies are successfully used for cancer therapy, they can have very severe adverse effects such as cytokine release syndrome (CRS). The animal models and in vitro human PBMC assays presently in use do not reliably predict CRS in patients. Currently, the only widely accepted predictors of CRS are cancer burden and therapeutic dose. Despite this, most pre-clinical assays that evaluate CRS do not incorporate cancer cells and the safety of drug combinations has not been widely explored. A predictive assay that identifies patient/cancer/therapy combinations at risk for developing CRS upfront in addition to treatment efficacy would improve the safety of immune-oncology drug development. **Methods:** We have developed sensitive in vivo humanized mouse models for quantitating CRS that are rapid, reproducible and able to show variation among PBMC donors. The NSG mouse and its derivatives are engrafted with cancer cells and human PBMCs. Mice are then dosed with checkpoint inhibitors or bi-specific antibodies as a single therapy or in combination. Cytokine release is evaluated 2-6 hours post dosing. This assay can be modified to also evaluate efficacy by using luciferase labeled cancer cells and monitoring tumor burden using the Xenogen IVIS imaging system. **Results:** For all therapy groups, each cytokine tested (including human IFN-γ, IL-2, IL-6, IL-10 and TNF) was upregulated 2-6 hours after drug treatment, but different PBMC donors had various cytokines release levels. Cytokine release levels correlated with a dose response, PBMC engraftment levels and tumor burden. We can demonstrate additive and synergistic cytokine release in the combination treated groups and compare efficacy versus single agents. Our in vivo method was able to determine CRS missed in the in vitro testing method. **Conclusions:** We have developed a rapid, sensitive and reproducible novel in vivo PBMC humanized mouse model that can differentiate human PBMC donors based on individual safety response to single agent and combination therapeutics of immune checkpoint inhibitors and bispecific T-cell-engaging antibodies. Additionally, this assay can utilize luciferase labelled cell lines to measure treatment efficacy. Using this assay, we can potentially evaluate both cytokine release and efficacy of current immune-oncology therapies as single agents and in combination. This assay has immediate utility in current and future drug development. Research Sponsor: None.

3115 Poster Session (Board #179), Fri, 8:00 AM-11:00 AM

Association between immune and tumor gene signatures with response or resistance to tislelizumab monotherapy or in combination with chemotherapy in gastroesophageal adenocarcinoma. *First Author: Jianming Xu, Department of Gastrointestinal Oncology, The Fifth Medical Center, General Hospital of People's Liberation Army, Beijing, China*

Background: Tislelizumab, an anti-PD-1 monoclonal antibody, has demonstrated clinical benefit as a single agent and in combination with chemotherapy for patients (pts) with gastroesophageal adenocarcinoma (GEA), including gastric, gastroesophageal junction (G/GEJ), and esophageal adenocarcinoma (EAC). Immune- and tumor-transcriptomic features of response and resistance to tislelizumab were assessed from data collected in two monotherapy studies (NCT02407990, CTR20160872) and one tislelizumab plus chemotherapy study (NCT03469557). **Methods:** Gene expression profiling (GEP), using the 1392-gene HTG EdgeSeq panel, was performed on baseline tumor samples from 103 pts with GEA receiving monotherapy and 13 receiving combination therapy. Signature scores were calculated using the Gene Set Variation Analysis package with publicly available gene signatures (GS). Differential gene signature (DEG) analysis was performed between responders and nonresponders (NRs) using Wilcoxon rank-sum test; GS associated with survival were evaluated using Cox proportional hazards model. **Results:** Of the 76 pts with available GEP data, 64 (n=51 G/GEJ; n=13 EAC) had evaluable responses. Across these pts with GEA, tislelizumab demonstrated antitumor activity (Table). In pts treated with monotherapy, DEG showed IFNγ GS (*IFNG*, *CXCL9*, *CXCL10*, *HLA-DRA*, *IDO1*, *STAT1*) scores were positively correlated with response (P=0.03) as well as progression-free (HR=0.5, 95% CI: 0.27–0.93) and overall survival (HR=0.44, 95% CI: 0.21–0.89). Monotherapy NRs could be clustered into distinct GEP subgroups. Compared with responders, two NR subgroups had lower IFNγ GS (P=0.002, 0.047) along with either higher epithelial-mesenchymal transition (EMT; P=0.027), and angiogenesis (P=0.002) or cell cycle (CC; P=0.097) GS expression. A third NR subgroup showed higher CC GS scores compared with responders (P=0.015), despite high IFNγ GS levels. Unlike tislelizumab monotherapy, responders to combination therapy showed higher CC GS expression versus NRs (P=0.089). **Conclusions:** While higher IFNγ GS was associated with clinical benefit with monotherapy, elevated EMT/angiogenesis and CC GS levels may indicate resistance. The effects of these signatures in pts treated with combination therapy may vary. Both immune- and tumor-intrinsic factors may be considered for validation in a phase 3 study (NCT03777657). Research Sponsor: BeiGene, Ltd.

	Monotherapy (n=53)	Combination (n=11)
Median follow-up, mo	14.3	16.3
ORR, %	13.2	54.5

3116 Poster Session (Board #180), Fri, 8:00 AM-11:00 AM

Investigating the tumor immune infiltrate for populations that predict immune-related adverse events (irAEs) in patients receiving PD-1 inhibitors. *First Author: Steven Michael Blum, Massachusetts General Hospital and Dana-Farber Cancer Institute, Boston, MA*

Background: The mechanistic relationship between clinical benefit and immune-related adverse events (irAEs) in response to immune checkpoint inhibitors (ICIs) remains unclear, with several clinical studies reporting that irAEs are biomarkers of responses. Single-cell RNA sequencing (scRNAseq) analysis of tumors from patients with advanced melanoma before and after treatment with ICIs have identified immune cells that correlate with response to ICIs. We sought to evaluate if these populations were also associated with irAEs. **Methods:** A published scRNAseq data set generated with the Smart-Seq2 protocol (Sade-Feldman M, et al. Cell 2018.) was re-analyzed, stratified by two definitions of irAEs: (1) toxicity requiring systemic immunosuppression (prednisone $>$ 10mg/day) or (2) systemic immunosuppression and/or endocrinopathy. Unbiased single-cell analysis was performed, followed by sub-clustering of T cell populations. The percentage of cells in each cluster was determined on a per sample basis. **Results:** 13,184 immune cells from 39 samples collected from 25 patients were re-analyzed. 27 samples were from patients who did not respond to ICIs, while 12 samples came from responding patients. 21 samples came from patients who required immunosuppression, 5 samples from patients with isolated thyroiditis, and 13 samples from patients who met neither irAE criteria. Unsupervised scRNAseq analyses focused on ICI efficacy re-capitulated published associations between response and populations that included B-cells ($p < 0.01$) and TCF7 expressing T-cells ($p < 0.01$). While these cell populations were not associated with either definition of toxicity, we observed a non-Treg CD4 expressing T cell population (0.8-10.5% cells/sample) that positively correlated with either definition of toxicity ($p < 0.05$) but not efficacy. **Conclusions:** In a patient cohort with advanced melanoma, tumor-infiltrating immune cell populations associated with response to ICI therapy were not associated with irAEs. This suggests that biomarkers of ICI response may not function as biomarkers of irAEs, and ongoing analysis will seek to validate this result. Understanding the differences between ICI response and irAEs may identify new therapeutic targets for maximizing efficacy while mitigating toxicity. Research Sponsor: U.S. National Institutes of Health.

3117 Poster Session (Board #181), Fri, 8:00 AM-11:00 AM

Validation of an immunomodulatory gene signature algorithm to predict response to neoadjuvant immunochemotherapy in patients with primary triple-negative breast cancer. *First Author: Toshiaki Iwase, Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: A 101-gene algorithm established as a molecular subtyping method for triple-negative breast cancer (TNBC) includes assignment of an immunomodulatory (IM) subtype based on genes active in immune cell processes. Recently, we isolated the IM concept to an independent 27-gene algorithm and its predictive ability for immunotherapy response was demonstrated in lung cancer. The objective of this study was to validate the predictive accuracy of the IM subtype as determined by the 27-gene algorithm for pathological complete response (pCR) compared with PD-L1 immunohistochemistry (IHC) staining in TNBC. **Methods:** We obtained RNA sequencing data from pretreatment core needle biopsies in 55 patients with stage I-III primary TNBC who received neoadjuvant immunotherapy (durvalumab with weekly nab-paclitaxel followed by ddAC) in phase I/II trial (NCT02489448). The 27-gene algorithm was used to determine IM positivity using a cutoff point previously validated from 71 lung cancer biopsy patients treated with immunotherapy. Results from the algorithm and PD-L1 IHC (antibody, SP263) were compared with pCR. Predictive accuracy of both methods was determined by diagnostic indicators. In cases positive for the IM subtype and pCR, we analyzed the immune microenvironment by deconvoluting the immune infiltration using a computational algorithm. **Results:** Of the 55 patients, 25 (45%) had pCR. Compared with previous subtyping methods, the 27-gene algorithm showed stronger predictive value (odds ratio, 4.125; 95% CI, 1.36-13.47; $P < 0.015$). For PD-L1 IHC, the odds ratio was 2.63 (95% CI, 0.82-9.21; $P = 0.11$). The positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio for PD-L1 IHC were 0.55, 0.68, 1.43, and 0.54, respectively. For the 27-gene algorithm, these metrics were 0.65, 0.69, 2.09, and 0.51, indicating its superior accuracy for predicting pCR. The computational algorithm showed that the IM subtype and pCR were negatively associated with a macrophage-enriched microenvironment. CD4+ T cells and dendritic cells were significantly increased among the baseline immune cell population in IM-positive patients. **Conclusions:** We conclude that 27-gene algorithm is a clinically applicable and a possible predictive marker for response to neoadjuvant immunochemotherapy for patients with primary TNBC. Our immune microenvironment results suggest that antigen-presenting immune cells have a crucial role in immunochemotherapy response. Research Sponsor: Astra Zeneca.

3118 Poster Session (Board #182), Fri, 8:00 AM-11:00 AM

Significance of meflin-positive cancer-associated fibroblasts in predicting response to immune checkpoint inhibitors in non-small cell lung cancer. *First Author: Yuki Miyai, Department of Clinical Oncology and Chemotherapy, Nagoya University Hospital, Nagoya, Japan*

Background: Tumor immunity is regulated by complex interactions between cancer and immune cells, which also involves other components of the tumor microenvironment (TME). Recently, cancer-associated fibroblasts (CAFs), a major constituent of the TME, have emerged as important regulators of tumor immunity. Specifically, for example, α-smooth muscle actin or leucine-rich repeat containing 15-positive CAFs have been shown to be crucial for the suppression of tumor immunity. However, a comprehensive picture of how other CAF subset(s) are involved in tumor immunity is still lacking. Here, we show the involvement of a CAF subset highly expressing Meflin, which was recently identified as a marker of cancer-restraining CAFs in pancreatic cancer (Mizutani et al., Cancer Res, 2019), in the response of non-small cell lung cancer (NSCLC) patients to immune checkpoint inhibitors (ICIs). **Methods:** A sample cohort of 122 subjects with NSCLC who had received ICI monotherapy with nivolumab, pembrolizumab, or atezolizumab was identified at the Department of Respiratory Medicine at Nagoya University Hospital. We selected 92 eligible patients, collected formalin-fixed paraffin-embedded tumor tissues, and prepared 4–μm-thick slides for the analysis of Meflin expression by RNA-in situ hybridization assay, followed by the evaluation of treatment response of 88 patients using the iRECIST criteria. We assessed the number of Meflin-positive CAFs and divided the patients into Meflin-High (20% and more CAFs express Meflin) and -Low groups. The cut-off value was obtained by the ROC analysis. Primarily, objective response rate (ORR) was compared between Meflin-High and –Low groups. Overall survival (OS), and progression free survival (PFS) were also assessed. **Results:** Patients who started to receive ICIs till the end of March 2019 were enrolled and followed-up until the end of 2019. Analysis of the tumor tissues revealed that 24 (40.7%) of 59 Meflin-High patients responded to the ICI monotherapy. In contrast, none (0%) of 29 Meflin-Low patients showed any significant response (p-value: 0.0000174). Meflin-High groups showed statistically significant prolongations in both OS and PFS with the hazard ratios of 0.3114 [0.1591-0.6094] and 0.3997 [0.2290-0.6976], respectively. **Conclusions:** This retrospective observation indicated that the high infiltration of Meflin-positive CAFs may shape tumor-suppressive immune response and increase the sensitivity to ICIs, which differs from those of other CAF subsets. Research Sponsor: the Ministry of Education, Culture, Sports, Science and Technology, Japan.

3119 Poster Session (Board #183), Fri, 8:00 AM-11:00 AM

Deep learning-based immune phenotype analysis reveals distinct resistance pattern of immune checkpoint inhibitor in non-small cell lung cancer. *First Author: Chan-Young Ock, Lunit Inc., Seoul, South Korea*

Background: Resistance pattern and biological mechanism of immune checkpoint inhibitor (ICI) has been poorly understood. Sine suggested resistance mechanisms would be either innate resistance caused by lack of immune recruitment or acquired immune evasion after durable response of ICI treatment, we hypothesized that resistance pattern of tumor microenvironment would be distinct according to duration of ICI response in non-small cell lung carcinoma (NSCLC). In the current study, we applied deep-learning-based classification of three immune phenotypes (3IP): *inflamed*, *excluded*, and *desert*, to objectively assess the immunologic status of tumor microenvironment. **Methods:** Deep-learning algorithm of H&E Whole-Slide Images (WSI), called Lunit-SCOPE, was trained with 1,824 H&E WSI of NSCLC from Samsung Medical Center (SMC). WSI was divided into patches and each patch (~10 high-power fields) was classified as *inflamed*, *excluded* and *desert*, based on both quantity and localization of immune cells. Among NSCLC patients treated with ICI in SMC, 87 paired treatment-naïve (Pre, patch N = 15,415) and post-progression (Post, patch N = 18,197) tumor tissues were analyzed for Lunit-SCOPE. **Results:** In 87-paired samples, proportions of excluded and desert phenotypes were increased in post-progression tumor tissues (excluded; Pre 26.8% versus Post 32.5%, desert; Pre 19.5% versus Post 25.3%). Focused on 29 patients classified as inflamed in treatment-naïve, proportion of immune phenotypes of post-progression were clearly different according to duration of response, divided by median progression-free survival (PFS) of 3.7 m. Patients with rapid progression without ICI response (PFS $<$ 3.7 m) turned into desert type (46.2%), whereas durable responder (PFS $\geq$ 3.7 m) either still remained on inflamed phenotype (42.9%) or turned into excluded phenotype (21.4%). Patients who remained on inflamed phenotype had favorable overall survival after progression on ICI, compared to turned into desert type (median survival not reached versus 6.6 m, P= 0.0296). **Conclusions:** Resistance patterns of ICI are distinct according to duration of response in patients with inflamed phenotype. Rapid progressor turns off immune into desert phenotype whereas most durable responder keeps immune recruitment into tumor microenvironment, which needs tailored strategy to overcome ICI resistance. Research Sponsor: Lunit Inc.

3120 Poster Session (Board #184), Fri, 8:00 AM-11:00 AM

Deep-learning analysis of H&E images to define three immune phenotypes to reveal loss-of-target in excluded immune cells as a novel resistance mechanism of immune checkpoint inhibitor in non-small cell lung cancer. *First Author: Sehhoon Park, Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

Background: Discovery of predictive biomarker to enrich the responder of immune checkpoint inhibitor (ICI) in PD-L1-low ($<$ 50%) non-small cell lung cancer (NSCLC) is still challenging. Recent study showed that loss of heterozygosity (LOH) of *HLA* led to immune evasion. In the current study, we hypothesized that 3 immune phenotype (3IP): *inflamed*, *excluded* and *desert* would be reliably classified by deep-learning algorithm of H&E image, called Lunit-SCOPE, which would dictate the responder in PD-L1-low NSCLC patients and discover a unique resistance pathway in *excluded* phenotype. **Methods:** Lunit-SCOPE was trained with 1,824 H&E Whole-Slide Image (WSI) of NSCLC from Samsung Medical Center (SMC). WSI was divided into patches (~10 high-power fields) which was classified for 3IP, based on both quantity and localization of immune cells. The 3IP was trained and optimized by considering clinical outcome of 119 NSCLC patients with PD-(L)1 inhibitor (training cohort, patches = 25,897), and validated in 62 patients enrolled in LC-biomarker study (NCT03578185, validation cohort, patches = 8,929). Tumor Proportion Score (TPS) of PD-L1 22C3 immunohistochemistry was assessed by pathologists. Tumor Mutational Burden (TMB) was calculated as number of nonsynonymous alterations throughout whole-exome and *HLA* LOH was called by LOHHLA algorithm. **Results:** Interactive analysis to classify 3IP in training cohort showed that 8,726 (33.7%), 10,965 (42.3%), and 6,206 (24.0%) patches were classified as *inflamed*, *excluded*, and *desert*, respectively. In validation cohort, median progression-free survival (mPFS) of *inflamed* phenotype was 10.1 m, significantly prolonged compared to either *excluded* phenotype (3.0 m, P= 0.0053) or *desert* phenotype (1.4 m, P= 0.0011). *Inflamed* phenotype independently dictated favorable ICI outcome in PD-L1-low (TPS $<$ 50%, mPFS of *inflamed*: 14.3 m vs *excluded/desert*: 1.4 m, P= 0.0233) as well as in PD-L1-high (TPS$\geq$50%, 10.1 m vs 4.2 m, P= 0.0361), respectively. *Excluded* phenotype had higher TMB compared to *inflamed* phenotype had (median 177 vs 107), and *HLA* LOH was also enriched in *excluded* phenotype (31.0%) compared to *inflamed* (17.6%) and *desert* (16.7%) phenotypes. **Conclusions:** Lunit-SCOPE based 3IP classification can predict ICI outcome especially in PD-L1-low ($<$ 50%) patients. *Excluded* phenotype showed poor ICI outcome even with high TMB, partially explained by *HLA* LOH resulting in loss-of-target, as a novel resistance mechanism of ICI. Research Sponsor: Lunit Inc.

3121 Poster Session (Board #185), Fri, 8:00 AM-11:00 AM

Gene signature of antigen processing and presentation machinery (APM) as highly predictive of response to checkpoint blockade in lung cancer and melanoma. *First Author: Jeffrey C. Thompson, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA*

Background: Treatment of non-small cell lung cancer (NSCLC) with immune checkpoint blockade (ICB) has resulted in striking clinical responses, but only in a subset of patients (pts), underscoring the need to identify genomic and molecular determinants of immune evasion. Limited data exist on the potential role of alterations in HLA Class I antigen processing and presentation machinery (APM) in mediating response to ICB. **Methods:** We conducted a retrospective cohort study analyzing transcriptional profiles from pre-treatment tumor samples of chemotherapy-refractory advanced NSCLC pts treated with ICB. RNA was analyzed using the AmpliSeq transcriptomic platform. An APM signature was generated utilizing 8 genes associated with antigen processing (*B2M, CALR, NLRC5, PSMB9, PSME1, PSME3, RFX5, HSP90AB1*) and was examined for its association with response to therapy and progression-free and overall survival (PFS, OS). The APM signature was then evaluated in two independent melanoma cohorts treated with ICB. **Results:** We analyzed pre-treatment tumor samples from 51 advanced NSCLC pts treated with ICB, median age 64 (range 31-92), smokers (n = 43), adenocarcinoma (n = 31). There were 23 responders and 28 non-responders. The APM signature was significantly higher in responders compared to non-responders (average z-score 2.69 vs. -2.49, p = 0.0001). An APM score above the median value for the entire cohort was significantly associated with improved PFS (HR 0.24, 95% CI, 0.12-0.47, log-rank = 0.001) and OS (HR 0.34, 95% CI, 0.18-0.67, log-rank = 0.005). The APM score was significantly correlated with the well-validated T-cell-inflamed resistance gene expression profile (GEP) score (R^2 = 0.32, p $<$ 0.0001). However, the APM score demonstrated improved ability to predict response to ICB relative to the GEP score with AUCs of 0.83 and 0.69, respectively. In an independent cohort of 14 high-risk resectable stage III/IV melanoma pts treated with neoadjuvant anti-PD1 therapy, upregulation of genes involved in antigen processing was associated with improved disease free survival (HR: 0.08, 95% CI, 0.01-0.50, p = 0.0065). In an additional independent melanoma cohort of 28 metastatic pts treated with ICB, a higher APM score was associated with improved overall survival (HR 0.31, 95% CI, 0.09-0.89, log-rank = 0.044). **Conclusions:** Our data demonstrate that defects in antigen presentation may be an important feature in predicting outcomes to ICB in both lung cancer and melanoma. Research Sponsor: U.S. National Institutes of Health.

3122 Poster Session (Board #186), Fri, 8:00 AM-11:00 AM

A machine learning-based approach for the inference of immunotherapy biomarker status in lung adenocarcinoma from hematoxylin and eosin (H&E) histopathology images. *First Author: Cory Batenchuk, Verily Life Sciences, South San Francisco, CA*

Background: The current standard work-up for both diagnosis and predictive biomarker testing in metastatic non-small cell lung cancer (NSCLC), can exhaust an entire tumor specimen. Notably, gene mutation panels or tumor mutation burden (TMB) testing currently requires 10 tissue slides and ranges from 10 days to 3 weeks from sample acquisition to test result. As more companion diagnostic (CDx)-restricted drugs are developed for NSCLC, rapid, tissue-sparing tests are sorely needed. We investigated whether TMB, T-effector (TEFF) gene signatures and PD-L1 status can be inferred from H&E images alone using a machine learning approach. **Methods:** Algorithm development included two steps: First, a neural network was trained to segment hand-annotated, pathologist-confirmed biological features from H&E images, such as tumor architecture and cell types. Second, these feature maps were fed into a classification model to predict the biomarker status. Ground truth biomarker status of the H&E-associated tumor samples came from whole exome sequencing (WES) for TMB, RNAseq for the TEFF gene signatures or reverse-phase protein array for PD-L1. Digital H&E images of NSCLC adenocarcinoma for model development were obtained from the cancer genome atlas (TCGA) and commercial sources. **Results:** This approach achieves $>$ 75% accuracy in predicting TMB, TEFF and PD-L1 status, offers a way to interpret the model, and provides biological insights into the tumor-host microenvironment. **Conclusions:** These findings suggest that biomarker inference from H&E images is feasible, and may be sufficiently accurate to supplement or replace current tissue-based tests in a clinical setting. Our approach utilizes biological features for inference, and is thus robust, interpretable, and readily verifiable by pathologists. Finally, biomarker status inference from a single H&E image may enable testing in patients whose tumor tissue has been exhausted, spare further tissue use, and return test results within hours to enable rapid treatment decision-making to maximize patient benefit. Research Sponsor: Verily Life Sciences.

3123 Poster Session (Board #187), Fri, 8:00 AM-11:00 AM

Extrachromosomal DNA (ecDNA) carrying amplified oncogenes as a biomarker for insensitivity to pembrolizumab treatment in gastric cancer patients. *First Author: Jason H. Christiansen, Boundless Bio, Inc., La Jolla, CA*

Background: In the KEYNOTE-059 study, the anti-PD-1 checkpoint inhibitor pembrolizumab was shown to have a modest overall response of 11.6%. Common predictors of response including, high microsatellite instability (MSI-H), PD-L1 expression, tumor mutational burden (TMB) and tumor inflammation signature (TIS), were not individually sufficient for patient selection. Recent pancancer studies have highlighted a unique population of cancer patients whose tumors appear to be driven by oncogene amplifications on extrachromosomal DNA (ecDNA). These ecDNA-driven tumors are aggressive and characterized by high levels of genomic instability. We sought to understand if tumors that possess ecDNA may represent a subset of the patient group that is non-responsive to anti-PD-1 therapy. **Methods:** We determined the ecDNA status of gastric cancer patients (N = 108) using whole genome sequencing (WGS) from the TCGA Pan-cancer dataset These patients had been previously subtyped for EBV status, genomic stability (GS), microsatellite instability (MSI), and chromosomal instability (CIN). Patients that were ecDNA+ were re-classified into a set regardless of gastric subtype. Additionally, TMB, TIS, and PD-L1 expression levels were collected. **Results:** 32% of gastric cancer patients were positive for ecDNA signatures and mutually exclusive from the 23% of MSI-H patients. We found that ecDNA positive tumors had statistically significantly lower TIS than all other groups (p-value < 0.05) except CIN tumors (p-value = 0.09). The ecDNA positive tumors also had lower PD-L1 expression than all but GS tumors. Only MSI-H showed statistically significantly higher TMB scores compared to every other group (p-value < 0.001), no difference in TMB scores were observed between every other pair of groups. **Conclusions:** Patients whose tumors are ecDNA positive represent a unique population that display signatures for non-response to checkpoint inhibitor therapy, including MSS, low TIS, and PD-L1 expression. Thus, the determination of tumor ecDNA status may have utility as an additional patient selection strategy for checkpoint inhibitor therapy. As ecDNA are not limited to gastric cancers, this study highlights the importance of the development of a clinical diagnostic test for ecDNA status and the need for further research on ecDNA biology, its impact on immunotherapy response, and potential ecDNA-directed therapeutics Research Sponsor: Boundless Bio, Inc.

3124 Poster Session (Board #188), Fri, 8:00 AM-11:00 AM

The prevalence of HLA LOH across 10 cancer types in Chinese patients. *First Author: Jian'An Huang, The First Affiliated Hospital of Soochow University, Suzhou, China*

Background: Recognition of tumor neoantigen is the key to generating immune response. The expression and integrity of human leukocyte antigen (HLA) are the prerequisites for neoantigen presentation, and loss of heterozygosity in HLA (HLA LOH) may facilitate immune evasion. However, the incidence of HLA LOH in Chinese cancer patients is unknown. **Methods:** In this study, 45 samples sequenced with both 1021-gene panel and whole-exome sequencing(WES) were used to evaluate the consistency of HLA LOH in the two testing strategies. The prevalence of HLA LOH analysis was performed in 1546 advanced patients across 10 diverse cancer types and 114 early-stage lung cancer patients who had undergone tumor profiling using 1021-gene panel. Exon 2, exon 3 and bilateral introns of *HLA-A/B/C* genes were well covered in 1021-gene panel. HLA LOH were analysis using LOHHLA algorithm (McGranahan, et al. 2017). **Results:** In the HLA LOH analysis of 45 samples, the consistency of 1021-gene panel and WES was 95.6% (43/45). Among the 1660 samples, 1.3% (21) were detected as HLA homozygous at all of the three site. HLA LOH was found in 45.1% (697/1546) of all the advanced patients, range from 24.1% to 59.7%. In colorectal cancer, the HLA LOH ratio of MSS samples was significantly higher than that of MSI-H samples (46.2%, 61/132 vs 16.7%, 3/18 p =0.0214). For NSCLC, the proportion of HLALOH in early-stage (I-IIIa) lung adenocarcinoma and lung squamous cell carcinoma was 25.7% (18/70) and 65.9% (29/44), respectively, consistent with the report. However, advanced (IIIa-IV) lung adenocarcinoma and lung squamous cell carcinoma were 49.4%(168/340) and 58.7%(179/305), respectively. The reason for the difference between early-stage lung adenocarcinoma and advanced lung adenocarcinoma needs further study. In 43.8% of cases (326/744), LOH occurred simultaneously in HLA-A, B and C,suggesting that the Class I locus was often lost together. **Conclusions:** We can use multi-gene panel for HLA LOH analysis, provided that the relevant regions are well captured. The prevalenceof HLA LOHpresent differences among cancer types.Understanding these distributions may provide more information for immunotherapy research. Research Sponsor: None.

HLA statusacross 10 cancer types in advanced patients.

Cancer types	Percent with HLA LOH
Breast cancer	42.1% (53/126)
Cervical cancer	59.7% (43/72)
Colorectal cancer	43.8% (70/160)
Endometrial cancer	23.8% (10/42)
Gastric and esophageal cancers	39.6% (57/144)
Kidney cancer	32.1% (25/78)
Liver cancer	24.1% (19/79)
Non-small-cell lung cancers	53.7% (347/645)
Ovarian cancer	38.2% (52136)
Pancreatic cancer	32.8% (21/64)

3125 Poster Session (Board #189), Fri, 8:00 AM-11:00 AM

CIMAC-CIDC tissue imaging harmonization. *First Author: Guray Akturk, Icahn School of Medicine at Mount Sinai, New York City, NY*

Background: The Cancer Immune Monitoring and Analysis Centers Cancer Immunology Data Commons (CIMAC-CIDC) network is a NCI Cancer Moonshots initiative to provide state-of-the-art technology and expertise for immunotherapy clinical trials. Multiplex tissue immunostaining is an integral assay provided that examines density and spatial distribution of immune cells and markers in tissues, for their prognostic or predictive value. Two approaches were evaluated for sensitivity, specificity, and reproducibility and subsequently harmonized: chromogenic-based Multiplex Immunohistochemical Consecutive Staining on Single Slide (MICSSS) and Multiplex Immunofluorescence (mIF) based tyramide signal amplification system. **Methods:** Harmonization was performed across CIMACs (Mount Sinai, Dana Farber Cancer Institute, MD Anderson Cancer Center) in multiple steps to prove that comparable data can be generated independent of site and platform. Goals: 1) harmonize image analysis platforms alone using tissues pre-stained with single chromogenic IHC for CD3 (membrane), Ki67 (nuclear), and CD68 (cytoplasmic), 2) compare image acquisition platforms, 3) streamline Antibody (Ab) clones and assess PD-L1 detection in relation to CLIA- assays, 4) harmonize staining protocols, image acquisition, and analysis platforms on 2 test head and neck tumor samples using MICSSS and mIF, 5) validate harmonization results with a tissue microarray on 27 tissues representing multiple tumors. For last steps, each CIMAC used their platforms for PD-L1, PD-1, CD3, CD8, and pan-cytokeratin (PanCK) staining on one of three consecutive slides from serial sections and compared densities of each marker. **Results:** Variables as PD-1 Ab clone, positive control reference tissues, sigma value for nuclear segmentation, and use of machine-learning based cell classifier were found to be key to produce accurate, reliable, comparable data. After visual quality control assessment and comparisons of each Region Of Interest (ROI), an overall inter-site Spearman correlation coefficient of ≥ 0.85 was achieved per marker within each tissue and across tissue types (expect pan-Cytokeratin, ≥ 0.7), with average coefficient of variation ≤ 0.1. **Conclusions:** These results show for the first time that two platforms can deliver harmonized data, despite differences in protocols, platforms, reagents, and analysis tools. Data resulting from retrospective and prospective CIMAC-CIDC analyses may be used with confidence for statistical associations with clinical parameters and outcome. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

3127 Poster Session (Board #191), Fri, 8:00 AM-11:00 AM

VCAN accumulation and proteolysis as predictors of T lymphocyte-excluded and permissive tumor microenvironments. *First Author: Philip Emmerich, University of Wisconsin Carbone Cancer Center, Madison, WI*

Background: Immune checkpoint inhibitors (ICIs) represent a major advance for treating solid tumors. However, only a minority of patients (pts) benefit from these therapies and markers that predict response have been elusive. Versican (VCAN) is an immunosuppressive proteoglycan in the tumor microenvironment (TME), which releases an immunostimulatory N-terminal fragment versikine (Vkine) when cleaved by ADAMTS proteases. We have demonstrated in colorectal cancers (CRC) that a low VCAN/high Vkine (VCAN proteolytic predominant [VPP]) phenotype correlates with increased tumor-infiltrating $CD8^+$ T lymphocytes (TILs). Here we examine the accumulation of VCAN as a marker of immune exclusion and its proteolysis as a marker of an immune-permissive TME. **Methods:** Immunohistochemistry for VCAN, Vkine and CD8+ was performed on samples from 1662 pts across breast (BC), CRC, endometrial cancer, pancreatic adenocarcinoma (PDAC), esophageal cancers and neuroendocrine tumors (NETs), across stages of disease (I-IV) and with diverse prior treatments. Stromal intensities of VCAN and Vkine staining quantified in collaboration with blinded surgical pathologists using a 0-3+ scale. 0/1+ were considered "low" for both VCAN and Vkine, whereas 2/3+ were considered "high". The number of $CD8^+$ TILs were counted using 400x magnification, the equivalent of a high power field (hpf). **Results:** Across the entire cohort VCAN phenotypes were diverse (VCAN high/Vkine low, 21%; VCAN high/Vkine high, 23%; VCAN low/Vkine low, 29%; VCAN low/Vkine high (VPP), 27%). Consistent with VCAN accumulation as a marker of T cell exclusion, VCAN low cancers had increased TILs compared to VCAN high (4.8 vs 18.3 TILs/hpf, $p < 0.001$). Low VCAN was identified in 85% esophageal, 79% NET (including small cell lung cancer [SCLC]) 72% endometrial, 47% MSI-H CRCs, 28% triple-negative BC and only 22% MSS CRC, 18% PDAC, 17% ER+ BCs. The VPP subgroup had the highest TILs per hpf across tumors. VPP was identified in 47% of esophageal, 45% endometrial, 41% NETs (including SCLC), 24% MSI-H CRCs, and only 9% MSS CRC, 7% ER+ BCs, 3% triple-negative BCs, and 0% of PDAC (n = 131 PDAC pts). **Conclusions:** VCAN accumulation correlates with T lymphocyte exclusion, while VCAN proteolysis predicts an immune permissive phenotype. VCAN accumulation and proteolysis are now incorporated into ICI clinical trials as a potential marker of response. Future studies will clarify the role of these biomarkers in predicting benefits of immuno-oncology treatment strategies. Research Sponsor: Funk Out Cancer, Bowlin for Colons.

3128 Poster Session (Board #192), Fri, 8:00 AM-11:00 AM

The HLA Ligand Atlas: A novel immuno-oncology resource for T-cell antigen discovery. *First Author: Ana Marcu, University of Tübingen, Cluster of Excellence iFIT (EXC 2180) "Image-Guided and Functionally Instructed Tumor Therapies", Tübingen, Germany*

Background: The human leukocyte antigen (HLA) complex regulates the adaptive immune response by showcasing the intracellular and extracellular protein content to the immune system, which is the basis for T cell-dependent tumor rejection. Therefore, a comprehensive map of the entirety of both HLA class I- and class II-presented peptides from various benign tissues is a highly sought after resource, as it enables the definition of tumor-association on the immunologically pivotal level of the HLA ligandome. **Methods:** Human tissue samples were snap frozen *post mortem* during autopsy. The study was approved by the local IRB. HLA ligands were immunopurified and characterized using an Orbitrap Fusion Lumos mass spectrometer coupled to an Ultimate 3000 RSLC Nano UHPLC System. Data acquisition was performed as technical triplicates in data-dependent mode, and data were analyzed using the containerized, computational pipeline MHCquant. **Results:** In this work, we describe the HLA Ligand Atlas, a comprehensive collection of matched HLA class I and class II ligandomes from 29 non-malignant tissues and 13 human subjects (208 samples in total), covering 38 HLA class I, and 17 HLA*DRB alleles and comprising 48,381 HLA class I and 16,146 HLA class II peptides. Nearly 50% of HLA ligands have not been previously described. The HLA Ligand Atlas is publicly available as a raw data resource, but also in the form of a user-friendly web interface that allows users to quickly formulate complex queries against the data set. Both downloadable data and the query interface are available at www.hla-ligand-atlas.org. **Conclusions:** This data set provides a valuable tool for research in diverse fields such as systems biology, general immunology, autoimmune disease and organ transplantation. Most importantly, the HLA Ligand Atlas provides essential information for translational applications in immuno-oncology. The knowledge of HLA ligands from benign tissues strongly supports the informed design of proteogenomic HLA-dependent target discovery approaches. Research Sponsor: Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) under Germany's Excellence Strategy - EXC 2180 – 390900677; Deutsche Forschungsgemeinschaft (DFG) SFB 685 "Immunotherapy: Molecular Basis and Clinical Application"; funded by ERC Ad.

3130 Poster Session (Board #194), Fri, 8:00 AM-11:00 AM

Machine learning-based identification of predictive features of the tumor micro-environment and vasculature in NSCLC patients using the IMpower150 study. *First Author: Amaro Taylor-Weiner, PathAI, Boston, MA*

Background: IMpower150 is a phase 3 study measuring the effect of carboplatin and paclitaxel (CP) combined with atezolizumab (A) and/or bevacizumab (B) in patients with advanced nonsquamous NSCLC, testing the hypothesis that anti-PD-L1 therapy may be enhanced by the blockade of VEGF. Here, we apply a machine-learning based approach to quantify the tumor micro-environment (TME) and vasculature and identify associations with clinical outcome in IMpower150. **Methods:** Digitized H&E images were registered onto the PathAI research platform (n=1027). Over 200K annotations from 90 pathologists were used to train convolutional neural networks (CNNs) that classify human-interpretable features (HIFs) of cells and tissue structures from images. Blood vessel compression (BVC) indices were calculated using the long versus short axes for each predicted blood vessel. HIFs were clustered to reduce redundancy, and selected features were associated with progression free survival (PFS) within each arm (ABCP, ACP, and BCP) using Cox proportional hazard models. **Results:** We used the trained CNNs to generate 4,534 features summarizing each patient's histopathology and TME. After association with survival and correction for multiple comparisons we identified clusters that were significantly associated with survival in at least one arm. Among patients receiving treatments that target PD-L1 (ABCP and ACP), high lymphocyte to fibroblast ratio (LFR) was associated with improved PFS (HR=0.64 (0.51, 0.81), $p < 0.001$) and showed no significant association with PFS among patients treated with BCP alone (HR=1.13 (0.85, 1.51), p=0.4). Among BCP treated patients, a higher average BVC within the tumor tissue was associated with improved PFS (HR=0.67 (0.50,0.90), p=0.01) and worse PFS among patients treated with ACP (HR=1.50 (1.10,2.06), p=0.009). **Conclusions:** We developed a deep learning-based assay for quantifying pathology features of the TME and vasculature from H&E images. Application of this system to Impower150 identified an association between high LFR and improved PFS among patients receiving PD-L1 targeting therapy, and between low BVC and improved PFS among patients receiving BCP. These findings support the importance of the TME and vasculature in determining response to PD-L1 and VEGF-targeting therapies. Research Sponsor: Genentech.

3131 Poster Session (Board #195), Fri, 8:00 AM-11:00 AM

Effect of chemokine signaling signatures on resolving discrepancy between TMB and checkpoint expression. *First Author: Christopher Szeto, ImmunityBio, Inc, Santa Cruz, CA*

Background: Tumor mutation burden (TMB) and *PD1/L1* expression are independent biomarkers for immune checkpoint blockade therapy, as seen in the Checkmate227 trial. Here we explore whether chemokine activity, an intermediate step between neoantigen presentation and immune-infiltration, can resolve this lack of association between existing biomarkers. We further use this novel biomarker to corroborate recent findings from Crowther et al. for a role of MHC class 1-related gene (*MR1)* downregulation in immune evasion. **Methods:** 1,395 clinical samples from the NantHealth database with matched tumor:normal whole exomes and deep whole-transcriptomic sequencing (> 200M reads) were available for analysis. The most common indications in the cohort were Breast (18%), Colon (9.8%), Lung (7.8%), Soft-tissue/Sarcomas (7.7%), and Pancreatic (6.1%). TMB was calculated by counting non-synonymous exonic mutations as per Rizvi, 2015. Immune-infiltration and chemokine signaling were inferred from RNAseq expression of published immune-cell-specific genesets (Bindea, 2013) and chemokine ligands (Nagarsheth, 2017) respectively. Significant associations between TMB, chemokine activity, immune-infiltration, and checkpoint expression were analyzed by ranksums test and corrected for multiple-hypothesis testing using Benjamini-Hochberg adjustment. **Results:** As expected, TMB and *PD1/L1* mRNA expression were not correlated in this cohort (r = 0.08 and r = 0.07 respectively). 36.3% of patients classified as highly immune-infiltrated by unsupervised clustering of immune-cell scores, and this subgroup significantly overexpressed all 11 targetable checkpoint genes analyzed including *PD1*, *PDL1, CTLA4, IDO1,* and *VISTA* (adj. p 9.7e-68 to 4e-168). There was no association between immune-infiltrated samples and TMB (t = 0.9, p = 0.35). Twice as many patients classified as chemokine-active (70.0%) and there was significant agreement between immune-infiltrated and chemokine-active patients (OR = 34.8, p = 6.5e-81). Interestingly, there was a weak but significant association between high chemokine-activity and increased TMB (t = 3.3, p = 0.001). Within patients that were chemokine-active but lacked immune-infiltration, *MR1* expression was significantly depleted (t = -10.7, p = 1e-26). **Conclusions:** Chemokine signatures can help resolve discordance between TMB and checkpoint expression. Analysis of discordance between chemokine-active but immune-depleted tumors may aid in identifying targets for converting from cold to hot tumor microenvironments. Research Sponsor: ImmunityBio, Inc.

3134 Poster Session (Board #198), Fri, 8:00 AM-11:00 AM

Personalized neoantigen/cancer testis antigen nanovaccine (PVAC) in combination with PD-1 monoclonal antibody and/or antiangiogenic treatment in patients with metastatic solid tumors. *First Author: Jia Wei, The Comprehensive Cancer Center of Drum Tower Hospital, Medical School of Nanjing University & Clinical Cancer Institute of Nanjing University, Nanjing, China*

Background: T-cell targeting of mutation-derived epitopes (neoantigens) has been demonstrated to drive anti-tumor responses. Nanotechnology has been reported to enhance immune responses of vaccines. Moreover, immunizing patients against such neoantigens, in combination with checkpoint inhibitor (CPI) and/or antiangiogenic drugs may elicit greater anti-tumor responses. **Methods:** Patient-specific mutation-containing neoantigens were selected on the basis of tumour-specific mutations whole-exome sequencing (WES) and RNA sequencing. Cancer testis antigens were obtained according to immunohistochemical staining and HLA-binding affinity prediction. Personalized neoantigen/cancer testis antigen nanovaccine (PVAC) is an amphiphiles nanovaccine loaded with personalized vaccine encoding multiple neoantigens designed to induce neoantigen specific T cells responses. Patients will receive PVAC in combination with PD-1 monoclonal antibody and/or antiangiogenic drugs. Primary end points include safety and tolerability. **Results:** 13 microsatellite stability (MSS) patients, which had relapsed from standard treatments, are enrolled in this study. 5 patients (1 gastric cancer, 1 liver cancer, 1 cervical carcinoma, 1 soft tissue sarcoma, 1 renal carcinoma) received PVAC in combination with PD-1 mAb, and another 8 patients (3 gastric cancer, 2 colon cancer, 1 NSCLC, 1 renal carcinoma) received PVAC in combination with PD-1 mAb and antiangiogenic therapy. No DLTs were reported. Five patients developed grade 1 and one patients developed grade 2 subcutaneous indurations in the injection sites, which collected with nanovaccine. One patient had grade 2 rash caused by anti-angiogenic drug. No drug related SAEs have been observed. There are 1 CR, 6 PR, 4 SD and 2 PD. Neoantigen specific T cell responses have been detected by IFN-γ ELISpot from PBMCs. **Conclusions:** PVAC is safe and well tolerated. Clinical responses have been observed in combination with PD-1 mAb and antiangiogenic drugs and neoantigen-specific T cell response have been observed after vaccination. Clinical trial information: ChiCTR1900022986. Research Sponsor: the National Natural Science Foundation of China.

3135 Poster Session (Board #199), Fri, 8:00 AM-11:00 AM

ESR1 mutations provide novel targets for breast cancer immunotherapy. *First Author: Jonathan Goldberg, Dana–Farber Cancer Institute, Boston, MA*

Background: Estrogen receptor (ER)-positive breast cancer is not considered immunogenic. Standard treatment is endocrine therapy to include aromatase inhibitors (AI). However, constitutively activating mutations in estrogen receptor alpha (*ESR1*) emerge with treatment making tumors resistant to AI therapy. While these mutations represent a pathway of resistance, they also represent potential neoepitopes that can be targeted with immunotherapy. Here we characterize the role of *ESR1* mutations as novel targets for breast cancer immunotherapy. **Methods:** Immunogenic epitopes derived from mutated *ESR1* (i.e. D538G, Y537S and E380Q) were identified in silico using the Immune Epitope Database and by determining overlapping peptides. In vitro T2 binding assays were used to measure the affinities of these peptides to HLA class-I, specifically HLA-A*0201. Dissociation assays were employed to characterize the stability of the peptide-HLA complex. Peptide-HLA-A*0201 tetramer staining was used to determine the expansion potential of peptide-specific cytotoxic T lymphocytes (CTL) from peripheral blood of healthy females. Cytotoxicity assays were used to determine the ability of peptide-specific CTLs to lyse cells presenting mutated ESR1-derived peptides. **Results:** We identified 22 nonameric and decameric peptides derived from the most common ESR1 mutations; 10/22 demonstrated high affinity (i.e. IC50 $<$ 500nM) binding to HLA-A*0201. The 3 highest predicted peptides demonstrated low IC50 values (13 nM, 19.5 nM and 56.6 nM), indicating very tight binding to HLA-*0201. *In vitro* assays confirmed high affinity binding for 10 of the 22 *in silico*-predicted peptides with an average fold change of 1.52 compared to non-pulsed T2 cells, and a median dissociation half-life of 6.45 hours. Tetramer staining of peptide specific CTLs from normal donor peripheral blood mononuclear cells showed relatively high expansion frequencies, with the highest three frequencies noted for D538G (1.04%), Y537S (0.49%) and V392I (0.27%). Using 4-hour *in vitro* cytotoxicity assays, in comparison with non-pulsed T2 cells, there was significantly higher lysis of peptide pulsed T2 cells that were cocultured with matching peptide-specific CTL: D538G (67.1 % vs 36.9%, $P < 0.001$), Y537S (59.5% vs 37.5%, $P < 0.01$), and E380Q (36.3% vs 7.8%, $P < 0.001$). **Conclusions:** These data confirm the immunogenicity of epitopes derived from the most common ESR1 mutations. Further investigation of these peptides as part of novel immunotherapies, to include vaccine strategies is warranted. Research Sponsor: Parker Institute for Cancer Immunotherapy.

3136 Poster Session (Board #200), Fri, 8:00 AM-11:00 AM

A shared tumor-antigen RNA-lipoplex vaccine with/without anti-PD1 in patients with checkpoint-inhibition experienced melanoma. *First Author: Carmen Loquai, Department of Dermatology, University Medical Center of the Johannes Gutenberg University, Mainz, Germany*

Background: Cancer vaccines are considered unsuitable for patients with advanced tumours and have not been clinically successful. **Methods:** Lipo-MERIT is an ongoing phase 1/2 trial (NCT02410733) with melanoma FixVac, a liposomal RNA vaccine targeting four non-mutant shared tumour-associated antigens (TAAs) (MAGE-A3, NY-ESO-1, tyrosinase, TPTE). Patients with stage IIIB-C and IV melanoma are eligible. The trial comprises 7 dose escalation and 3 dose expansion cohorts, the latter with FixVac alone or combined with anti-PD1. Eight doses of FixVac are administered i.v. weekly/bi-weekly followed by optional continued monthly treatment. This abstract summarizes the findings of an exploratory interim analysis (cut-off JUL2019) of 89 patients. **Results:** 42 of 89 patients had measurable disease at baseline and were eligible for assessment of best objective overall response. All but one patient were stage IV and had undergone previous lines of treatment, 41 patients were checkpoint-inhibitor (CPI)-experienced, and 35 had been exposed to both anti-CTLA4 and anti-PD1 therapy. In the vaccine monotherapy group (n = 25) three patients experienced a partial response (PR) and 7 patients had stable disease (SD). An additional patient showed a complete metabolic remission of metastatic lesions based on [^{18}F]-FDG PET/CT imaging. In the group of patients treated with melanoma FixVac and PD1 blockade, 6 of 17 patients developed a PR. Patients with PR showed induction of poly-epitopic and strong CD4$^+$ and CD8$^+$ T cell immunity against the vaccine antigens. The number of antigen-specific cytotoxic T cells in some responders reached up to low 2-digit percentages of circulating CD8$^+$ T cells and was maintained at high levels by continued vaccination. Overall, 75% of the 50 patients tested by *ex vivo* IFNg ELISpot analysis and all 20 patients tested by IFNg ELISpot after *in vitro* stimulation showed vaccine-induced immune responses against at least one vaccine antigen. Typically, antigen-specific T cells ramped up within the first 4-8 weeks to single-digit and low double-digit percent fractions of circulating CD8$^+$ T cells. Immune responses were of effector memory phenotype and their strength and frequency did not depend on disease status at baseline (measurable *versus* non-measurable disease), on vaccine dose or on treatment (FixVac alone *versus* in combination with anti-PD1). **Conclusions:** FixVac alone and in combination with anti-PD1 mediates durable objective responses in pre-treated, CPI experienced patients with advanced progressing melanoma. Clinical trial information: NCT02410733. Research Sponsor: BioNTech RNA Pharmaceuticals GmbH.

3137 Poster Session (Board #201), Fri, 8:00 AM-11:00 AM

Personalized viral-based prime/boost immunotherapy targeting patient-specific or shared neoantigens: Immunogenicity, safety, and efficacy results from two ongoing phase I studies. *First Author: Charles G. Drake, Herbert Irving Comprehensive Cancer Center, New York, NY*

Background: Neoantigens are key targets of a tumor-specific immune response and CD8 T cells targeting neoantigens drive clinical benefit in patients (pts) treated with checkpoint inhibitors. **Methods:** Two Phase I studies are being conducted to assess the safety, immunogenicity, and early clinical activity of a viral-based neoantigen-targeting prime/boost immunotherapy aimed at maximizing the CD8 T cell response. Both studies use a chimpanzee adenovirus prime followed by increasing doses of repeat boosts with a self-amplifying mRNA in combination with IV nivolumab +/- SC ipilimumab. In the first study, GO-004, patient-specific neoantigens are predicted using Gritstone's EDGE model and incorporated into both prime/boost vectors. In GO-005, shared neoantigens derived from common driver mutations (including several from *KRAS*) are encoded in off-the-shelf prime/boost vectors. **Results:** To date, 12 pts have been treated: 6 pts with GEA, NSCLC, or MSS-CRC (GO-004) and 6 pts with NSCLC, MSS-CRC, or PDA (GO-005) with all pts receiving IV nivolumab and 5 pts also receiving SC ipilimumab. Nine pts continue to receive study treatment. No DLTs have been observed. Treatment-related AEs are reversible and include Grade 1/2 fever (7/12), injection site reactions (4/12), fatigue (3/12), diarrhea (2/12), hypotension (2/12), pruritus (2/12), skin reactions (2/12), anorexia (1/12), dyspnea (1/12), hyponatremia (1/12), infusion-related reactions (1/12), myalgia (1/12), and asymptomatic Grade 3 CK elevation (1/12). At the time of analysis, 8 of 12 pts with $\geq$ 1 radiographic assessment have a best response of stable disease (SD) (3) and progressive disease (PD) (4), and one pt with no evaluable disease at baseline continues on study $>$ 8 months. In GO-005, 1 pt with SD has a 20% reduction in tumor dimensions that correlates with a decrease in ctDNA. In 4 pts in GO-004 analyzed to date, all pts showed substantial neoantigen-specific CD8 T cell responses to multiple neoantigens after priming which increase further in 2 of 3 pts analyzed after subsequent boosts. In GO-005, 1 of 3 pts showed a robust KRAS G12C-specific CD8 T cell response. Induced T cells express IFNg and granzyme B, consistent with an effector response. **Conclusions:** Taken together, these early data support the tolerability of a viral-based prime/boost immunotherapy, demonstrate marked immunogenicity, and are consistent with potential clinical activity. Additional pts and data at higher dose levels will be presented. Clinical trial information: NCT03639714, NCT03953235. Research Sponsor: Gritstone Oncology, Inc.

3138 Poster Session (Board #202), Fri, 8:00 AM-11:00 AM

Multi-antigen active specific immunotherapy induced long-term remission and prevent colorectal cancer relapse. *First Author: Juan Pablo Marquez-Manriquez, CICS USA, Seattle, WA*

Background: Clinical effective multi-antigen active immunotherapy for colorectal cancer (CRC) is still limited and most studies have failed. We consider this is because the targets in some of the studies are not oncogenic drivers. This is especially important for patients that progressed to standard of care treatment. Also, most of the studies with Immune checkpoint inhibitors (ICH) have failed in CRC but potentially may impact and provide better outcomes if used as combination therapies. We treated CRC patients with progressive disease in a pilot study n = 15 and found clinical responses that correlate with the CD8, delayed-type hypersensitivity (DTH) and Th1 parameters. After patients achieved remission we used the same peptides to prevent relapse with clinical and statistics significance. **Methods:** N = 15 CRC patients were enrolled in this pilot trial after approval for the ethic IRB committee from CICS Mexico. Patients were treated with an intradermal vaccine every week for four weeks, every two weeks four times in axillary and inguinal lymph nodes (LN) areas, and finally subcutaneously every month six times in the sites with tumor activity. Previously to the treatment we perform Granzyme B ELISPOT, ELISA, DTH and CT scan as initial controls. We delivered intradermal four peptides from sixteen peptides predicted from four proteins such as Fascin-1, Ape-1, VCP and RCAS1. **Results:** 86% of the patients had an objective clinical responses and 14% stable disease. All the patients had a correlation with the immunological assays as following. 58% of patients had an increased in the CD8 cells demonstrated by Granzyme B; DTH reactions were gradually increasing and by the first month of treatment the DTH were positive for Fascin-1 (78%), Ape-1 (85%), VCP (95%) and RCAS1 (83%) peptides. The more immunogenic peptides by ELISA were Fascin-1 A ($P = 0.001$), Fascin-1 D ($P = 0.005$), Ape-1 C ($p = 0.001$), VCP A ($P = 0.003$), RCAS1 A ($p = 0.001$) and RCAS1 B ($P = 0.01$). **Conclusions:** The treatment was effective with CR and SD responses. Once we validate this data we are planning a clinical study combining the treatment with low dose of ICH. Currently all the patients with CR are now under relapse prevention. We are still treating the patients with SD until disease progression. Importantly we believe that this data may impact the PFS and OS in CRC patients who have Karnoksky $>$ to 80% despite progressive disease to standard of care. Research Sponsor: Sonora Cancer Research Center Foundation from Ciudad Obregon, Sonora, Mexico.

3139 Poster Session (Board #203), Fri, 8:00 AM-11:00 AM

Safety and tolerability of intratumorally administered OH2, an oncolytic herpes simplex virus 2, in patients with advanced solid tumors: A phase I dose escalation clinical study. *First Author: Jing Huang, Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: There have been limited reports concerning treatment outcomes of oncolytic viruses in solid tumors other than melanoma. OH2 is a genetically engineered oncolytic herpes simplex virus type 2 designed to selectively amplify in tumor cells and express GM-CSF to enhance tumor-specific immune responses. **Methods:** We conducted an open-label, single-center, phase 1 study. Eligible pts were 18-75 years of age; had histologically confirmed advanced solid tumor; had progressed after standard systemic treatments. Pts were required to have tumor(s) deemed safe to inject, with a longest diameter of at least 0.5cm. Other eligibility criteria included measurable lesion as per RECIST v1.1; ECOGPS score of 0-1 and adequate organ functions. A 3+3 dose-escalation strategy was used in the study and 3 dose levels (10^6, 10^7 and 10^8 CCID50/mL) of OH2 were assessed. OH2 was administered intratumorally every 3 weeks for the first cycle and every 2 weeks.Treatment may continue afterwards in ptswith potential clinical benefit at the discretion of the investigators. The primary objective was the safety and tolerability of OH2 injection as defined by the dose limiting toxicities (DLTs) within the first 3 weeks of therapy, and the maximum tolerated dose (MTD). Secondary objectives included efficacy and immunogenicity of OH2. **Results:** 11 pts were enrolled between April 17, 2019 and November 4, 2019. The median follow-up duration was 8.36 months (95%CI: 5.64-11.08). OH2 was well-tolerated as no DLTs were reported and no MTD reached. Before the end of the DLT assessment period,1 pt withdrew consent, and 1 pt died of arrhythmia unrelated to OH2, with negative OH2 DNA copies in serum, urine and saliva samples. Most treatment-related adverse events (TRAEs) observed were of grade 1-2, except that 1 pt in the 10^8 CCID50/mL group developed grade 3 fever. The most common TRAEs were fever (n =5) and blood bilirubin level increase (n = 4). There were no grade 4 or 5 TRAEs. One pt(rectal cancer) had PR and 2 (appendix cancer and ovarian cancer) had SD as per RECIST v1.1. One patient (esophageal cancer) achieved iPR as per iRECIST criteria. The duration of follow-up for the 2 responders were 9.70 months and 8.36 months, respectively, and both had ongoing responses. Notably, regression of a non-injected lesion was observed in 1 patient. **Conclusions:** OH2 had a favorable safety profile with no DLTs and MTD. The dose expansion study in selected tumor types is currently underway. Clinical trial information: NCT03866525. Research Sponsor: Wuhan Binhui Biotechnology Co., Ltd.

3140 Poster Session (Board #204), Fri, 8:00 AM-11:00 AM

Inhaled corticosteroid use and risk of pneumonitis in patients treated with immune checkpoint inhibitors. *First Author: Mingjia Li, The Ohio State University Wexner Medical Center, Division of Hospital Medicine, Columbus, OH*

Background: The identification of risk factors for immune-related adverse events (irAEs) is an important area of research. Among irAEs, pneumonitis carries one of the highest morbidities. There is a lack of strong predictors for pneumonitis in patients (pts) treated with ICI. We sought to identify predictors for the development of pneumonitis, and whether the use of inhaled corticosteroids (ICS) at time of ICI could be protective. **Methods:** Pts with advanced cancer treated with ICI from 2011 and 2018 were included in this retrospective study. Pneumonitis attribution to ICI was determined by treating physician at time of diagnosis. Time to pneumonitis was defined as days from the start of ICI to pneumonitis diagnosis. Pts who never had pneumonitis were censored at the time of last follow up or death. Predictors of pneumonitis were assessed by univariate Cox proportional hazard models at a significance threshold of alpha = 0.05. **Results:** A total of 837 pts were identified, and 30 (3.6%) pts developed any grade pneumonitis (12 grade 2, 14 grade 3, 1 grade 4, 3 grade 5) after receiving ICI (Table). Pts with age ≥65 years (y) had increased risk of developing pneumonitis over pts with age < 65y (HR 2.1, 95 CI: 1.02-4.4, p=0.041). 82 (9.7%) of the total cohort were on inhaled corticosteroid (ICS) at time of ICI, and 9 (11%) developed pneumonitis. Rather than being protective, pts on ICS had higher risk of pneumonitis (HR 4.2, 95 CI: 1.9-9.2, p=0.001). Pts with lung cancer had an increased risk for pneumonitis compared to pts with other cancers (HR 3.2, 95 CI: 1.5-6.4, p =0.003). Other risk factors included performance status, smoking history, line of therapy, or prior treatment including radiation were not statistically significant. **Conclusions:** Rather than a protective effect of ICS, our analysis found a higher risk of pneumonitis in pts treated with ICS. We confirmed an increased risk of pneumonitis for lung cancer pts compared to pts with other cancers, and higher risk of pneumonitis in pts age >65y. We hypothesize that the increased inflammatory status in chronic lung inflammation may predispose pts to pneumonitis that was not ameliorated by ICS. Future study is needed in prospective cohorts to further clarify the underlying inflammatory mechanism. Research Sponsor: Research support provided by the REDCap project and The Ohio State University Center for Clinical and Translational Science grant support (National Center for Advancing Translational Sciences, Grant UL1TR002733). Dr. Owen is a Paul Calabresi Scholar suppo.

	Pt Count	Pneumonitis Count		Pt Count	Pneumonitis Count
Age <65y	483 (58%)	12 (2.5%)	on ICS	82 (9.8%)	9(11%)
Age ≥65y	354(42%)	18 (5.1%)	Not on ICS	755 (92.2%)	21 (2.8%)
Cancer Types					
Melanoma	310 (37%)	7 (2.3%)			
Lung Cancers	209 (25%)	14 (6.7%)			
Renal Cell	73 (9%)	2 (2.7%)			
Other	245 (29%)	7 (2.8%)			

3141 Poster Session (Board #205), Fri, 8:00 AM-11:00 AM

Response criteria for intratumoral immunotherapy in solid tumors: itRECIST. *First Author: Gregory V. Goldmacher, Merck & Co., Inc., Kenilworth, NJ*

Background: The approval of intratumoral (IT) immunotherapy for metastatic melanoma and the active development of numerous novel IT drugs have created a need for standardized evaluation of response to this unique treatment strategy. The Response Evaluation Criteria in Solid Tumors (RECIST) is not suitable for assessing responses separately for injected and noninjected tumors. Building on RECIST concepts, we propose an IT immunotherapy RECIST (itRECIST) to capture data and assess local and systemic responses in a standardized fashion for clinical trials involving IT immunotherapies. **Methods:** itRECIST will address the unique needs of IT immunotherapy trials but, where possible, aligns with RECIST 1.1 and iRECIST. It does not dictate which lesions to inject but provides guidelines for collecting data and assessing response as treatment evolves. **Results:** itRECIST enables overall response assessment, separate response assessments in injected and noninjected lesions, and continued assessment following modifications of therapy at initial progression. At baseline, lesions are classified into 4 categories: target injected, target noninjected, nontarget injected, and nontarget noninjected. After baseline, lesions can be reclassified from noninjected to injected if the investigator decides to change the lesions to inject, but target and nontarget designations never change. Overall response at each assessment is based on target lesion response (injected and noninjected), nontarget lesion response, and absence/appearance of new lesions. Noninjected lesion response is determined by comparing tumor burden with baseline and nadir values. Injected lesion assessment is based on visit-to-visit changes in the lesions injected during treatment and on a combined assessment once the patient is off treatment. A new response category is defined to capture progression that would be "confirmed" per iRECIST even though injected lesions are responding and therapy continues. Multiple examples have been created to aid in training and adoption. **Conclusions:** itRECIST is an important step toward a standardized method of response assessment for this promising and evolving therapeutic modality. The proposed guidelines can be adopted into trial protocols and routine clinical practice without the need for complex additional assessments by treating physicians. Until there is evidence to support wider use, itRECIST is intended only to support standardized collection of data and to facilitate exploratory analysis. Authors G.V.G. and A.D.K. contributed equally to this work. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

3142 Poster Session (Board #206), Fri, 8:00 AM-11:00 AM

Analysis of mutation detection of POLD1/pole in pan-cancer. *First Author: Gao Yang, Xiangya Hospital, Central South University, Changsha, China*

Background: Previous studies proved that mutation of *POLD1* and *POLE* elevates base-substitution mutations and lead to the elevation of tumor mutation burden (TMB). Other signature needs to explore to identify driver mutations in these two genes. **Methods:** Using gene-panel target-capture next generation sequencing, we analyzed the TMB and *POLD1/POLE* mutation in 17383 tumor tissue or plasma ctDNA samples from different patients. **Results:** Tumor mutation burdens were calculated of all the 17383 samples. According to the present research and our panel, we use 10 and 100 Mut/Mb to define hypermutation and ultra-hypermutation. Samples with hypermutation possessed 18.8% (n = 3268) and ultra-hypermutation possessed 0.3% (n = 58). In unselected, hypermutation and ultra-hypermutation group, *POLD1* or/and *POLE* mutations were identified in 3.5% (n = 625), 56.1% (n = 32) and 87.9%(n = 372) samples. There were 0.5% (n = 81), 17.0% (n = 73) and 87.7%(n = 51) identified more than one mutation. These results showed that *POLD1* or/and *POLE* mutations were enriched in samples with high TMB. We screened every known *POLE* and *POLD1* driver mutations. There were 22 ultra-hypermutation samples identified these mutations, including A456P(3), P286R(10), V411L(6), M444K(1), S459F(1) in *POLE* and R1016H(1) in *POLD1*. Interestingly, all of them were identified in microsatellite stable (MSS) samples , which suggest that driver mutation may enriched in MSS samples. These already known driver mutation was not detect in 24 high-level microsatellite instability (MSI-H) and ultra-hypermutation samples. We further analyzed 10 *POLD1/POLE* mutations in other 5 MSS and ultra-hypermutation samples. *POLE* L424V was a pathogenic germline mutation but not defined as a driver mutation clearly before. *POLE* P286C had not been biochemically characterized but had different residue with P286R in the same position. Others had not been biochemically characterized (R232H, A234T, V945M, S1064I, Y467H in *POLD1*, D462N and R749Q, E1956D in *POLE*). These mutations were potential driver mutations and further research need to be support. **Conclusions:** We found that not only *POLD1* or/and *POLE* mutations were enriched in samples with high TMB, but also driver mutations were enriched in microsatellite stable tumors. Further researches need to continue to identify more driver mutations of *POLD1* and *POLE*. Research Sponsor: None.

3143 Poster Session (Board #207), Fri, 8:00 AM-11:00 AM

Percutaneous hepatic injection of rose bengal disodium (PV-10) in metastatic uveal melanoma. *First Author: Sapna Pradyuman Patel, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: PV-10 is a small molecule autolytic immunotherapy in clinical development for treatment of solid tumors. When administered by intralesional (IL) injection, PV-10 can produce immunogenic cell death that may induce a T cell-mediated immune response against treatment refractory and immunologically cold tumors. Given this mechanism of action and clinical data that metastatic uveal melanoma (MUM) generates low response rates to immune checkpoint blockade (CB), we investigated treatment of MUM with percutaneously-delivered PV-10. **Methods:** This open-label Phase 1 basket study (NCT00986661) is evaluating the safety, tolerability, and preliminary efficacy of intralesional PV-10 in patients (pts) with solid tumors of the liver. PV-10 is injected into one or more designated hepatic tumor(s) with a maximum sum of diameters ≤4.9 cm. Response assessments using 2D EASL criteria are performed at Day 28, then every 3 months. Pts with additional injectable tumors are eligible to receive further PV-10 after Day 28. Pts can receive standard of care CB immunotherapy during treatment with PV-10. **Results:** As of February 1, 2020, the initial cohort of 15 pts with MUM to the liver was fully enrolled. Pts had received at least 1 IL injection of PV-10, with an average of 2 hepatic lesions injected per pt (range 1-4). Of these, 4 pts were refractory to prior CB. Three pts received PV-10 alone, 3 received PV-10 + anti-PD-1 and 9 received PV-10 + anti-PD-1 + anti-CTLA-4. Adverse events (AEs) were consistent with established patterns for PV-10 and CB: AEs attributed to PV-10 were transient and included 3 cases of Grade 3/4 transaminitis that resolved within 72 hrs, injection site pain, photosensitivity, and pink discoloration of skin, urine or feces; AEs attributed to CB included nausea, decreased WBC, and fatigue. Response assessments on 24 injected tumors were: 2 complete response (8%), 7 partial response (29%) and 11 stable disease (46%), per 2D EASL. Among the 4 CB-refractory pts, median overall survival (OS) was 9.2 months (range 5.3 - 11.4 months, with 2 pts alive at 5.3 months each), while among the 11 CB-naïve pts OS was undefined (range 0.5 - 21.9+ months, with 1 death at 7.9 months). Pts receiving PV-10 alone (1 CB-refractory, 2 naïve) achieved a median OS of 7.9 months with one CB-naïve pt alive with partial overall response at 21.9 months. **Conclusions:** Response indicative of regression or stabilization in a majority (83%) of injected lesions is encouraging in a disease of major unmet need. Enrollment and follow-up for safety, duration of response and survival are ongoing. Clinical trial information: NCT00986661. Research Sponsor: Provectus Biopharmaceuticals.

3144 Poster Session (Board #208), Fri, 8:00 AM-11:00 AM

Immune-mediated adverse events following concomitant radiotherapy and immunotherapy in patients with melanoma and Merkel cell carcinoma: A preliminary report from an evolving retrospective registry. *First Author: Nikolaos Andreatos, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH*

Background: Radiotherapy (RT) potentiates immune-mediated responses against tumor antigens, an effect that is enhanced by checkpoint inhibitors (CPIs) and may hold therapeutic promise. However, the mechanisms underlying this abscopal effect can theoretically increase the rate of immune-mediated adverse events (irAEs). We estimated the incidence of irAEs in a single-institution cohort treated with concomitant RT and immunotherapy. **Methods:** We retrospectively screened 731 patients that received RT and CPIs at our institution. Patients diagnosed with melanoma or Merkel cell carcinoma (MCC) who underwent RT concurrently or within 30 days of CPI administration were eligible. A radiation period (RP) comprised the interval between the first and last treatment days (≤90 days); a patient could contribute multiple RPs. Data on new irAEs diagnosed within 3 months after RT and relevant demographic and clinicopathologic variables were collected; univariate analysis was performed with the chi-squared test. **Results:** 35 patients (23 male, 12 female) contributed 43 RPs; mean age was 65.5 years (range: 39-90). Five had MCC, and 30 had melanoma (24 cutaneous, 1 uveal and 5 urogenital melanomas). PD-1 inhibitors were most commonly employed (22 RPs), followed by ipilimumab-nivolumab (14 RPs), ipilimumab (4 RPs), and avelumab (3 RPs). CPIs were administered concurrently with RT in 32 RPs and sequentially in 11 RPs. Fourteen RPs comprised intracranial radiation. Importantly, 45.7% of patients (16/35) experienced irAEs, which manifested within a month of RT in 25.7% (9/35). Four patients experienced grade ≥3 irAEs leading to hospitalization; one died of respiratory failure after developing pneumonitis. On univariate analysis, no significant association between tumor type, CPI regimen, concurrent RT, intracranial vs. extracranial RT, and irAE incidence was noted. A trend for increased irAEs within the ipilimumab-nivolumab group was observed ($p = 0.27$). **Conclusions:** Almost half of patients developed new irAEs following RT, with 25% (4/16) of cases warranting hospitalization; these incidence rates appear to exceed rates from historical data and raise concerns about the additive toxicity of CPIs and RT. Comparison to non-RT cohorts and survival analyses are ongoing. Research Sponsor: None.

TPS3145 Poster Session (Board #209), Fri, 8:00 AM-11:00 AM

ZW25, an anti-HER2 bispecific antibody, plus chemotherapy with/without tislelizumab as first-line treatment for patients with advanced HER2-positive breast cancer or gastric/gastroesophageal junction adenocarcinoma: A phase 1B/2 trial-in-progress. *First Author: Do-Youn Oh, Seoul National University Hospital, Seoul, South Korea*

Background: ZW25 is a novel HER2-targeted antibody that binds two distinct extracellular domains of HER2, allowing for multiple mechanisms of action, including activation of ADCC and inhibition of ligand-dependent and -independent cellular growth. ZW25 is well tolerated and showed single-agent antitumor activity in patients (pts) with advanced HER2-positive cancers. Previous reports suggested that tislelizumab, an investigational anti-PD-1 antibody engineered to minimize binding of FcgR on macrophages in order to abrogate antibody-dependent phagocytosis, was generally well tolerated and had antitumor activity alone and in combination with chemotherapy in pts with advanced solid tumors. Combining HER2-targeted agents with chemotherapy has resulted in improved survival; the highly immunogenic nature of HER2 tumors has led to the development of therapies combining anti-HER2 therapies with immune checkpoint blockade. **Methods:** This open-label, two cohort phase 1B/2 study is designed to evaluate ZW25 plus chemotherapy ± tislelizumab as first-line therapy in pts (n≈50) with HER2-positive metastatic breast cancer (mBC; cohort 1) or advanced gastric/gastroesophageal junction adenocarcinoma (GC/GEJC; cohort 2). In cohort 1, pts with HER2-positive (IHC3+ or ISH amplified) mBC must be treatment-naïve for metastatic disease and will receive intravenous (IV) ZW25 30 mg/kg plus docetaxel 75 mg/m^2 IV once every 3 weeks (Q3W). In cohort 2, treatment-naïve pts with HER2-positive (IHC3+ or IHC2+ with ISH amplification) advanced GC/GEJC will receive ZW25 30 mg/kg plus tislelizumab 200 mg IV and chemotherapy (CAPOX regimen: capecitabine 1000 mg/m^2 twice daily and oxaliplatin 130 mg/m^2 IV) Q3W. A safety lead-in phase is designed for the first six pts in cohort 2, followed by dose expansion after a safety monitoring committee review. Primary endpoints are the safety/tolerability profile and objective response rate; secondary endpoints include duration of response, time to response, progression-free survival, disease control rate, and overall survival. Clinical trial information: Registered, NCT number pending will provide as soon as available. Research Sponsor: BeiGene, Ltd.

TPS3146 Poster Session (Board #210), Fri, 8:00 AM-11:00 AM

Bgb-A425, an investigational anti-TIM-3 monoclonal antibody, in combination with tislelizumab, an anti-PD-1 monoclonal antibody, in patients with advanced solid tumors: A phase I/II trial in progress. *First Author: Jayesh Desai, Peter MacCallum Cancer Centre, Melbourne, Australia*

Background: While immune surveillance plays a critical role in preventing tumor proliferation and metastasis, tumors develop resistance mechanisms to suppress and/or escape the immune system. T-cell immunoglobulin and mucin-domain containing-3 (TIM-3) and programmed cell death protein-1 (PD-1) function as immune checkpoint receptors on tumor-infiltrating lymphocytes. Overlap in expression and function suggests TIM-3 and PD-1 cooperate to maximize effector T-cell exhaustion, leading to a decreased antitumor immune response. Although blockade of TIM-3 alone is unlikely to result in an efficacious antitumor immune response, combined TIM-3/PD-1 blockade may enhance the antitumor properties of anti-PD-1 therapies alone. BGB-A425 is an investigational IgG1-variant monoclonal antibody against TIM-3. Tislelizumab, an anti-PD-1 antibody, was engineered to minimize binding to FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. This phase 1/2 study will assess the safety/tolerability, pharmacokinetic (PK) profile, and antitumor activity of BGB-A425 in combination with tislelizumab in patients with advanced solid tumors. **Methods:** This is an open-label phase 1/2 study (NCT03744468) of BGB-A425 in combination with tislelizumab in patients with histologically/cytologically confirmed advanced, metastatic, unresectable solid tumors. Phase 1 will determine the recommended phase 2 dose (RP2D) for combination treatment; phase 2 will assess the antitumor effects of the combination in select tumor types. In phase 1, up to 42 patients will be enrolled into sequential cohorts of increasing doses of intravenous (IV) BGB-A425 in combination with tislelizumab 200 mg IV, based on a 3+3 study design. During Cycle 1, patients will receive BGB-A425 alone on Day 1 followed by tislelizumab alone on Day 8. If no dose-limiting toxicities are observed, patients will receive both BGB-A425 and tislelizumab sequentially on Day 29 and every 21 days thereafter. Once the RP2D is determined, the combination therapy will be evaluated in up to 120 patients with select tumor types in phase 2. Safety/tolerability profile and RP2D determination (phase 1) and objective response rate per RECIST v1.1 (phase 2) are primary objectives; secondary objectives include antitumor activity, PK profile, and immunogenicity of combination therapy. Clinical trial information: NCT03744468. Research Sponsor: BeiGene, Ltd.

TPS3147 Poster Session (Board #211), Fri, 8:00 AM-11:00 AM

A phase I study of CD40 agonist ABBV-927 plus OX40 agonist ABBV-368 with or without the PD-1 inhibitor budigalimab in patients with advanced solid tumors. *First Author: John D. Powderly, Carolina BioOncology Institute, Huntersville, NC*

Background: CD40 is a key costimulatory molecule for both the innate and adaptive immune systems that is essential for T-cell activation and proliferation. OX40 is a costimulatory molecule that is involved in enhancing nascent immune responses and concomitantly acts to suppress regulatory T-cell activity. ABBV-927 and ABBV-368 are potent agonistic antibodies against CD40 and OX40, respectively. This open-label, Phase 1 study will evaluate the doublet combination of ABBV-927 and ABBV-368 and the triplet combination of ABBV-927, ABBV-368, and the programmed cell death protein-1 (PD-1) inhibitor budigalimab in patients with advanced solid tumors. **Methods:** For this study (NCT03893955), patients must be ≥18 y with an Eastern Cooperative Oncology Group performance status of 0-1. Patients must have an advanced solid tumor that has progressed on standard therapies. Disease-specific cohorts will include patients with non-small cell lung cancer (NSCLC) and triple-negative breast cancer (TNBC). Patients with NSCLC must have previously received a PD-1/PD-ligand 1 inhibitor and a platinum-based therapy and no more than one prior immunotherapy. Patients with TNBC must not have received immunotherapy. Patients with uncontrolled central nervous system metastases will be excluded. The recommended Phase 2 dose (RP2D) will first be identified with ABBV-927 + ABBV-368 in patients with solid tumors (Arm A) and will be expanded in disease-specific cohorts including TNBC. The RP2D of ABBV-927 + ABBV-368 + budigalimab will be identified in patients with NSCLC (Arm B). The primary endpoints are determination of the RP2D of ABBV-927 + ABBV-368, the RP2D of ABBV-927 + ABBV-368 + budigalimab, and overall response rate; duration of response, progression-free survival, safety, and pharmacokinetics are secondary endpoints. Screening began on 21 May 2019, and enrollment is ongoing. Clinical trial information: NCT03893955. Research Sponsor: Abbvie, Inc.

TPS3148 Poster Session (Board #212), Fri, 8:00 AM-11:00 AM

A phase II open-label multicenter study to assess the efficacy and safety of AFM13 in patients with relapsed or refractory CD30-positive peripheral T-cell lymphoma or transformed mycosis fungoides: The REDIRECT study design and rationale. *First Author: Cassandra Choe-Juliak, Affimed Inc, NY, NY*

Background: AFM13 is a tetravalent, bispecific (anti-CD30/anti-CD16A) recombinant antibody being developed for the treatment of CD30-positive T-cell malignancies and Hodgkin lymphoma. AFM13 selectively kills CD30-positive tumor cells by engaging and activating natural killer cells and macrophages. AFM13 was well tolerated at doses of 0.01 to 7 mg/kg and showed clinical activity in patients with relapsed/refractory (R/R) Hodgkin lymphoma in a Phase 1 study. In an ongoing biomarker Phase 1b/2a study in patients with R/R CD30-positive lymphomas with cutaneous involvement, 4 of 8 patients responded (at different doses) including one CR. Based on these findings, this Phase 2 study (REDIRECT) has been initiated. **Methods:** This is a Phase 2, open-label, multicenter global study investigating the efficacy and safety of AFM13 in patients with R/R CD30-positive peripheral T cell lymphoma (PTCL) or transformed mycosis fungoides (TMF). AFM13 is administered at 200 mg weekly via an intravenous infusion until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent. Cohorts A and B include PTCL patients with ≥10%, and ≥1% to <10% CD30 expression by IHC, respectively. Cohort C includes patients with TMF who express ≥1% CD30. Eligible PTCL patients must have received at least 1 prior line of systemic therapy and, if diagnosed with systemic anaplastic large cell lymphoma, must have failed or be intolerant to brentuximab vedotin. Eligible patients with TMF must have received at least 1 prior line of systemic therapy and have exhausted systemic therapies with regular approval for their disease. This global trial started enrollment in Oct 2019. The primary endpoint is objective response rate as confirmed by an Independent Review Committee for all cohorts. The study will also assess investigator-measured efficacy parameters, safety, PK, immunogenicity and QOL. Disease assessment will be done at screening and every 8 weeks for the first 3 assessments, then every 12 weeks thereafter, regardless of any treatment/cycle delays that may occur. ClinicalTrials.gov identifier: NCT04101331. References: Reusch U et al. *mAbs.* 2014;6(3):728-739. Rothe A et al. *Blood.* 2015;125(26):4024-4031. Clinical trial information: NCT04101331. Research Sponsor: Affimed GmbH.

TPS3149 Poster Session (Board #213), Fri, 8:00 AM-11:00 AM

KITE-439: A phase I study of HPV16 E7 T cell receptor-engineered T cells in patients with relapsed/refractory HPV16-positive cancers. *First Author: Kedar Kirtane, Moffitt Cancer Center, Tampa, FL*

Background: Human papillomavirus 16 (HPV16) is the most prominent subtype across invasive head and neck cancers, as well as cervical cancer and other anogenital cancers (Saraiya M, et al. *J Natl Cancer Inst.* 2015). The HPV16 E7 (E7) viral antigen is important for the survival of HPV-positive tumor cells but is absent from normal human tissue, making it an attractive target for anti-cancer therapy. Preclinical efficacy has been observed with MHC class I-restricted T cell receptor (TCR)-engineered T cells targeting E7 on HPV16-positive tumor cells (Jin BY, et al. *JCI Insight.* 2018). This Phase 1, first-in-human, open-label, multicenter study (NCT03912831) will evaluate the safety and efficacy of KITE-439, an autologous TCR-engineered T cell therapy targeting E7, in HLA-A*02:01–positive patients with relapsed/refractory HPV16-positive cancers. **Methods:** A single-patient dose-escalation schema will be used in Phase 1A of the study, enrolling up to 30 patients. Phase 1A will evaluate safety and inform the recommended dose of KITE-439 for Phase 1B. Approximately 45 patients with squamous cell cancer of the head and neck, cervical cancer, and other HPV16-positive tumors will be included in Phase 1B. Patients in Phase 1A and Phase 1B may receive optional bridging therapy followed by cyclophosphamide and fludarabine conditioning chemotherapy. Patients will then receive an infusion of KITE-439 at 1×10^6 up to 1×10^8 TCR-transduced T cells/kg along with daily subcutaneous IL-2 therapy for a maximum of 14 doses post-infusion. The primary endpoint for Phase 1A is the incidence of adverse events defined as dose-limiting toxicities. The primary endpoint for Phase 1B is investigator-assessed objective response rate per modified RECIST v1.1 criteria (Eisenhauer EA, et al. *Eur J Cancer.* 2009). Secondary endpoints for Phase 1B include duration of response, progression-free survival, overall survival, and safety. Patients ≥ 18 years must be HLA-A*02:01–positive and have relapsed/refractory HPV16-positive cancer, an ECOG PS of ≤ 1, and adequate bone marrow and organ function. Key exclusion criteria include a history of stroke, myocardial infarction, or symptomatic deep vein thrombosis/pulmonary embolism, known infection with human immunodeficiency virus, detectable hepatitis C, or detectable hepatitis B. This study is currently open and accruing patients. Clinical trial information: NCT03912831. Research Sponsor: Kite, a Gilead Company.

TPS3150 Poster Session (Board #214), Fri, 8:00 AM-11:00 AM

Phase I trial of drug resistant immunotherapy: A first-in-class combination of MGMT-modified γδ t cells and temozolomide chemotherapy in newly diagnosed glioblastoma multiforme. *First Author: Lawrence S. Lamb, Incysus Therapeutics, New York, NY*

Background: Temozolomide (TMZ) transiently upregulates GBM-specific stress-induced NKG2D ligands that are targeted by innate immune effector cells. Leveraging this effect is problematic, however, due to the lymphodepleting effects of TMZ.Genetic modification of *ex vivo* expanded and activated with an MGMT-expressing lentivector allows simultaneous chemotherapy and γδ T cell therapy that targets the tumor when NKG2DL are maximally expressed. We have termed this Drug Resistant Immunotherapy (DRI). Patient-derived xenograft mouse models of both primary and recurrent GBM treated with DRI have shown a significant survival advantage that were otherwise impervious to either cell therapy or TMZ. These preclinical findings and associated safety data provide the rationale to initiate a Phase I trial of DRI in primary GBM. **Methods:** This first in human study will evaluate the safety and optimal dosing frequency of the DRI with TMZ (NCT04165941).Eligibility criteria include the following: GBM eligible for resection, ≥18y, adequate organ and marrow function, and KPS≥70. Six to 12patients with newly diagnosed GBM are being enrolled in a 3 + 3 design into 1 of 2 fixed dose levels (DL) of DRI. Following tumor resection and immediately prior to induction chemo/radiotherapy, an apheresis product is collected and γδ T cells expanded in Zoledronic Acid (Novartis) and rhIL-12 (Miltenyi) and transduced with a P140K-MGMT lentivector (Miltenyi Lentigen, Gaithersburg, MD), harvested, and cryopreserved. At initiation of maintenance phase TMZ therapy, patients receive 150mg/m^2 intravenous TMZ concurrently with intracranial injection of 1 x 10^7 γδ T cells (DL1) delivered through a Rickham reservoir previously inserted into the tumor cavity at resection. The patient then receives 4 daily doses of oral TMZ followed by 24d rest. Treatment cycles escalate from 1 to 3 (DL2) DRI doses following a safety observation period and absence of dose limiting toxicity. Maintenance TMZ treatment will continue for 6 cycles. Safety evaluations consist of routine laboratory analyses, clinical measurements (physical exams, vital signs), neurological function and evidence DRI γδ T cell related toxicity. Peripheral blood will be obtained for comprehensive immuno-phenotyping and T cell function analysis. Clinical benefit of DRI will be characterized by evaluating responses (CR, PR, SD and PD) and determining progression-free, median, and overall survival. As of February 2020, enrollment into DL 1 is ongoing. Clinical trial information: NCT04165941. Research Sponsor: Incysus Therapeutics, Inc.

TPS3151 Poster Session (Board #215), Fri, 8:00 AM-11:00 AM

A phase Ia/Ib, open-label first-in-human study of the safety, tolerability, and feasibility of gene-edited autologous NeoTCR-T cells (NeoTCR-P1) administered to patients with locally advanced or metastatic solid tumors. *First Author: Bartosz Chmielowski, UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA*

Background: Neoepitopes (neoE) derived from private tumor-exclusive mutations represent compelling targets for personalized TCR-T cell therapy. An ultra-sensitive and high-throughput process was developed to capture tumor mutation-targeted CD8 T cells from patient blood. NeoTCRs cloned from the captured CD8 T cells, when engineered into fresh CD8 and CD4 T cells, effected killing of patients' autologous tumor cells in vitro. These observations have been leveraged for the development of a fully personalized adoptive T cell therapy (NeoTCR-P1). A Phase 1 clinical trial testing NeoTCR-P1 in subjects with solid tumors is ongoing (NCT03970382). **Methods:** During the initial trial phase, escalating doses of NeoTCR-P1 T cells administered without and with IL-2 in the regimen, and following conditioning chemotherapy, will be evaluated in subjects with advanced or metastatic solid tumors (melanoma, urothelial cancer, colorectal cancer, ovarian cancer, HR^+ breast cancer, and prostate cancer). The objective of the Phase 1a study is to establish a recommended Phase 2 dose. Primary endpoints include the incidence and nature of DLTs and overall process feasibility. The proliferation, persistence, and trafficking of NeoTCR-T cells will be characterized. In the expansion trial phase, preliminary anti-tumor activity of NeoTCR-P1 will be assessed in selected tumors. The combination of NeoTCR-P1 dosing plus nivolumab will be tested in a Phase 1b study. Conclusion: This is the first clinical study of an autologous, fully personalized adoptive T cell therapy directed against private tumor-exclusive mutations, generated without using recombinant viral vectors. Clinical trial information: NCT03970382. Research Sponsor: PACT Pharma.

TPS3152 Poster Session (Board #216), Fri, 8:00 AM-11:00 AM

Quilt-3.064: An open-label phase I study of PD-L1 t-haNK in subjects with locally advanced or metastatic solid cancers. *First Author: Tara Elisabeth Seery, Chan Soon Shiong Institute for Medicine, El Segundo, CA*

Background: Tumor cells can escape immunosurveillance through upregulation of PD-L1, which inhibits the proliferation and antitumor activity of T cells. T cells genetically altered to express chimeric antigen receptors (CARs) that recognize tumor-associated antigens have mediated potent responses in patients with hematologic cancers, but have shown limited efficacy in solid tumor cancers and can be associated with severe toxicity, ie, cytokine release syndrome (CRS). Like T cells, NK cells can be genetically modified to express CARs that can specifically recognize and lyse cancer cells. Unlike T cells, NK cell cytotoxicity does not require prior sensitization and is not HLA-restricted, making NK cells an attractive choice for clinical immunotherapy. In addition to their innate cytotoxicity, NK cells mediate antibody-dependent cellular cytotoxicity (ADCC) via expression of CD16. PD-L1 t-haNK is an off-the-shelf, human, allogeneic, NK cell line engineered to express a CAR targeting PD-L1. It can be easily and continuously expanded in culture and preclinical in vitro and in vivo studies have demonstrated effective PD-L1 CAR–mediated antitumor activity against $PD\text{-}L1^+$ MDSCs. PD-L1 t-haNK has also been engineered to express the high-affinity variant of the Fcγ receptor (FcγRIIIa/CD16a 158V), and thus has enhanced CD16-targeted ADCC capabilities, particularly when combined with a monoclonal antibody. As such, a dual-targeted NK approach may be more effective at potentiating antitumor activity and reversing suppression in multiple cancers that express PD-L1 in the tumor microenvironment. **Methods:** This is a dose-escalation study of PD-L1 t-haNK in subjects with locally advanced or metastatic solid cancers, regardless of PD-L1 expression. Dose escalation will involve a standard 3 + 3 design. The primary objectives are to determine safety, maximum tolerated dose (MTD), and designate a recommended phase 2 dose. Secondary objectives include estimates of preliminary efficacy by objective response rate, progression-free survival, and overall survival. Subjects in Cohort 1 will receive $\sim 2 \times 10^9$ PD-L1 t-haNK cells twice per week and assessed for dose-limiting toxicities (DLTs). If no DLTs occur, the dose may increase to $\sim 4 \times 10^9$ cells twice per week in Cohort 2. Dose expansion will occur when the MTD has been determined. PD-L1 t-haNK is administered by IV infusion in an outpatient setting. Enrollment in Cohort 1 has been completed ($N = 6$, > 100 doses total) without DLTs or CRS. Enrollment into Cohort 2 began December 2019. Clinical trial information: NCT04050709. Research Sponsor: NantKwest.

TPS3154 Poster Session (Board #218), Fri, 8:00 AM-11:00 AM

Alliance A151804: Establishment of a national biorepository to advance studies of immune-related adverse events. *First Author: David E. Kozono, Dana-Farber Cancer Institute, Boston, MA*

Background: Immune-related Adverse Events (irAEs) are rare but serious sequelae of treatment with immuno-oncology (IO) therapeutics. These therapeutics, including monoclonal antibodies targeting programmed cell death protein 1 (PD-1), programmed death-ligand 1 (PD-L1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), have had transformative effects on outcomes for patients (pts) with advanced cancers. Although most pts tolerate the therapies well, a few experience irAEs ranging in severity up to life-threatening. These irAEs involve diverse organs including the heart, kidney, liver and lung, and gastrointestinal, musculoskeletal, central and peripheral nervous systems. Because of the relatively low incidence and wide variety of irAEs due to various immunotherapies for multiple tumor types, establishment of an efficient centralized repository for acquisition and organized distribution of well-annotated biospecimens is vital for translational studies that improve understanding of the molecular pathogenesis and treatment of these significant toxicities. **Methods:** This multi-institutional study is open at sites across the National Clinical Trial Network to pts who received $\geq$ 1 IO therapeutics (e.g., CTLA-4, PD-1 or PD-L1 inhibitor) and experienced 1) $\geq$ 1 serious (grade 3–5) adverse events that are likely immune-related, 2) rare infection or 3) tumor hyperprogression. IrAEs of interest include myocarditis, colitis, hepatitis, nephritis, myositis, pneumonitis, meningitis/encephalitis, dermatitis, endocrinopathies and neuropathy. Pts may be on an NCTN or non-NCTN IO trial or be receiving standard-of-care therapy. Registration must occur $\leq$ 72 hours after confirmation of the irAE event. Clinical data are collected at registration, 1 month after registration and for up to 1 year. Biospecimens (tumor blocks, biopsies of inflammatory tissues used to establish irAE diagnosis, and serial blood samples for isolation of plasma, serum and peripheral blood mononuclear cells) are collected at 1-2 timepoints. Stool samples are collected from pts experiencing colitis. Imaging data are collected for pts with hyperprogression or pneumonitis. Goal accrual is 240 pts. Biospecimens and data will be made available to investigators following future submission and approval of proposals. Support: U10CA180821, U10CA180882, U24CA196171; U10CA180820 (ECOG-ACRIN); U10CA180888 (SWOG); U10CA180868 (NRG); https://acknowledgments.alliancefound.org; Clinical trial information: NCT04242095. Research Sponsor: U.S. National Institutes of Health.

TPS3155 Poster Session (Board #219), Fri, 8:00 AM-11:00 AM

A phase I study of AK112, a bispecific antibody that targets PD-1 and VEGF co-expressing T cells, in patients with advanced solid tumors. *First Author: Jermaine Coward, Icon Cancer Care, Brisbane, Australia*

Background: AK112 is a humanized IgG1 bispecific anti-PD-1/VEGF antibody. VEGF blockade potentiates PD-1 inhibition by, *inter alia*, opposing the immunosuppressive effects of VEGF-A, which include suppression of dendritic cell activity and enhancement of checkpoint molecule expression on CD8+ T cells and proliferation of regulatory T cells. Combination therapies involving PD-(L)1 and VEGF inhibitors have been approved for the treatment of selected patients with metastatic non-small cell lung carcinoma, advanced renal cell carcinoma and advanced endometrial carcinoma. A supplemental Biologics License Application has been submitted for an anti-PD-L1 + anti-VEGF combination for the first-line treatment of unresectable hepatocellular carcinoma. Given the strong correlation between VEGF and PD-1 expression in the tumor microenvironment, the simultaneous blockade of these 2 targets by AK112 as a single agent might achieve higher target binding specificities and synergistically produce enhanced antitumor activity compared to co-administration of anti-PD-(L)1 and anti-VEGF therapies. **Methods:** This is a Phase 1a/1b, first-in-human, multicenter, open-label study in patients with advanced or metastatic solid tumor that is refractory/relapsed to standard therapies. The primary objective is to assess safety, tolerability and DLTs; and to determine the Maximum Tolerated Dose (MTD) or Maximum Administered Dose of AK112. Antitumor activity, PK and immunogenicity of AK112 will be studied as secondary objectives. As exploratory endpoints, tumor tissue samples may be evaluated for PD-L1 expression, mRNA expression profile and biomarkers (e.g. CD8+, FoxP3, Granzyme B, apelin and EPHB4). PD-1 receptor occupancy on circulating T-cells and serum VEGF level may also be measured as indications of target engagement. The dose-escalation phase will evaluate 5 dose levels of AK112 (up to 20 mg/kg Q2W IV) using a 3+3+3 study design. Additional subjects (up to 18 subjects) may be enrolled at any dose level not exceeding the MTD for additional PK, PD and safety evaluations to determine the optimal dose level for the dose-expansion phase. Cohorts 1 and 2 have been completed and enrollment to Cohort 3 began in January 2020. The dose-expansion phase will be performed in patients with selected advanced solid tumors who had no prior exposure to drugs targeting T-cell co-stimulation or immune checkpoint pathways. Clinical trial information: NCT04047290. Research Sponsor: Akeso BioPharma, Inc.

TPS3156 **Poster Session (Board #220), Fri, 8:00 AM-11:00 AM**

A phase II study of olaparib in combination with pembrolizumab in patients with previously treated advanced solid tumors with homologous recombination repair mutation (HRRm) and/or homologous recombination repair deficiency (HRD): KEYLYNK-007. *First Author: Timothy A Yap, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: The anti-PD-1 antibody pembrolizumab (pembro) has improved clinical outcomes in multiple previously treated advanced solid tumors. The poly (ADP-ribose) polymerase (PARP) inhibitor olaparib (ola) has shown antitumor activity as monotherapy in previously treated advanced cancers with *BRCA1*/*BRCA2* mutations (BRCAm), other HRRm, and ovarian cancer with HRD phenotype. Antitumor activity of PD-(L)1 plus PARP inhibition was reportedly higher than expected with either agent alone in patients (pts) with recurrent ovarian cancer regardless of BRCAm or HRD status and in pts with BRCAm breast cancer. KEYLYNK-007 (NCT04123366) evaluates antitumor activity and safety of ola plus pembro in pts with advanced solid tumors with HRRm and/or HRD. **Methods:** This phase 2, nonrandomized, multicenter, open-label study plans to enroll ~300 pts aged ≥18 y with histologically/cytologically confirmed, previously treated, advanced solid tumors with HRRm and/or HRD per Lynparza HRR-HRD assay (Foundation Medicine, Inc., Cambridge, MA, USA) and ECOG PS 0-1. Pts will be grouped by biomarker status: (1) BRCAm; (2) HRRm without BRCAm; (3) HRD positive without HRRm (loss of heterozygosity score ≥16 per Lynparza HRR-HRD assay). Pts will receive ola 300 mg BID + pembro 200 mg IV Q3W (35 cycles) until PD, unacceptable AEs, intercurrent illness, investigator decision, withdrawal, or pregnancy. Tumor imaging assessment by blinded independent central review (BICR) per RECIST v1.1 or Prostate Cancer Working Group (PCWG)-modified RECIST v1.1 for prostate cancer will occur Q9W for 12 mo, then Q12W until PD, start of new anticancer treatment, withdrawal, pregnancy, or death. AEs will be monitored throughout the study and for 30 days after final dose (90 days for serious AEs) and graded by NCI CTCAE v5. The primary endpoint is ORR (RECIST v1.1 or PCWG-modified RECIST v1.1 by BICR). Secondary endpoints include DOR, PFS (RECIST v1.1 or PCWG-modified RECIST v1.1 by BICR), OS, and safety. ORR will be analyzed by the Clopper-Pearson method; and DOR, PFS, and OS by the Kaplan-Meier method. Clinical trial information: NCT04123366. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

TPS3157 **Poster Session (Board #221), Fri, 8:00 AM-11:00 AM**

AGEN1181, a clinical stage Fc-engineered anti-CTLA-4 antibody with improved therapeutic potential for the treatment of patients with advanced malignancies. *First Author: Steven O'Day, John Wayne Cancer Institute, Santa Monica, CA*

Background: AGEN1181 is a novel Fc-optimized anti-CTLA4 antibody, currently being evaluated in an ongoing multi-center, open-label, phase 1 study in all advanced solid tumors as mono-therapy and combination with anti-PD-1 antibody, AGEN2034 (NCT03860272). AGEN1181 is Fc-engineered to harness a novel mechanism for enhanced FcγR-dependent functionality relative to first-generation CTLA-4 antibodies. In pre-clinical models, AGEN1181 enhances T cell priming, depletion of intratumoral regulatory T cells (Treg) and improved memory formation compared to first-generation anti-CTLA-4 antibodies. Most notably, AGEN1181 demonstrates improved binding to FcγRIIIA and superior T cell responsiveness in populations that only express the low affinity FcγRIIIA receptor relative to first-generation IgG1 CTLA-4 antibodies. The combination of AGEN1181 and AGEN2034 further enhances T cell activation and effector function. **Methods:** This phase 1 study is an open-label, multi-center dose-escalation designed to evaluate the safety, tolerability, dose limiting toxicity (DLT) PK, and pharmacodynamic profiles of patients with refractory advanced solid tumors who did not receive an anti-CTLA4 previously. The study is being conducted in 3 arms; with patients assigned using a standard 3+3 dose escalation design in the mono-therapy arms with AGEN1181 and an accelerated design in the combination with AGEN2034 arm. AGEN1181 is administered as IV infusion as mono-therapy on Day 1 of every 3 weeks (0.1,0.3,1,2,4 mg/kg), every 6-weeks (1,2,4 mg/kg) in parallel cohorts and every 6-weeks (0.1,0.3,1,2,4 mg/kg) in combination with AGEN2034 (3mg/kg Q2Weeks) until disease progression or unacceptable toxicity (maximum 2 years). All 3 Arms are open and enrolling patients. The study is expected to enroll approximately 80 evaluable patients with solid tumors. Dose reductions are not allowed in the event of AGEN1181-related toxicities. Currently 3 cohorts have been completed, first cohort in the combination arm and the fourth cohort in the monotherapy arm are enrolling. Preclinical and clinical assessment of AGEN1181 supports continued development as a potential therapy for refractory or relapsed advanced solid tumors. Clinical trial information: NCT03860272. Research Sponsor: Agenusbio.

TPS3158 **Poster Session (Board #222), Fri, 8:00 AM-11:00 AM**

A phase Ib study of nivolumab in patients with autoimmune disorders and advanced malignancies (AIM-NIVO). *First Author: Ecaterina Elena Ileana Dumbrava, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Immune checkpoint inhibitors (ICI) such as anti-PD-1/PD-L1 antibodies have become a pivotal approach to cancer therapy. Nivolumab is an anti-PD1 antibody approved for an increasing number of solid tumors and hematological malignancies. However, patients (pts) with history of autoimmune disorders are excluded from the majority of clinical trials testing ICI. Consequently, the risks of flares and worsening of pre-existing autoimmune disorders in pts with tumor types who otherwise stand to benefit from ICI therapy are largely unknown, posing a challenge for oncologists. We are conducting a phase Ib study to test the hypothesis that nivolumab can be safely administered to pts with varying severity of Dermatomyositis, Systemic Sclerosis, Rheumatoid Arthritis, Systemic Lupus Erythematosus, Inflammatory Bowel Disease, Multiple Sclerosis, Sjögren's Syndrome and Other Autoimmune Disorders (AIM-Nivo). **Methods:** AIM-Nivo is an open-label, multi-center ongoing phase Ib study with nivolumab 480mg IV every 28 days in pts with autoimmune diseases and advanced malignancies (NCT03816345). The study has autoimmune disease-specific cohorts overseen by a multidisciplinary group of experts. The primary objective is to assess the overall safety and toxicity profile of nivolumab in pts with autoimmune disorders and advanced malignancies. Secondary objectives are to evaluate the antitumor efficacy, the impact of nivolumab on the autoimmune disease severity indices, and to explore potential biomarkers of response, resistance or toxicity. Key overall inclusion criteria include age ≥18 years, histologically confirmed advanced malignancies in which ICI are approved or have shown clinical activity. Key overall exclusion criteria include prior therapy with anti-PD-1/PD-L1 antibodies. Specific eligibility criteria are defined for each disease-specific cohort. For each autoimmune disorder, severity level of the disease as defined by disease-specific severity indices will be assessed, and up to a total of 12 pts will be included in each disease cohort at each severity level. Primary endpoints are dose-limiting toxicities, adverse events (AEs) and serious AEs. Continuous monitoring of toxicity will be conducted. Key secondary endpoints are best objective response, progression free and overall survival and cohort specific tumor tissue, blood and non-tumor tissue-based biomarkers. The AIM-Nivo trial opened in May 2019 and is enrolling pts through the National Cancer Institute Experimental Therapeutics Clinical Trials Network (ETCTN). Clinical trial information: NCT03816345. Research Sponsor: U.S. National Institutes of Health.

TPS3159 **Poster Session (Board #223), Fri, 8:00 AM-11:00 AM**

First-in-human phase I/II clinical trial of ONC-392: Preserving CTLA-4 immune tolerance checkpoint for safer and more effective cancer immunotherapy. *First Author: Christian Diego Rolfo, University of Maryland Marlene & Stewart Greenebaum Comprehensive Cancer Center, Baltimore, MD*

Background: A major paradigm in cancer immunotherapy is to use checkpoint inhibitors to break regulatory mechanisms that guard the host against autoimmune diseases. CTLA-4-targeting immunotherapy was the first example to establish this paradigm. However, the clinically tested anti-CTLA-4 antibodies exhibit suboptimal efficacy but high toxicity. Our recent studies have demonstrated that immunotherapy-related adverse events (irAE) and the cancer immunotherapeutic effect (CITE) represent distinct and therapeutically separable activities of anti-CTLA-4 antibodies. The irAEs are attributable to inactivation of the CTLA-4 checkpoint, while the CITE is effective through selective depletion of regulatory T cells (Treg) in the tumor microenvironment. We hypothesize that a safer and more effective CTLA-4-targeting immunotherapy should preserve the CTLA-4 checkpoint while enhancing the efficacy and selectivity of Treg-depletion in tumor microenvironment. In preparation to test this ground-breaking hypothesis clinically, we have generated a next generation of anti-CTLA-4 antibody that preserves the CTLA-4 immune checkpoint by avoiding lysosomal degradation of CTLA-4. The new antibody, ONC-392, has dramatically lower irAEs in a humanized mouse model and significantly more potent activity in depleting tumor-infiltrating Tregs, resulting in more effective CITE. **Methods:** This is an open label Phase IA/IB clinical study to test the safety, pharmacokinetics (PK), and efficacy of ONC-392 as a single agent and in combination with Pembrolizumab in advanced solid tumors and non-small cell lung cancer patients. The study consists of two linked parts: Part A is a dose-finding rapid titration study, with ONC-392 as a single agent in patients with advanced disease of various histology. The aim of this trial is to define the recommended Phase II dose for ONC-392 monotherapy (RP2D-M), Part B is a Phase IA/IB trial of ONC-392 in combination with a standard dose of 200 mg Pembrolizumab in patients with NSCLC. The trial consists of a dose-finding, dose escalation or de-escalation, Phase IA component aimed at defining the recommended phase II dose for ONC-392 in combination with a standard dose of Pembrolizumab (RP2D-C), then progressing into two parallel, single arm, Phase IB expansion cohorts to test for safety and initial efficacy in two groups of patients with NSCLC: Stage IV NSCLC anti-PD(L)1 immunotherapy naïve with PD-L1-positive (PD-L1 TPS ≥ 1%); Stage IV NSCLC refractory/resistant to anti-PD(L)1 immunotherapy. Clinical trial information: NCT04140526. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

TPS3160 Poster Session (Board #224), Fri, 8:00 AM-11:00 AM

A phase Ib, open-label, dose-escalation trial of naptumomab estafenatox (Nap) in combination with durvalumab (MEDI4736) in subjects with selected advanced or metastatic solid tumors. *First Author: Ravit Geva, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel*

Background: Immunotherapy with the anti-PD-(L)1 checkpoint inhibitors (CPIs) has been largely ineffective in so-called non-immunogenic "cold tumors". Facilitating T cell infiltration is necessary to invoke an immune response which may be augmented or complemented by the activity of CPIs like durvalumab. Selective T cell Redirection Proteins (STRs) are fusion proteins that consist of genetically engineered Superantigen (Sag) linked to Fragment antigen binding (Fab) moieties directed to tumor-associated antigens. Nap is a first in class STR compound, recognizing the tumor-associated oncofetal antigen 5T4, whereas the SAg moiety selectively engages the T cell receptor β variable (TRBV) 7-9. Nap has been shown to induce specific T cells expansion, activation and infiltration into the tumor in pre-clinical and clinical studies. Pre-clinical data demonstrated that the combination of STR with CPI may lead to long term durable responses not possible in most patients receiving single agent CPI therapy and suggests that combining CPIs with STR may be a promising therapeutic strategy for patients with solid tumors. **Methods:** Patients will be treated with the combination of Nap and durvalumab using a flat dose of durvalumab (1120 mg) and the 3+3 design for Nap dose escalation (2, 5, 10, 15 and 20 mcg/kg). The MTD of Nap for the combination treatment will be established based on DLTs occurring during the first treatment cycle. The dose escalation part will be followed by MTD expansion cohort in which 10–15 patients will be treated with MTD of Nap and 1120 mg durvalumab (Clinical trial registry number NCT03983954). Major eligibility criteria include patients with pretreated advanced or metastatic, 5T4 expressing solid tumors, including patients previously progressed on CPI therapy. As of January 2020, enrollment to dose levels 2, 5 and 10 mcg/kg has been completed without DLT, enrollment to dose level 15 mcg/kg will start on February 2020. Clinical trial information: NCT03983954. Research Sponsor: NeoTX Therapeutics Ltd., Pharmaceutical/Biotech Company

TPS3161 Poster Session (Board #225), Fri, 8:00 AM-11:00 AM

Phase II trial of Voyager-V1 (vesicular stomatitis virus expressing human IFNβ and NIS, VV1), in combination with cemiplimab (C) in patients with NSCLC, melanoma, HCC or endometrial carcinoma. *First Author: Mario Sznol, Yale School of Medicine and Smilow Cancer Center, Yale-New Haven Hospital, New Haven, CT*

Background: VV1 is an oncolytic vesicular stomatitis virus engineered to express human IFNβ to enhance cellular anti-tumor immune responses and tumor selectivity, and the human sodium iodide symporter (NIS) for virus tracking by SPECT imaging. Cancer cells are often hyporesponsive to IFNβ, enabling the efficient spread of VV1 and resulting in increased oncolysis. Differently from other oncolytic viruses, VV1 is suitable for both intra-tumoral (IT) and/or intra-venous (IV) administration. Despite considerable anti-tumor activity with checkpoint inhibitors (CPI) among some malignancies, long term survival and overall cures remain elusive. Prior Ph 1 studies have shown significant anti-tumor activity among several malignancies when VV1 was administered either as monotherapy or in combination with a CPI, despite progression on prior CPI monotherapy. Furthermore, pre- and post-treatment biopsy evaluations after VV1 treatment have demonstrated T cell infiltration and inflammation in both IT injected and non-injected lesions. Among IV treated patients (pts), IFNβ was detectable in the serum correlating with viral replication, making it an effective biomarker. C is a high-affinity potent human IgG4 anti-PD-1 monoclonal antibody. Though approved for use in cutaneous squamous cell carcinoma, C has shown anti-tumor activity, similar to other CPI, in several other indications. Therefore, VV1 and C could be an attractive combination for the immunotherapy for several solid tumors. This study represents the first clinical evaluation of VV1 in combination with C in pts with advanced solid tumors. **Methods:** The Ph 2 Simon 2 stage five-arm study of IV administration VV1 in combination with IV C will enroll pts with advanced NSCLC, HCC, melanoma & endometrial cancer. Enrolled pts with NSCLC & melanoma will be recent CPI-progressors, whereas enrolled HCC & endometrial cancer will be CPI-naïve. The study's objectives include assessment of preliminary anti-tumor activity, safety, & immuno-regulatory activity of the combination. Pts will receive IV VV1 once on D1 and IV C once every 3 weeks until confirmed disease progression or intolerable toxicity. Pts enrolled in one melanoma cohort will also receive IT VV1 administered to palpable lesions. Response will be assessed every 9 weeks per RECIST v1.1. The null hypothesis of each cohort's ORR will be tested versus a one-sided alternative yielding a Type I error rate of 5% and power of 80%. Cohorts will be expanded based on signal of activity. Clinical trial information: NCT. Research Sponsor: Vyriad Inc.

TPS3162 Poster Session (Board #226), Fri, 8:00 AM-11:00 AM

A phase Ia/Ib dose-escalation study of intravenously administered SB 11285 alone and in combination with nivolumab in patients with advanced solid tumors. *First Author: Filip Janku, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, MD Anderson Cancer Center, Houston, TX*

Background: Activation of the Stimulator of Interferon Genes (STING) pathway in immune cells in the tumor microenvironment (TME) and tumor cells results in the induction of innate and adaptive immunity and subsequent activation of cytotoxic T cells and NK cells for durable anti-tumor responses. SB 11285 is a novel agonist of the STING pathway leading to the activation of tumor-resident APCs and priming of tumor antigen specific CD8+ T cells. In our preclinical studies using multiple tumor-derived cell lines, SB 11285 has been observed to cause the induction of cytokines, such as INF-b, INF- a, TNFa and others consistent with engagement of the STING target, as well as tumor cell death by STING-mediated apoptosis. SB 11285 reduced tumor volumes in multiple rodent tumor models when administered intravenously, intraperitoneally or intratumorally as monotherapy or in combination with checkpoint inhibitors such as anti-CTLA-4 or anti-PD-1 antibody. Systemic administration could additionally facilitate trafficking of newly activated CD8+T cells from periphery into the tumor site. **Methods:** This open-label, multicenter phase 1a/1b clinical trial (NCT04096638) aims to enroll approximately 110 patients in the dose escalation (Part 1) and expansion cohorts (Part 2). Part 1 of the trial is a dose escalation study with IV SB 11285 monotherapy followed by combination with the checkpoint inhibitor nivolumab. Part 1 Dose Escalation of the study will evaluate ascending doses of intravenously administered SB 11285 with respect to dose-limiting toxicities (DLTs), maximum tolerated dose (MTD), recommended phase 2 dose (RP2D) and the pharmacokinetic (PK)/pharmacodynamic profile as monotherapy and in combination with nivolumab. SB 11285, with a starting dose of 0.3μg/kg, will be administered as monotherapy weekly on Days 1, 8, 15, and 22 of repeated 28-day cycles in escalating doses and in combination with nivolumab administered on Q4W schedule. Part 2 Expansion Cohorts of the study will explore initial signs of efficacy in pre-specified tumor types (such as Melanoma, Head and Neck squamous cell carcinoma) using the recommended phase 2 dose (RP2D) of SB 11285 in combination with nivolumab. In addition, the biological effects of SB 11285 will be evaluated by changes in immune cell types and activation state, serum cytokines, and gene expression patterns indicative of activation of the immune compartment. The trial is being conducted at multiple sites in the U.S . Clinical trial information: NCT04096638. Research Sponsor: Spring Bank Pharmaceuticals, Inc.

TPS3163 Poster Session (Board #227), Fri, 8:00 AM-11:00 AM

Phase I/II dose-escalation and expansion study of FLX475 alone and in combination with pembrolizumab in advanced cancer. *First Author: John D. Powderly, Carolina BioOncology Institute, Huntersville, NC*

Background: Regulatory T cells (T_{reg}) can dampen anti-tumor immune responses in the tumor microenvironment (TME). The predominant chemokine receptor on human T_{reg} is CCR4, the receptor for the chemokines CCL17 and CCL22, which are produced by tumor cells, tumor-associated macrophages and dendritic cells, as well as by effector T cells (T_{eff}) in the setting of an inflammatory anti-tumor response. Preclinical studies with orally-available CCR4 antagonists have demonstrated potent inhibition of T_{reg} migration into tumors, an increase in the intratumoral T_{eff}/T_{reg} ratio, and anti-tumor efficacy as a single agent and in combination with checkpoint inhibitors. In a first-in-human trial conducted in healthy volunteers, the oral CCR4 antagonist FLX475 was demonstrated to be well tolerated with outstanding PK properties. A robust PD assay measuring receptor occupancy on circulating T_{reg} demonstrated the ability to safely achieve exposure levels predicted to maximally inhibit T_{reg} recruitment into tumors via CCR4 signaling. These human PK, PD, and safety data have enabled a streamlined design of a Phase 1/2 study of FLX475 in cancer patients both as monotherapy and in combination with checkpoint inhibitor. **Methods:** This clinical trial is a Phase 1/2, open-label, dose-escalation and cohort expansion study to determine the safety and preliminary anti-tumor activity of FLX475 as monotherapy and in combination with pembrolizumab. The study is being conducted in 2 parts, a dose-escalation phase (Part 1) and a cohort expansion phase (Part 2). In Part 1 (Phase 1) of the study, at least 3 to 6 eligible subjects are being enrolled in sequential cohorts treated with successively higher doses of FLX475 as monotherapy (Part 1a) or in combination with pembrolizumab (Part 1b). In Part 2 (Phase 2) of the study, expansion cohorts of both checkpoint-naïve and checkpoint-experienced patients with tumor types predicted to be enriched for T_{reg} and/or CCR4 ligand expression (i.e. "charged tumors") -- including both EBV^+ and HPV^+ tumors and NSCLC, HNSCC, and TNBC -- will be enrolled using a Simon 2-stage design. As of February 4, 2020, Phase 1 dose escalation has been completed and a recommended Phase 2 dose chosen for both FLX475 monotherapy and combination therapy with pembrolizumab. Enrollment into Phase 2 expansion cohorts has been initiated. Clinical trial information: NCT03674567. Research Sponsor: RAPT Therapeutics.

TPS3164 Poster Session (Board #228), Fri, 8:00 AM-11:00 AM

AST-008: A novel approach to TLR9 agonism with PD-1 blockade for anti-PD-1 refractory Merkel cell carcinoma (MCC) and cutaneous squamous cell carcinoma (CSCC). *First Author: Mohammed M. Milhem, Holden Comprehensive Cancer Center, University of Iowa, Iowa City, IA*

Background: AST-008 is a potent spherical nucleic acid configuration of a toll-like receptor (TLR) 9 agonist oligonucleotide being developed for the treatment of MCC and CSCC in patients (pts) progressing on immune checkpoint inhibitor (CPI) monotherapy. Previously presented data suggests AST-008 elicits a Th1-type cytokine response and immune cell activation. This parallel-arm phase II design will permit assessment of efficacy in two advanced skin cancers with high unmet medical need. **Methods:** The study has an open label, multicenter phase Ib/II dose escalation/expansion design. The phase 1b dose escalation used a 3+3 design with increasing doses of intratumoral (IT) AST-008 plus standard flat dose pembrolizumab. The phase II dose expansion is using the recommended regimen (RP2D) of IT AST-008 plus flat dose pembrolizumab or cemiplimab to treat two cohorts of pts with advanced/metastatic MCC or CSCC, respectively. The key objective of the phase II expansion is to provide an estimate of preliminary efficacy of IT AST-008 with pembrolizumab or cemiplimab in pts whose disease progressed on a single-agent CPI therapy. Endpoints also include safety, pharmacokinetic and pharmacodynamic assessments. Pts must have at least two evaluable lesions by RECIST v1.1. One or more lesions may be injected with AST-008, but one lesion (the "witness" lesion) must remain un-injected throughout the study to differentially assess effects of AST-008 on the injected and witness lesions. The RP2D of AST-008 was derived from the dose escalation phase together with pembrolizumab. That RP2D is being used not only in the MCC cohort where AST-008 is combined with pembrolizumab, but also in the CSCC cohort where AST-008 is combined with cemiplimab. To ensure safety of the AST-008/cemiplimab combination, the first 6 pts in the CSCC cohort will be monitored for dose limiting toxicities through the first 5 weeks of dosing, and then the data review committee will assess safety before approving additional patient enrollment to that cohort. Each expansion cohort will enroll up to 29 pts with a Simon two-stage optimal design. In the first stage, 10 pts will be accrued. If there are 0 responses in these 10 pts, enrollment in that arm will be stopped. Otherwise, 19 additional pts will be accrued for a total of 29. The null hypothesis will be rejected if 4 or more responses are observed in 29 pts. This design yields a type I error rate of 0.05 and power of 80% when the true response rate is 20%. The planned phase II enrollment is 58 pts across about 15 US-based sites. Clinical trial information: NCT03684785. Research Sponsor: Exicure Inc.

TPS3165 Poster Session (Board #229), Fri, 8:00 AM-11:00 AM

A phase I/II first-in-human study of a novel anti-MAGE-A4 TCR/anti-CD3 bispecific (IMC-C103C) as monotherapy and in combination with atezolizumab in HLA-A*02:01-positive patients with MAGE-A4-positive advanced solid tumors (IMC-C103C-101). *First Author: George R. Blumenschein, Jr., Department of Thoracic and Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: ImmTAC bispecifics are unique T cell receptor (TCR)/anti-CD3 bispecific molecules that are designed to redirect polyclonal T cells against intracellular antigens, in contrast to antibody-based therapies, which are limited to extracellular antigens. ImmTAC molecules recognize a specific peptide presented on defined Class I HLA molecules via an affinity enhanced, engineered, soluble TCR. Through the addition of an anti-CD3 scFv effector domain fused to the TCR targeting domain, ImmTAC molecules redirect T cell activity against cancer cells, regardless of the specificity of the T cell. IMC-C103C is an ImmTAC being investigated against MAGE-A4, which is among the most commonly expressed cancer testis antigens in solid malignancies, but with minimal to absent expression on normal tissues and/or hematopoietic cells. The most advanced ImmTAC in development, tebentafusp (IMCgp100), directed against melanocyte-associated lineage antigen gp100, has shown monotherapy activity in uveal melanoma and PD-1 refractory advanced cutaneous and uveal melanoma. Tebentafusp is being further evaluated in combination with durvalumab and tremelimumab. **Methods:** IMC-C103C-101 is a multi-center, open-label, Phase 1/2 first-in-human study of IMC-C103C as monotherapy and combination with atezolizumab in HLA-A*02:01-positive patients with MAGE-A4-positive advanced cancers. The study includes IMC-C103C monotherapy (Q1W) dose escalation, followed by expansion into indication specific arms to test for efficacy in defined patient cohorts. Concurrently, combinations with atezolizumab are planned. Primary objectives of dose escalation are to identify the MTD/RP2D, and characterize safety/tolerability. Secondary objectives include an assessment of efficacy (best overall response by RECIST v1.1), PK, PD, and ADA. IMC-C103C monotherapy dose escalation is in progress. Clinical trial information: NCT03973333. Research Sponsor: Immunocore Ltd, Pharmaceutical/Biotech Company.

TPS3166 Poster Session (Board #230), Fri, 8:00 AM-11:00 AM

Trial in progress: A phase I/II, open-label, dose-escalation, safety and tolerability study of NC318 in subjects with advanced or metastatic solid tumors. *First Author: Martin Gutierrez, Hackensack University Medical Center, Hackensack, NJ*

Background: Siglec-15 (S15) is a member of the Siglec family (Sialic acid-binding Immunoglobulin Lectins), a distinct subgroup of immunoglobulin (Ig) superfamily proteins involved in discriminating self from non-self-immune regulation (Macauley MS et al. 2014). Nonclinical models demonstrate S15 mediates suppression of T cell proliferation and negatively regulates T cell function. NC318 is a first-in-class monoclonal antibody that blocks S15-mediated immune suppression and prevents tumor growth by normalizing T cell function and restoring anti-tumor immunity in the tumor microenvironment (Wang J et al. 2019). The clinical hypothesis of this study is that NC318 targeting of S15 can improve anti-tumor immune response and provide benefit in multiple oncology indications. **Methods:** This is a multi-center, first in human, phase 1/2, open-label, non-randomized study to determine the safety and tolerability, define maximum tolerated dose and/or pharmacologically active dose, assess preliminary efficacy, and explore predictive and pharmacodynamic biomarkers of NC318 in subjects with advanced or metastatic solid tumors. Key eligibility criteria included measurable disease based on RECIST v1.1 and consent for collection of biopsies at screening and on treatment (optional for phase 1). Phase 1 used a 3+3 dose escalation design to determine the recommended phase 2 dose (RP2D) and schedule of NC318 while identifying drug related toxicities (DLTs). Phase 2 enrollment is limited to non-small cell lung, ovarian, head and neck, and triple negative breast cancer subjects with PD-L1 tumor proportion scores $<$50% (additional tumor types are being evaluated for inclusion). Ongoing exploratory analyses include the assessment of predictive biomarkers associated with treatment benefit, and pharmacodynamic markers associated with study drug activity (e.g. evaluation of tumor biopsies and peripheral markers of inflammation). Phase 1 enrollment began October 2018 and completed in August 2019. The RP2D was defined and the phase 2 opened to enrollment October 2019. Clinical trial information: NCT03665285. Research Sponsor: NextCure, Inc.

TPS3167 Poster Session (Board #231), Fri, 8:00 AM-11:00 AM

Phase II basket trial of olaparib and durvalumab in patients (pts) with isocitrate dehydrogenase (IDH) mutated solid tumors. *First Author: Eric Xueyu Chen, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada*

Background: Somatic IDH mutations are common in low grade gliomas, and rare in other solid tumors with the exception of intrahepatic cholangiocarcinoma (ICA) and certain subtypes of chondrosarcoma. IDH mutations confer a gain-of-function neomorphic activity, such that mutant IDH enzymes preferentially convert αKG to 2-hydroxyglutarate (2HG), resulting in abnormal accumulation of 2HG. 2HG competitively inhibits αKG-dependent dioxygenases, many of which are involved in DNA repair. Preclinical studies show that IDH mutated cancer cells have defective homologous recombination repair and are exquisitely sensitive to poly (adenosine 5'-diphophate-ribose) polymerase (PARP) inhibition. **Methods:** This is a single arm phase II basket study (NCT03991832). Pts with IDH mutated solid tumors are divided into three cohorts; A: low-grade glioma; B: cholangiocarinoma; C: all other solid tumors. Pts are treated with olaparib 300 mg twice daily continuously and durvalumab 1500 mg every 4 weeks until progression, intolerable toxicity or consent withdrawal. Radiological assessment is performed after every 2 cycles of study treatments. Major eligibility criteria include IDH mutation by immunohistochemistry or sequencing, up to 2 lines of systemic therapy for advanced disease, performance status 0 – 2 and adequate organ function. Pts are excluded if they received prior PARP inhibitors and anti-PD-1/PD-L1 antibody. The Simon's optimal 2-stage design is applied for Cohorts A and B. 10 pts will be enrolled in each of Cohort A and B initially. If 2 or more partial responses (PR) are seen in these 10 pts, additional 19 pts will be enrolled for a total of 29 pts in that cohort. The combination is considered to be of clinical interest for further development if $\geq$ 6 PRs are seen in each cohort. Cohort C will enroll 20 pts. Archival tumor tissues and serial blood samples will be collected on study. 2HG levels will be measured and correlated with responses. The study was activated in December 2019. 3 pts have been enrolled into Cohort B. Clinical trial information: NCT03991832. Research Sponsor: None.

TPS3168 Poster Session (Board #232), Fri, 8:00 AM-11:00 AM

First-in-human phase Ib study of ATRC-101, an engineered version of a patient-derived antibody targeting a tumor-restricted ribonucleoprotein complex. *First Author: Jonathan Eliot Benjamin, Atreca, Inc., South San Francisco, CA*

Background: ATRC-101 is a fully human, engineered IgG1 version of an antibody discovered through a a target-agnostic screen to identify patient-derived antibodies that bind selectively to public tumor antigens. The parental antibody was identified from B cells in the active immune response of a patient receiving checkpoint therapy for Stage IV non-small cell lung cancer (NSCLC). A fluorescently conjugated version of ATRC-101 binds selectively to human tumor specimens including a majority of NSCLC, acral melanoma, breast, colorectal, and ovarian cancer samples. No reactivity of toxicological significance is found across a wide range of normal human tissues. ATRC-101 displays dose-dependent, single-agent activity in syngeneic mouse tumor models, including the EMT6 breast cancer model, which displays a T cell-excluded microenvironment often observed in human tumors, and in which checkpoint inhibitors targeting the PD-1 axis exhibit limited activity. Dosing with ATRC-101 in the EMT6 model causes marked changes in the tumor microenvironment, including a shift from the M2 to the M1 macrophage phenotype and infiltration of T cells. ATRC-101 does not appear to act via NK cell-driven ADCC; instead, activity *in vivo* is dependent both on Fc region interactions with Fc receptors, likely on myeloid rather than lymphoid cells, and on the presence of CD8+ T cells. ATRC-101 binds to a target that is a ribonucleoprotein (RNP) complex containing polyadenylate-binding protein 1 (PABP-1) bound to poly(A)RNA. Whereas both PABP-1 and poly(A)RNA are ubiquitously expressed at high levels in normal tissues and have been localized intracellularly, the ATRC-101 target is detected extracellularly on tumor cells grown *in vivo*. The basis for the tumor-selectivity of ATRC-101 as well as the extracellular localization of the target is under investigation. Ascending doses of ATRC-101 were well tolerated in multiple non-clinical safety studies. **Methods:** ATRC-101-A01 is an open-label, 3+3, Phase 1b safety study in patients with acral melanoma, NSCLC, breast, ovarian, and colorectal cancers. Participants are accruing in the first dose cohort. ATRC-101 is administered every 21 days up to 24 months or until disease progression. The primary objective of the trial is to determine the safety and tolerability of ATRC-101. Secondary objectives are to characterize the pharmacokinetic profiles of ATRC-101 and to assess antitumor activity as determined by RECIST 1.1 and lymphocytic infiltration in the tumor microenvironment. Clinical trial information: NCT04244552. Research Sponsor: Atreca, Inc.

TPS3170 Poster Session (Board #234), Fri, 8:00 AM-11:00 AM

Phase I/II open label nonrandomized safety and efficacy study of the viral vectored ChAdOx1-MVA 5T4 immunotherapy in combination with PD-1 checkpoint blockade in intermediate-risk localized or locally advanced prostate cancer and advanced metastatic prostate cancer. *First Author: Mark Tuthill, The Jenner Institute, University of Oxford, Oxford, United Kingdom*

Background: Antigen-specific immunotherapy (Sipuleucel-T) is licenced for the treatment for castrate resistant prostate cancer, but has modest clinical efficacy and is complex to administer to patients. New therapeutic antigen-specific approaches are required to generate and sustain therapeutic immune responses against tumour specific antigens in men with early and advanced prostate cancer. We have previously reported immunogenicity and efficacy data of a novel viral vectored vaccines-based immunotherapy based on two replication-deficient viruses, chimpanzee adenovirus (ChAdOx1) and MVA, targeting an oncofetal self-antigen 5T4, administered as a single agent and in combination with anti-PD-1 in mouse tumour models. We tested this immunotherapy alone in a first-in-human trial, VANCE (NCT02390063), in intermediate risk prostate cancer patients. Based on encouraging safety and exceptional T cell immunogenicity of the VANCE study, the phase I/II trial, ADVANCE (NCT03815942) is being undertaken to test the immunotherapy safety and efficacy in combination with PD-1 blockade in intermediate risk disease and metastatic prostate cancer. **Methods:** Study design: ADVANCE, an open label non-randomised phase I/II study, will recruit 12 patients with intermediate-risk prostate cancer patients (Gleason score $\leq$ 7, local tumour stage $\leq$T3c, PSA$\leq$ 20 ng/ml) scheduled to undergo radical prostatectomy (Cohort 1) and 24 mCRPC patients with disease progression on anti-androgen therapy with either enzalutamide or abiraterone (Cohort 2). Cohort 1 will receive one cycle of ChAdOx1-MVA 5T4 immunotherapy and a single nivolumab infusion. Cohort 2 will receive 2 cycles of ChAdOx1-MVA 5T4 vaccination and three nivolumab infusions. Primary endpoint: Cohort 1 - PSA change from baseline to surgery, Cohort 2 – composite response rate measured as either $\geq$50% reduction of circulating tumour DNA or $\geq$50% serum PSA decrease from baseline at 24-week assessment and the maximal response rate. Secondary and exploratory endpoints include 5T4-specific immune response in the periphery, progression-free and overall survival and reduction of circulating tumour cells. 23 of planned 24 patients have been enrolled in Cohort 2. Enrolment to the Cohort 1 is ongoing. The data analysis is expected to be completed by Q4 2020 for Cohort 2. Clinical trial information: NCT03815942. Research Sponsor: Grant agreement No. 602705.

TPS3171 Poster Session (Board #235), Fri, 8:00 AM-11:00 AM

A phase I/II study of HB-201, an arenavirus-based cancer immunotherapy, alone, or in combination with anti-PD-1 in patients with HPV16+ cancers. *First Author: Bharat Burman, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Human Papillomavirus 16 (HPV16) is linked to several cancer types; treatment options are limited for patients with HPV16+ recurrent or metastatic cancers. The generation and maintenance of the HPV16+ malignant state requires the stable expression of HPV16-specific E7 and E6 oncogenes, which can also serve as immunogenic tumor-associated antigens. HB-201 is a replication-competent live-attenuated vector based on the arenavirus LCMV encoding a non-oncogenic E7 and E6 fusion protein. In preclinical models, both intravenously (IV) and intratumorally (IT) administered HB-201 demonstrate potent immunogenicity by induction of HPV16-specific cytotoxic T cells and associated efficacy. **Methods:** This is a first in human, Phase I/II study of HB-201 monotherapy or in combination with PD-1 immune checkpoint inhibitor (anti-PD-1) in HPV16+ confirmed recurrent/metastatic cancers. Phase I consists of 2 treatment groups, each conducted with a 3+3 dose escalation design. Group 1 is enrolling patients with HPV16+ head and neck squamous cell carcinoma who will receive HB-201 IV only. Group 2 is enrolling HPV16+ cancer patients with a safely accessible tumor site who will receive HB-201 IT for the first dose, followed by HB-201 IV for subsequent doses (IT-IV). HB-201 will be administered every 21 days. The Phase II component will be conducted with the recommended Phase II doses (RP2Ds) defined in Phase I and will consist of 3 groups: Group A (HB-201 IV only), Group B (HB-201 IV plus anti-PD-1), and Group C (HB-201 IT-IV). Key eligibility criteria include age $>$ 18, ECOG performance status 0-1, confirmed HPV16+ recurrent or metastatic cancer, disease progression from at least 1 systemic standard of care therapy, and measurable disease per RECIST v1.1. The Phase I primary objective is to determine RP2Ds for IV and IT HB-201. The Phase II primary objective is to assess antitumor activity. Secondary endpoints for both phases include safety, tolerability, overall survival, progression-free survival, and duration of response. Exploratory objectives include characterization of immunogenicity of HB-201 and biomarkers associated with immune or antitumor response. Enrollment to Groups 1 and 2 began in December 2019. Clinical trial information: NCT04180215. Research Sponsor: Hookipa Pharma.

TPS3172 Poster Session (Board #236), Fri, 8:00 AM-11:00 AM

Safety and efficacy of neoadjuvant intravesical oncolytic MV-NIS in patients undergoing radical cystectomy (RC) for urothelial carcinoma but ineligible for neoadjuvant cisplatin-based chemotherapy. *First Author: Bradley C. Leibovich, Mayo Clinic, Rochester, MN*

Background: Bladder cancer is a leading cause of cancer death in the United States. Over 90% of bladder cancer cases are urothelial carcinomas (UC) that may present as a non-muscle-invasive (NMIBC) or muscle-invasive disease (MIBC). Standard of care for NMIBC includes transurethral resection of bladder tumor (TURBT), intravesical chemotherapy and immunotherapy with Bacillus Calmette-Guerin (BCG). Patients (pts) with high-grade BCG-refractory NMIBC or MIBC undergo RC, which involves complete bladder removal and pelvic lymphadenectomy. RC severely impacts quality of life with significant morbidity. Oncolytic viruses are showing promise in UC, and MV-NIS has proven efficacy in other tumor types. MV-NIS is an investigational oncolytic measles virus with an excellent safety profile, irrespective of route of administration ($n > 100$). MV-NIS-related adverse events are limited to infusion reactions and transient CBC changes, and little local toxicity is anticipated with intravesical therapy. Clinical efficacy of this oncolytic may be related to absence of measles immunity. Based on this, the clinical strategy for MV-NIS is focused on targeting immune-privileged sites via intra-tumoral or intravesical routes, alone or in combination with checkpoint inhibitors. We hypothesize that intravesical therapy with oncolytic MV-NIS can improve clinical outcomes for (a) BCG refractory NMIBC pts to avoid or delay the need for RC; and (b) MIBC pts undergoing RC. **Methods:** This study is enrolling pts undergoing RC who are ineligible to receive neoadjuvant chemotherapy. The trial has 2 stages to (a) determine the safety and tolerability of intravesical MV-NIS, and (b) assess preliminary efficacy. Part (a) includes 4-24 pts in a timing cohort with doses administered at increasing durations (1-4 weeks) prior to RC to establish safety of a single MV-NIS dose. Part (b) includes an expansion cohort ($n = 12$) to evaluate the safety and efficacy of 2 intravesical doses of MV-NIS at 2-week intervals prior to RC. Safety is assessed using NCI-CTCAE V5 and Clavien-Dindo grading of operative complications. The efficacy endpoint is pathologic stage at time of RC (pT0 rate), which can be compared to pre-study TURBT stage. Additional exploratory studies include PK and PD analyses in urine, blood and tumor. Enrollment is ongoing at 2 Mayo Clinic sites (Rochester, MN and Jacksonville, FL) and the study has now progressed from the timing cohort into the expansion cohort. Clinical trial information: NCT03171493. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

TPS3173 Poster Session (Board #237), Fri, 8:00 AM-11:00 AM

Phase I study of NBTXR3 activated by radiotherapy in patients with advanced cancers treated with an anti-PD-1 therapy. *First Author: Colette Shen, University of North Carolina at Chapel Hill, Chapel Hill, NC*

Background: Despite the past decade of transformative advances in immuno-oncology, the response rate to checkpoint inhibitors (ICIs) remains low (~15%). There is significant interest in developing strategies to overcome resistance to these treatments, thus increasing response rate. Emerging evidence suggests that radiation therapy (RT) could potentially augment the antitumor response to ICIs through synergic effect. However, RT dose and ultimate efficacy are limited by toxicity related to exposure of healthy tissues. NBTXR3 is a first-in-class radioenhancer administered by direct intratumoral injection, designed at the nanoscale to increase RT dose deposition within tumor cells and RT-dependent tumor cell killing, without increasing surrounding normal tissue toxicity. Preclinical and early clinical data suggest NBTXR3 activated by RT can trigger an anti-tumor immune response, producing both local and systemic (abscopal) effects. We hypothesize that NBTXR3 activated by RT, in combination with anti-PD-1 therapy (R3/RT/PD-1), will act synergistically to maximize the local RT effect and produce a systemic response sufficient to increase the proportion of ICI responders or convert ICI non-responders to responders. **Methods:** This trial [NCT03589339] is a multicenter, open-label, phase I study to evaluate safety and tolerability of R3/RT/PD-1 in three cohorts: (1) Locoregional recurrent or recurrent and metastatic head and neck squamous cell carcinoma (HNSCC) amenable to re-irradiation of the HN field, (2) Lung metastases, or (3) Liver metastases, both from any primary cancer eligible for anti-PD-1 treatment. Approximately two-thirds of patients in each cohort will be anti-PD-1 non-responders. NBTXR3 injected volume is based on a percentage of gross tumor volume (GTV). The primary objective is to determine the R3/RT/PD-1 recommended phase 2 dose in each cohort. Secondary objectives are to evaluate anti-tumor response (objective response rate; ORR), safety and feasibility of NBTXR3 injection, and NBTXR3 body kinetic profile. Exploratory objectives will assess biomarkers of R3/RT/PD-1 response, including PD-L1 status by IHC, as well as mRNA and cytokine immune marker profiling. To date, three patients have been treated, one in cohort 1, two in cohort 2. Clinical trial information: NCT03589339. Research Sponsor: Nanobiotix, SA.

3500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

First-in-human phase I study of ARV-110, an androgen receptor (AR) PROTAC degrader in patients (pts) with metastatic castrate-resistant prostate cancer (mCRPC) following enzalutamide (ENZ) and/or abiraterone (ABI). *First Author: Daniel Peter Petrylak, Smilow Cancer Center, Yale University, New Haven, CT*

Background: Proteolysis Targeting Chimera (PROTAC) protein degraders induce selective degradation of targeted proteins by engaging the ubiquitin proteasome system. ARV-110 is an orally bioavailable PROTAC that specifically degrades AR ≥ 95% and achieves anti-tumor activity in ENZ-naïve and -resistant prostate cancer xenograft models. **Methods:** To define the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D) of ARV-110, pts with ≥ 2 prior therapies for mCRPC, including ENZ and/or ABI, received ARV-110 orally once daily. Dose escalation is per 3+3 design. Endpoints include dose limiting toxicities (DLTs), adverse events (AEs), pharmacokinetics (PK), biomarkers (e.g., AR mutation analysis), RECIST and PSA response. **Results:** By January 2020, 18 pts were dosed: 35 mg (N = 3), 70 mg (N = 4), 140 mg (N = 8), 280 mg (N = 3). 12 pts received both ENZ and ABI; 14 received prior chemotherapy. 1 of 18 pts experienced a DLT (280 mg) of Grade (Gr) 4 elevated AST/ALT followed by acute renal failure while taking rosuvastatin (ROS). A 2nd pt had Gr 3 AST/ALT with ROS that resolved off ROS, permitting ARV-110 retreatment. ROS plasma concentrations demonstrated significant increases concurrent with AST/ALT elevations in both pts. Subsequently, ROS was prohibited without further ≥Gr 2 AST/ALT AEs. No other related Gr 3/4 AEs were reported. ARV-110 PK was generally dose proportional and at 140 mg reached levels associated with preclinical anti-tumor activity. 15 pts were evaluable for PSA response (excludes 1 pt stopped after 1 dose for early progression and 2 pts initiated 2 weeks before cutoff, all at 140 mg). Of these, 8 pts initiated dosing at ≥140 mg. 2 pts achieved confirmed PSA declines of >50%, both at 140 mg. Prior therapy in both pts included ENZ and ABI, chemotherapy, bicalutamide and radium-223 plus other regimens. 1 pt had 2 AR mutations known to confer ENZ resistance. The 2nd pt also achieved an unconfirmed RECIST partial response (confirmatory scan pending). Both responses were ongoing at data cutoff (8+ and 21+ weeks of treatment). **Conclusions:** To date, ARV-110 has an acceptable safety profile. Concurrent ROS is now prohibited. MTD has not yet been established; determination of RP2D continues. ARV-110 demonstrates antitumor activity in mCRPC after ENZ/ABI with 2 ongoing confirmed PSA responses, one of which was associated with tumor reduction. Updated data for this first PROTAC in clinical testing will be presented. Clinical trial information: NCT03888612. Research Sponsor: Arvinas.

3501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase I/II study of avadomide (CC-122) in combination with R-CHOP for newly diagnosed DLBCL. *First Author: Neha Mehta-Shah, Washington University School of Medicine, St. Louis, MO*

Background: In certain subsets of patients (pts) with diffuse large B-cell lymphoma (DLBCL), the failure rate of standard R-CHOP treatment is high. Pts with high-risk disease (International Prognostic score [IPI] 3-5) have a particularly poor prognosis, with 3-y survival rates of ~62% with R-CHOP alone. The cereblon E3 ligase modulator avadomide (CC-122) showed activity in pts with relapsed or refractory DLBCL. We report results of avadomide plus R-CHOP in previously untreated pts with high-risk DLBCL. **Methods:** CC-122-DLBCL-002 (NCT03283202) is a phase 1/2 study of avadomide plus R-CHOP-21 in pts newly diagnosed with DLBCL not otherwise specified with IPI scores 3-5 who were aged ≥18 y. Pts received standard R-CHOP and escalating doses (1-3 mg) of oral avadomide for up to six 21-d cycles (Table). All pts received pegfilgrastim support. Primary objectives were to assess safety, tolerability, and complete response (CR) rate. Secondary objectives include evaluation of additional efficacy parameters (objective response rate [ORR], progression-free survival [PFS], and overall survival) and biomarkers. **Results:** As of July 30, 2019, 35 pts were enrolled in the phase 1 part of the study. Median age was 66 y (range, 20-75), 23 pts (66%) were aged > 60 y, 18 (51%) had an IPI score of 3, and 17 (49%) had an IPI score of 4-5. Thirty-two pts (91%) completed 6 cycles of treatment. Median relative total dose intensity of avadomide was 99% and the average relative dose intensity of R-CHOP was 95%. Six pts had dose-limiting toxicities: 1 pt had neutropenia and bacterial hepatic infection; 1 had pneumonia; 1 had febrile neutropenia (FN); 1 had FN and hypotension; 1 had FN due to skin infections; and 1 had sepsis. The recommended phase 2 dose was 3 mg 2/3 wk. Grade 3/4 adverse events in ≥10% of pts were neutropenia (54%), anemia (20%), leukopenia (20%), lymphopenia (14%), hypophosphatemia (14%), and FN (11%). Among 34 efficacy-evaluable pts, the ORR was 88% (n = 30/34), including a CR rate of 79% (n = 27/34) at the end of treatment. With a median follow-up of 10 mo, the 1-y PFS rate was 80% (95% CI, 58-92). Correlative analyses will be presented at the meeting. **Conclusions:** Avadomide plus R-CHOP was well-tolerated with no significant additive toxicities. The promising efficacy in this high-risk pt population warrants further evaluation of immunomodulatory drugs combined with immunochemotherapy for pts with previously untreated DLBCL. Clinical trial information: NCT03283202.Research Sponsor: Celgene, a wholly owned subsidiary of Bristol-Myers Squibb.

Dose Level	Avadomide Dose	Schedule
1	1 mg	D1-5 & D8-12 (5/7 d; 2/3 wk)
2	2 mg	D1-5 & D8-12 (5/7 d; 2/3 wk)
3	3 mg	D1-5 & D8-12 (5/7 d; 2/3 wk)
4	3 mg	D1-5, D8-12, & D15-19 (5/7 d; 3/3 wk)

3502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

CX-2029, a PROBODY drug conjugate targeting CD71 (transferrin receptor): Results from a first-in-human study (PROCLAIM-CX-2029) in patients (Pts) with advanced cancer. *First Author: Melissa Lynne Johnson, Sarah Cannon Research Institute, Nashville, TN*

Background: CX-2029 is a PROBODY drug conjugate (PDC) of MMAE, a potent microtubule inhibitor, directed against CD71 (transferrin receptor 1). In addition to being an abundant tumor antigen, CD71 is highly expressed on normal cells, precluding targeting by a traditional antibody drug conjugate (ADC). PDCs are masked ADCs, unmasked predominantly by tumor-associated proteases, thereby restricting target engagement to tumors. Both a CD71 PDC and ADC displayed broad activity in multiple xenograft tumor models; in toxicology studies, the PDC was tolerable at doses consistent with efficacy in non-clinical tumor models while the ADC was not. **Methods:** In a phase 1/2 first-in-human study of PDC CX-2029 in advanced solid tumors (NCT03543813), pts with ECOG 0–1 and ≥1 prior systemic therapy were enrolled into escalating dose cohorts of the PDC CX-2029 given IV every 21 days. Endpoints included evaluation of MTD, safety, antitumor activity, and potential biomarkers; plasma and tissue samples were collected for PK/PD analyses. Preliminary results are reported. **Results:** As of 30 November 2019, 34 pts were enrolled (median age 59 y; 59% male; 71% ECOG 1; median [range] of 3 [1–16] prior therapies). Pts received a median of 3 (1–12) CX-2029 doses. Starting dose for escalation was 0.1 mg/kg. Following a single CX-2029 dose, median molar ratio of masked CX-2029 to total CX-2029 for AUC_{tau} was 0.938 (0.864–0.942); the ratio of free MMAE to total CX-2029 was <0.03. Infusion-related reactions were the most common treatment-related AE (TRAE) of any grade (88%; primarily low grade and with first infusion), followed by anemia (56%), fatigue and nausea (24% each), neutropenia (21%), and leukopenia (12%). Grade 3+ TRAEs in ≥10% pts were anemia (35%) and neutropenia (18%). In 32 response-evaluable pts, 1 pt had a confirmed partial response (squamous NSCLC); 9 had stable disease including 1 pt with ocular melanoma treated for 36 weeks. **Conclusions:** The observed safety profile for CX-2029 effectively reduces on-target toxicity for this previously undruggable target, supporting the PROBODY platform. Evidence of anti-tumor activity was observed. Dose escalation continues. Clinical trial information: NCT03543813. Research Sponsor: CytomX Therapeutics, Inc.

3503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Results from a phase I, open-label study of ceralasertib (AZD6738), a novel DNA damage repair agent, in combination with weekly paclitaxel in refractory cancer (NCT02630199). *First Author: Jeeyun Lee, Samsung Medical Center, Seoul, South Korea*

Background: Ataxia Telangiectasia and Rad3 Related (ATR) is an apical kinase with a critical role in the DNA-damage response. During normal DNA replication, ATR is recruited at stalled replication forks which can progress to double strand breaks if left unrepaired. AZD6738 is an oral inhibitor of the serine/threonine protein kinase ATR, a member of the phosphoinositide 3-kinase related kinase (PIKK) family. **Methods:** Eligible patients (pts) with advanced solid tumours were administered AZD6738 in combination with fixed dose paclitaxel 80 mg/m2 D1, D8, D15 in 28-day cycles. The dose of AZD6738 was escalated to reach a maximum tolerated dose (MTD) in a rolling 6 design. The trial evaluated safety, MTD, pharmacokinetics (PK) and pharmacodynamics (PD). Translational studies on plasma samples included cytokine analysis, panel sequencing of ctDNA, as well as IHC and immunofluorescence of immune cell markers. **Results:** 58 pts (34 melanoma, 15 gastric cancer (GC), 4 sarcoma, 3 colon cancer, 1 neuroendocrine and 1 hepatocellular cancer) were enrolled in 7 dose cohorts ranging 40mg OD to 240 mg BID. One dose-limiting toxicity (DLT) of neutropenic fever occurred in each cohort of n = 6 evaluable pts at AZD6738 160 mg BD and 240 mg BD days 1-14. Per protocol, the maximum tolerated dose of AZD6738 is 240 mg BID days 1-14. The most common toxicities (all causality, all grade) were: anorexia/nausea (n = 15, 26%), leukopenia (n = 11, 19%) and anemia (n = 11, 19%). 51 pts are evaluable for efficacy; we observed 1 complete response (1.9 %, melanoma), 12 confirmed partial responses (23.5%; 2 gastric, 10 melanoma all of which were post-immunotherapy), 18 stable disease (35.3%) and 20 disease progression (39.2%). The overall confirmed response rate from the dose escalation is 25.5%. Genomic analysis of baseline plasma (27 pts) revealed enrichment of NF1 somatic mutations and activating NRAS mutations amongst melanoma pts (6/18 and 4/18, respectively). Cyclical changes in interleukin-12 levels were observed in three pts with disease control which could reflect an immunological component to the mechanism of response. We will present a comprehensive case report of a patient with dramatic and durable response. **Conclusions:** We conclude that AZD6738 can be safely combined with weekly paclitaxel and propose a recommended phase II dose and schedule. The combination of AZD6738 and paclitaxel demonstrated promising anti-tumor activity with durable responses, especially in melanoma pts after failing anti-PD1 therapy. Clinical trial information: NCT02630199. Research Sponsor: None.

3504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase I monotherapy dose escalation of RGX-202, a first-in-class oral inhibitor of the SLC6a8/CKB pathway, in patients with advanced gastrointestinal (GI) solid tumors. *First Author: Johanna C. Bendell, Sarah Cannon Research Institute, Tennessee Oncology, PLLC, Nashville, TN*

Background: About 65% of advanced colorectal cancer (CRC) patients (pts) have creatine kinase B (CKB) expressing tumors. CKB expressing (CKB+) GI cancer cells import creatine via the creatine transporter SLC6a8 and utilize it to generate intracellular ATP. RGX-202, a small molecule inhibitor of SLC6a8, reduces intracellular creatine and ATP levels, leading to apoptosis. RGX-202 treatment triggers complete tumor regressions in multiple CKB+ preclinical models, including KRAS mutant CRC. **Methods:** RGX-202-001 is a phase I escalation/expansion study of RGX-202 +/- FOLFIRI in pts with advanced GI tumors. The primary safety objective during dose escalation is to identify the maximum tolerated dose (MTD), or the maximum tested dose at which multiple dose-limiting toxicities (DLTs) are not observed. The primary efficacy objective is to estimate the antitumor activity of RGX-202 by RECIST. **Results:** As of January 31, 2020, 17 pts have been treated in 4 single agent dose escalation cohorts: 600 mg BID (3 pts), 1200 mg BID (4 pts), 2400mg BID (5 pts) and 3600mg BID (5pts) given continuously. No DLTs were observed and an MTD was not reached. Treatment-related adverse events (TRAEs) occurring in $>$ 2 pts are shown in the Table. There were no Grade 4 TRAEs. At the highest dose, 2 of 3 CRC pts had prolonged disease control: a patient with a KRAS G13D mutant cancer had SD for 14 weeks; and a patient with KRAS G12V mutant (MSS) cancer had a confirmed PR ongoing at 30 weeks. Exposure to RGX-202 was greater than dose-proportional and the average $AUC_{0\text{-}24}$ ranged from ~15,700 ng-hr/mL in cohort 1 to 241,097 ng-hr/mL in in Cohort 4. Serum and urine creatine levels, pharmacodynamic markers of SLC6a8 inhibition, correlated with systemic exposure to RGX-202. **Conclusions:** Among 17 patients treated with single agent therapy, no DLTs occurred; notably, exposures predicted to be sufficient to inhibit human tumor growth from preclinical models were achieved along with concomitant pharmacodynamic effects. These data, along with a durable PR observed in the highest dose cohort, support further development of RGX-202. Consequently, dose escalation in combination with FOLFIRI in patients with advanced GI cancers is underway with plans for expansion in CKB+ CRC pts. Clinical trial information: NCT03597581.Research Sponsor: Rgenix.

	All Patients (N=17) n (%)	
TRAE Term	**Any Grade**	**Grade 3**
Nausea	8 (47)	1 (6)
Vomiting	7 (41)	1 (6)
Diarrhoea	5 (29)	0
Decreased appetite	4 (24)	0
Fatigue	4 (24)	0
Blood alkaline phosphatase increased	2 (12)	0
Muscle spasms	2 (12)	0
Weight decreased	2 (12)	0

3505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Tolerability and preliminary efficacy of BXQ-350 for refractory solid tumors and high-grade gliomas: First-in-human, first-in-class phase I trial. *First Author: Olivier Rixe, GRU Cancer Center, Augusta, GA*

Background: BXQ-350 is a first-in-class agent comprised of Saposin C (SapC) and dioleoyl phosphatidylserine (DOPS). SapC, a multifunctional lysosomal-activator glycoprotein that preferentially interacts with tumor cell phospholipids, has demonstrated anti-tumor effects in both *in vitro* and *in vivo* preclinical models. The tolerability and preliminary efficacy of BXQ-350 in the first-in-human study are summarized here. **Methods:** Eighty-six refractory solid tumor (ST) or high-grade glioma (HGG) patients age $\geq$18 (36F: 50M, age 24-81) were enrolled in a 3-part first-in-human trial (NCT02859857) from 2016-2019 and received at least one dose of BXQ-350. Doses were administered via intravenous infusion during 28-day cycles until disease progression occurred. The previously reported part 1 dose escalation portion of the study (9 HGG, 9 ST patients) established the highest planned dose of 2.4mg/kg as safe but did not identify a maximum tolerated dose. The part 2 expansion cohort treated 37 patients (18 HGG and 19 ST) and an additional part 3 cohort treated 31 ST gastrointestinal (GI) patients, both at the 2.4 mg/kg dose level. Preliminary antitumor activity was evaluated (RECISTv1.1 or RANO). **Results:** There were no BXQ-350-related serious adverse events, dose limiting toxicities or withdrawals with the exception of 1 allergic type reaction. Three patients (Glioblastoma, Ependymoma, Appendiceal) demonstrated a partial response per RECIST/RANO. Two HGG patients with progressive radiologic enhancement were seen to have treatment effect at surgery, and hence considered to have stable disease. Seven patients (2 HGG, 3 GI, 2 other ST) remain on study and have received treatment for 9+ to 41+ months, with 5 patients treated for $>$ 1 year. A continuing treatment protocol is planned in order to allow these patients to remain on BXQ-350 treatment. **Conclusions:** BXQ-350 was well tolerated with no significant dose-limiting toxicities at the highest planed dose level. Preliminary results indicate this novel agent demonstrated possible anti-tumor activity in refractory solid tumors and HGG. Clinical trial information: NCT03967093). Research Sponsor: Bexion Pharmaceuticals.

3506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase II study of copanlisib in patients with tumors with *PIK3CA* mutations (*PTEN* loss allowed): NCI MATCH EAY131-Z1F. *First Author: Senthil Damodaran, Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: The NCI-MATCH (EAY131) is a platform trial that enrolls patients (pts) with solid tumors, lymphomas, or multiple myeloma to targeted therapies based on matching genomic alterations of interest (NCT02465060). Arm Z1F evaluated copanlisib, a highly selective, pan-Class 1 PI3K inhibitor with predominant activity against both the δ and α isoforms in pts with *PIK3CA* mutations. **Methods:** Pts received copanlisib (60 mg IV) on days 1, 8, and 15 in 28-day cycles until progression/toxicity. Tumor assessment was every 2 cycles. The primary endpoint was objective response rate (ORR); secondary endpoints were PFS, 6-month PFS, and predictive biomarkers. Pts with *KRAS* mutations, HER2+ve breast cancers, lymphomas were excluded. **Results:** 35 pts were enrolled (from 8/2/18 to 12/27/18), of which, 28 pts were available for analysis (7 patients, not eligible or did not start therapy). Multiple histologies were enrolled with gynecologic (n = 7), gastrointestinal (n = 6), and genitourinary (n = 5) the most common tumors. Median age 61 (range 42-78). 75% of pts had $\geq$ 3 lines of prior therapy. 54% of *PIK3CA* mutations were located in the helical domain, 32% in kinase domain and 14% in other domains. Twenty-six pts had co-occurring gene alterations (median 3; range 1-9), with 9 patients having 4 or more gene alterations. The ORR was 11% (3/28, 90% CI: 3%-25%). Partial responses were seen in uterine cancer, clear cell carcinoma of anterior abdominal wall, and liposarcoma. 6 pts had $>$ 6 months of stable disease and clinical benefit rate was 32% (9/28). Two pts are still on treatment. The most common reason for protocol discontinuation was disease progression (n = 18, 69%). Thirty pts were included for toxicity analysis. Ten pts (33%) had grade 1 or 2 toxicities, 16 pts (53%) had grade 3 toxicities, and one patient (3%) had grade 4 toxicity (CTCAE v5.0). Most common toxicities include hyperglycemia (n = 19), fatigue (n = 11), hypertension (n = 10), diarrhea (n = 10), and nausea (n = 9). Total of 5 deaths were reported, none related to treatment. **Conclusions:** Copanlisib showed meaningful clinical activity across various tumors with *PIK3CA* mutation in the late-line refractory setting. Further study either alone or in combinations in select tumors is warranted. G3/4 toxicities observed were consistent with reported toxicities for PI3K pathway inhibition. Clinical trial information: NCT02465060. Research Sponsor: U.S. National Institutes of Health.

3507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase I study of 9-ing-41, a small molecule selective glycogen synthase kinase-3 beta (GSK-3β) inhibitor, as a single agent and combined with chemotherapy, in patients with refractory tumors. *First Author: Benedito A. Carneiro, Brown University, Lifespan Cancer Institute, Providence, RI*

Background: Overexpression of GSK-3β, a serine/threonine kinase, is associated with advanced stage malignancies, aggressive tumor growth, and chemotherapy resistance. 9-ING-41 is a GSK-3β inhibitor with significant broad spectrum preclinical antitumor activity, including chemotherapy-resistant models. This first-in-human study (NCT03678883) is evaluating the safety, pharmacokinetics (PK), and efficacy of 9-ING-41 monotherapy and in combination with chemotherapy in patients (pts) with refractory malignancies. **Methods:** 9-ING-41 is given intravenously (IV) twice-weekly as a single-agent (21-day cycle) or combined with gemcitabine, gemcitabine/nab-paclitaxel, carboplatin, carboplatin/paclitaxel, doxorubicin, lomustine or irinotecan in patients previously treated with the same chemotherapy. **Results:** As of Jan 2020, 101 pts were enrolled. Tumor types: 25 pancreatic (PDAC), 14 colorectal (CRC), 10 non-small cell lung cancer (NSCLC), 8 GBM and other gliomas, 7 melanoma, 5 appendiceal, 4 breast (BC), 30 others. Seven single agent dose levels (DL) completed (1, 2, 3.3, 5, 7, 9.3, 12.4 mg/kg) without any 9-ING-41-attributable SAEs. 9-ING-41 attributable AEs include: transient visual change (color perception; n = 29), starting at DL 3 (3.3mg/kg), all G1/2; infusion reactions (n = 14), all G1/2, starting at DL 5 (7mg/kg). 9-ING-41's mean terminal half-life is 12-20 hrs. C_{max} and $AUC_{0\text{-}72}$, are dose proportional with no accumulation. One BRAFV600K-mutated melanoma with $>$ 20 brain metastases, post checkpoint/BRAF/MEK failure has an ongoing CR starting at cycle 2 and sustained after 9 months on treatment. 32 (31%) pts had SD as best response (6 PDAC, 6 CRC, 3 appendiceal, 2 BC, 2 salivary gland, 2 melanoma, 1 Merkel cell, 2 GBM/glioma, 1 RCC, 1 HCC, 1 NSCLC, 1 esophageal, 1 parotid gland, 1 nasopharyngeal, 1 peritoneal, 1 T cell-ALL). 8 pts remained on study treatment $>$ 5 months (1 melanoma, 3 PDAC, 1 appendiceal, 1 GBM, 1 peritoneal, 1 salivary gland) with median treatment duration of 198 days (range 163-261). 32 pts continue to receive 9-ING-41. **Conclusions:** 9-ING-41 has dose-proportional PK, is well tolerated with significant antitumor activity as monotherapy and in combination with chemotherapy in pts with refractory tumors. 1 ongoing CR was observed in a refractory BRAF-mutated melanoma. A biologically active dose has been reached, although MTD has not been determined. Enrollment is ongoing. Clinical trial information: NCT03678883. Research Sponsor: Actuate Therapeutics.

3508 Poster Discussion Session; Displayed in Poster Session (Board #238), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase Ib study of a novel bivalent IAP antagonist APG-1387 in combination of pembrolizumab for patients with advanced solid tumors. *First Author: Drew W. Rasco, South Texas Accelerated Research Therapeutics, San Antonio, TX*

Background: APG-1387 is an IAP (inhibitor of apoptosis proteins) antagonist that has strong antitumor activity in multiple xenograft cancer models and acts as a host immune modulator, supporting its exploration for use in combination with checkpoint inhibitors for cancer therapy. **Methods:** This "3+3" dose escalation and dose expansion study evaluated APG-1387 combined with pembrolizumab in patients with refractory or intolerant advanced solid tumors (NCT03386526). APG-1387 was administered IV once weekly with pembrolizumab 200 mg on day 1 of a 21-day cycle. Study aims were to assess safety/tolerability, recommended phase 2 dose (RP2D), pharmacokinetics (PK), pharmacodynamics (PD), and efficacy. **Results:** As of December 25, 2019, total 28 patients had been treated in 3 dose cohorts of APG-1387: 20 mg (n = 4), 30 mg (n = 3), and 45 mg (n = 21, 18 in dose expansion). The median line of prior systemic cancer therapies was 3.0 (1-12). No dose-limiting toxicity was observed. The most common treatment-related adverse events (TRAEs; ≥10%) were fatigue (28.6%), arthralgia (14.3%), headache (14.3%), and tumor pain (10.7%). One patient in the 45-mg cohort had grade 2 Bell's Palsy. G3^{+} TRAEs were autoimmune colitis, hypoxia, increased lipase, mucosal inflammation, pneumonitis, and tumor pain in 1 patient each (3.6%). Treatment-related SAEs were 1 G3 autoimmune colitis, 1 G2 myocarditis, and 1 G3 pneumonitis. The maximum tolerated dose (MTD)/RP2D for APG-1387 was 45 mg. Among 25 efficacy-evaluable patients, 1 with ER^{+}, HER2^{-} breast cancer receiving APG-1387 30 mg after failing 5 lines of therapy (PD-1 treatment-naïve, microsatellite stable) achieved confirmed PR (-79.2%) for 6 cycles but discontinued due to pneumonitis; another patient with PD-L1^{-} non–small-cell lung cancer treated at 45 mg had confirmed PR (-65.0%) for 6 cycles (ongoing). Other 11 patients had SD for 2-11 cycles. The disease control rate was 52%. Preliminary PK data showed a dose-proportional increase in APG-1387 exposure from 20 mg to 45 mg. Preliminary PD data showed that APG-1387 induced rapid degradation of cellular IAP1 and X-linked IAP in peripheral blood mononuclear cell samples; Increased serum release of interleukins (IL-12, IL-10) and monocyte chemotactic protein 4 was dose and time dependent. **Conclusions:** APG-1387 combined with pembrolizumab is well tolerated. Encouraging antitumor effects were observed in patients with several tumor types. The ongoing study will further evaluate the efficacy of this combination. Clinical trial information: NCT03386526. Research Sponsor: Ascentage Pharma Group Inc., Rockville, MD.

3509 Poster Discussion Session; Displayed in Poster Session (Board #239), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

First-in-human study of palcitoclax (APG-1252), a novel dual Bcl-2/Bcl-xL inhibitor, demonstrated advantages in platelet safety while maintaining anticancer effect in U.S. patients with metastatic solid tumors. *First Author: Nehal J. Lakhani, START-Midwest, Grand Rapids, MI*

Background: Targeting Bcl-2/Bcl-xL proteins is considered as an important approach for anticancer drug development. Palcitoclax (APG-1252) was being developed to reduce on-target platelet toxicity without diminishing antitumor potency. **Methods:** The phase 1 study was to evaluate the safety/tolerability, pharmacokinetics (PK), and preliminary efficacy (assessed per RECIST 1.1) of palcitoclax in US patients with metastatic small-cell lung cancer (SCLC) or other solid tumors (NCT03080311). A standard "3+3" design was applied to the dose-escalation stage. Palcitoclax was administered IV infusion for 30 minutes, twice a week (BIW) or once a week (QW) for 3 weeks in a 28-day cycle. Once the maximum tolerated dose / recommended phase 2 dose (MTD/RP2D) was determined, additional patients were treated in a dose-expansion stage. **Results:** The dose-escalation phase has been completed with 42 patients (31 on BIW and 11 on QW) who received palcitoclax at 8 dose cohorts ranging 10 mg - 400 mg. Most adverse events (AEs) were grade 1 or 2 (G1 or G2), and 26.2% patients had ≥ G3 TRAEs. The most common TRAEs were platelet count decreased (14.3%), aspartate aminotransferase increased (9.5%), and alanine aminotransferase increased (7.1%). Rapid platelet drop was observed in patients treated at 320 mg and 400 mg, which was transient and resolved rapidly within 2-6 days. Palcitoclax at 240 mg once weekly was determined to be MTD/RP2D. Of 36 efficacy-evaluable patients, 3 patients with SCLC, neuroendocrine prostate cancer, and ovarian cancer respectively achieved partial response (PR) and 8 patients had stable disease (SD) as their best overall response. One patient with SCLC had a PR that lasted over 21 cycles. Preliminary PK analyses showed that C_{max} and AUC were approximately dose proportional over the range of 10 mg to 320 mg following the IV infusion on Day 1, with a mean $T_{1/2}$ of 3.0-13.0 hours. **Conclusions:** Palcitoclax is safe and well tolerated, with a favorable platelet toxicity profile. Its promising antitumor effect supports its further development in combination therapies for treatment of patients with SCLC and other solid tumors. Clinical trial information: NCT03080311. Research Sponsor: Ascentage Pharma Group Inc., Rockville, MD.

3510 Poster Discussion Session; Displayed in Poster Session (Board #240), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Safety and efficacy of pyrotinib in patients with NSCLC and other advanced solid tumors with activating *HER2* alterations: A phase I basket trial. *First Author: Bob T. Li, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Pyrotinib is a potent, irreversible tyrosine kinase inhibitor (TKI) that blocks signal transduction through the erythroblastic leukemia viral oncogene homolog (erbB) receptors, which has previously demonstrated promising antitumor activity in patients (pts) with breast cancers. We studied the safety and efficacy of pyrotinib in pts with non-small cell lung cancer (NSCLC) and other solid tumors with activating human epidermal growth factor receptor 2 (*HER2, ERBB2)* alterations. **Methods:** This is an open-label, multicenter phase 1 dose expansion basket trial of pyrotinib given 400mg oral daily at 28-day cycles. Expansion cohorts included pts with *HER2*-mutant NSCLC and advanced solid tumors with *HER2* mutation or amplification. *HER2* testing was conducted using next generation sequencing or fluorescence *in situ* hybridization. Primary endpoints included toxicities as evaluated by NCI CTCAE v5.0, and overall response rate (ORR) as evaluated by RECIST v1.1. Secondary objectives included progression-free survival (PFS). **Results:** A total of 62 pts were enrolled. The median age was 67 (range 40 – 86 years), 61% were female and the median lines of prior systemic therapy was 3 (range 1-11). There were no treatment related deaths. The most common adverse events were diarrhea (96.8%), nausea (82.3%) and vomiting (41.9%). The only ≥ grade 3 treatment related toxicity was diarrhea (24.2%). Prophylactic anti-diarrhea treatment was introduced to facilitate continuation of pyrotinib. At the Jan 13, 2020 cut-off, 24 pts with *HER2*-mutant NSCLC (20, i.e. 65% of which were the A775_G776insYVMA mutation) and 18 pts with *HER2*-mutant or amplified solid tumors completed end of Cycle 2 imaging scan and were evaluable for tumor responses. The ORR was 19% (8/42, 95% CI 7-31%); confirmed responses include a complete response (CR) and 3 partial responses (PRs) in *HER2*-mutant NSCLC, and 4 PRs in *HER2*-amplified cholangiocarcinoma, ovarian, endometrial and salivary gland carcinomas. There were 7 stable disease ≥ 6 months. Median progression-free survival was 5.4 months (95% CI 4.4-7.3). **Conclusions:** Pyrotinib demonstrated a manageable safety profile and encouraging efficacy in pts with heavily pre-treated *HER2*-mutant NSCLC. Furthermore, it is the first TKI to produce durable responses in pts with *HER2*-amplified biliary tract, ovarian, endometrial and salivary gland cancers. These results warrant further clinical development of pyrotinib. Clinical trial information: NCT02500199. Research Sponsor: Hengrui Therapeutics Inc.

3511 Poster Discussion Session; Displayed in Poster Session (Board #241), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

CodeBreak 100: Phase I study of AMG 510, a novel KRAS^{G12C} inhibitor, in patients (pts) with advanced solid tumors other than non-small cell lung cancer (NSCLC) and colorectal cancer (CRC). *First Author: David S. Hong, MD Anderson Cancer Center, Houston, TX*

Background: Kirsten rat sarcoma viral oncogene homolog (*KRAS*) p.G12C mutation occurs in approximately 13% of NSCLC and 1%–3% of CRC and other solid tumors. AMG 510 is a first-in-class small molecule that specifically and irreversibly inhibits KRAS^{G12C}. Previously, AMG 510 showed preliminary antitumor activity and favorable tolerability in pts with *KRAS* p.G12C mutant NSCLC or CRC in the phase 1, first-in-human trial. Here, we report results in pts with other tumor types from the same trial. **Methods:** This study evaluates AMG 510 in pts with locally-advanced or metastatic *KRAS* p.G12C mutant solid tumors. Key inclusion criteria: *KRAS* p.G12C mutation via local testing and prior systemic anticancer treatment (tx). Oral daily doses of 180, 360, 720, and 960 mg were tested in the dose escalation, and 960 mg was selected for expansion. Primary endpoint is safety; key secondary endpoints include pharmacokinetics and objective response rate as assessed per RECIST 1.1. Response is assessed every 6 weeks (wks) for 24 wks then every 12 wks thereafter. **Results:** As of January 8, 2020, 25 pts (9 female, median age 60 years [range: 40–75]) with tumor types categorized by investigators as histology other than NSCLC and CRC were enrolled and dosed (10 pancreatic cancer, 4 appendiceal cancer, 2 endometrial cancer, 2 unknown primary cancer, 1 bile duct cancer, 1 sinonasal cancer, 1 ampullary cancer, 1 small bowel cancer, 1 melanoma, 1 small cell lung cancer, and 1 esophageal cancer). 23 pts received 960 mg dose. 20 pts (80.0%) had ≥2 prior lines of tx. At data cutoff, 13 pts (52.0%) remained on tx; 9 (36.0%) and 3 (12.0%) pts remained on tx for ≥3 and ≥6 months, respectively. Median follow up was 4.3 months (range: 0.1–12.6). Tx-related adverse events (TRAEs) occurred in 9 pts (36.0%). 2 pts (8.0%) had grade 3 TRAEs, including diarrhea (1/25) and pneumonia (1/25, serious AE). No dose-limiting toxicities, grade ≥4, or fatal TRAEs were reported. No TRAEs led to tx discontinuation. 3 pts had not been followed up for ≥7 wks by the data cutoff. 22 pts were followed up for ≥7 wks, and their best overall responses were: 3 confirmed partial response (1 appendiceal, 1 melanoma, and 1 endometrial), 13 stable disease (6 pancreatic, 2 appendiceal, 1 ampullary, 1 bile duct, 1 endometrial, 1 sinonasal, and 1 unknown primary), and 6 progressive disease. **Conclusions:** AMG 510 was well tolerated and demonstrated clinical activity in pts with advanced *KRAS* p.G12C mutant solid tumors other than NSCLC and CRC. Clinical trial information: NCT03600883. Research Sponsor: Amgen Inc.

3512 Poster Discussion Session; Displayed in Poster Session (Board #242), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase Ib study of a novel, small-molecule MDM2 inhibitor APG-115 combined with pembrolizumab in U.S. patients with metastatic solid tumors. *First Author: Anthony W. Tolcher, NEXT Oncology, San Antonio, TX*

Background: APG-115 activates p53-mediated apoptosis in tumor cells retaining wild-type *TP53*. It also functions as a host immune modulator and enhances antitumor activities when combined with PD-1 blockade preclinically. MDM2 amplification is associated with hyperprogression in patients treated with checkpoint inhibitors. **Methods:** The Phase Ib / II study was designed to evaluate APG-115 combined with pembrolizumab in patients with metastatic solid tumors (NCT03611868). APG-115 was administered orally every other day for 2 weeks, at dose ranging from 50 mg – 200 mg, with pembrolizumab at 200 mg IV on Day 1 of a 21-day cycle. Study objectives were to assess safety including dose-limiting toxicity (DLT), serious adverse events (SAEs), treatment-related AEs (TRAEs), pharmacokinetics (PK), pharmacodynamics (PD), and efficacy (assessed by RECIST v1.1), to determine recommended phase 2 dose (RP2D). **Results:** As of December 25, 2019, the enrollment of phase 1b study was completed. Total 19 patients had been treated in four APG-115 cohorts: 50 mg (n = 3), 100 mg (n = 3), 150 mg (n = 6), and 200 mg (n = 7). No DLT was observed, The TRAEs (≥15%) were nausea (47.4%), fatigue (36.8%), decreased platelet count (26.3%), and decreased appetite (21.1%), as well as diarrhea, vomiting, decreased neutrophil or white blood cell count, and hypothyroidism in 15.8% each. Grade > 3 TRAEs included decreased neutrophil and thrombocytopenia in 15.8% each. Two SAEs were treatment related: G3 febrile neutropenia and G3 adrenal insufficiency. No new safety finding from combination with Pembrolizumab. The RP2D of APG-115 was 150 mg. One patient with ovarian cancer has a CR lasting for 15 months, 2 patients had PR for 8-9 months: one NSCLC failed IO therapy, another with appendix cancer, and 7 had SD for 1.5-7 months. The objective response rate was 15.8%, and the disease control rate (DCR) was 52.6%. PK data indicated an approximately dose-proportional increase in APG-115 exposure over the range of 50-200 mg on Day 1. PD-PK analyses showed that serum macrophage inhibitory cytokine-1 (MIC-1) increase was time and dose dependent, the MIC-1 elevation correlated with APG-115 exposure, indicating p53 activation in these patients. **Conclusions:** APG-115 in combination with pembrolizumab is well tolerated. Encouraging antitumor effects were observed in several tumor types. The phase II study is ongoing in the cancer patients with specific bio-marker profiling. Clinical trial information: NCT03611868. Research Sponsor: Ascentage Pharma Group Inc., Rockville, MD.

3513 Poster Discussion Session; Displayed in Poster Session (Board #243), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase I study of rucaparib and irinotecan in advanced solid tumors with homologous recombination deficiency (HRD) mutations. *First Author: Mallika Sachdev Dhawan, Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA*

Background: Poly (ADP-ribose) polymerase inhibitors (PARPi) are approved for multiple tumor types with HRD mutations. In efforts to prolong durations of response, combination treatments of PARPi and chemotherapy are being explored. However, expected overlapping toxicities have previously limited the tolerability of PARPi-chemotherapy combinations. Preclinical studies suggest that the inhibition of PARP will prevent the repair of topoisomerase induced DNA strand breaks. In this Phase I trial, we test whether pulse dosing and alternate treatment schedules of rucaparib and irinotecan are safe and tolerable. **Methods:** Rucaparib and irinotecan were dose escalated in a 3+3 design. Patients with advanced solid tumors and somatic or germline known or suspected pathogenic mutations in HRD were accepted on trial. 15 patients have been enrolled in 3 cohorts and treated with rucaparib 400 mg BID (days 1-7) and irinotecan 65 mg/m2 (cohort 1) or 100 mg/m2 (cohort 2) every 2 weeks or 100 mg/m2 every 3 weeks (cohort 2i). **Results:** Tumor types on trial are heterogeneous and include pancreatic ductal adenocarcinoma (PDAC: 3), cholangiocarcinoma, neuroendocrine carcinoma of the pancreas, ovarian cancer/primary peritoneal carcinoma (3), prostate cancer, small bowel carcinoma, squamous cell carcinoma of the tonsil, testicular cancer, triple negative breast cancer, and urothelial carcinoma. 14/15 patients had 3+ prior lines of therapy. Mutation types include: 7 ATM, 3 BRCA1, 3 BRCA2, 1 CHEK2, and 1 PALB2. All patients were previously exposed to platinum chemotherapies; 8/15 had progressive disease while on platinum. 5/15 patients had prior PARPi with progression. There were 3 DLT events, all of which were related to grade 3 or 4 neutropenia. Of the 13 patients evaluable for response, there was one confirmed partial response (PR). 5 patients have remained on study for longer than 6 months and 3 patients with ATM mutations have remained on study for longer than one year (primary peritoneal cancer, small bowel carcinoma, PNET). 4/5 patients with clinical benefit had prior platinum progression and 1/5 had previously progressed on a PARPi. Our current recommended phase 2 dose is rucaparib 400 mg BID days 1-7 and irinotecan 100 mg/m2 every 3 weeks. **Conclusions:** The pulse dosing schedule of rucaparib and irinotecan has allowed for long term tolerability and exposure to both agents with encouraging efficacy in patients with ATM mutations. Further testing of PARPi and topoisomerase inhibitors at this schedule in patients with ATM mutations is planned. Clinical trial information: NCT03318445. Research Sponsor: Clovis.

3514 Poster Discussion Session; Displayed in Poster Session (Board #244), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Lurbinectedin (LUR) in combination with Irinotecan (IRI) in patients (pts) with advanced solid tumors: Updated results from a phase Ib-II trial. *First Author: Santiago Ponce Aix, Hospital Universitario 12 De Octubre, Madrid, Spain*

Background: LUR is a novel agent that exerts antitumor activity through inhibition of trans-activated transcription and modulation of tumor microenvironment. Preclinical synergism/additivity in combination with IRI has been reported, thus prompting the conduct of this clinical trial. **Methods:** Phase Ib-II trial to evaluate escalating doses of LUR on Day (D) 1 plus a fixed dose of IRI 75 mg/m^2 on D1 and D8 every 3 weeks (q3w) in pts with advanced solid tumors (+/- G-CSF, if dose-limiting toxicities [DLTs] were neutropenia). Starting dose was LUR 1.0 m/m^2 + IRI 75 mg/m^2. **Results:** 77 pts have been treated to date at 5 dose levels, 51 of them at the recommended dose (RD). Baseline characteristics of all 77 pts were: 48% females, 68% ECOG PS=1; median age 57 years (range, 19-75 years); median of 2 prior lines (range, 0−4 lines). The maximum tolerated dose (MTD) was LUR 2.4 mg/m^2 + IRI 75 mg/m^2 with G-CSF, and the RD was LUR 2.0 mg/m^2 + IRI 75 mg/m^2 with G-CSF. DLTs in Cycle 1 occurred in 2/3 evaluable pts at the MTD and 3/13 evaluable pts at the RD, and comprised omission of IRI D8 infusion due to grade (G) 3/4 neutropenia (n=3 pts) or G2-4 thrombocytopenia (n=2). At the RD (n=51), common G1/2 non-hematological toxicities were nausea, vomiting, fatigue, diarrhea, anorexia and neuropathy. G3 non-hematological toxicities (diarrhea 10%, fatigue 10%) and G3/4 hematological abnormalities (neutropenia 49%, thrombocytopenia 10%) were transient. **Conclusions:** The combination of LUR and IRI had acceptable tolerance, with no unexpected toxicities. Transient myelosuppression was dose-limiting. The RD is LUR 2.0 mg/m^2 on D1 + IRI 75 mg/m^2 on D1 and D8 q3w with G-CSF. Antitumor activity was observed at the RD in SCLC pts, as well as in endometrial carcinoma pts. Hints of activity were also observed in STS pts. Updated results will be presented. Clinical trial information: NCT02611024. Research Sponsor: PharmaMar SA.

Main efficacy data for selected tumors at the RD are shown below.

Tumor type evaluable	SCLC (n=13)	Endometrial Ca. (n=10)	STS (n=9)	Glioblastoma (n=13)
ORR (PR)	8 (61.5%)	3 (30%)	0%	0%
DCR (PR+SD)	84.6%	100%	88.9%	38.5%
PFS at 6 months (95% CI)	36.3% (4.1-68.4%)	66.7% (36.0-97.5%)	50.8% (16.2-85.4%)	0%

Ca, carcinoma; CI, confidence interval; DCR, disease control rate; n, number of evaluable patients; ORR, overall response rate as per RECIST v.1.1; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors; SCLC, small cell lung cancer; SD, stable disease; STS, soft tissue sarcoma.

3515 Poster Discussion Session; Displayed in Poster Session (Board #245), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Pen-866, a miniature drug conjugate of a heat shock protein 90 (HSP90) ligand linked to SN38 for patients with advanced solid malignancies: Phase I and expansion cohort results. *First Author: Gerald Steven Falchook, Sarah Cannon Research Institute at HealthONE, Denver, CO*

Background: PEN-866 is a miniature drug conjugate which links a HSP90 binding small molecule to a SN-38 cytotoxic payload. HSP90 is highly expressed in advanced malignancies. PEN-866 targets and binds to activated tumor HSP90 protein, releases its cytotoxic payload, and results in complete tumor regressions in multiple xenograft models. This first-in-human study assessed safety, tolerability, pharmacokinetics (PK), and preliminary efficacy of PEN-866. **Methods:** Patients (pts) with progressive, advanced solid malignancies were enrolled in escalating cohorts of 2-9 pts. The primary objective was to determine the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D) of PEN-866 given weekly (3 out of 4 weeks in a 28-day cycle). **Results:** 30 pts were treated in 8 cohorts (range 30-360 mg flat dosing or 150–200 mg/m^2 BSA-based dosing). As of 9Jan20, the total median/mean exposure was 7.05/12.4 weeks. No dose limiting toxicities (DLTs) occurred in the first 4 cohorts (30-240 mg; 14 pts). In cohort 5 (360 mg), 1 of 3 pts had a DLT of grade (G) 3 transient diarrhea, and 2 other pts had G3 uncomplicated transient neutropenia. A change to BSA-based dosing was instituted for cohort 6 (175 mg/m^2), on which no DLTs were observed, although 1 pt experienced G3 uncomplicated transient neutropenia. At 200 mg/m^2, 2 of 5 pts experienced DLTs (G5 dehydration, G3 fatigue). The MTD and RP2D were determined to be 175 mg/m^2. The most frequent (≥20% pts) related adverse events were nausea (50%), fatigue (43%), diarrhea (40%), vomiting (27%), and anemia (23%). PK was nonlinear. Plasma exposures increased greater than dose proportionally. Median $t_{1/2}$ ~7 h. Cleaved SN38 never exceeded 3% of PEN-866 plasma AUC at all dose levels. Tissue PK confirmed tumor accumulation and retention of both the conjugate and released payload. As of 9Jan20, 26 pts were evaluable for response. 11 pts had stable disease at 8 weeks, of which 7 lasted 12–58 weeks. One pt with anal squamous cell carcinoma achieved a confirmed partial response. Decreased target lesion size was observed in 6 additional pts. **Conclusions:** PEN-866 was well tolerated and demonstrated preliminary evidence of antitumor activity. PEN-866 will be evaluated in Phase 2a expansion cohorts enrolling multiple solid tumors (NCT03221400). Clinical trial information: NCT03221400. Research Sponsor: Tarveda Therapeutics, Inc.

3516 Poster Discussion Session; Displayed in Poster Session (Board #246), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Utility of circulating tumor DNA (ctDNA) versus tumor tissue clinical sequencing for enrolling patients (pts) with advanced non-colorectal (non-CRC) gastrointestinal (GI) cancer to matched clinical trials: SCRUM-Japan GI-SCREEN and GOZILA combined analysis. *First Author: Akihiro Ohba, National Cancer Center Hospital, Tokyo, Japan*

Background: We recently reported that clinical assessment of genomic biomarkers using ctDNA had advantages over tumor tissue-based sequencing for enrollment into matched clinical trials across a wide range of GI cancers. Herein we investigated the utility of ctDNA in non-CRC cancers in a SCRUM-Japan GI-SCREEN and GOZILA combined analysis. **Methods:** In GI-SCREEN, tumor tissue samples of pts with non-CRC were analyzed by a next generation sequencing (NGS)-based assay, Oncomine Comprehensive Assay, since Feb 2015. In GOZILA, plasma samples of non-CRC pts were analyzed by an NGS-based ctDNA assay, Guardant360, since Feb 2018. **Results:** As of Apr 2019, 2,952 pts in GI-SCREEN and 633 pts in GOZILA were enrolled. Baseline characteristics between the groups were well matched except that GOZILA included more pancreatic ($P < 0.0001$) and liver cancers ($P = 0.016$) but fewer gastric cancers ($P < 0.0001$) and GIST ($P = 0.020$) than GI-SCREEN. The success rates of the tests were 86.6% in GI-SCREEN and 87.3% in GOZILA ($P = 0.649$). Median turnaround time (TAT) was 37 days in GI-SCREEN and 12 days in GOZILA ($P < 0.0001$). The proportion of cases with actionable alterations detected (tissue vs blood; 29.8% vs 46.8%, $P < 0.0001$) and enrolled into matched clinical trials (4.8% vs 6.5%, $P = 0.286$) for each group by cancer type are shown in the Table. Pts with upper GI cancers, especially those in GOZILA, were more often enrolled into matched trials; trial enrollment for those with hepatobiliary and pancreatic (HBP) or other cancers was similar regardless of testing method. Median time from GI-SCREEN or GOZILA enrollment to clinical trial enrollment was 5.0 and 1.0 months (mo), respectively ($P < 0.0001$). Objective response rates (ORR) and progression-free survival (PFS) were not significantly different (tissue vs. blood; ORR: 14.6 vs. 26.3%, P = 0.30: median PFS: 3.3 vs. 2.6 mo, P = 0.71). **Conclusions:** Clinical sequencing of ctDNA, with its shorter TAT, contributed to rapid enrollment of non-CRC pts into matched clinical trials compared to those tested by tumor tissue sequencing, particularly for those with upper GI cancer, without compromising efficacy. Clinical trial information: UMIN000029315.Research Sponsor: SCRUM-Japan.

	Actionable alterations-Tissue (n = 855)	Matched trial-Tissue (n = 41)	Actionable alterations-Blood (n = 292)	Matched trial-Blood (n = 19)
Upper GI	346 (23.4%)	24 (6.9%)	84 (35.3%)	14 (16.7%)
HBP	401 (36.6%)	14 (3.5%)	196 (56.8%)	5 (2.6%)
Others	108 (37.5%)	3 (2.8%)	12 (29.3%)	0 (0%)

3517 Poster Discussion Session; Displayed in Poster Session (Board #247), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Pan-tumor analyses of kinase fusions detected in circulating tumor DNA (ctDNA) and concordance with paired tissue. *First Author: Jessica Kim Lee, Foundation Medicine, Inc., Cambridge, MA*

Background: Oncogenic kinase gene fusions are targetable with approved and investigational therapies and can also emerge as acquired resistance (AR) to targeted therapy. To understand the clinical validity of liquid biopsy comprehensive genomic profiling (CGP) to detect kinase fusions, we compared patient-matched plasma and tissue-based CGP. **Methods:** Hybrid capture-based CGP was performed on 28,743 plasma and 325,131 tumor tissue samples in the course of clinical care. Complete exonic regions of 13 kinases involved in oncogenic fusions plus select introns in *ALK, EGFR, FGFR2/3, PDGFRA, RET,* and *ROS1* were sequenced to capture fusions with well characterized breakpoints. ctDNA fraction was estimated by maximum somatic allele frequency (MSAF). **Results:** 86% of cases had detectable ctDNA in plasma (MSAF > 0). Kinase fusions were detected in 2.1% of ctDNA cases (478/23,294) and were most prevalent in patients (pts) with bladder cancer (4.5%), non-small cell lung cancer (NSCLC) (4.3%), and cholangiocarcinoma (3.9%). The most commonly rearranged kinases were *ALK* (60%, 162/271) and *RET* (19%, 51/271) in NSCLC, *FGFR2* (85%, 11/13) in cholangiocarcinoma, and *FGFR3* (88%, 7/8) in bladder cancer. *ALK* fusions were detected in 26% (54/207) of fusion+ non-NSCLC cases. Paired tissue and ctDNA samples where ≥1 sample harbored a kinase fusion were available for 147 pts; median time between sample collection was 150 days (interquartile range: 444 days). Positive percent agreement (PPA) to tissue and liquid biopsies was 76% and 80%. Median MSAF in concordant and discordant ctDNA samples was 2.3% and 0.41% ($p = 0.04$) and median time between specimen collection for concordant and discordant pairs was 110 and 344 days ($p = 0.04$). PPA to tissue and liquid was 86% and 88% for pairs collected < 60 days apart (n = 53), versus 70% and 74% for pairs collected > 60 days apart. 6 pts with paired samples all collected > 196 days apart (median 593 days) had initial tissue samples with *EGFR* driver mutations and had an acquired kinase fusion (4 *ALK*, 1 *FGFR2*, 1 *FGFR3*) in the 2nd ctDNA sample, likely representing AR. **Conclusions:** Kinase gene fusions identified by tissue-based CGP were detected by liquid biopsy CGP in 85% of temporally-matched plasma samples. Kinase fusion detection by liquid biopsy CGP is feasible and had high PPA to tissue-based CGP. Subsequent sampling by liquid biopsy identified acquired fusions in *EGFR* driver positive cases consistent with known mechanisms of resistance to EGFR inhibitors suggesting utility of liquid biopsy at progression to identify targetable mechanisms of AR. Research Sponsor: Foundation Medicine.

3518 Poster Discussion Session; Displayed in Poster Session (Board #248), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Early plasma circulating tumor DNA (ctDNA) changes to predict response to first-line pembrolizumab +/- chemotherapy in non-small cell lung cancer (NSCLC). *First Author: Biagio Ricciuti, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute, Boston, MA*

Background: ctDNA shedding into plasma can be prognostic in lung cancer, and changes in plasma ctDNA levels correlate with response to systemic therapy. However, is unknown whether early detection of ctDNA levels change predicts response to first-line pembrolizumab +/- chemotherapy. We hypothesized that serial assessment of plasma ctDNA by next generation sequencing would enable early detection of response to immunotherapy in NSCLC prior to radiological assessment. **Methods:** Patients (pts) with advanced NSCLC who received first-line treatment with pembrolizumab +/- platinum doublet chemotherapy at the Dana-Farber Cancer Institute were enrolled in this study. Plasma collected from pts prior to starting therapy and serially after starting therapy was analyzed by NGS using enhanced tagged-amplicon sequencing (eTAm-Seq) of hotspots and coding regions from 36 genes (InVisionFirst-Lung). ctDNA allele fractions (AF) change was correlated with treatment responses. **Results:** Among 38 pts who received first-line pembrolizumab +/- platinum/pemetrexed, 9 (23.7%) had no ctDNA detected at baseline while 29 had alterations detected. Pembrolizumab was administered as monotherapy in 19 of the 29 pts (65.5%) and in combination with chemotherapy in 10 (34.5%). The median time to the first ctDNA assessment was 21 days (IQR:21-24). Pts who had a decrease in the max AF at the first blood drawn compared to pre-treatment AF had a significantly higher response rate to treatment with pembrolizumab +/- platinum doublet chemotherapy than those with an AF increase (64.5% vs 7.7%, $P < 0.01$). The median PFS (mPFS) and median OS (mOS) were significantly longer among pts with early AF decrease compared to those with an AF increase mPFS: 13.7 vs 3.4 months, HR:0.20, $P < 0.01$; mOS: 32.8 vs 14.7 months, HR:0.06, $P < 0.01$). The median change in allele fraction at the first on-treatment blood draw was -90% (range: -100 to +65), -71% (range: -100 to +100) and +35% (range: +17 to +100) in pts with subsequent radiological response (N = 11), stable disease (N = 11) and progressive disease (N = 7), respectively ($P < 0.01$). Among the 9 cases with no detected ctDNA at baseline, 2 pts with emergence of cfDNA within 8 weeks developed progressive disease. In the other 7 cases, ctDNA remained undetected. **Conclusions:** In pts with advanced NSCLC, rapid decreases in ctDNA prior to radiological assessment correlated with clinical benefit. These results suggest a potential role for ctDNA as an early pharmacodynamic biomarker of response or resistance to immunotherapies. Research Sponsor: None.

3519 Poster Discussion Session; Displayed in Poster Session (Board #249), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Acquired genomic alterations in circulating tumor DNA from patients receiving abemaciclib alone or in combination with endocrine therapy. *First Author: Matthew P. Goetz, Mayo Clinic, Rochester, MN*

Background: An understanding of the mechanisms of acquired resistance to CDK4 & 6 inhibitors, either alone or with endocrine therapy (ET), is an unmet need. Abemaciclib is a CDK4 & 6 inhibitor approved for treatment of HR+, HER2- advanced breast cancer (ABC). Here we evaluated acquired genomic alterations detected in circulating tumor DNA (ctDNA) from patients (pts) treated with abemaciclib + nonsteroidal aromatase inhibitor (AI) or placebo + AI in MONARCH 3 or abemaciclib monotherapy in nextMONARCH 1. **Methods:** MONARCH 3 randomized postmenopausal women with HR+, HER2- ABC with no prior systemic therapy in the advanced setting to abemaciclib (150 mg Q12H) or placebo + AI. nextMONARCH 1 randomized women with HR+, HER2- metastatic breast cancer who had progressed on or after prior ET and CT to abemaciclib (150 mg Q12H) + tamoxifen, abemaciclib (150 mg Q12H), or abemaciclib (200 mg Q12H) + loperamide. Plasma from pts in the abemaciclib or placebo + AI arms (MONARCH 3) or abemaciclib monotherapy arms (nextMONARCH 1) was analyzed by the Guardant360 assay to identify potential tumor-related genomic alterations including point mutations, indels, amplifications, and fusions acquired at EOT in comparison with baseline. **Results:** For MONARCH 3, commonly acquired alterations at EOT included *ESR1* (17%), *TP53* (10%), *EGFR* (8%), *FGFR1* (7%), and *PDGFRA* (7%) in the abemaciclib + AI arm, and *ESR1* (31%), *TP53* (10%), and *BRCA1* (7%) in the placebo + AI arm. Acquired alterations more frequent for abemaciclib + AI pts included *RB1* (6%), *MYC* (5%), and *AR* (5%), compared to 0% in the placebo + AI arm ($p = 0.008$ *RB1*; $p = 0.015$ *MYC* or *AR*). In contrast, acquired *ESR1* alterations were less frequent with abemaciclib + AI vs placebo + AI (17% vs 31%, $p = 0.038$). In nextMONARCH 1, the most commonly acquired alterations with abemaciclib monotherapy were in *TP53* (10%), *EGFR* (9%), *RB1* (9%), *MYC* (9%), and *MET* (8%). In addition, acquired alterations in *ESR1* (6%) and *AR* (3%) were also found. *PIK3CA* alterations were not frequently acquired (abemaciclib + AI 1%, placebo + AI 6%, abemaciclib monotherapy 5%). **Conclusions:** Acquired genomic alterations potentially associated with emerging mechanisms of resistance to abemaciclib alone or in combination with AI may include *RB1*, *MYC*, or *AR* alterations, while the acquisition of *ESR1* alterations was less common in pts treated with abemaciclib + AI compared to placebo + AI. These findings are hypothesis-generating and provide insight into mechanisms of resistance to abemaciclib vs ET. Clinical trial information: NCT02246621, NCT02747004. Research Sponsor: Eli Lilly and Company.

3520 Poster Session (Board #250), Fri, 8:00 AM-11:00 AM

An open-label, multicenter, phase II study of ceritinib in patients with advanced ALK+ non-lung solid tumors and hematological malignancies (ASCEND-10). *First Author: Victor Moreno, START Madrid-FJD, Fundación Jiménez Díaz University Hospital, Madrid, Spain*

Background: Prior studies have confirmed the efficacy and safety of ceritinib in patients (pts) with advanced *ALK*+ non-small cell lung cancer (Soria, et al, Lancet 2017; Shaw et al, Lancet Oncol 2017; Cho et al, JTO 2019). Ceritinib also demonstrated antitumor activity in pediatric pts with *ALK*+ inflammatory myofibroblastic tumor (IMT) and ALCL (Georger et al, ASCO 2015 [abstract#10005]). Long-term clinical benefits of ceritinib treatment were shown in pts with anaplastic large cell lymphoma (ALCL) (Richly et al, Blood 2015). The aim of the current study was to examine ceritinib efficacy and safety in pts with advanced *ALK*+ non-lung solid tumors and hematological malignancies. **Methods:** In this open-label, multi-arm, phase 2 (NCT02465528) trial, adult pts with *ALK* gene abnormalities who had received ≥1 prior systemic therapy were administered oral ceritinib 750 mg/day, under fasted conditions. Primary endpoint: investigator assessed disease control rate (DCR); secondary endpoints: investigator assessed overall response rate (ORR), duration of response (DOR), time to response (TTR), progression-free survival (PFS), and safety. **Results:** Overall, 22 pts (ALCL [n = 1], IMT [n = 4], glioblastoma multiforme [GBM, n = 12] and others [n = 5]) were enrolled; median (m) age: 52.5 years; male: 50%; Stage ≥IV: 95.4%. Key efficacy results are shown in the Table. mTTR in pts with confirmed complete response (CR) or partial response (PR) [n = 4] was 7.4 (range, 6–25) weeks. mDOR was not reached. mPFS (95% CI) was 2.6 (1.6, 3.7) weeks. Most common adverse events (AEs; ≥30%) were: diarrhea and nausea (59.1% each), vomiting (50.0%) and increased alanine aminotransferase (31.8%). Most common grade ≥3 AEs (≥10%): hyperglycemia (18.2%), increased gamma-glutamyl transferase, thrombocytopenia, and anemia (13.6% each). Clinical trial information: NCT02465528. **Conclusions:** Ceritinib 750 mg/day under fasted conditions showed antitumor activity in pts with *ALK*+ ALCL and IMT; however, data interpretation is limited due to the small sample size. Safety findings were consistent with the known ceritinib safety profile.Research Sponsor: Novartis.

	ALCL (n = 1)	IMT (n = 4)	GBM (n = 12)	Others* (n = 5)	All pts (n = 22)
CR, n (%)	1 (100.0)	0	0	0	1 (4.5)
PR, n (%)	0	3 (75.0)	0	0	3 (13.6)
SD, n (%)	0	0	0	2 (40.0)	2 (9.1)
ORR: CR+PR, % (95% CI)	100.0 (2.5, 100.0)	75.0 (19.4, 99.4)	0 (0, 26.5)	0 (0, 52.2)	18.2 (5.2, 40.3)
DCR: CR+PR+SD, % (95% CI)	100.0 (2.5, 100.0)	75.0 (19.4, 99.4)	0 (0, 26.5)	40.0 (5.3, 85.3)	27.3 (10.7, 50.2)

*Pts with primary tumor in soft tissue (n = 3), colon (n = 1) and stomach (n = 1).
SD, stable disease.

3522 Poster Session (Board #252), Fri, 8:00 AM-11:00 AM

Longitudinal cumulative dose: A novel measure to assess multiple dimensions of chemotherapy adherence over time. *First Author: Michael Webster-Clark, University of North Carolina at Chapel Hill, Chapel Hill, NC*

Background: Adjuvant chemotherapy regimens take months to complete. Despite this, trials and observational studies evaluate chemotherapy adherence via measures assessed at the end of treatment (e.g. number of patients missing any dose, relative dose intensity [RDI]). This approach misses information that impacts outcomes, like treatment delays. We propose longitudinal cumulative dose (LCD) as a way to integrate the impact of dose reductions, missed doses, and dose delays at each cycle over time. **Methods:** We obtained data from the 2,246 participants in the Multicenter International Study of Oxaliplatin/5FU-LV in the Adjuvant Treatment of Colon Cancer (MOSAIC). We evaluated proportions of patients stopping treatment early and reducing (based on protocol), missing, or delaying a dose in each arm for each chemo agent at each visit. We obtained LCD, the fraction of the final standard dose a participant reached by a given day, for each participant and each chemo agent. We compared LCD medians over time and at the end of a standard regimen (24 weeks) between treatment arms and by age and performance status. We assessed agreement between oxaliplatin LCD and RDI with Fleiss' kappa (Table). **Results:** Participants randomized to FOLFOX were more likely than those randomized to 5FU to stop treatment, reduce doses, miss doses, or delay visits; these differences increased over time. Median LCD for oxaliplatin in the FOLFOX arm at 24 weeks was 77%. Graphs of median LCD for 5FU showed a clear difference between arms (FOLFOX arm median LCD: 81%; 5FU arm median LCD, 96%). While 5FU LCD decreased with age in the FOLFOX arm (median LCD in those age <40: 85%; 40-64, 82%; 65-75, 76%), it was similar across ages in the 5FU arm (median LCD 94%, 96%, and 96%, respectively), with smaller performance status trends. RDI and LCD showed fair agreement (Fleiss' kappa=0.34); 19% of those with RDI over 85% had LCD under 60%. **Conclusions:** Visualizing LCD highlighted the timing and scale of deviations from standard administration, with major differences in 5FU LCD across arms. Next steps include evaluating if LCD predicts clinical outcomes. Research Sponsor: Patient Centered Outcomes Research Institute.

Comparison of oxaliplatin LCD versus RDI.

	RDI <60%	RDI 60%-85%	RDI > 85%
LCD <60%	133	62	84
LCD 60%-85%	55	165	25
LCD >85%	10	244	332

3523 Poster Session (Board #253), Fri, 8:00 AM-11:00 AM

A phase Ib study of simmitecan (LP) single-agent and in combination with 5-fluorouracil/leucovorin (5-FU/LV) or thalidomide (T) in patients with advanced solid tumor. *First Author: Jifang Gong, Gastrointestinal Medical Oncology, Beijing Cancer Hospital, Beijing, China*

Background: Simmitecan (LP), a novel 9-substituted lipophilic camptothecin derivative, is a potent inhibitor of topoisomerase I with anti-tumor activity single agent or in combination with other anti-tumor agents, i.e. thalidomide or anti-PD-1 antibody in xenograft models. In this phase Ib study (NCT02870036), we evaluate the safety and anti-tumor effects of LP as monotherapy or in combination therapies in patients (pts) with advanced solid tumors. **Methods:** This open-label, multi-cohort phase Ib study was conducted at 3 academic centers in China. Eligible pts had advanced cancer without standard treatment options. Prior irinotecan treated failure pts was eligible. In the single agent study, enrolled pts was allocated to received intravenous(iv) 50, 80, or 120 mg/m^2 of LP Q2W to determine the safety of LP. After single agent study finished, enrolled pts allocated in LP+5-FU/LV cohorts received 50, 65, or 80 mg/m^2 of LP then LV 400 mg/m^2 and 5-FU bolus at 400 mg/m^2 followed by 5-FU continuous iv of 2400 mg/m^2 Q2W; pts in LP+T cohorts received LP 65 mg/m^2 Q2W + thalidomide 50mg QD or thalidomide 100mg QD, or LP 80 mg/m^2 Q2W + thalidomide 50mg QD. Treatment repeated in 28-day cycles until disease progression or unacceptable toxicity. **Results:** Between October 2016 to February 2019, 41 pts, median age of 55.1 (range 29-69) years, were enrolled, 13 in LP monotherapy, 10 in LP + 5-FU/LV and 18 in LP + T. Over all, no dose limited toxicity (DLT) occurred. The most common (≥20%) grade 3/4 AE among three regimens was neutropenia (44%, 70% and 89% respectively in LP, LP+5FU/LV and LP+T),and treatment related SAEs were similar, i.e. anemia and febrile neutropenia (11.1% each) in LP, diarrhea (10%) in LP+5-FU/LV, febrile neutropenia (5.6%) in LP+T. Majority of enrolled pts (24/41, 59%) had progressed on prior irinotecan, nevertheless, partial response (PR) was observed in 1 colorectal cancer pt treated with LP 80 mg/m^2 + thalidomide 50mg. Disease control rate (DCR, SD≥12 weeks or CR or PR) were 60%, 80% and 61% and median progress free survival were 2.71, 4.17 and 2.76 months respectively in LP, LP + 5-FU/LV and LP+T cohorts. **Conclusions:** This study showed the safety profiles are manageable, either LP monotherapy or combination therapies, no DLT or safety concern was elicited in combination compared to single agent, and the LP + 5-FU/LV regimen showed higher DCR. A phase II study in pts with metastatic NEC is on-going to explore safety and efficacy of LP + 5-FU/LV regimen combined with toripalimab, an anti-PD-1 antibody. Clinical trial information: 02870036. Research Sponsor: Shanghai HaiHe Pharmaceutical Co.,Ltd.

3524 Poster Session (Board #254), Fri, 8:00 AM-11:00 AM

Intratumoral exposure levels of pentaglutamated pemetrexed following treatment with LEAF-1401 and pemetrexed. *First Author: Gwangseong Kim, L.E.A.F. Pharmaceuticals LLC, Woburn, MA*

Background: The activity of pemetrexed is highly dependent on the intracellular enzyme folypolyglutamate synthase (FPGS) which adds glutamates to pemetrexed and yields very potent pemetrexed polyglutamates. Pemetrexed pentaglutamate (tetraglutamated pemetrexed) is 80-fold more potent than pemetrexed in inhibiting thymidylate synthase. Yet it is a poor drug candidate because it cannot readily cross the negatively charged cell membrane due to its own negative charge. We are developing LEAF-1401, a novel nanoliposomal encapsulation of gamma L-pentaglutamated pemetrexed. Because liposomes can readily be taken up by tumor cells, for its anti-tumor effect, LEAF-1401 can directly deliver pentaglutamated pemetrexed into tumor cells, bypassing the need for transmembrane folate carriers and FPGS which are both downregulated in resistant tumors. **Methods:** To measure drug levels in tumor, blood and various tissues (biodistribution), *in vivo* testing of LEAF-1401 and pemetrexed was conducted in a CT-26 murine colorectal carcinoma xenograft model. Animals were treated with a single dose of either LEAF-1401 (80mg/kg; equivalent to 32 mg/kg pemetrexed) or pemetrexed (118mg/kg). Tumor growth inhibition and clinical assessments were conducted. Animals were sacrificed: 5 mice per timepoint in each group and tumor, blood, liver, spleen and other tissues were harvested. Pentaglutamated pemetrexed levels were quantitatively analyzed by LC/MS/MS. **Results:** Compared to pemetrexed, LEAF-1401 treatment resulted in a 19-fold increase in exposure levels of pentaglutamated pemetrexed in the tumor and significant tumor growth inhibition. Plasma levels of pentaglutamated pemetrexed were high with LEAF-1401, but undetectable with pemetrexed. Like other liposomes, LEAF-1401 also resulted in accumulation of pentaglutamated pemetrexed in the liver and spleen (See Table below). Treatment appeared to be generally well tolerated. **Conclusions:** LEAF-1401, given at approximately a quarter of the equivalent pemetrexed dose, resulted in a 19-fold increase in pentaglutamate pemetrexed in tumor tissue compared to regular pemetrexed. LEAF-1401 represents a promising new class of novel nanoliposomal antifolates, that enhance the intratumoral delivery of potent polyglutamate antifolates, and improve antitumor activity while retaining an acceptable safety profile. Research Sponsor: L.E.A.F. Pharmaceuticals.

	Tissue Pentaglutamated Pemetrexed Levels (AUC: h*mg/mL)	
	LEAF-1401 dosed group	Pemetrexed dosed group
Tumor	0.38	0.02
Blood (plasma)	76.37	< LLOQ
Liver	9.22	< LLOQ
Spleen	1.35	0.0004

3525 Poster Session (Board #255), Fri, 8:00 AM-11:00 AM

Liquid biopsies to enable non-invasive real-time functional chemoresistance profiling in solid organ cancers. *First Author: Dadasaheb B Akolkar, Datar Cancer Genetics Limited, Nasik, India*

Background: Despite the development of targeted therapy agents and immune checkpoint inhibitors (ICI), cytotoxic anticancer agents remain the mainstay of treatment in several solid organ cancers. However, instances of innate and acquired resistance towards these anticancer agents can lead to treatment failures, which remain undetectable until clinical or radiological manifestation of symptoms suggestive of disease progression. There are presently no viable means or markers to detect or monitor for chemoresistance in real time. Owing to this unmet need, cancer treatment strategies face risks of failure and poor outcomes. **Methods:** We obtained 15 mL blood from 3,662 patients with various solid organ cancers, of various states and including treatment-naïve and pretreated patients. Circulating Tumor Associated Cells (C-TACs) were enriched and harvested from PBMCs using an epigenetically activating medium that is cytotoxic towards non-malignant epithelial and hematolymphoid cells in blood, but confers survival benefit on apoptosis resistant cells of tumorigenic origin (Circulating Tumor Associated Cells, C-TACs). In a subset of patients, fresh tumor tissue was also obtained from which viable tumor derived cells (TDCs) were obtained. Viable TDCs and C-TACs were treated with a panel of anticancer agents and the surviving cell fraction estimated to determine chemoresistance. **Results:** Among the 1,325 therapy naïve patients, resistance towards treatment agents was observed in C-TACs from 56.3 % of samples. Among 2,201 pretreated patients' samples, resistance towards treatment agents was observed in C-TACs from 77.8% of samples. The increased resistance in C-TACs from pretreated patients indicated that the C-TACs had been resistance-educated by prior therapies. In a subset of patients, Chemoresistance profile of C-TACs was observed to be 96.9% concordant with that of tumor derived cells (TDCs) which were concurrently obtained from tumor tissue indicating that C-TACs accurately represent chemo-antecedents of the tumor. **Conclusions:** Non-invasive chemoresistance profiling of C-TACs is a viable strategy to monitor treatment efficacy in real time. Adoption of this strategy in the clinic will not only guide treatment selection with reduced risk of failure, but will also enable timely therapeutic course correction upon detection of acquired chemoresistance. Research Sponsor: None.

3526 Poster Session (Board #256), Fri, 8:00 AM-11:00 AM

Pharmacokinetics, safety, and early activity of a nanoparticle micellar formulation of docetaxel in women with metastatic breast cancer: Results of two randomized trials (phase I and II). *First Author: Markus Joerger, Department of Oncology/Hematology, Cantonal Hospital St. Gallen, St. Gallen, Switzerland*

Background: Docetaxel micellar (DM) is a nano-sized particle formulation of docetaxel in which a retinoic acid derivative is used as solubilizer with a high drug to excipient ratio possibly resulting in reduced systemic toxicity or hypersensitivity reactions due to the excipient. DM is given without standard use of premedication, avoiding steroid-associated immunosuppression. Here we present the pharmacokinetics (PK) after a single dose of DM or polysorbate-solubilized docetaxel (D) as well as safety and early activity including overall response rate (ORR) in female patients with metastatic breast cancer. **Methods:** The PK study was a two-cycle, cross-over study where 30 patients were included and randomized to either DM followed by D or D followed by DM, both given as a 1-hour intravenous infusion at a dose of 100mg/m^2. The phase II study was a prospective, multicenter, open-label, third-party blinded, randomized, parallel group, active-controlled study including 200 patients to compare the early activity and safety of DM and D, both given as 100 mg/m^2 1-hour intravenous infusion every 21 days (1 cycle) for a total of 6 cycles. **Results:** Bioequivalence of total docetaxel in plasma, AUC0-last and Cmax, was demonstrated for DM compared to D. The incidence of adverse events was higher in the D arm than in the DM arm for the majority of SOCs and PTs in the phase II study. Overall, Grade 3 or 4 AEs were reported for 82.7% of patients from DM arm and 99.0% of patients from D arm. Twelve (12.2%) patients in the DM arm and 24 (24.0%) patients in the D arm needed at least one dose reduction due to AEs. The primary efficacy endpoint in the phase II study was based on the assessment according to Response Evaluation Criteria in Soldid Tumors (RECIST) 1.1 and non-inferiority was not reached based on the pre-defined non-inferiority margin. A post-hoc analysis investigating the ORR based on tumour assessment at the end of chemotherapy, and non-inferiority of DM as compared to D was shown (ITT population). **Conclusions:** DM is bioequivalent to D regarding total drug in plasma and provides a docetaxel formulation that spares patients steroid premedication. An improved safety profile for DM compared to D was shown while additional efficacy data is needed for future development of DM. Eudra CT: 2012-005161-12 and 2013-004889-33. Clinical trial information: 2012-005161-12 and 2013-004889-33. Research Sponsor: Oasmia Pharmaceutical AB.

3527 Poster Session (Board #257), Fri, 8:00 AM-11:00 AM

Liquid biopsy: A community-based oncology practice experience. *First Author: Khalil Choucair, Kansas University School of Medicine, Wichita, KS*

Background: Liquid biopsy is a promising and minimally invasive genetic test examining plasma circulating tumor DNA. Coupled with the rapidly developing next-generation sequencing (NGS) technologies, it holds the potential for implementation in selecting signal-matched therapeutic options. **Methods:** A retrospective chart review was conducted on adult patients with advanced solid tumors whose tumors were tested with Guardant360 assay, between December 2018 and December 2019. A total of 178 patients were referred for testing by 12 oncologists within a single community cancer center. **Results:** Referral rates varied widely (2.25% - 22%). The majority of patients (98%) were tested upfront for molecular marker evaluation, in either newly diagnosed advanced cancer patients, or in recurrent patients without enough tissue for testing. Other patients (2%) were evaluated after failure of 1 st line therapy to assess for acquired mutations. A total of 18 histological types were tested, with lung (LCa; n = 90; 50.56%), breast (BCa; n = 31; 17.42%), and colorectal (CRCa; n = 14; 7.87%) cancers being the most common types. In 86.11% of all tests (n = 180), $\geq$ 1 alteration was detected, while 13.89 % of tests did not reveal any tumor-related mutation, and were considered negative. The average number of alterations per test was 3.1 ($\pm$2.14; n = 481), and varied across types: CRCa (4.36), prostate cancer (2.73), BCa (2.97), and LCa (2.59), had the highest average number of alterations per test. Similarly, LCa (48.44%), BCa (19.13%), and CRCa (12.68%), harbored most of the detected somatic alterations (n = 481). Of all the alterations of practical significance (n = 457), *TP53* (32.17%), *PIK3CA* (8.53%), *EGFR* (7.66%) and *KRAS* (7.22%), were the most commonly altered genes. Only 1 patient had a positive MSI-H status, amenable to immune-therapy. Of those with positive test results (n = 155), 31 (20%) had $\geq$ 1 FDA approved, target-matched therapeutic opportunity. Similarly, 71 patients (45.81%) had $\geq$ 1 target-matched therapeutic opportunity, outside current indications. Lastly, when no FDA-approved target-matched therapy was available (n = 39), results from liquid biopsy testing offered signal-based clinical trial opportunity in 39/39 patients. **Conclusions:** Implementation of NGS-based liquid biopsy testing is feasible within a community practice. In the era of precision oncology, such assays have the potential to expedite the efforts towards target-matched therapies and signal-based clinical trial opportunities. Further studies are warranted to identify the most-cost effective testing strategies. Research Sponsor: None.

3528 Poster Session (Board #258), Fri, 8:00 AM-11:00 AM

Exosomal circular RNAs derived from serum: Promising biomarkers for therapeutic targets and prognosis of triple-negative breast cancer (TNBC). *First Author: Sujin Yang, Department of General Surgery, the First Affiliated Hospital with Nanjing Medical University, Nanjing, China*

Background: Exosomes are well known by the "exosomal shuttle" that delivers oncogenic microRNAs (miRNAs), mRNAs, circular RNAs (circRNAs) and proteins to the recipient cells and tumor microenvironment, and may be used as promising biomarkers for disease diagnosis. This study aims to provide a theoretical basis to use stable exosomal circRNAs as new biomarkers for predicting the development, metastasis and therapeutic targets of TNBC. **Methods:** A strategy combining RNA-sequencing technique, bioinformatic analysis and RT-qPCR was used to determine the level of differential expressed circRNAs in serum exosomes samples (n = 43) from TNBC patients compared with non-TNBC patients. The expression of circHSDL2 were also detected in tumor tissues (n = 20) from TNBC patients and breast cancer cell lines by qRT-PCR. Cell cycle analysis, the wound healing assays and transwell assays were used to investigate the function of circHSDL2 in proliferation, invasion and metastasis of TNBC cells. FISH, dual-luciferase reporter and functional assays were performed to confirm the interaction between circHSDL2 and let-7a-2-3p in TNBC cells. **Results:** We profiled the circRNAs in the serum exosomes samples from TNBC patients and non-TNBC patients by RNA sequencing and detected 803 significantly differentially-expressed circRNAs. After bioinformatic analysis, circHSDL2 was chose to further study. RT-qPCR results showed that higher expression of circHSDL2 in TNBC cell lines and tumor tissues from TNBC patients. Moreover, overexpression of circHSDL2 promoted TNBC cells proliferation and invasion, while knockdown of circHSDL2 inhibited TNBC cells proliferation and invasion. Mechanistically, circHSDL2 acted as a "miRNAs sponge" to absorb let-7a-2-3p; let-7a-2-3p inhibited TNBC cell invasion and metastasis. Kaplan-Meier plots showed lower expression of let-7a-2-3p was connected to poor prognosis in TNBC metastasis patients from TCGA database. **Conclusions:** The expression of circHSDL2 was found significantly upregulated in serum exosomes and tumor tissues from TNBC patients. Moreover, circHSDL2 could promote cell proliferation, invasion and metastasis in TNBC cells. CircHSDL2 might be function as competing endogenous RNAs (ceRNAs) by targeting let-7a-2-3p in the progression of TNBC. Therefore, this study provides a fresh perspective on novel therapeutic targets and potential biomarkers for TNBC from exosomal circRNAs. Research Sponsor: National Natural Science Foundation of China (No. 81872365).

3529 Poster Session (Board #259), Fri, 8:00 AM-11:00 AM

MSK-ACCESS for noninvasive somatic mutation profiling of lung cancers utilizing circulating tumor DNA. *First Author: Emily S. Lebow, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Circulating cell-free DNA (cfDNA) next-generation sequencing (NGS) is a promising strategy for non-invasive molecular profiling of cancers. MSK-ACCESS (Analysis of Circulating cfDNA to Evaluate Somatic Status) is a hybridization-capture targeted NGS assay that detects somatic variants in select exons of 129 genes with matched white blood cell sequencing. We present the initial clinical experience with MSK-ACCESS among patients with advanced non-small cell lung cancer (NSCLC). **Methods:** Patients with stage IV NSCLC underwent prospective MSK-ACCESS testing at initial diagnosis or progression of disease on targeted therapy between June 2019 and January 2020. A subset of patients had matched tissue-based NGS testing with the MSK-IMPACT 468 gene assay. We assessed oncogenic driver detection, turnaround time, plasma-tissue concordance, and matching to therapy. National Comprehensive-Cancer Network designated driver alterations were included in evaluation of tissue-plasma concordance (EGFR, ALK, KRAS, MET, RET, BRAF, HER2, ROS1, NTRK). Turnaround time was compared by a two-sided Wilcoxon signed-rank test. **Results:** A total of 201 patients with NSCLC had MSK-ACCESS testing at initial diagnosis (n = 79) or following progression of disease (n = 122). The median turn-around-time from plasma collection to MSK-ACCESS report was 16 days (range: 9 – 36 days) compared to 19 days from lab receipt of tissue to report (range: 12 – 57) for MSK-IMPACT ($p < 0.001$). Among patients with a driver detected on MSK-ACCESS, 100% (92/92) had an identical driver detected on MSK-IMPACT. Among patients with a driver detected on MSK-IMPACT, 75% (92/123) had an identical driver detected on MSK-ACCESS. This rate was similar among patients who were treatment-naive (74%; 64/86) and had disease progression (76%, 28/37) at the time of MSK-ACCESS. MSK-ACCESS identified driver alterations that directly guided first-line targeted therapy (n = 18) with response in all patients with available radiographic follow-up (n = 10), including a patient without confirmatory tissue testing. MSK-ACCESS identified resistance alterations among patients with disease progression including EGFR T790M, EGFR C797S, ROS1 G2032R, as well as a BRAF fusion. **Conclusions:** MSK-ACCESS successfully identified driver alterations with high concordance to tissue-based testing, directly guided patients to therapy with clinical responses, and detected known and novel resistance mechanisms. This assay warrants further clinical development to guide and facilitate precision oncology. Research Sponsor: None.

3530 Poster Session (Board #260), Fri, 8:00 AM-11:00 AM

Exploitation of treatment induced tumor lysis to enhance sensitivity of ctDNA analysis: A first-in-human pilot study. *First Author: Daniel Adam Breadner, London Regional Cancer Program, London, ON, Canada*

Background: Blood based liquid biopsies examining circulating tumour DNA (ctDNA) have increasing applications in non-small cell lung cancer (NSCLC). Limitations in sensitivity remains a barrier to ctDNA replacing tissue-based testing. There is a paucity of data regarding the dynamics of ctDNA levels in the hours to days following a new treatment. We hypothesize that chemotherapy or radiation will yield an increased abundance of ctDNA in plasma by inducing tumor lysis, allowing for the detection of genetic alterations that were occult in baseline testing. **Methods:** Two prospective cohorts of 20 patients (pts) with stage III/IV NSCLC were enrolled. Cohort 1 (C1) contained pts starting the first cycle of platinum doublet chemoradiation (C1a, n=10) or the first cycle of platinum doublet cytotoxic chemotherapy ± immunotherapy without radiation (RT) (C1b, n=10). Cohort 2 (C2) contained pts receiving palliative RT alone. Two baseline samples were collected, the first ≤ 14 days prior to starting treatment and one immediately prior to treatment. In C1, subsequent samples were collected 3, 6, 24 and 48 hours post initiation of chemotherapy. Pts in C2 had samples collected immediately prior to RT fractions 2, 3, and 4. Samples were analyzed for ctDNA using the 36-gene amplicon-based NGS Inivata InVisionFirst-Lung assay. **Results:** Complete results were available for the first 35 of 40 enrolled pts, C1a – 10 pts, C1b – 9 pts, C2 – 16 pts. Detectable ctDNA was present at baseline in 27 pts (77%), 4 additional pts (11%) had detectable ctDNA in post treatment samples. Four of the patients with detectable ctDNA at baseline (15%) had new genetic alterations detected in post treatment samples. A total of 8/35 pts (23%) had new genetic alterations detected in the post treatment samples. Mutant molecule numbers increased with treatment in 23 of 31 (74%) pts with detectable ctDNA, C1 - 13 of 19 pts (68%) and C2 - 10 of 16 pts (63%). ctDNA levels peaked a median of 2.2 hours (IQR: 1.5 – 2.9 hours) after the initiation of chemotherapy and a median of 1 day (IQR: 1-2 days) after radiation was commenced. The percentage increase in ctDNA levels was a median of 29% (IQR: -18 to +112%) in C1. C2 had a median increase of 16% (IQR: 0 to +131%). **Conclusions:** ctDNA levels increase in the hours to days after starting treatment. ctDNA testing in the acute post treatment phase can yield results that were not evident in pretreatment testing. Application of this principle could improve ctDNA utility as an alternate to tissue-based testing and improve sensitivity for the detection of treatment-resistant clones. Research Sponsor: None.

3531 Poster Session (Board #261), Fri, 8:00 AM-11:00 AM

Longitudinal and personalized detection of circulating tumor DNA (ctDNA) for monitoring efficacy of atezolizumab plus bevacizumab in patients with unresectable hepatocellular carcinoma (HCC). *First Author: Chih-Hung Hsu, National Taiwan University Cancer Center, Taipei City, Taiwan*

Background: ctDNA has emerged as a promising biomarker for noninvasive monitoring of treatment response and disease progression in many tumor types. However, the clinical use of ctDNA in patients with HCC has not been established. Here, we evaluated longitudinal and personalized detection of ctDNA for monitoring the treatment response to atezolizumab (atezo) + bevacizumab (bev) in patients with unresectable HCC not previously treated with systemic therapy. **Methods:** A subset (n = 48) of 104 patients with HCC who enrolled in Arm A of GO30140 (NCT02715531; Phase 1b) and received atezo + bev treatment were included in this study. These patients had 10 CR, 11 PR, 12 SD and 15 PD per IRF-assessed RECIST 1.1. Serial plasma samples were collected at baseline (Cycle [C]1 Day [D]1), during treatment (C2D1, C4D1) and at disease progression. Somatic mutations in individual tumors were identified via whole exome sequencing of archival tumor tissues or fresh biopsies collected before treatment. Personalized ctDNA assays (Signatera 16-plex multiplex PCR next-generation sequencing assay) specific to each patient's tumor mutational signatures were successfully designed for 47 of 48 patients. **Results:** At C1D1, a median of 25.7 ng of cell-free DNA was extracted from 2-mL plasma samples. ctDNA was detected in 45 of 47 patients (96%), with a median of 70.6 mean tumor molecules/mL of plasma (MTM/mL) and a median of 1.8% mean variant allele frequency (mean VAF) in plasma. Higher ctDNA levels detected at C1D1 appeared to be associated with increased tumor burden ($P < 0.03$). Dynamic changes in ctDNA levels post-treatment were associated with response at C4D1. ctDNA status changed from positive at baseline to negative in 7 of 10 CR (70%), 3 of 11 PR (27%), 1 of 11 SD (9%) and 0 of 11 PD (0%) patients. Longer PFS was observed in patients whose ctDNA became undetectable post-treatment. The median PFS in patients with ctDNA present vs cleared at C4D1 was 6.5 months and not reached, respectively (HR, 12 [1.7-93], log-rank $P < 0.00029$). **Conclusions:** Our study showed that Signatera, a personalized and tumor-informed ctDNA assay, could be used as a sensitive method for detecting ctDNA in patients with unresectable HCC. More importantly, our results illustrate the promise of ctDNA as an emerging biomarker that may potentially help to monitor treatment responses and disease progression in patients with HCC. Research Sponsor: F. Hoffmann-La Roche, Ltd.

3532 Poster Session (Board #262), Fri, 8:00 AM-11:00 AM

Comprehensive genomic profiling of 216 Chinese patients with renal cell carcinoma. *First Author: Congwang Zhang, GloriousMed Technology Co., Ltd., Shanghai, China*

Background: Renal cell carcinoma (RCC), a global public health problem, has exhibited a gradual rise in incidence. Unfortunately, the scarcity of effective biomarkers in the clinical became a major limitation of the progress of biological therapies. Therefore, it is imperative to accurately comprehend RCC genomic profiling for exploring its clinical treatment strategies. **Methods:** Formalin Fixed Paraffin Embedded (FFPE) tumor and matched blood samples of 216 Chinese RCC patients were obtained for next-generation sequencing (NGS)-based 620 cancer genes panel assay and RCC genomic profiling was evaluated. **Results:** In our Chinese RCC cohort, multiple histological subtypes, encompassing clear cell (96/216, 44.44%), papillary (14/216, 6.48%), chromophobe (2/216, 0.93%), and undefined subtypes (104/216, 48.15%) were included. The top ranked genomic alterations in Chinese RCC patients were VHL (45.83%), PBRM1 (17.1%), BAP1(13.89%), TP53 (10.65%), SETD2 (9.29%), MTOR (8.67%), ARID1A (5.6%), PTEN (5.09%). Interestingly, BAP1, PBRM1 were co-mutated with VHL, and MET, NF2 were mutually exclusive with VHL (all $p < 0.05$). Of these patients, 87.9% (190/216) of RCC patients had at least one genomic alteration, indicating the potential clinical benefits of targeted therapies. Out of 15 most common canonical pathways, potentially targetable genomic alterations were mainly identified in HIF (45.83%), chromatin remodeling (42.59%), PI3K/AKT (24.07%), DNA damage response (19.44%), RTK-RAS (18.06%), TP53 (15.74%), NOTCH (9.72%), Hippo (9.72%), and WNT (5.56%) pathway. Additionally, HIF pathway was commonly co-altered with chromatin remodeling pathway, and WNT and NOTCH pathways were significantly co-altered with TP53 pathway. Rare mutation types such as CDKN2A-DMRTA1 and HOOK1-ALK were also detected. Across samples, the median TMB was 2.2 (0-18.6) mutations/Mb. Only 2 Chinese RCC patients had TMB-high (> 10 mutations/Mb). **Conclusions:** Our results displayed the landscape of genomic alterations in 216 Chinese RCC patients. The genomic alterations identified in our study may provide an opportunity to discover potential strategies for targeted and immunotherapy in RCC. Future studies should account for these genomic alterations. Research Sponsor: None.

3533 Poster Session (Board #263), Fri, 8:00 AM-11:00 AM

Genomically informed longitudinal monitoring of circulating tumor DNA (ctDNA) to predict outcomes of cancer therapy. *First Author: Mohamed Alaa Gouda, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Short fragments of ctDNA can be detected and quantified from blood samples of patients with cancer. We hypothesize that dynamic changes in quantity of ctDNA in patients with advanced solid cancers during the first few weeks of therapy can predict treatment outcomes reported by standard imaging. **Methods:** We enrolled patients with advanced cancers treated with experimental therapies, who had blood collection for ctDNA isolation and testing at baseline, mid-cycle and at the time of restaging imaging. Patients who were treated with multiple treatment lines were included with separate record for each therapy. Genomically informed molecular testing of ctDNA was performed using unamplified droplet digital PCR (QX200, Bio-Rad) designed based on known molecular profile of tumor tissue and ctDNA was quantified as aggregate variant allele frequency (VAF%) for detected molecular aberrations. Patients were classified based on results of their first restaging imaging as responders (complete [CR] or partial response [PR]) vs. non-responders (stable disease [SD], progressive disease [PD]) and progressors (PD) vs. non-progressors (CR, PR, SD). **Results:** Total of 85 patients who received 132 courses of therapies between May 2012 and June 2019 were analyzed. Breast (N = 21), melanoma (N = 14) and cholangiocarcinoma (N = 14) were most frequent tumor types. Aggregate VAF at mid-cycle was higher in non-responders (3.98%) compared to responders (0.40%, P = 0.016) and in progressors (4.40%) compared to non-progressors (2.10%, P = 0.019) as measured by 5% trimmed mean. Similarly, aggregate VAFs at first imaging restaging was higher in non-responders (5.10%) compared to responders (0.10%, P = 0.001) and in progressors (10.80%) compared to non-progressors (0.90%, P < 0.001). Progressors demonstrated increase in ctDNA VAF at the time of the first imaging restaging compared to decrease in non-progressors (0.7% vs. -4%, P = 0.015). In addition, increase in ctDNA VAF at the first imaging restaging was associated with more PD (44% vs. 8%, P = 0.019) and less PR/CR (0% vs. 31%, P < 0.001). Median time-to-treatment failure was shorter in patients with increase in ctDNA VAF at the time of the first imaging restaging (52 days vs. 89 days, P = 0.002). **Conclusions:** Dynamic changes in quantity of blood-derived ctDNA within the first few weeks of therapy correspond with treatment outcomes reported by the first restaging imaging and time-to-treatment failure. Research Sponsor: NCI NIH Cancer Center support grant, Rising Tide Foundation, Sabin Family Foundation.

3534 Poster Session (Board #264), Fri, 8:00 AM-11:00 AM

Subcellular partitioning of Kaiso (ZBTB33) as a biomarker to predict overall breast cancer survival. *First Author: Sandeep K Singhal, Department of Pathology, School of Medicine and Health Sciences, University of North Dakota, Grand Forks, ND*

Background: The epigenetic transcriptional regulator, Kaiso (ZBTB33) has been identified as a member of the C2H2 zinc finger proteins containing a BTB/POZ -zinc finger family of transcription factors that are implicated in development of cancer. Although, our understanding of clinical relevance of subcellular distribution (cytoplasmic/nuclear) Kaiso in the growth and survival of human Breast cancer (BC) is limited. **Methods:** We examined a cohort of 555 BC patients who underwent surgery for their primary BC in Greenville, NC using AI and SM approach. **Results:** The sub-classification BC shows, cytoplasmic Kaiso is differentially enriched in ER- BC (p=0.001) compared nuclear Kaiso (p=0.8) and is significantly enriched in the more aggressive classes LumB (p=0.0017), HER2+ (p=0.05) and TNBC (p=6.1e-07) with respect to LumA BC patients. Additionally, the survival analysis of different compartments of Kaiso demonstrates that high cytoplasmic Kaiso (HR = 16.29 (7.6 – 34.8), p = 5.5e−13) is much more predictive of poor survival compared to nuclear Kaiso (HR = 2.83 (2.02 – 3.8), p = 6.1e−11). At gene expression level, ZBTB33 mRNA levels do not correlate with either nuclear (Spearman correlation: -0.03157, p= 0.7267) or cytoplasmic levels (Spearman correlation: -0.03526, p= 0.6962) of Kaiso. Surprisingly, ZBTB33 mRNA abundance is predictive of poor overall BC survival as demonstrated in two independent publicly available BC cohorts Metabric (HR = 2.14 (1.49 − 3.08), p = 2.7e−05) and Gyorffy B et al. (HR = 1.81 (1.55 − 2.12), p = 2.5e−14). Nuclear and cytoplasmic levels of Kaiso do not show significant differences based on race p=0.27 and p=0.1 respectively. **Conclusions:** Our data suggest subcellular distribution of high Kaiso is associated with poor prognosis of BC survival and subcellular localizations of Kaiso may play differential biological roles in BC prognosis. Research Sponsor: the NCI and the National Institute on Minority Health and Health Disparities, Bethesda Maryland, 20892, The NIH/NCI Cancer Center Support Grant P30CA013696, the Susan G. Komen (Sponsor ID: SAC160072) Grant in support of the Triple-Negative Breast Cancer i.

3535 Poster Session (Board #265), Fri, 8:00 AM-11:00 AM

Circulating stromal cells as a potential blood-based biomarker for screening invasive solid tumors. *First Author: Daniel Adams, Creatv MicroTech, Inc., Monmouth Junction, NJ*

Background: Peripheral blood allows for a simple non-invasive method for isolating various cancer associated circulating stromal cells (CStCs) which may predict for cancer presence. Cancer Associated Macrophage-Like cells (CAMLs), a specific CStC, are phagocytic myeloid cells that derive from an immunological response to cancer and emanate from primary tumors. Using a filtration platform we screened the peripheral blood of untreated newly diagnosed cancer patients (n = 308) for CAMLs. In parallel, we screened patients with newly diagnosed non-malignant diseases, i.e. lupus, benign cysts, etc. (n = 39), and healthy control samples (n = 76). We found that CAMLs are highly prevalent (87%) in the blood of cancer patients, but uncommon in non-malignant conditions (20%) & absent in healthy individuals (0%). **Methods:** Anonymized peripheral blood were taken from 308 cancer patients after confirmation of invasive malignancy [stage I (n = 76), stage II (n = 73), stage III (n = 72), stage IV (n = 65) and unstaged non-metastatic (n = 22)] with pathologically confirmed lung (n = 65), pancreas (n = 53), breast (n = 52), prostate (n = 40), esophageal (n = 30), renal cell (n = 18), hepatocellular (n = 15), neuroblastoma (n = 10), melanoma (n = 8), and other (n = 17). Further, anonymized blood was taken from patients with untreated non-malignant conditions including benign breast masses (n = 19), lupus (n = 11), liver cirrhosis (n = 5), benign prostatic hyperplasia (BPH) (n = 3), and viral infection (n = 1); or from healthy control volunteers (n = 76). CAMLs were isolated from whole peripheral blood by the CellSieve™ microfiltration technique and defined as enlarged, multinuclear cells with cytokeratin and/or CD45/CD14 positive. **Results:** CAMLs were found in 87% of all cancer patients regardless of stage, ~5.4 CAMLs/7.5mL blood. Specifically, CAMLs were found in 80% of Stage I, 90% Stage II, 89% Stage III, and 97% Stage IV patients. No CAMLs were found in any healthy controls, but were found in 26% of benign breast masses, 18% of lupus, 0% of BPH and 0% of cirrhosis. In total, CAML sensitivity in cancer vs healthy was 87% (CI95% 82-90%), specificity = 100% (CI95% 95-100%), PPV = 100% (CI95% 100%), NPV = 67% (CI95% 58-71%). CAML sensitivity in cancer vs benign was 87% (CI95% 82-90%), specificity = 80% (CI95% 64-91%), PPV = 97% (CI95% 95-98%), NPV = 43% (CI95% 35-51%). **Conclusions:** CAMLs, a Circulating Stromal Cell subtype, is a sensitive blood based biomarker found in all stages of cancer that is rare in non-malignant conditions and absent in healthy individuals. Research Sponsor: U.S. National Institutes of Health, Other Government Agency.

3536 Poster Session (Board #266), Fri, 8:00 AM-11:00 AM

Clinical potential of ctDNA-based TMB in small cell lung cancer recieving chemoradiotherapy. *First Author: Ying Jin, Institute of Cancer and Basic Medicine, Chinese Academy of Sciences, Department of Medical Oncology, Cancer Hospital of the University of Chinese Academy of Sciences & Zhejiang Cancer Hospital, Zhejiang Key Laboratory of Radiation Oncology, Hangzhou, China*

Background: Small cell lung cancer (SCLC) is an aggressive tumor with poor prognosis. Chemotherapy and / or radiotherapy is the main choice of SCLC treatment. Circulating tumor DNA (ctDNA) has received substantial attention in recent years owing to the potential of patient stratification and monitoring. Here, we assessed the value of prediction and prognosis using ctDNA in SCLC. **Methods:** SCLC patients (pts) with limited-stage disease (LD) receiving chemoradiotherapy and extensive-stage disease (ED) receiving chemotherapy were enrolled. Baseline plasma samples were collected for NGS using a 1021-gene-panel. Mutational features and blood-based tumor mutation burden (bTMB) were analyzed using ctDNA. pyClone software was used to cluster the mutations. The mutations in the cluster with the highest cancer cell fraction (CCF) were defined as clonal mutations. Progression-free survival (PFS) was followed. **Results:** 58 SCLC pts (35 LD and 23 ED) and 58 plasma samples were enrolled. Smoking pts accounted for 84% (49/58). In all samples, recurrent genes were TP53 (86%), RB1 (57%), LRP1B (34%), CREBBP (26%), and MLL3 (22%). The median of bTMB and clone count were 7.9 [0-26] and 7 [0-25]. Significant higher bTMB and clone count were observed in ED pts compared with LD (Mann Whitney test, p = 0.019 and p = 0.041, respectively). Mutated *CREBBP* (10/23 ED versus 5/35 LD) was enriched in ED (Fisher exact test, p = 0.017 and OR = 0.223). Mutations in NOTCH signaling pathway were enriched in ED (l6/23 ED versus 13/35 LD, p = 0.031, OR = 0.265). In LD group, there were trend toward prolonged PFS in pts with higher bTMB(p = 0.065), and pts with higher clonal bTMB (cbTMB) exhibited significant longer PFS (p = 0.016, HR 0.37, 95% CI [0.12-1.11]). Patients with alteration in PIK3CA showed shorter PFS than wild type (p < 0.001, HR 0.11, 95% CI [0-2.86]). There were no significant difference in median PFS in LD stage pts with any detectable pathway alterations. Whereas, LD pts whose ctDNA contained RTK-RAS signaling pathway alterations exhibited shorter PFS than pts without those alterations (p = 0.135). In ED pts, NOTCH1 gene wild type displayed longer PFS than mutant type (p = 0.036, HR 0.38, 95% CI [0.1-1.53]). There were no difference in PFS between pts with higher and lower bTMB and cbTMB. **Conclusions:** ctDNA can characterize the mutational feature of SCLC. There are differences in the molecular characteristics between ED and LD pts. Clonal bTMB is a potential prognostic biomarker for LD SCLC chemoradiotherapy. The prognostic marker of ED chemotherapy is different from LD. Research Sponsor: None.

3537 Poster Session (Board #267), Fri, 8:00 AM-11:00 AM

Circulating tumor DNA dynamics to predict cancer recurrence/metastasis in Chinese pathologic stage I lung adenocarcinoma. *First Author: Chao Cheng, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Pathologic(p)stage I lung adenocarcinoma (LUAD) patients exhibit high levels of genetic heterogeneity and the association between the genomic characteristics of (p)stage I LUADs and tumor recurrence remains poorly understood. Circulating tumor DNA (ctDNA) monitoring after resection represents a useful tool to predict response to therapy and tumor recurrence but its application in (p)stage I LUAD patients remains controversial. In addition, it is of great clinical interest to decipher the difference of genetic features between ground-glass opacity (GGO) and solid nodules (non-GGO) subgroups. **Methods:** Tumor tissues and matched post-operative plasma samples were collected from a total of 86 Chinese (p)stage I LUAD patients who were enrolled in a clinical study (NCT03172156). Comprehensive genomic profiling was performed using capture-based hybrid next generation sequencing by targeting 422 cancer relevant genes. **Results:** *EGFR* and *TP53* represent commonly mutated genes in this cohort of (p) stage I lung adenocarcinoma, followed by alterations in *ALK*, *PIK3CA*, *STK11*and *MYC*. For a median follow up period of 21.54 months after surgical resection, we observed that ctDNA positivity significantly correlated with an increased probability of early tumor recurrence or metastasis (P= 0.03, HR = 7.9), and in particular, the *EGFR* mutation status of ctDNA samples rather than that of primary tumor samples significantly correlated with shorter disease-free survival (DFS). Further comparison between GGO and non-GGO subgroups indicated that the frequency of *TP53* mutations in non-GGO was markedly higher than that in GGO (48% vs 20%, $P<$ 0.05). In addition, pathway analysis showed that the epigenetic regulation pathway was more frequently affected in the GGO subgroup, while impaired apoptosis/cell cycle pathway was more enriched in the non-GGO LUADs. **Conclusions:** Our data show that ctDNA positivity, including the *EGFR* mutation status, significantly correlated with early relapse or metastasis after surgery, representing a useful tool to predict treatment response and tumor relapse in (p)stage I LUAD patients. Mutated *TP53* was more abundant in non-GGO comparing to GGO (p)stage I LUADs that may act as potential oncogenic driver in LUAD development and/or disease progression. Clinical trial information: NCT03172156. Research Sponsor: National Natural Science Foundation of China (81572391), National Natural Science Foundation of China (11671409) and the Project for Science and Technology Development of Guangdong Province, China (2017A020215167).

3538 Poster Session (Board #268), Fri, 8:00 AM-11:00 AM

Evaluation of Genexus system that automates specimen-to-report for cancer genomic profiling within a day using liquid biopsy. *First Author: Siew-Kee Kee Low, Cancer Precision Medicine Center, Japanese Foundation for Cancer Research, Tokyo, Japan*

Background: Genomic profiling of patients' tumors using NGS system help in facilitating molecular-guided therapy. The turnaround time from specimen to report by the NGS system is important to deliver result timely for clinical decisions. The Genexus Integrated Sequencer automates all steps of the targeted NGS workflow starting from nucleic acid of formalin-fixed paraffin-embedded tissues or plasma that significantly reduce laborious procedures. Importantly, the whole specimen-to-report workflow delivers results in a single day. In this study, we evaluated detection rate of alteration using Oncomine Precision Assay (OPA) on Genexus system with cell-free DNA (cfDNA) from non-small cell lung cancer (NSCLC). **Methods:** Among the cfDNA from 48 plasma samples of NSCLC were evaluated, 19 were newly-diagnosed cases with *EGFR* mutations in cancer tissues and 29 cases were patients who experienced progression of disease after first line of EGFR, ALK or ROS1-targeted therapy. 13-20ng of input cfDNA were subjected to automated Genexus Integrated Sequencer for library construction using OPA panel, templating and sequencing. OPA panel covers actionable hotspot mutations, copy number gains or loss, fusion drivers. The concordance of mutation profiles between the tumor tissue and cfDNA and detection of a resistance mutation(s) during molecular-targeted therapy were evaluated. **Results:** The sequencing resulted in median overall reads of 8,698,358, median overall depth of 30,648 (range 15,069-48,707) and median molecular coverage of 1,595 (range 859-2,550). Among 48 samples examined, 44 were detected to carry at least one somatic mutation, giving the detection rate of 92%. A total of 17 of 19 newly diagnosed EGFR-positive patients were also detected to carry *EGFR* mutations. Importantly, these 17 patients carry the same mutation that was found in tissue samples implying complete concordance. In addition, we found novel resistance mutations in plasma of the patients who were under EGFR, ALK or ROS1 targeted therapies. **Conclusions:** Genexus Integrated Sequencer is a fully automated and highly accurate NGS system with a 1-day turnaround time that could assist clinicians to make more timely decision. Novel actionable, resistance mutations were detected using OPA panel that provide potential options for molecular-guided therapy and may help the better understanding of resistance mechanism of targeted therapy. Research Sponsor: Council for Science, Technology and Innovation (CSTI), cross-ministerial Strategic Innovation Promotion Program (SIP), "Innovative AI Hospital System".

3540 Poster Session (Board #270), Fri, 8:00 AM-11:00 AM

A pan-cancer analysis of ARID1A as a potential biomarker for immune checkpoint therapy. *First Author: Dongyong Yang, Department of Pulmonary and Critical Care Medicine, Second Affiliated Hospital of Fujian Medical University, Quanzhou, China*

Background: AT-rich interactive domain 1A (ARID1A), encoding a subunit of the BAF (SWI/SNF) chromatin remodeling complex, is correlated with the origination and progress of tumor. Previous research on ARID1A gene revealed that ARID1A deficiency was associated with mismatch repair (MMR) and higher tumor mutation burden (TMB) level in cancer, which might cooperate with immune checkpoint blockade therapy. **Methods:** Next generation sequencing (NGS) data of 10336 pan-cancer patients were obtained from the MSK-IMPACT Clinical Sequencing cohort (MSKCC). NGS data of 15849 pan-cancer patients from Chinese clinical dataset were analyzed to explore the association between ARID1A gene mutation and TMB. TMB was defined as total number of somatic non-synonymous mutations in coding region. 853 advanced NSCLC patients from two independent cohorts (OAK study cohort and POPLAR study cohort) were used to analyze the correlation between ARID1A alteration and the efficacy of immune checkpoint blockade immunotherapies (ICIs). **Results:** In total, 8.62% (891/10336) of pan-cancer patients in MSKCC harbored ARID1A mutation and 8.47% (3188/37628) in Chinese cohort. In MSKCC cohort, the highest ARID1A mutation frequency tumor type was endometrial cancer (31.64%, 69/218), bladder cancer (26.95%, 114/423) and hepatobiliary cancer (17.18%, 61/355) come in second and third, respectively. While in Chinese cohort, the top three ARID1A mutation frequency tumor types were endometrial cancer (39.29%, 88/224), gastric carcinoma (17.80%, 318/1787) and urothelial carcinoma (17.18%, 83/483), respectively. ARID1A gene mutation was also associated with higher TMB in the Chinese pan-cancer cohort ($P < 0.0001$). The highest medium TMB level of ARID1A mutation tumor type was Urothelial carcinoma with 18.63 Muts/Mb (n = 65). In addition, the TMB level and prognositic analysis were performed on patients in two independent NSCLC cohorts with ICIs, TMB level of ARID1A mutant group was higher than wild-type group with significant difference ($P < 0.0001$). The overall survival (OS) of ARID1A mutation group were significantly shorter than wild-type group (OS, median, 6.80 vs 10.28 months; HR, 1.47; P = 0.0474), and a decreasing trend on progression-free survival (PFS) without significant difference (median, 1.46 vs 2.99 months; HR, 1.27; P = 0.1584). **Conclusions:** The results indicated that ARID1A gene mutation was associated with a higher TMB level in Chinese pan-cancer patients, and patients harboring these genes mutations might easily benefit from ICIs. Research Sponsor: None.

3541 Poster Session (Board #271), Fri, 8:00 AM-11:00 AM

The predictive role of plasma mutant allele fraction to antiangiogenic drugs in patients with mCRC: An expanded analysis of surrogate biomarkers of response to first-line treatment with bevacizumab. *First Author: Giulia Martini, Medical Oncology, Università degli Studi della Campania "Luigi Vanvitelli", Naples, Italy*

Background: So far, no biomarkers of response to anti-angiogenic drugs are available in colorectal cancer (CRC) treatment. Liquid biopsy tracks dynamic mutational changes in CRC patients (pts). RAS mutant allele fraction in plasma (plMAF) is an independent prognostic marker in metastatic CRC (mCRC). We explored the predictive value of plMAF in RAS mutant pts treated in 1st line with chemotherapy +/- bevacizumab (bev). **Methods:** A multicentric prospective/retrospective analysis was conducted. We collected data from 226 mCRC pts and selected the subset not eligible for metastasis resection with basal plMAF sample evaluable for RAS mutant MAF quantification with digital PCR (BEAMing). Pts were stratified as high ($\geq$ 5.8%) or low ($<$ 5.8%) plMAF. We investigated associations between clinicopathological variables and progression-free survival (PFS) stratified by plMAF RAS levels using Cox regression models and survival data were calculated by Kaplan-Meier method. Computational analysis of baseline CT scan data extracted 93 radiomics features of all the lesions per patient including 1) 1st class from density histogram distribution and texture analysis by 2) 2nd order and 3) higher order feature classes. The radiomic features distribution between pts with high and low plMAF was assessed with Student's t-test analysis. **Results:** From October 17 to May 19, 63 basal plasma samples were analysed with BEAMing. 42 pts (67.7%) were classified as high and 21 pts (32,3%) as low plMAF. In high plMAF subgroup, a statistically significant longer PFS favouring FOLFOX+bev was observed, compared to FOLFOX alone (10.7 vs 6.9 mts; HR: 0.30; p = 0.002). In low RAS plMAF subgroup, no differences in terms of PFS were observed in either arm (8.9 vs 8.7 mts; HR: 0.7; p = 0.6). Multivariate PFS model showed no association between RAS plMAF and clinicopathological variables, except for high RAS plMAF and treatment benefit with FOLFOX+bev. The CT-radiomics signature, that may translate tumor vascularization, differentiated patients with high vs low plMAF (p = 0.002). 58 patients (92%) had similar radiomic score; 5 patients with high plMAF (8%) presented very heterogeneous radiomic score distribution. **Conclusions:** Tumor-borne RAS plMAFs may constitute a potential predictive biomarker of efficacy for anti-angiogenic drugs in mCRC. Next steps will include the identification of -histological, transcriptomic and radiomic- surrogate biomarkers of response that reflect tumor irrigational status. Research Sponsor: aecc.

3542 Poster Session (Board #272), Fri, 8:00 AM-11:00 AM

Analytical validation of digital cytometry (iSort) for leukocyte enumeration using stored blood. *First Author: Aaron M. Newman, Stanford Cancer Institute, Stanford, CA*

Background: Blood leukocyte enumeration is a cornerstone for clinical diagnosis and immune monitoring of diverse cancers and immunotherapies. Existing methods rely on intact/living cells and can thus be limiting due to handling time constraints and need for predefined antibody panels. While indirect cytometry methods including digital cytometry can overcome this limitation on archival specimens, their clinical performance has not been extensively characterized. We developed iSort, a novel transcriptome deconvolution method based on CIBERSORTx. Here, we comprehensively evaluated iSort and validated it against established diagnostic standards. **Methods:** We recruited 36 healthy adult blood donors and characterized their blood leukocyte profiles. We used several established clinical cytometry methods requiring intact cells in a CLIA laboratory including Complete Blood Count [CBC] and 6-color TBNK [TBNK]. We also immunophenotyped leukocytes by a research flow cytometry panel (FACS) and by mass cytometry (CyTOF). We then used these techniques as standards for validating leukocyte populations enumerated by iSort. iSort was performed on whole blood through deconvolution of 22 subsets from RNA-Seq. We assessed iSort's analytical detection performance by spiking purified lymphocyte subsets into lymphodepleted human blood and by simulating blood mixtures using defined leukocyte mixtures within latin square designs. We assessed iSort concordance with an FDA approved IVD assay (TBNK) comparing distinct RNA-Seq library preparation chemistries. **Results:** iSort was highly correlated with TBNK/CBC across CD4 T, CD8 T, B cells, NK cells, monocytes, and neutrophils ($r \geq 0.95$). When comparing correlations to TBNK/CBC, we found no significant differences between iSort, CyTOF, and FACS, nor between RNA-Seq library chemistries. iSort demonstrated high linearity at low abundance levels (0.1 - 1%, $r = 0.99$, B-cells spiked into lymphodepleted blood samples after Rituximab) and at higher abundance levels (0.5 - 90%, $r > 0.99$) across lymphoid and myeloid subsets. iSort also showed high reproducibility among triplicate blood tubes for each population (median CV = 11%). **Conclusions:** iSort digital cytometry achieves highly accurate and robust leukocyte enumeration for diverse hematopoietic subsets. Given its favorable performance against existing clinical standards that require intact/living cells, iSort is a promising approach for the development of immunotherapy biomarkers. Research Sponsor: CiberMed, Inc.

3543 Poster Session (Board #273), Fri, 8:00 AM-11:00 AM

Noninvasive identification of lineage-specific circular RNA for ER-positive breast cancer. *First Author: Jason Brown, Department of Internal Medicine, University of Michigan, Ann Arbor, MI*

Background: Non-invasive testing in plasma using RNA biomarkers has been limited by exoribonuclease-mediated degradation of RNA. Circular RNA (circRNA) are covalently closed RNA structures that resist this degradation due to their circular structure. Therefore circRNA are more stable than their linear counterparts. CircRNA are formed by alternative backsplicing of the 3' end of a downstream exon to the 5' end of an upstream exon. Here, we propose a novel method for non-invasive identification of circRNA and demonstrate circularized forms of several lineage and cancer specific targets for estrogen receptor-positive breast cancer. **Methods:** Capture RNA sequencing on cancer tissue was previously performed to determine the relative expression of potential circRNA isoforms in breast cancer patients. These isoforms as well as those predicted by intron length were screened using a quantitative PCR-based assay on ER-positive breast cancer cells. RNA extracted from breast cancer cells are exposed to ribonuclease R to demonstrate stability of circRNA. CircRNA derived from targets with known universal expression are used as positive controls as well as for analysis on plasma. **Results:** We identify the circRNA isoforms with highest expression for five genes, including ESR1, that are differentially expressed in ER-positive breast cancer compared to other cancers and normal breast tissue. We determine that the circRNA corresponding to all five targets is specifically expressed in breast cancer cell lines with at least 1000-fold higher expression than in non-ER positive breast cancer cell lines. We demonstrate that the highest expressing circRNA isoforms are resistant to degradation by ribonuclease R, whereas corresponding linear mRNA is susceptible. We also demonstrate the presence and stability of positive control circRNA in plasma from patients without cancer. **Conclusions:** CircRNA are promising biomarkers for early non-invasive detection of cancer due to their stability in plasma. This assay reliably detects ER-positive breast cancer specific circRNA, and exoribonuclease resistance has been validated. Application of this diagnostic assay to plasma from breast cancer patients is underway. Research Sponsor: U.S. National Institutes of Health.

3544 Poster Session (Board #274), Fri, 8:00 AM-11:00 AM

Circulating microtumors: A functional hallmark for cancer detection and management. *First Author: Vineet Datta, Datar Cancer Genetics Limited, Nasik, India*

Background: There are presently no accepted non-invasive means for detection of cancers in asymptomatic individuals or suspected cases. Radiological and serological investigations, though non-invasive, are not confirmatory and necessitate an invasive biopsy to establish malignant status of suspected findings. Invasive biopsies, in turn, face challenges due to non-representative tumor tissue or in cases where biopsy is impossible or unviable. We hypothesized that Circulating Microtumors (also called as C-ETACs: Circulating Ensembles of Tumor Associated Cells) in peripheral blood are universally present in solid organ cancers and their detection can be linked to malignant status. **Methods:** We obtained peripheral blood from 14,138 patients with various solid organ cancers as well as 10,625 asymptomatic individuals with age associated elevated risk of cancer. Out of the 14,138 patients with cancer, 25.1 % had local (non-metastatic) disease and 56.4% had metastatic disease as confirmed by radiological evaluation. C-ETACs were enriched and harvested from PBMCs using an epigenetically activating medium that is cytotoxic towards non-malignant epithelial and hematolymphoid cells in blood but confers survival benefit on apoptosis resistant circulating cells of tumorigenic origin and their heterotypic clusters (C-ETACs) in peripheral blood. Viable C-ETACs were identified and further characterized by immunocytochemistry (ICC) profiling. **Results:** C-ETACs were detected in 89.7% of samples from solid organ cancers irrespective of stage, treatment or present radiological status. C-ETACs were rarely detected (3.0%) in asymptomatic individuals. The asymptomatic individuals where C-ETACs were detected are being followed up periodically so as to enable detection of cancer based on clinical or radiological manifestation of symptoms. **Conclusions:** C-ETACs are ubiquitous in cancers and unexpected in asymptomatic individuals. Detection of C-ETACs in asymptomatic individuals may be indicative of risk of latent undiagnosed malignancy. The non-invasiveness of this approach makes it convenient for screening large populations for cancer. Research Sponsor: None.

3545 Poster Session (Board #275), Fri, 8:00 AM-11:00 AM

Identification of *FGFR2/3* fusions from clinical cfDNA NGS using a de novo fusion caller. *First Author: Arielle Yablonovitch, Bioinformatics, Guardant Health, Redwood City, CA*

Background: *FGFR2/3* rearrangements are promising therapeutic targets, especially in advanced urothelial cancer (aUC) with FDA-approved erdafitinib. Liquid biopsy is an attractive non-invasive method to identify these fusions, but detection in cfDNA is technically challenging due to low tumor shedding levels, short molecules, and wide variation in gene partners. To address this, we developed an assembly-based fusion detection algorithm to call rearrangements in a *de novo* fashion without reliance on a fixed partner set and applied it to $>$ 15,000 clinical samples. **Methods:** A cohort of 15,218 patients with mixed cancer types (including 698 aUC patients, as well as breast, cholangiocarcinoma, colorectal, and gastric), plus 276 healthy control samples were previously tested with Guardant360(R), a clinical 74-gene cfDNA NGS-based assay. The median unique molecule coverage was approximately 3,000 molecules sequenced to 15,000x read depth. Samples were reanalyzed *in silico* using the novel algorithm: in brief, reads aligned to candidate fusion breakpoints were assembled into de Bruijn graphs. Resulting contigs were aligned to the reference and filters were applied to remove technical artifacts. **Results:** The majority of *FGFR2* (86%) and *FGFR3* fusion partners (73%) in the mixed cancer cohort were observed only once, consistent with previous reports (Helsten 2016). *FGFR3-TACC3* was the most common fusion, occurring in 72% of *FGFR3* fusion-positive patients. In 37% of *FGFR2* fusion positive patients, the *de novo* caller detected partners not previously described. In the aUC cohort, *FGFR3* fusions were detected in 3.3% of patients, with 8/10 (80%) partner genes/intergenic regions occurring only once, which is in line with previous reports (Nassar 2018). No fusions were identified in 276 healthy control samples. In the mixed cancer cohort, common mutations co-occurring with *FGFR2* fusions were *FGFR2* N549K, *PIK3CA* H1047R, and *TP53* R175H (5.6% each); *KRAS* Q61H was observed in 28% of patients with *FGFR3* fusions. **Conclusions:** *FGFR2/3* fusion partners detected by a highly specific assembly-based *de novo* fusion caller were heterogeneous and individually rare, highlighting the importance of a *de novo* approach. We observed an *FGFR3* fusion prevalence in cfDNA from aUC patients that is comparable to previous reports for tissue testing, demonstrating an ability to capture targetable genomic rearrangements with plasma-based NGS in this patient population. Research Sponsor: Guardant Health.

3546 Poster Session (Board #276), Fri, 8:00 AM-11:00 AM

Demonstrating the value of liquid biopsy for lung cancer in a public health care system. *First Author: Rosalyn A. Juergens, Juravinski Cancer Centre, McMaster University, Hamilton, ON, Canada*

Background: Given the challenges of molecular profiling in patients with advanced lung cancer, this prospective study examines clinical outcomes and utility of liquid biopsy in treatment naive stage IV lung adenocarcinoma patients (Cohort 1) and in the setting of resistance to targeted therapy (Cohort 2; not reported here). **Methods:** This study is being conducted at 6 Canadian centres (NCT03576937) using Guardant 360 (G360), a validated cell-free DNA next-generation sequencing assay that identifies variants in 74 cancer-associated genes, including fusions and copy number gain. Cohort 1 (N = 150) includes patients with treatment-naïve advanced non-squamous lung carcinoma, ≤10 pack-year smoking history, and measurable disease. Patients received standard of care tumour tissue (TT) molecular profiling (*EGFR, ALK +/- ROS1*) and liquid biopsy (LB). The primary endpoint was response rate to first-line therapy (RECIST 1.1); secondary endpoints include incremental targetable alterations identified through G360 (*EGFR, ALK, BRAF, ERBB2, KRAS (G12C), NTRK, MET (amplification, exon 14 skipping), RET, ROS1*), turn-around time (TAT) and successful molecular profiling rates. **Results:** To date, 84 eligible patients with clinical data have been accrued to Cohort 1. Median age is 64 (range 23-91), 64% are female, 85% never smokers, 96% have adenocarcinoma. Actionable targets have been identified in 55% of patients using G360 (*EGFR/ALK* in 37%), 39% using standard TT profiling. Eight *EGFR/ALK* aberrations were identified in TT but not LB, while 6 were identified in LB but not TT. TT profiling for *EGFR/ALK* was unsuccessful in 8% of patients (insufficient tissue, failed biopsy). Fourteen patients (17%) had no ctDNA alterations detected by G360 (low disease burden vs. non-shedding). Of 75 patients receiving first-line treatment, 57% received targeted therapy, 28% chemotherapy combinations, 11% checkpoint inhibitors and 4% were observed. Treatment decisions were informed by G360 alone in 37% and by G360+TT results in 27% (by physician report). Among 46 evaluable patients, ORR was 54% (25/46). Using G360, ORR was 75% (15/20) in those with actionable alterations and 38.5% (10/26) in those without. Using TT, ORR was 67% (14/21) in those with actionable alterations and 44% (11/25) in those without. Mean TAT was 7.9 days (SD+/-1.7) for LB vs 19.9 days (SD+/- 9.8) for TT. **Conclusions:** Liquid biopsy using G360 identifies actionable targets beyond tissue profiling alone in newly diagnosed lung cancer patients, has faster TAT and yields similar outcomes with targeted and non-targeted therapy. Clinical trial information: NCT03576937. Research Sponsor: Guardant Health, Other Foundation.

3547 Poster Session (Board #277), Fri, 8:00 AM-11:00 AM

The prevalence of $KRAS^{G12C}$ mutations utilizing circulating tumor DNA (ctDNA) in 80,911 patients with cancer. *First Author: Kyaw Thein, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Kirsten rat sarcoma viral oncogene homolog (KRAS) is the most commonly mutated proto-oncogene identified in cancer and still remains an arduous therapeutic challenge. Recently, $KRAS^{G12C}$ mutation has become special interest since it has now been considered potentially druggable after the introduction of covalent small-molecule $KRAS^{G12C}$ inhibitors. Advances in next-generation sequencing (NGS) and embracing utilization of ctDNA have uncovered more genetic alterations in many cancers. We present a comprehensive analysis on the prevalence of $KRAS^{G12C}$ mutations identified by ctDNA. **Methods:** We conducted a 5-year (July 2014 to June 2019) retrospective review of ctDNA NGS analysis in the Guardant360 CLIA database inclusive of treatment-naïve and previously treated patients with metastatic solid tumors. Data were retrieved from the 80,911 unique patients with ctDNA detected. Clonality and co-occurrence of cancer type were analyzed. Clonality was defined as variant allele fraction(AF) / maximum somatic AF in the sample. **Results:** 80,911 patients, which included more than 100 tumor histologies, were identified. 2,985 patients (3.7%) with > 40 tumor types had $KRAS^{G12C}$ mutations identified in ctDNA. $KRAS^{G12C}$ prevalence by cancer type were as follows: sarcomatoid lung carcinoma (13.5%), lung cancer NOS (9%), large cell lung carcinoma (9%), lung adenocarcinoma (7.4%), NSCLC (6.9%), carcinoma of unknown primary (CUP) (4.1%), lung carcinoid (4%), CRC (3.5%), squamous cell lung carcinoma (2%), small cell lung carcinoma (1.5%), pancreatic ductal adenocarcinoma (PDAC) (1.2%), cholangiocarcinoma (1.2%), bladder cancer (0.6%), ovarian cancer (0.6%) and breast cancer (0.3%). 53 additional patients with $KRAS^{G12C}$ were identified across 24 other tumor types. The $KRAS^{G12C}$ mutation was found to be clonal (clonality > 0.9%) in the majority of patients with lung adenocarcinoma, NSCLC, CUP, squamous cell lung carcinoma, and PDAC, compared to patients with CRC and breast cancer who had bimodal distribution of clonal and sub clonal mutations. **Conclusions:** To our knowledge, this is the largest analysis on the prevalence of $KRAS^{G12C}$ mutations identified by ctDNA. Our study demonstrated the feasibility of utilizing ctDNA to identify $KRAS^{G12C}$ mutations across solid tumors with the highest prevalence in lung cancer as previously reported in tissue. The clonality information available from ctDNA-based genotyping may provide insights into the clinical efficacy of targeting $KRAS^{G12C}$ in different tumor types. Research Sponsor: None.

3548 Poster Session (Board #278), Fri, 8:00 AM-11:00 AM

Exploring the Cancer Genome Atlas (TCGA) for the molecular profile of young onset colorectal cancers. *First Author: Seyed Ali Khalessi Hosseini, NYU Langone Medical Center, New York, NY*

Background: Colorectal cancer (CRC) incidence and mortality has been declining, in part due to increased implementation of screening, but the incidence among patients under 50 (young onset, YO) is increasing at a rate of 2% per year. The cause of this increasing incidence remains poorly understood, but differences in mutation profiles can help understand pathogenesis, prognosis, and identify targets for therapy. **Methods:** Genomic and clinical data for 488 TCGA CRC patients was used to evaluate differences in genetic alterations between YO and patients over 50. Chi-squared tests were used to determine differences in somatic mutation frequency in critical pathways implicated in CRC: DNA MMR, P53, WNT, RAS-MAPK, PI3K/AKT/mTOR, and TGF-B pathways. For 85 of the patients, proteomic data via RPPA was also available and analyzed. **Results:** The average age of included patients was 66 (SD 12.8). 76 (12.2%) were under 50 at time of diagnosis. When comparing YO with those over 50, there were no differences in microsatellite instability, histologic type (adeno or mucinous), location (colon or rectal), tumor size, or metastasis. YO patients were more likely to have nodal involvement (p = 0.007) and higher histological grade (p = 0.022). YO patients were more likely to have mutations in the MMR pathway (43% vs 23%, p = 0.002) and the PI3K/AKT/mTOR pathway (70% vs 54%, p = 0.024). Specifically, YO were more likely to have mutations in MSH2 (7% vs 1%, p = 0.001), MSH6 (24% vs 7%, p = 0.000); ATM (46% vs 30%, p = 0.015); FZD10 (7% vs 2%, p = 0.007); ERBB2 (15% vs 7%, p = 0.027); PIK3R1 (20% vs 9%, p = 0.014), PTEN (61% vs 35%, p = 0.000), and TGFBR2 (13% vs 4%, p = 0.004). When looking at proteomic data, YO were more likely to have decreased expression of MSH2 (p = 0.003) and MSH6 (p = 0.005). **Conclusions:** Patients with YO CRC are more likely to have somatic mutations in genes involved in the MMR pathway and the PI3K/AKT/mTOR pathway. Specifically, in MSH2, MSH6, ATM, FZD10, ERBB2, PIK3R1, PTEN and TGFBR2. When including proteomic data, significant differences were only seen in expression of MSH2/6. Some of these genes (e.g. ERBB2/HER2) are targets for existing therapies, and others are being actively investigated as potential therapeutic targets. Establishing differences in tumor genetic profiles is a first step towards understanding the increase in YO CRC, and simultaneously identifies targets for therapy. However, because of post-transcriptional changes (e.g. RNAi, methylation), genetic profiling alone cannot always reliably establish differences in protein expression, and thus therapy targets. Research Sponsor: None.

3549 Poster Session (Board #279), Fri, 8:00 AM-11:00 AM

Phase I expansion study of XMT-1536, a novel NaPi2b-targeting antibody-drug conjugate (ADC): Preliminary efficacy, safety, and biomarker results in patients with previously treated metastatic ovarian cancer (OC) or non-small cell lung cancer (NSCLC). *First Author: Debra L. Richardson, Stephenson Cancer Center/Sarah Cannon Research Institute at the University of Oklahoma Health Sciences Center, Oklahoma City, OK*

Background: XMT-1536 is a first-in-class ADC targeting the sodium-dependent phosphate transport protein NaPi2b, broadly expressed in NSCLC and ovarian cancer. XMT-1536 utilizes the Dolaflexin platform to deliver 10-12 DolaLock auristatin payload molecules per antibody. In the dose-escalation portion of the Phase I study (NCT03319628), XMT-1536 showed clinical activity at doses >20mg/m^2 with confirmed responses and prolonged stable disease in heavily pretreated OC and NSCLC patients, without preselection for NaPi2b expression. XMT-1536 was generally well-tolerated without the severe toxicities observed with other ADC platforms such as neutropenia, peripheral neuropathy, or ocular toxicity (Tolcher et al., ASCO 2019; Richardson et al., SGO 2020). Here, we report on the expansion (EXP) cohort, which included patients with fewer prior lines of therapy, in the ongoing Phase I study. **Methods:** Doses administered intravenously every 4 weeks (q4w) of 36 and 43 mg/m^2 were evaluated in two cohorts (1) high grade serous ovarian, fallopian tube, or primary peritoneal cancer (OC) with up to 4 prior lines of therapy and (2) NSCLC adenocarcinoma; prior treatment with a platinum-based therapy, immune checkpoint inhibitor, and TKI, if indicated. Archival tumor tissue and tissue from a new tumor biopsy were required for retrospective evaluation of NaPi2b expression. **Results:** As of 10 February 2020, 23 patients (19 OC and 4 NSCLC) were enrolled in the EXP cohort: 16 dosed at 36 mg/m^2 and 7 dosed at 43 mg/m^2. Adverse events were generally similar to those previously reported, including transient AST elevation, fatigue, nausea, and pyrexia. Clinical responses and stable diseases have been observed. Efficacy data (objective response rate) and initial correlation of NaPi2b score with clinical response will be reported. Available data from all patients with data cutoff in May 2020 will be included. **Conclusions:** Overall, XMT-1536 treatment demonstrated clinical activity in high grade serous ovarian cancer and NSCLC adenocarcinoma and was generally well-tolerated with no new safety signal trends identified in the EXP. Clinical efficacy and the relevance of NaPi2b expression for treatment with XMT-1536 will be presented. Clinical trial information: NCT03319628. Research Sponsor: Mersana Therapeutics.

3550 Poster Session (Board #280), Fri, 8:00 AM-11:00 AM

First-in-human dose-escalation study of anti-EGFR ADC MRG003 in patients with relapsed/refractory solid tumors. *First Author: Rui-hua Xu, Sun Yat-Sen University Cancer Center, Guangzhou, China*

Background: MRG003 is a novel antibody drug conjugate (ADC) composed of a fully human anti-EGFR IgG1 monoclonal antibody conjugated to a microtubule disrupting agent monomethyl auristatin E (MMAE). MRG003 is presently being tested in an ongoing phase I study for safety, pharmacokinetics, and preliminary antitumor activity in patients (pts) with solid tumors (CTR20180310). **Methods:** In the phase I dose escalation study of a traditional (3+3) design, pts with relapsed or refractory cancers received single agent MRG003 once every 3 weeks (Q3W) for a maximum of 8 treatment cycles. The starting dose of MRG003 is 0.1 mg/kg, followed by 0.3, 0.6, 1.0, 1.5, 2.0, 2.5, and 3.0 mg/kg. Observations included adverse events (AEs), dose-limiting toxicity (DLT), and antitumor activity which is assessed every two cycles. **Results:** A total of twenty-two pts with colorectal (CRC, n = 15), nasopharyngeal (NPC, n = 3), head and neck (H&N, n = 2), esophageal (EC, n = 1), and duodenal (DC, n = 1) cancer were enrolled in the dose escalation. The median age of pts was 56.5 years. The MTD identified was 2.5 mg/kg. Commonly observed adverse events were anemia (50%), AST increase (41%), decreased appetite (41%), rash (36%), pruritus (36%), asthenia (36%), and proteinuria (32%). Majority of AEs were mild to moderate in severity. EGFR expression in patients' tumor samples was determined retrospectively by a validated IHC method in a central laboratory. Nine out of 22 pts tested were EGFR positive. Among these 9 EGFR positive pts, one with NPC in the 2.5 mg/kg cohort had partial response, four had stable disease (one with H&N in the 1.5 mg/kg, one each with NPC and H&N in the 2.0 mg/kg, and one with EC in the 2.5 mg/kg cohorts). The disease control rate (DCR) at doses ≥1.5 mg/kg was 100% for the EGFR positive pts. **Conclusions:** The dose escalation study of MRG003 showed manageable safety profiles and encouraging preliminary antitumor activity in pts with EGFR-positive solid tumors. MRG003 is currently being evaluated as a single agent in phase I dose expansion cohorts to further assess safety, PK, and antitumor activity. Clinical trial information: CTR20180310. Research Sponsor: Shanghai Miracogen Inc.

3551 Poster Session (Board #281), Fri, 8:00 AM-11:00 AM

First-in-human phase I study of ALT-P7, a HER2-targeting antibody-drug conjugate in patients with HER2-positive advanced breast cancer. *First Author: Yeon Hee Park, Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

Background: ALT-P7 is an antibody-drug conjugate, in which two molecules of monomethyl auristatin E (MMAE) are site-specifically conjugated to a cysteine-containing peptide motif of trastuzumab variant. This is the first-in-human study evaluating safety and pharmacokinetics of ALT-P7 in patients with HER2-positive advanced breast cancer. **Methods:** This was an open label, 3+3 dose-escalation phase 1 trial. Eligible patients were with HER2-positive advanced breast cancer progressive to at least two kinds of prior anti-HER2 treatment. ALT-P7 at doses from 0.3mg/kg to 4.8mg/kg were intravenously administered once every 3 weeks. Dose limiting toxicities were evaluated over the first cycle of 21 days. Primary objective was to define the maximum tolerated dose. **Results:** ALT-P7 were administered in 27 patients (n=4 at 0.3mg/kg, n=3 at each of 0.6, 1.2, 2.4, 3.6, 4.2, 4.5 mg/kg, n=5 at 4.8mg/kg) between Jan 2018 and Feb 2020. The median number of previous line of systemic therapy was six, including median four prior anti-HER2 agents. The most common grade (G) 3/4 adverse event (AE) was neutropenia (n=4). The other common drug-related AEs of all grade were myalgia (n=9), fatigue (n=7), sensory neuropathy (n=6), alopecia (n=6), pruritus (n=6), and neutropenia (n=6). Dose limiting toxicities(DLTs) were observed in three patients at 4.8mg/kg (G4 febrile neutropenia, G4 thrombocytopenia, G4 hyperbilirubinemia, G3 myalgia, G4 hyponatremia). No DLTs have been observed up to 4.2mg/kg, and safety evaluation at 4.5mg/kg is currently ongoing. Toxicokinetic analysis for total antibody, drug-conjugated antibody, and free payload suggested that there were no accumulation of ALT-P7 upon repeated injection. In 22 patients with response evaluation, disease control rate at 6 weeks of ALT-P7 treatment was 77.3%(17/22) and partial response was achieved in two out of fifteen patients with measurable lesion. The median PFS at doses from 2.4 to 4.8mg/kg was 6.2 months (95% CI 2.5-9.9 months). **Conclusions:** ALT-P7 was well tolerated to a dose of 4.2mg/kg in heavily pretreated HER2-positive advanced breast cancer. DLTs were observed at 4.8mg/kg, and 4.5mg/kg is under evaluation. The observed clinical activity warrants further evaluation in a phase 2 trial. Clinical trial information: NCT03281824. Clinical trial information: NCT03281824. Research Sponsor: Alteogen, Inc., Korea Drug Development Fund (KDDF) funded by MSIT, MOTIE and MOHW

3552 Poster Session (Board #282), Fri, 8:00 AM-11:00 AM

A phase I/II study of rovalpituzumab tesirine in delta-like 3-expressing, advanced solid tumors. *First Author: Aaron Scott Mansfield, Mayo Clinic, Rochester, MN*

Background: Delta-like 3 (DLL3) is highly and specifically expressed in solid tumors, such as neuroendocrine carcinomas (NECs), malignant melanoma (MM), and medullary thyroid carcinoma (MTC). Rovalpituzumab tesirine (Rova-T) is a DLL3-targeting antibody-drug conjugate. **Methods:** This Phase 1/2 study (NCT02709889) enrolled patients with relapsed/refractory DLL3+ (>1% by IHC) advanced solid tumors and ECOG performance status of 0-1. Rova-T was given IV at 0.2, 0.3, or 0.4 mg/kg on d 1 of each 6-wk cycle (q6wk) for dose escalation (3+3 design) in disease-specific cohorts in Phase I. The recommended Phase 2 dose (RP2D) was tested in Phase II. Safety and dose-limiting toxicities (DLTs) were primary endpoints; efficacy outcomes were secondary endpoints. **Results:** The study enrolled 200 patients; 101 had NECs (large cell NEC [n=13], neuroendocrine prostate cancer [n=21], high-grade gastroenteropancreatic NEC [n=36], other [n=31]) and 99 had other solid tumors (MM [n=20], MTC [n=13], glioblastoma [GBM; n=23], other [n=43]). The median age was 61 y (range, 28-84); 63% were male. The RP2D was 0.3 mg/kg q6wk for 2 cycles in all cohorts. There were 7 DLTs in 5 patients: 2 with 0.2 mg/kg (Grade [Gr] 3 photosensitivity reaction, Gr 3 dyspnea), 2 with 0.3 mg/kg (1 with Gr 2 effusion, Gr 3 tumor lysis syndrome, and Gr 3 rhabdomyolysis; 1 with Gr 4 kidney injury), and 1 with 0.4 mg/kg (Gr 4 thrombocytopenia). Despite only 1 DLT identified with 0.4 mg/kg, the totality of the safety data suggested that this dose is not well tolerated. Common adverse events (AEs) in patients given 0.3 mg/kg (n=145) are shown (Table). Serious AEs occurred in 77/145 patients (53%), most commonly (≥3%) malignant neoplasm progression (n=18; 12%), pleural effusion (n=7; 5%), pericardial effusion (n=6; 4%), and dyspnea (n=5; 3%). The objective response rate (ORR) was 11% (21/200): 14 had NEC, 2 had MM, 2 had MTC, 2 had small cell carcinoma (SCC) not of lung origin (all partial responses), and 1 had GBM (complete response). In patients with NECs given 0.3 mg/kg, ORR, clinical benefit rate, and progression-free survival trended in favor of those with high DLL3-expressing tumors (≥50% by IHC) which represented 51% of NECs. **Conclusions:** Rova-T was tolerable in patients with advanced solid tumors at 0.3 mg/kg q6wk for 2 cycles. Antitumor activity was observed in patients with NEC, MM, MTC, SCC, and GBM. Clinical trial information: NCT02709889.Research Sponsor: Abbvie, Inc.

AEs in ≥30% of patients given 0.3 mg/kg q6wk Rova-T (n=145).

AE, n (%)	Any Gr	Gr ≥3
Any	144 (99)	99 (68)
Fatigue	75 (52)	6 (4)
Nausea	53 (37)	5 (3)
Thrombocytopenia	48 (33)	22 (15)
Pleural effusion	48 (33)	4 (3)
Peripheral edema	44 (30)	1 (1)

3553 Poster Session (Board #283), Fri, 8:00 AM-11:00 AM

Phase I study of mesothelin-targeted immunotoxin LMB-100 given as a long infusion with or without nab-paclitaxel. *First Author: Guillaume Joe Pegna, National Cancer Institute Center for Cancer Research, Bethesda, MD*

Background: LMB-100 recombinant immunotoxin consists of a mesothelin-binding Fab for targeting a modified *Pseudomonas* exotoxin A payload. Previous Phase 1 clinical testing of a 30-minute LMB-100 "short" infusion format identified a serum half-life of ~1 hour. Pre-clinical data suggested that extending infusion time could improve anti-tumor efficacy by increasing tumor cell duration of exposure to LMB-100. The primary objective of this study was to determine the safety and tolerability of administering LMB-100 in a long infusion format over 24-48 hours alone or with nab-paclitaxel chemotherapy in patients with mesothelin-expressing solid tumors. **Methods:** Patients (n = 15) with pancreatic adenocarcinoma and other mesothelin-expressing solid tumors (n = 3; mesothelioma, colon, and ampullary cancers) treated on 3 dose levels received long infusion of LMB-100 (65 or 100 mcg/kg/day) for 24 hour on Days 1 and 4 (n = 6) or 48 hour on Day 1 (n = 9) with or without a loading dose (40 mcg/kg over 30 minutes) for up to 2 cycles. In the second arm, patients (n = 5) with pancreatic adenocarcinoma were treated with LMB-100 over 24 hours on Day 1 concurrently with nab-paclitaxel (125 mg/m^2) for up to 3 cycles. **Results:** DLT of proteinuria (grade 3) in one patient and acute kidney injury (grade 1) in one patient were observed amongst patients receiving 100 mcg/kg/day over 48 hours and 24 hours, respectively. No objective responses were seen but all patients receiving nab-paclitaxel had > 50% decrease in CA 19-9. Patients at all single agent dose levels (8 of 10 evaluable) developed high titer anti-drug antibodies (ADAs) against LMB-100. Those with ADAs (8 of 8) had undetectable cycle 2 peak plasma LMB-100 concentration. Development of high titer ADAs occurred more frequently with long infusion than seen previously with "short" infusion LMB-100. Most long infusion patients (19 of 20) developed increased serum IL-6 within 24 hours of LMB-100 infusion. However, the systemic inflammatory response to LMB-100 (as measured by increased serum CRP) which occurs in most "short" infusion patients was not observed. **Conclusions:** Long infusion format LMB-100 is generally well tolerated but immunogenicity limits treatment to 1 effective cycle. No antitumor efficacy of the single agent was observed. Clinical trial information: NCT02810418. Research Sponsor: U.S. National Institutes of Health.

3555 Poster Session (Board #285), Fri, 8:00 AM-11:00 AM

Anaplastic lymphoma kinase (ALK) partners identified by next-generation sequencing in Chinese patients with solid tumors. *First Author: Sheng Yang, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: Anaplastic lymphoma kinase (ALK) rearrangement is a validated therapeutic driver gene in non-small cell lung cancer (NSCLC). More than 30 different fusion partner genes of ALK in NSCLC have been reportedand most of these ALK fusions respond well to ALK inhibitors crizotinib. With the development of next-generation sequencing (NGS), more novel partners for ALK rearrangement have been identified. Here, we aimed to report the landscape of ALK rearrangement in Chinese patients with solid tumors. **Methods:** Tissue or blood samples were subjected to NGS in a College of American Pathologists-certified and Clinical Laboratory Improvement Amendments-accredited lab for ALK arrangement. **Results:** In total, we profiled more than 40,000 patients, among which 72 cases with 52 ALK fusion partner, harboring 17 reported partners and 35 novel partners. The average ALK rearrangement patients' age was 53 years (range, 17-76 years). Among all the ALK fusion cases (n = 72), lung cancer were the largest proportion with 77.8% (n = 56), colorectal cancer accounted for, 5.5% (n = 4), liver cancer accounted for 4.2% (n = 3), biliary cancer, melanoma, carcinosarcoma and inflammatory myofibroblastic tumor accounted for 2.8% (n = 2) respectively, and only one case (n = 1) was malignant peritoneal mesothelioma. The most common ALK fusion partners were KIF5B (n = 6), DCTN1 (n = 5) and STRN (n = 5). In 38 cases, 35 novel ALK fusion partners were discovered. The novel CLIP4-ALK, EHBP1-ALK, PLB1-ALK occurred twice in 6 patients, which were two lung cancer patients with CLIP4-ALK fusion, two lung cancer patients with PLB1-ALK fusion, one hepatic cellular cancer patients with EHBP1-ALK, and one melanoma patients with EHBP1-ALK. There were two special lung cancer cases with two ALK fusions. One case detected the novel LRIG1-ALK fusion and novel PLB1-ALK fusion, the other case detected novel GLI3-ALK fusion and reported HIP1-ALK fusion. **Conclusions:** Novel ALK fusions are detected in patients with not only NSCLC but also other solid tumors. NGS fusion assay is an optional method for screening novel fusions. Research Sponsor: None.

3556 Poster Session (Board #286), Fri, 8:00 AM-11:00 AM

High intratumoral tryptophan metabolism is a poor predictor of response to pembrolizumab (pembro) in metastatic melanoma (MM): Results from a prospective trial using baseline C11-labeled alpha-methyl tryptophan (C11-AMT) PET imaging for response prediction. *First Author: Jorge D. Oldan, Department of Radiology, The University of North Carolina at Chapel Hill, Chapel Hill, NC*

Background: Molecular imaging of metabolic pathways critical for effector T cell response other than glucose could predict response to PD1 inhibitors. We have previously shown that high expression of tryptophan metabolic pathway enzymes in stage III/IV melanoma correlates with reduced abundance of tumor-infiltrating lymphocytes (TILs, ASCO 2019, e21014). Here we investigated C11-AMT, a PET tracer that images tryptophan metabolism, as a predictor of response to pembro in patients (pts) with PD1 inhibitor-naïve MM. **Methods:** In this trial (NCT03089606) pts must have had measurable MM by RECIST, have undergone IV contrast CT, FDG-PET, and C11-AMT PET scan (30-40 min dynamic imaging), plus a mandatory tumor biopsy prior to pembro treatment. **Results:** 21 pts (16 males; 15 stage IV; median age 61) had all 3 baseline scans and evaluable research biopsies. 13 pts were non-progressors (CR = 4, PR = 6, and SD = 3). At a median f/u of 13.7 mons (2.8-25.1+), 6 pts are dead from MM, 11 are alive without MM and 4 are alive with MM. 46 tumor lesions were assessed by all 3 scans. Of the pts with tumor lesion, C11-AMT PET $SUV_{max} < 7$ and skewness $< +0.3$ of the tumor lesion with the highest C11-AMT SUV_{max} was associated with non-progression by RECIST ($SUV_{max} < 7$/skewness $< +0.3$ in progressors vs. non-progressors; Fisher's 2-tail test $p = 0.055$). The corresponding association between baseline FDG-PET ($SUV_{max} < 14$ and skewness $< +0.3$) with treatment response was insignificant ($p = 0.08$). There was a weak (Spearman $\rho = 0.33$) but significant correlation ($p = 0.001$) in SUV_{max} between FDG-PET and C11-AMT among the 46 tumors analyzed. There was no significant correlation between melanoma-specific expression of the tryptophan- (TPH1, TPH2, IDO1, TDO2, LAT1) and glucose-metabolizing enzymes (GLUT1, HK1, HK3) by immunohistochemistry. Response to pembro trends to associate with present TILs (Fisher's $p = 0.087$). **Conclusions:** Baseline C11-AMT PET imaging using simple radiomics measures (highest metabolic activity, SUVmax, and tumor heterogeneity, skewness) may better predict clinical benefit from pembro in MM than FDG PET. Variability in C11-AMT's SUV_{max} cannot be solely explained by FDG-PET's SUV_{max}, suggesting that these two imaging modalities may provide complementary information about intratumoral metabolic dysregulation that may relate with pembro response. Texture analysis using LifeX v4.0 will be presented at the meeting. Clinical trial information: NCT03089606. Research Sponsor: Merck.

3557 Poster Session (Board #287), Fri, 8:00 AM-11:00 AM

First in-human study of in vivo imaging of ex vivo labeled CAR T cells with dual PET-MR. *First Author: Ritu Singla, Cell Therapies, Peter MacCallum Cancer Centre, Melbourne, Australia*

Background: This is a first in human in-vivo biodistribution of ex-vivo labelled CAR T cells assessed in a cohort of patients. Cells were labelled with novel Cu-64 labelled superparamagnetic iron oxide nanoparticles (SPION) and infused IV into patients with solid tumors & tracked using clinical dual PET-MR. The study validates the clinical translation of CAR T cell in-vivo tracking in real time. **Methods:** Cu-64 radioisotope was bound to silica coated SPION using electrolysis plating with tin & palladium seeding. Cellular uptake of Cu-64 SPION was facilitated with a transfecting agent. Functional assays including ^{51}Chromium release, cytometric bead array demonstrated that labelling process did not affect cytotoxicity & cytokine secretion (TNFα & IFN-g). T cells were transduced with retroviral vector constructs encoding for second-generation chimeric T-cell receptor specific for carbohydrate Lewis Y antigen. Modified T-cells were expanded ex-vivo & were labelled with Cu-64 (~300 MBq) prior to re-infusion (3 $x10^8$ labelled cells). Scanning is performed with Siemens 3T dual PET-MR scanner. **Results:** In this first in human in-vivo study (HREC/16/PMCC/30) a cohort of patients received ex-vivo labelled CAR T cells to determine how many labelled cells distribute to solid tumor sites within 3-5 days. Our results demonstrate that cells can be efficiently labelled (≤60%) with high cell viability (≥85%) at a sensitivity sufficient to detect labelled cells at tumor site for up to 5 days. An observed trend in SUV_{mean} & SUV_{max} provided insight into efficacy & individual response to therapy. Early time points showed moderate uptake of labelled cells in lungs posterior basal segments without increased activity over next few days, suggesting a transient process. Mild, diffuse bone marrow & relatively intense uptake of labelled cells in liver & spleen suggests margination of cells to reticulo-endothelial system. Distinct PET signal at some of the tumor sites at 24 h suggests antigen specific localization & time taken to reach these sites. Excretion via hepatobiliary indicated reabsorption from GI tract & re-circulation of labelled cells. Minimal uptake in brain & heart supported safety profile of labeling agent. **Conclusions:** This is first in human in-vivo study to provide highly valuable visual and dynamic data in real time and provides insight into individual responses to therapy. CAR T cell functionality largely remain unchanged due to labeling process. The findings indicate that labelled cells traffic to tumor sites at later time points & remain persistent for extended period of time. Research Sponsor: Juno Therapeutics, Australian Global Innovation Linkage Grant.

3558 Poster Session (Board #288), Fri, 8:00 AM-11:00 AM

Clinically aggressive malignancies associated with STK11 germline mutations (STK11GCa): A comprehensive genomic profiling (CGP) study. *First Author: Ethan Sokol, Foundation Medicine, Inc., Cambridge, MA*

Background: Germline mutations in the *STK11* (*LKB1*) mTOR pathway gene are associated with Peutz-Jehger's Syndrome and a variety of malignancies of variable clinical aggressiveness. Recent evidence also links *STK11* inactivation with failure to benefit from anti-cancer immune checkpoint inhibitor (IO) therapy in NSCLC. **Methods:** Using hybrid capture based CGP on extracted tumor DNA and a published "somatic-germline-zygosity" SGZ data analysis algorithm on 212,470 samples of clinically advanced malignancies, we identified 103 (0.05%) STK11GCa inactivating base substitutions or indels. Tumor mutational burden (TMB) was determined on up to 1.1 Mbp of sequenced DNA and microsatellite instability (MSI) was determined on 114 loci. PD-L1 expression was determined by IHC (Dako 22C3). **Results:** 57 (55%) STK11GCa cases were NSCLC, 7 (7%) STK11GCa cases each were CRC, breast, pancreatic and unknown primary carcinomas, and 3 (3%) were gynecologic cancers. Amongst all samples included in this analysis, *STK11* germline alterations were found in 0.15% NSCLC, 0.03% CRC, 0.03% breast, 0.08% pancreas, 0.06% unknown primary carcinoma and 0.03% of gynecologic cancers. Additional malignancies harboring STK11GCa included melanoma, gastroesophageal, HNSCC, bladder, HCC, lymphoma and mesothelioma. In STK11GCa, the median patient age at sequencing was 61 years (range 2 to > 89 years); gender distribution was 52% female and 48% male. STK11GCa cases had a median of 6.5 genomic alterations (GA)/tumor and *KEAP1*, another IO resistance gene, was co-altered in 10%. Currently untargetable GA were detected in *TP53* (50%), *KRAS* (38% with 9% in potentially targetable G12C), *CDKN2A* (32%), *CDKN2B* (22%), *SMARCA4* (19%), *MYC* (11%), and *APC* (10%). Potentially targetable GA, which have also been linked in some studies to IO efficacy, included GA in *BRAF* (10%), *EGFR* (9%) and *PBRM1* (4%). No targetable gene rearrangements or fusions were identified. No MSI High cases were identified. The median TMB was 5 mut/Mb with 23 % >10 mut/Mb and 4% >20 mut/Mb. 15% of 20 evaluated STK11GCA cases were PD-L1 high (>50% tumor cell staining). **Conclusions:** STK11GCa include a wide variety of primary tumors with a paucity of co-occurring targetable GA. Although these tumors have significant PD-L1 staining and a subset harbor other markers of potential IO efficacy, the inactivated *STK11* in these tumors may contribute to IO resistance and lack of responsiveness to immunotherapies. Research Sponsor: Foundation Medicine Inc.

3559 Poster Session (Board #289), Fri, 8:00 AM-11:00 AM

A prospective study of prognostic role of plasma circulating tumor DNA (ctDNA) in patients (pts) with early-stage malignancies. *First Author: Mikhail Fedyanin, Federal State Budgetary Institution N.N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russian Federation*

Background: Recently, conflicting evidence has emerged showing the association of ctDNA level and cancer progression. The aim of our study was the development of a method for detecting ctDNA in plasma and the investigation of the prognostic value of ctDNA retention after surgery in the prospective way. **Methods:** This prospective, single-center, sample collection study; pts with early-stage malignancies of the different origin were included. Tumor somatic mutations were determined by target sequencing of DNA from FFPE tumor blocks. Sequencing was performed using the custom NGS panel covering regions of frequent somatic mutations in 50 genes. Tumor-specific mutations were monitored in plasma samples taken before and after surgery. The median time between surgery and plasma collection was 7 days (5-15). Mutations of plasma ctDNA were determined by ddPCR. The plasma sample was considered "positive" if the content of ctDNA was more than 0.5 copies of mutant DNA in ml plasma. We needed 265 pts for improving 1-year disease free survival (DFS) from 60% to 80% with α=0.01, β=0.1, 10% loss of f.-up and duration of the study for 2 years. **Results:** The study comprised 271 pts with various cancers including colorectal – 91 (33,6%), pancreatic – 37 (13,7%), breast – 66 (24,4%), lung – 35 (12,9%) and gastric cancer – 42 (15,5%). Pts with stage I was 50 (18,5%), stage II – 118 (43,5%) and stage III – 103 (38%). The median time of the f.-up was 9 mos. (1-37). No significant association was found between the level of ctDNA before surgery and DFS either in the general group or in groups stratified by tumor sites (HR 2.4, 95%CI 0.8-7.1, p=0.12 and HR 1.5, 95%CI 0.4-6.3, p=0.5, correspondingly). ctDNA was detected in the plasma after surgery in 57 (10%) pts: 9 (9.9%) cases of colorectal, 10 (27%) - pancreatic, 9 (13.6%) - breast, 19 (54.3%) - lung, and 10 (23.8%) - gastric cancer. Progression of the disease was detected in 28/57 (49%) pts with ctDNA(+) and 17/214 (8%) - in ctDNA(-) pts ($p<0.001$). One-year DFS in ctDNA(+) and ctDNA(-) pts were 57% and 87%, respectively (HR 6.1, 95%CI 3.3-11.2, $p<0,001$). ctDNA positivity after surgery was an independent negative prognostic factor according to Cox regression model fitted to T, N, and adjuvant chemotherapy (HR 5.7, 95%CI 3.1-10.8, $p<0.001$). **Conclusions:** These results demonstrate the prognostic significance of ctDNA persisting after surgery in pts with the early stage of the different malignancies. Further clinical validation of this approach is required in trails with modifications of the adjuvant treatment, according to the content of ctDNA. Research Sponsor: This research is conducted under the auspices of the experimental governmental assignment of the Ministry of Health of the Russian Federation and coordinated by the FSBI "Center for Strategic Planning and Management of Biomedical Health Risks".

3560 Poster Session (Board #290), Fri, 8:00 AM-11:00 AM

Validation of RecurIndex (RI) for patients with early-stage breast cancer enrolled in a Taiwanese multicenter study. *First Author: Yi-Hsuan Lee, Departments of Pathology, National Taiwan University Hospital, Taipei, Taiwan*

Background: Numerous prospective studies, predominantly in Caucasian population, have proven the clinical utility of using multigene expression tests to prevent over-treatment in early breast cancer (EBC) patients. Since racial and ethnic disparities exist in genetic and biological factors that could influence the disease, the primary purpose of this study is to access the clinical utility of RecurIndex, a recurrence risk test, that is based on a genomic profiling derived from Asian women. **Methods:** A total of 298 patients with EBC, luminal subtype (85.6%), HER2 subtype (7.7%) and triple-negative subtype (6.7%), were enrolled in a retrospective study across Taiwan medical centers. Kaplan Meier and Cox Proportional Hazards model were used to, respectively, identify independent prognostic factors and calculate the survival rates. The prediction model was then tested using the area under the receiver operating characteristic curve (AUC). The primary endpoint was distant recurrence-free survival (DRFS). **Results:** The 10-year DRFS was significantly higher in the good-prognosis group than the poor-prognosis group (92.0% [95% CI, 86.1-98.2] versus 63.0% [95% CI, 49.9-79.5]) (Table). The overall hazard ratio for distant recurrence was 1.031 (95% CI, 1.017 ± 1.046) per RI score increment. In addition, in a subset of 179 cases (60.1%), the model yielded an 82.3% correct classification rate for predicting DR with a sensitivity of 87.0%, a specificity of 68.6% and negative predictive values of 97.3%. **Conclusions:** The present study provides robust evidence of the clinical utility of RI-DR to predict clinical outcomes. RecurIndex could be used to determine the utility of chemotherapy in Asian patients, especially in hormone-receptor positive and HER2 negative disease, leading to a meaningful reduction in adjuvant chemotherapy recommendations. Research Sponsor: Amwise Diagnostics Pte. Ltd.

Kaplan-Meier estimates of distant recurrence-free survival rates by RI-DR risk classification.

Risk group	10-year DRFS (%)	P value	Crude hazard ratio (95% CI)
All patients (n=298)		0.0011	
Good prognosis (n=145)	92.0		----
Poor prognosis (n=153)	63.0		3.621 (1.59 - 8.27)
Luminal patients (n=255)		0.0200	
Good prognosis (n=141)	91.6		----
Poor prognosis (n=114)	65.4		2.729 (1.13 - 6.58)
HER2/TNBC patients (n=43)		0.2500	
Good prognosis (n=4)	100.0		----
Poor prognosis (n=39)	61.2		----

Key words: Early breast cancer, Asian women, genomic assay, clinical utility, recurrence index (RI), distant recurrence (DR).

3561 Poster Session (Board #291), Fri, 8:00 AM-11:00 AM

Molecular profiling of metastatic breast cancer (MBC) and target-based therapeutic matching in an Asian tertiary phase I oncology unit. *First Author: Robert John Walsh, Department of Haematology-Oncology, National University Cancer Institute, National University Health System, Singapore, Singapore*

Background: Somatic profiling of MBC has highlighted actionable mutations and driven trials of matched targeted therapy (tx). Previous phase I studies have reported improved outcomes following matched therapies with tumour molecular profiles. Here, we review next generation sequencing (NGS) and treatment outcomes of Asian MBC patients (pts) in the phase I unit of a tertiary centre. **Methods:** Pts with MBC referred to a phase I unit underwent NGS (n = 152). Tumour tissue was sequenced via the amplicon based Ion Ampliseq Cancer (IAC) v2 (50 genes) platform from 2014-2017 prior to institutional change to Foundation Medicine 1 (FM1) (324 genes) 2017-2019. Patients were counselled on findings and enrolled onto matched therapeutic trials where available. **Results:** NGS was successfully performed in 107 pts (IAC 46%, FM1 54%) of which tumour subtypes include hormone receptor positive 63%, triple negative breast cancer (TNBC) 28% and Her2 positive 19%. Median lines of prior tx for MBC was 4 (range 0-12). 89% had prior chemotherapy (CT), 57% prior endocrine therapy (ET). 72/107 (67%) sequenced patients had further treatment and 18 (25%) were matched to tx based on NGS findings (15 clinical trial, 3 off trial). Matching rates on both NGS platforms were similar (IAC 22% *vs* FM1 28%). Mutated pathways with potential matched tx included PIK3CA/AKT/PTEN (52%), DNA damage response (DRR) (15%), and FGFR (11%) pathways. *PIK3* mutations were seen in 43% and associated with higher number of metastatic sites (p = 0.03); most prevalent aberrations were *PIK3CA H1047R* (41%) and *PIK3CA E542K* (13%). Matched cases were more heavily pretreated (mean lines of prior tx 5.3 matched *vs* 3.7, unmatched p = 0.05), and showed a median progression free survival (mPFS) of 24 weeks [w] and clinical benefit rate (complete/partial response or stable disease $\geq$ 12 weeks) of 53% on matched tx. Comparison by NGS platform showed improved mPFS for matched vs unmatched pts sequenced on FM1 *vs* IAC (FM1: 26 *vs* 19w, HR = 0.76 [95% CI: 0.3-1.9]; IAC: 8 *vs* 12w; HR = 1.21 [95% CI: 0.5-2.8]). Interestingly, 1 pt with *SMARCB* mutation, reportedly associated with the FGFR pathway, had a PFS of 70w on tx with a pan-FGFR inhibitor after progressing on 3 prior lines of tx (ET and CT). **Conclusions:** Molecular profiling of MBC in a phase I unit led to matched tx in 25% of cases. Matched pts showed encouraging mPFS with a suggestion of benefit in those matched after sequencing on a broader gene panel (FM1). Research Sponsor: NCIS Centre Grant - NMRC/CG/M005/2017_NCIS.

3562 Poster Session (Board #292), Fri, 8:00 AM-11:00 AM

Exomes and transcriptomes to reveal actionable findings in patients with negative-targeted panel sequencing. *First Author: Eric Y. Zhao, Canada's Michael Smith Genome Sciences Centre, Vancouver, BC, Canada*

Background: Next generation sequencing targeted panels increasingly inform clinical decisions, but may miss actionable findings detectable by whole exome sequencing (WES) and RNA-seq. There has been no direct comparison of WES plus RNA-seq against targeted panel sequencing to determine its added utility. To address this, we performed WES and RNA-seq analysis in a cohort of 100 patients with no actionable findings on prior panel sequencing. **Methods:** Ontario-wide Cancer Targeted Nucleic Acid Evaluation (OCTANE; NCT02906943) has sequenced 2,106 patients using a 161-gene Oncomine or 555-gene Hi5 panel. 100 patients (98 Hi5, 2 Oncomine) were chosen for further sequencing. Tumor (100x coverage) and normal (50x) exomes and tumor transcriptomes were sequenced on Illumina HiSeq2500 or NextSeq550. Interpretation included knowledgebase annotation (e.g. OncoKB, CIViC), mutation signatures, homologous recombination deficiency (HRD) scores, gene expression, and pathway analysis. Findings were deemed "actionable" if they could directly inform management or trial eligibility. **Results:** WES and RNA-seq identified one or more novel actionable findings in 38 patients. Of these, the main actionable finding was tumor mutation burden (TMB), mutation signature, or HRD score in 19 (50%), a copy number variant in 16 (42%), a fusion in 2 (5%), and a point mutation in 1 (2.6%). WES identified a *MALAT1-GLI1* fusion in a cancer of unknown primary (CUP) whose transcriptome was consistent with gastric cancer, together suggesting the diagnosis of a rare gastroblastoma. To date, two cases have received exome-supported targeted therapy: (1) a metastatic high grade serous ovarian cancer, HRD-high, treated with olaparib then cisplatin for a combined 15 months, and (2) a metastatic neuroendocrine rectal tumor with RICTOR amplification treated with everolimus starting in Dec 2016 until last follow-up in Sep 2019. Of 62 patients with no actionable finding, expanded sequencing identified one or more known cancer drivers in 25 (40%): 17 CNVs, 3 fusions, and 5 point mutations or indels. In 16 patients, an oncogenic variant found on panel was not captured by WES, and may represent artifacts, germline mutations, or subclonal/localized variants. **Conclusions:** WES and RNA-seq expanded detection of actionable biomarkers and oncogenic mutations, especially CNV, TMB/signatures, and HRD. Two cases have undergone exome-supported targeted treatment. We performed the first WES of a rare gastroblastoma, originally a CUP but reclassified by expanded fusion detection and RNA-seq. Research Sponsor: The Government of Ontario and The Princess Margaret Cancer Foundation.

3563 Poster Session (Board #293), Fri, 8:00 AM-11:00 AM

Machine learning radiomics signature on magnetic resonance imaging associated with phenotypes and disease-free survival in patients with breast cancer (RBC-01): A registry-based, multicenter cohort study. *First Author: Herui Yao, Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Department of Oncology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China*

Background: The early stage breast cancer patients can vary in disease-free survival (DFS), innovative predictors evaluate the prognostic capacity are urgently needed. We aimed to develop and independently validate a radiomics signature based on MRI associated with phenotypes and DFS in patients with breast cancer and to establish a radiomics nomogram that incorporates the radiomics signature and clinicopathological findings using computational algorithms. **Methods:** In this multicenter, retrospective, cohort study, we analyzed preoperative contrast–enhanced MRI data from the prospective cohort study (n = 123) of patients who had been treated with neoadjuvant chemotherapy in phase 3 trials and independent cohort (n = 438) at the Sun Yat-sen Memorial Hospital as training cohort to develop the radiomic signature, and validated it in validation cohort (Foshan cohort, n = 121; Dongguan cohort, n = 89) between November 17, 2011, and September 21, 2019, and validated in TGCA cohort (n = 84). Machine-learning algorithm to identify robust imaging subtypes and evaluated their clinical and biologic relevance. A nomogram combining the radiomic signature and clinicopathological findings to predict individual survival based on Cox regression model. The primary endpoint was disease-free survival (DFS). This study is registered with ClinicalTrials.gov, number NCT04003558, and Chinese Clinical Trail Registry, number ChiCTR1900024020. **Results:** A total of 855 breast cancer patients were included. Radiomics signature was generated to classify patients into high-risk and low-risk groups in the Guangzhou training cohort. Patients with low-risk scores in the training cohort had higher DFS (hazard ratio [HR] 0.55, 95% CI 0.31 to 0.99; *P*= 0.045) than patients with high-risk scores, and validated in in validation cohort (HR 0.14, 95% CI 0.03 to 0.62; *P*= 0.003). The nomogram combined radiomics score with clinicopathological factors could accurately predict DFS benefits in training cohort (C-index = 0.83; AUC, 1, 2, 3-year were 0.80, 0.85, 0.82, respectively) and validated in validation cohorts. **Conclusions:** The radiomics signature are significantly associated with the DFS in patients with breast cancer. Combining the radiomics nomogram improved individualized DFS pretiction. Clinical trial information: NCT04003558. Research Sponsor: None.

3564 Poster Session (Board #294), Fri, 8:00 AM-11:00 AM

Comparison of the clinical interpretation of high-dimensional molecular data by two molecular tumor boards. *First Author: Damian Tobias Rieke, Charité Universitätsmedizin Berlin, Berlin, Germany*

Background: The clinical interpretation of molecular data is a bottleneck of precision oncology. High-dimensional molecular data, such as RNA sequencing (RNA-seq) and whole-exome sequencing (WES), will likely increase the complexity of clinical interpretation. We compared the recommendations by two molecular tumor boards (MTBs) that independently interpreted the same high-dimensional molecular profiles. **Methods:** Patients with advanced solid tumors, no available standard therapy, an ECOG performance status of 0-1, and available fresh-frozen tissue underwent WES of tumor tissue and normal blood as well as RNA-seq of tumor tissue within the MASTER (Molecularly Aided Stratification for Tumor Eradication Research) precision oncology program of the German Cancer Consortium (DKTK). Data from 46 patients (WES and RNA-seq, n = 41; WES alone, n = 5) were independently discussed by two MTBs. Treatment recommendations were compared with regard to levels of evidence, therapeutic baskets, and types of biomarkers. **Results:** A total of 51,610 aberrations (median, 393 per patient) were considered for clinical interpretation (34,314 mutations/single-nucleotide variants, 7,115 mRNA expression changes, 6,144 DNA copy number variations, 4,037 gene fusions). 110 and 132 treatment options were identified by the two MTBs, respectively, with an overall agreement rate of 44.1%. The highest agreement rates were identified for treatment options based on clinical levels of evidence (Level 1, 60%; Level 2, 49.6%) and for poly(ADP-ribose)-polymerase inhibition (57.1%). The lowest agreement rates were identified when MTBs opted for traditional chemotherapy (0%), combination therapies (6.9%), therapies based on preclinical levels of evidence (Level 3, 35.9%; Level 4, 32%), and MAPK inhibition (35%). Similar agreement rates, ranging from 39% (gene fusions) to 54% (loss of heterozygosity), were observed for different types of biomarkers. **Conclusions:** Reproducible, evidence-based annotation of high-dimensional molecular data is feasible. Our experience provides a basis for ongoing harmonization and standardization efforts within the MTBs of the DKTK. Research Sponsor: Deutsches Konsortium für translationale Krebsforschung.

3565 Poster Session (Board #295), Fri, 8:00 AM-11:00 AM

ERBB2 amplifications and mutations in 109 advanced breast cancer patients by next-generation sequencing. *First Author: Ami N. Shah, Northwestern University, Chicago, IL*

Background: In advanced breast cancer (ABC) HER2 status is based on ASCO/CAP immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) criteria. Next generation sequencing (NGS) of tissue and blood can detect aberrations in *ERBB2* such as copy number gain/amplifications (cng/amp) and mutations. **Methods:** We retrospectively identified patients (pts) seen at Northwestern University between 2015 and 2019 with ABC and an alteration in *ERBB2* identified by tissue and/or circulating tumor DNA (ctDNA) NGS. We included pts with testing by Guardant360, TempusX, and/or FoundationOne platforms. NGS reports were evaluated for non-synonymous mutations and cng/amp. HR and HER2 status were determined based on the most recent pathologic assessment. Mutations were categorized as pathologic if they were consider oncogenic (level 1-2 evidence with direct functional data), likely oncogenic, or predicted oncogenic, based on OncoKB (Chakravarty et al., JCO PO 2017). **Results:** 109 cases of ABC (6 locally advanced, 103 metastatic) with *ERBB2* alterations were identified. Tissue NGS was available from 43%, ctDNA from 72%, and both from 19%. The positive predictive value (PPV) of *ERBB2* amp/cng by tissue NGS to predict HER2+ using the gold standard as IHC/FISH was 94% (33/35). The PPV of *ERBB2* amp by ctDNA was 93% (40/43). *ERBB2* mutations were detected in 52 pts. Of these, 23 pts were considered to harbor pathologic *ERBB2* mutations, (19 oncogenic, 2 likely oncogenic, 1 predicted oncogenic) detected by ctDNA and tissue in 4, ctDNA in 16, and tissue in 3 pts. The most frequently detected mutations were V777L and S310. Four pts had co-mutations of *ERBB2* V777L and S310F. Disease subtype among those with *ERBB2* pathologic mutations was HR+ HER2- in 57%, HER2+ in 26%, and triple negative in 17%. In all patients with serial ctDNA analysis and pathologic *ERBB2* mutations, the mutation was detected on the first analysis. Pathologic *ERBB2* mutation represented the mutant with the highest mutant allele frequency (MAF) in 30% and top 3 highest MAF in an additional 35%. *PIK3CA* was co-mutated in 48%. **Conclusions:** The PPV of *ERBB2* amp/cng by tissue and ctDNA NGS was high, and has potential utility for cancers where HER2 IHC/FISH is not standardly assessed or cases where biopsy is challenging. *ERBB2* pathologic mutations were found in all breast cancer subtypes. When present, they were identified on the initial ctDNA analysis and often represented a significant clone, supporting its role as a 'driver mutation'. Research Sponsor: None.

3566 Poster Session (Board #296), Fri, 8:00 AM-11:00 AM

Platform comparison of HTG EdgeSeq and RNA-Seq for gene expression profiling of tumor tissue specimens. *First Author: Di Ran, HTG Molecular Diagnostics, Tucson, AZ*

Background: Clinical biomarker studies are often hindered by the availability of tissue specimens of sufficient quality and quantity. While RNA-Seq is often considered the gold standard for measuring mRNA expression levels in cancer tissue, it typically requires multiple formalin-fixed paraffin-embedded (FFPE) tissue sections to extract a sufficient amount of quality RNA for subsequent gene expression profiling analysis. The HTG EdgeSeq technology is a gene expression profiling platform that combines quantitative nuclease protection assay technology with next-generation sequencing detection. Unlike RNA-Seq, the HTG EdgeSeq technology does not require RNA extraction, and can use small amounts of tissue material, typically several mm^2, to generate reproducible gene expression profiles. **Methods:** This study compares the performance of RNA-Seq and HTG's profiling panel, the HTG EdgeSeq Precision Immuno-Oncology Panel (PIP), which is designed to measure expression levels of 1,392 genes focused on tumor/immune interaction. Approximately 1,200 samples from three tumor indications (gastric cancer, colorectal cancer and ovarian cancer) were tested using both technologies. **Results:** Up to four FFPE slides were used for RNA extraction to support RNA-Seq testing; out of the 1,202 samples processed, 1,099 generated extracted RNA of sufficient quality and quantity (as measured by RNA concentration, RIN score and %DV200) to proceed to sequencing, which resulted in a pass rate of 91.4% for RNA-Seq. The HTG EdgeSeq PIP panel resulted in a pass rate of 97.3% (samples passing QC metrics) when the same 1,200 samples were tested, and required only a single FFPE section owing to the small sample requirement. The t-SNE (a non-linear dimensionality reduction method) analysis of the common 1,358 genes revealed similar clustering of the three cancer indications between the two methods. Correlations across individual genes by sample resulted in the mean Spearman correlation coefficient of 0.73 (95% confidence interval of 0.61 - 0.80). Additionally, gene-wise comparisons across all samples were also evaluated. **Conclusions:** These data demonstrate that HTG EdgeSeq gene expression panels can be used as a competitive alternative to RNA-Seq, generating equivalent gene expression results, while offering the added benefits of a small sample size requirement, lack of RNA extraction bias, and fully automated data analysis pipeline. Research Sponsor: HTG Molecular Diagnostics and Oncologie, Inc.

3567 Poster Session (Board #297), Fri, 8:00 AM-11:00 AM

Diagnosis of leptomeningeal metastasis (LM) through identification of circulating tumor cells (CTCs) in cerebrospinal fluid (CSF). *First Author: Kathleen Fenn, Department of Medicine at Columbia University Medical Center, New York, NY*

Background: Diagnosis of LM from solid tumors can be challenging. The TargetSelector (TS) CTC detection assay has demonstrated highly specific and sensitive CTC capture both for epithelial (CK+) and non-epithelial (CK-) subsets. The assay utilizes a ten-antibody (ab) capture cocktail followed by biotinylated secondary abs that bind to CTCs, enriched in a microfluidic device. TS targeted next-generation sequencing (NGS) assay detects somatic mutations in 12 breast cancer-related genes. The aim was to determine whether TS can improve sensitivity in the diagnosis of LM compared to CSF cytology by lumbar puncture (LP). **Methods:** CSF was collected prospectively from patients (pts) with a prior solid tumor diagnosis and suspicion of LM. CTCs were isolated from CSF using the TS platform. Cells were stained with cytokeratin (CK), CD45, streptavidin and DAPI. CTCs captured in a microchannel were classified as CK + or -. Peripheral blood samples obtained at time of LP underwent similar CTC analysis. Cell-free total nucleic acids (cfTNA) were extracted from plasma and CSF followed by NGS. Data analysis used the Ion Torrent Suite with annotation and report curation by Ion Reporter and Oncomine Knowledgebase Reporter software respectively. **Results:** There were 14 pts (13 women and 1 man), median age 56 years (range 32-75) with cancers of the breast (10), lung (1), colon (1), CNS lymphoma (1) or glioma (1). Pts had received a median of 2.5 lines of systemic metastatic therapy (range 0-8). CSF cytology was not sent for 1 pt and TS was not performed for 1 pt. TS and standard cytology had 89% agreement in pts with metastatic breast cancer (MBC, 8/9). Of the 6 pts for whom CTCs were detected in CSF by TS, 3 pts had + cytology (all MBC), 2 pts had - cytology and 1 pt with MBC was not tested by cytology. Of the 3 pts with + CSF by cytology (all MBC), all were detected by TS (Table). Among 5 MBC pts with CTCs present in CSF, ER status was concordant in 2 of 5 (40%). HER2 status was concordant in 3 of 4 (75%) evaluable pts and not determined in 1 pt. Analysis of cfDNA from CSF identified somatic mutations in 3 pts (TP53, PIK3CA, CCND1, respectively). In 1 of 3 pts, the mutation identified in the CSF (PIK3CA) in HR+/HER2- MBC was also identified in the blood. **Conclusions:** TargetSelector is a viable platform for the detection of breast cancer CTCs in the CSF. NGS performed on CSF samples can identify potentially actionable mutations. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

	LP CTC (+) (n = 6) no. (%)	LP CTC (–) (n = 7) no. (%)
Breast primary	5 (83)	5 (71)
Other primary	1 (17)	2 (29)
CSF cytology +	3 (50)	0 (0)
CSF mutation detected	2 (33)	1 (14)

3568 Poster Session (Board #298), Fri, 8:00 AM-11:00 AM

The utility of blood-based molecular tools-the NETest-to monitor and evaluate the efficacy of PRRT in neuroendocrine tumors. *First Author: Lisa Bodei, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Peptide receptor radionuclide therapy (PRRT) is an effective therapy for metastatic/inoperable neuroendocrine tumors (NETs). Tools to predict and monitor the efficacy of therapy are important adjuncts in the radio-oncology armamentarium. Standard blood biomarkers are not effective by new molecular based assays such as the PRRT Predictive Quotient (PPQ) and NETest are effective as real-time predictors and monitors of therapy. We aimed to prospectively evaluate whether: 1) the NETest functioned as a surrogate biomarker for image-based per RECIST evaluation of PRRT efficacy; 2) there was a correlation between changes in NETest levels during therapy, PPQ prediction and treatment efficacy. **Methods:** Three independent ^{177}Lu-PRRT-treated GEP-NET and BPNEN cohorts (Rotterdam, Netherlands: n= 41; Bad-Berka, Germany: n= 44; Meldola, Italy: n= 72). Treatment response: RECIST1.1 [Responder (stable, partial/complete response) vs Non-Responder]. Blood sampling: pre-PRRT, prior to each cycle and 6 months (median) after completion of all cycles. PPQ (positive/negative) and NETest (0-100 score) by PCR. Stable$<$40; progressive $>$ 40). CgA (ELISA) as comparator. Samples deidentified, measurement and analyses blinded. Kaplan-Meier survival and Mann-Whitney analyses. **Results:** 122 of 157 were evaluable. RECIST stabilization or response in 67%; 33% progressed. NETest significantly ($p<$ 0.0001) decreased in RECIST-"responders" (-47$\pm$3%); in "non-responders" it elevated (+79$\pm$19%, $p<$ 0.0005). NETest monitoring accuracy 98% (119/122). Follow-up levels $>$ 40 (progressive) vs stable ($<$40) significantly correlated with mPFS (not reached vs. 10 months; HR 0.04, 95%CI: 0.02-0.07). PPQ response prediction was accurate in 118 (97%); 99% accurate positive and 93% accurate negative prediction. NETest significantly ($p<$ 0.0001) decreased in PPQ-predicted responders (-46$\pm$3%) and remained increased in PPQ-predicted non-responders (+75$\pm$19%). Follow-up NETest categories stable vs progressive significantly correlated with PPQ prediction and mPFS (not reached vs. 10 months; HR 0.06, 95%CI: 0.03-0.12). In comparison, the standard biomarker, CgA, failed to predict or correlate with response to PRRT (p= NS). **Conclusions:** NETest accurately (98%) monitors PRRT response and is an effective surrogate marker for radiological response (image concordance 98%). A NETest decrease identified responders (99%) and correlated ($>$ 97%) with the pretreatment PPQ response predictor. Research Sponsor: None.

3569 Poster Session (Board #299), Fri, 8:00 AM-11:00 AM

High-risk breast cancer genes at 8q22-24 and their role in over 5,000 patients evaluated with the 70-gene risk of recurrence assay. *First Author: Sami Diab, Rocky Mountain Cancer Center-Aurora, Aurora, CO*

Background: Previous studies have shown that *CCNE2* expression is higher in patients' cancers resistant to CDK4/6 inhibitors. Increased expression of *CCNE2*, *MTDH,* or *TSPYL5*, genes contained within the 70-gene risk of distant recurrence signature (70GS), has also been implicated in breast oncogenesis, poor prognosis, and chemoresistance. These genes are located on chromosome region 8q22.1, one of the most recurrently amplified regions out of all 70GS genes in breast tumors (Fatima et al. 2017). *MYC*, located on 8q24, is overexpressed in 40% of all breast cancers (BC). Here we examined the expression of *CCNE2*, *MTDH,* and *TSPYL5* in relation to 70GS risk and the 80-gene molecular subtype signature (80GS), and their correlation with *MYC* expression in early stage BC patients. **Methods:** *CCNE2*, *MTDH*, *TSPYL5,* and *MYC* mRNA expression was measured in 5022 BC samples sent to Agendia (Irvine, CA) for 70GS and 80GS testing, which included FFPE microarray full-transcriptome data. 70GS was used to stratify patients into Ultra Low Risk (UL), Low Risk (LR), High Risk (HR), and Ultra High Risk (UH). Both 70GS and 80GS were used to classify patient samples into Luminal A, Luminal B, HER2, or Basal type. Wilcoxon rank sum test was used to assess expression differences. **Results:** The expression of *CCNE2*, *MTDH*, and *TSPYL5* significantly correlated with each other and was higher in HR patients compared to LR patients ($p < 0.001$) and higher in UH patients compared to HR patients ($p < 0.001$). Expression of these genes was highest in Basal type tumors, 83% of which were UH, followed by Luminal B type tumors, and lowest in Luminal A type tumors. *CCNE2* and *MYC* expression was elevated in LR compared to UL patients ($p < 0.001$ and $p = 0.0043$). There was no difference in *MYC* expression between HR vs. LR or UH vs. HR. Lastly, there was no association between the expression of 8q22.1 genes and *MYC* in any 70GS subgroup. **Conclusions:** Within the 70GS, *CCNE2, MTDH,* and *TSPYL5* have similar expression patterns and when overexpressed may identify an UH cohort of BC. This observation, in addition to their physical proximity at 8q22.1 suggests a possible amplicon in this region. The highest expression of *CCNE2*, *MTDH,* and *TSPYL5* associated with UH patients and is concordant with previous studies that support the role of these genes in BC metastasis. Furthermore, this analysis suggests *MYC* may not stratify patients based on metastatic potential. These data may be clinically relevant for stratifying patients in ongoing clinical trials evaluating response and resistance to targeted therapies in early stage BC. Research Sponsor: Agendia, Inc.

3570 Poster Session (Board #300), Fri, 8:00 AM-11:00 AM

Adding precision to 2018 ASCO/CAP HER2 testing guidelines in breast cancer with genomic profiling. *First Author: Adam Brufsky, Magee-Womens Hospital of UPMC, Pittsburgh, PA*

Background: Biological heterogeneity of HER2 positive breast cancers has been suggested by a modest benefit of HER2-targeted therapies reported in the APHINITY and ExteNET trials. This highlights the need for improved biomarkers that more precisely identify patients who benefit from HER2-directed agents. The 80-gene molecular subtyping signature (80GS) classifies breast tumors into Luminal, HER2 or Basal type based on the gene expression of downstream signaling pathways. Previous work showed a substantial proportion of tumors identified as HER2 equivocal or HER2 positive by 2013 ASCO/CAP guidelines may be reclassified as non-HER2 type by 80GS. In 2018, ASCO/CAP HER2 IHC/ISH classification guidelines were revised to reduce the frequency of HER2 equivocal cases, for which treatment recommendations have been ambiguous. Here we evaluated concordance between HER2 status by 2018 ASCO/CAP guideline classification and 80GS molecular subtyping. **Methods:** Pathology reports are provided by physicians for samples that are tested with the 70-gene risk of distant recurrence signature (70GS) and 80GS as part of routine diagnostic care. This analysis includes data sent to Agendia (Irvine, CA) from January 2019 to January 2020. HER2 IHC/ISH results based on ASCO/CAP 2018 guidelines were available for 1453 samples. **Results:** Of 1453 samples, 1336 (92%) were HER2 negative, 99 (7%) were HER2 positive, and 18 (1.2%) were HER2 equivocal under 2018 guidelines. 80GS reclassified 57 of 99 (58%) HER2 positive tumors as Luminal and 11 of 99 (11%) as Basal; the remaining 31% were confirmed HER2. Furthermore, 55 of 99 (55%) HER2 positive tumors were also ER and PR positive by IHC, with 48 (87%) of these reclassified as Luminal type. Of HER2 negative tumors, 80GS classified 94 of 1336 (7%) as Basal and 2 of 1336 (0.15%) as HER2. Of HER2 equivocal tumors, 16 of 18 (89%) reclassified as Luminal and 2 of 18 (11%) as Basal. **Conclusions:** In this real-world diagnostic dataset, 2018 ASCO/CAP guidelines resulted in few HER2 equivocal tumors overall, confirming the positive impact of the revised guidelines. However, 80GS reclassified 69% of HER2 positive tumors to non-HER2 molecular subtypes, suggesting these tumors may have suboptimal responses to HER2-directed therapy compared to HER2 enriched. All HER2 equivocal tumors reclassified to non-HER2 subtypes. Molecular classification by 80GS adds further precision in classifying HER2 positive patients and potential to predict responsiveness to HER2-targeted therapies. Further studies are warranted to validate the utility of HER2 status based on 80GS. Research Sponsor: Agendia, Inc.

3571 Poster Session (Board #301), Fri, 8:00 AM-11:00 AM

Genomic analysis of driver-negative lung adenocarcinoma (LA) in lifetime never smokers. *First Author: Aline Fusco Fares, Princess Margaret Hospital, Toronto, ON, Canada*

Background: Genomic events giving rise to driver negative LA in never smokers remain elusive. Here we report results of whole exome sequencing (WES) and targeted RNA sequencing in NS who had no mutation drivers found on routine clinical testing by targeted next generation sequencing (NGS). **Methods:** The cohort of never smokers with EGFR/ALK negative LA by clinical biomarker testing at Princess Margaret Cancer Centre, were first subjected to various clinical NGS profiling platforms (table). Where tissue was available, those negative for potential drivers in the clinical NGS then underwent WES (mean coverage > 200x) and Oncomine comprehensive v.3 RNA sequencing. We analyzed mutational signatures (MS) of the driver negative cohort based on the COSMIC catalog and assessed the median tumor mutation burden (mTMB mut/Mb -Megabase) in cases without a smoking MS, to avoid confounders. **Results:** Of 159 never smokers profiled with clinical NGS, potential drivers were found in 86 (54%): 75 (87%) with mutations in known LA driver genes and 11 (13%) with fusions. Among the remaining never smokers that tested negative by clinical NGS, 35 (48%) had available tissue for further testing. The Oncomine panel identified 9 cases (25%) with fusions or MET exon14 mutation (n = 7). Within the driver negative group, 24 (92%) underwent WES. Three tumors had WES base substitution patterns that were consistent with a smoking-related MS (MS4). Twenty-one patients exhibited signatures found common across all cancer types (MS 5), associated with DNA mismatch repair (MS 6, MS 20) or APOBEC over-activation (MS 2, MS13). In the driver-negative group, we identified 7 pts with somatic mutations in the KMT2 family (4 KMT2C, 4 KMT2A, 1 KMT2D), known for putative tumor suppressors and histone methyltransferases. mTMB on the driver negative group was 1.92, while one outlier with APOBEC MS and KMT2C/A mutations had a TMB of 16.8. **Conclusions:** Never smokers with driver negative LA are a heterogeneous group, with different MS and a wide TMB range. Mutations on KMT2 family are frequently found in driver negative LA in never smokers and warrant further investigations. Research Sponsor: Alan Brown Chair.

Never smokers EGFR/ALK negative with routine clinical NGS	**Drivers on NGS** N = 86 (54%)	**Mutations:** KRAS (35%) HER2 (33%) BRAF (9%) METex14 (7%) FGFR (4%)
N = 159 • 15 genes N = 89 • > 150genes N = 41 • Blood Guardant360 or Foundation blood N = 29		**Fusions:** ROS1 (6%) NRG1 (3%) RSPO2 (3%) RET (3%)
	No drivers on NGS N = 73 (46%)	**Tissue for WES and RNA panel** N = 35 (48%)
		Fusions N = 9 METex14 (20%) NTRK (3%) RSPO (3%)
		WES on driver negatives N = 24 (2 no material) KMT2 (29%), ATM (12%) SMAD4 (8%) ARID2 (4%)

3572 Poster Session (Board #302), Fri, 8:00 AM-11:00 AM

Ultrasensitive multiplex detection of structural rearrangements in *ALK*, *RET*, *ROS1* and *PD-L1* using a comprehensive next-generation sequencing assay. *First Author: Kao Chin Ngeow, Lucence Diagnostics, Singapore, Singapore*

Background: Oncogenic structural rearrangements (SR) in *ALK*, *RET* and *ROS1* are well-described in lung cancer, and confer sensitivity to targeted therapy. SR disrupting the 3'UTR of *PD-L1* gene have been reported in multiple cancer types and can potentially predict response to checkpoint immunotherapy. An amplicon-based next-generation sequencing (NGS) platform technology (AmpliMARK), previously optimized for detection of single nucleotide variations (SNVs), microsatellite instability and viral DNA, was extended to the multiplex detection of SR in *ALK*, *RET*, *ROS1* and *PD-L1* in cell-free DNA (cfDNA) and tumor tissue DNA. **Methods:** A hybrid primer-extension and adapter-ligation based method allowing detection of SR in a fusion-partner agnostic manner was utilized for multiplex target capture of genomic regions of *ALK*, *RET*, *ROS1* and *PD-L1* SR. Analytical validation was performed using admixtures of fragmented genomic DNA from an *ALK* SR-positive cell line, commercial standards containing *RET* and *ROS1* SR, and synthetic *PD-L1* SR gene constructs. Clinical performance was assessed in cfDNA samples from lung cancer patients and tumor tissue DNA samples from natural killer(NK)/T-cell lymphoma patients. **Results:** Detection of SR could be achieved to an allele frequency detection limit of 0.5% with sensitivity of 89.5% and specificity of 100% in admixture samples mimicking cfDNA. In an unselected series of 374 lung cancer cases, actionable SR for *ALK*, *RET* and *ROS1* were detected in cfDNA of 9 samples, for an overall detection rate of 2.4%, and 1.8% (3 out of 168) when restricted to treatment-naive lung cancer cases only. In 29 NK/T-cell lymphoma tumor tissue samples, 9 samples were positive for *PD-L1* SR, which were orthogonally confirmed by whole-genome sequencing, targeted sequencing or Sanger sequencing for a concordance rate of 100% across all samples. For 1 NK/T-cell lymphoma tumor tissue sample where matched plasma was available, the same *PD-L1* SR was also detected in cfDNA. **Conclusions:** We have demonstrated and validated a comprehensive amplicon-based NGS assay for ultrasensitive multiplex detection of structural rearrangements in *ALK*, *RET*, *ROS1* and *PD-L1* across both cfDNA and tumor tissue DNA in analytical and clinical contexts. Ongoing studies will further evaluate the performance and utility of this assay across a larger number of clinical samples for the detection of these SR as well as additional cancer-associated SR involving *NTRK1/2/3*, *FGFR2/3* and *TMPRSS2*. Research Sponsor: Lucence Diagnostics.

3573 Poster Session (Board #303), Fri, 8:00 AM-11:00 AM

^{89}Zr-durvalumab PD-L1 PET in recurrent or metastatic (R/M) squamous cell carcinoma of the head and neck. *First Author: Sarah Verhoeff, Department of Medical Oncology, Radboud University Medical Center, Nijmegen, Netherlands*

Background: Immune checkpoint inhibitors (ICI) targeting programmed cell death protein-1/ligand-1 (PD-1/PD-L1) have shown activity in R/M squamous cell carcinoma of the head and neck (SCCHN). Positron-emission-tomography (PET) with ^{89}Zr-labeled anti-PD-L1 antibodies could aid in predicting response to ICI. We present the dose-finding results of the first-in-human ^{89}Zr-durvalumab PD-L1 PET-imaging in patients with SCCHN participating in the ongoing phase II PINCH study (NCT03829007). **Methods:** Following baseline [^{18}F]FDG-PET and CT/MRI imaging, patients with incurable R/M SCCHN received 37 MBq ^{89}Zr-durvalumab and protein dose 2mg, 10mg or 50mg durvalumab. ^{89}Zr-durvalumab PD-L1 PET-scan was acquired day 5 post-injection. Plasma pharmacokinetic analyses were performed at day 0 and 5. Standardized uptake values (SUV, mean ± SD) were measured in [^{18}F]FDG-positive tumor lesion, liver, spleen, bone marrow and bloodpool. PD-L1-expression was assessed on archival tumor tissue using the Ventana PD-L1 (SP263) assay. **Results:** 14 patients were enrolled and no adverse events were reported. High tracer-retention was observed in liver and spleen, most prominent in patients receiving 2 or 10mg durvalumab. ^{89}Zr-durvalumab accumulation within tumors and between patients was heterogeneous and not all [^{18}F]FDG-positive lesions showed ^{89}Zr-durvalumab uptake. Tumor lesions were visualized best using 10 or 50mg durvalumab (SUV_{peak} 2mg: 3.86 ± 0.79, 10mg: 7.46 ± 2.18, 50mg: 5.57 ± 1.74). Tumor-to-blood-ratios for 10mg durvalumab were highest (2mg: 2.27 ± 0.33, 10mg: 3.44 ± 0.76, 50mg: 1.73 ± 0.99; p = 0.019). PK-analyses confirmed visual prolonged tracer-retention in bloodpool with increasing protein dose. PD-L1-expression was equally distributed amongst dose-groups. **Conclusions:** This is the first study to show feasibility of ^{89}Zr-durvalumab PD-L1 PET in SCCHN patients, demonstrating the highest tumor-to-blood radio with a total dose of 10mg durvalumab. So far, no correlation of tumor PD-L1 expression with ^{89}Zr-durvalumab-uptake and PD-L1 expression on archival tissue was found. Next step will be to correlate ^{89}Zr-durvalumab PD-L1 PET tumor uptake with durvalumab treatment response in the phase 2 part of the PINCH study. Clinical trial information: NCT03829007. Research Sponsor: Astra Zeneca, Radboud Institute for Health Sciences, Junior research project.

3574 Poster Session (Board #304), Fri, 8:00 AM-11:00 AM

PCR-based comprehensive genomic profiling (PCR-CGP): Feasibility from >20,000 tumor tissue specimens (TTS) and predicted impact on actionable biomarker identification versus hybrid capture (H)-CGP and plasma (P)-CGP. *First Author: Dan Rhodes, Strata Oncology, Ann Arbor, MI*

Background: Tissue-based h-CGP is increasingly utilized for treatment selection in patients with advanced solid tumors but has high tumor surface area [TSA] requirements (≥25mm^2 for leading commercial tests). P-CGP is recommended when tissue is insufficient for H-CGP. Here we assessed the feasibility and clinical impact on actionable biomarker identification of PCR-CGP. **Methods:** We performed a post-hoc, non-prespecified analysis on 21,743 consecutive subjects with advanced solid tumors who sent TTS for PCR-CGP from 5/17-12/19 as part of an ongoing observational trial at > 20 U.S. health systems (NCT03061305). PCR-CGP was performed using StrataNGS, a single-site laboratory developed test assessing all CGP biomarker classes (including microsatellite instability (MSI) status and tumor mutation burden [TMB]). We predicted actionable biomarker identification rates for PCR-CGP, H-CGP and P-CGP if applied to all U.S. patients with advanced solid tumors through incorporating population incidence, biomarker frequencies, test TSA and tumor content requirements (or cfDNA detection rates), and performance characteristics. Actionable biomarkers were the 30 in 11 tumor types from the MoIDX p-CGP local coverage determination (L38043), pan-tumor NTRK fusions and MSI, and TMB in lung cancer. **Results:** Among TTS from 21,734 patients with advanced cancer, 20,493 (94.3%) met TSA requirements for PCR-CGP (≥2mm^2) vs. 9,281 (42.7%) for H-CGP. PCR-CGP reported results for 98.0% and 95.0% of patients with large (≥25mm^2 TSA) and small (2-24mm^2) TS, respectively, in a median of 7 business days. Compared to 1,882 orthogonal actionable biomarker results, PCR-CGP accuracy was 96.6% and 96.5% in large and small TTS, respectively. Actionable biomarker frequency was highly correlated in PCR-CGP tested large vs. small TTS (r^2= 0.99), as well as in this PCR-CGP cohort vs. a MSKCC institutional pan-cancer H-CGP cohort (r^2= 0.92). If applied to all U.S. patients with advanced solid tumors, PCR-CGP has significantly greater predicted actionable biomarker identification rate (88.5%) compared to P-CGP (77.0%, N-1 chi-squared test, p < 0.0001) or H-CGP (54.3%, p < 0.0001). **Conclusions:** Half of TTS submitted for PCR-CGP did not meet H-CGP tissue requirements. PCR-CGP is feasible for the vast majority of patients and is predicted to expand the actionable biomarker evaluable proportion of patients with advanced solid tumors compared to H-CGP or P-CGP. Clinical trial information: NCT03061305. Research Sponsor: Strata Oncology.

3575 Poster Session (Board #305), Fri, 8:00 AM-11:00 AM

Hyperprogression in cancer patients on immunotherapeutic agents. *First Author: Sumi Dey, University of Michigan, Ann Arbor, MI*

Background: Patients (pts) treated with checkpoint inhibitors (CPI) may uncommonly experience accelerated progression in their tumor burden when compared to their rate of progression prior to receiving CPI. This hyperprogression has been varyingly defined and no biomarker has yet been identified. **Methods:** We reviewed the database from the Tumor Response Assessment Core (TRAC) at University of Michigan to identify these patients. Hyperprogression was defined as increase in tumor burden per specific immune RECIST criteria by at least 40% from baseline on the first follow-up scan with a minimum increase of 10 mm, and at least 2 times rate of growth than observed prior to start of CPI therapy. **Results:** Out of 741 pts who underwent baseline and 1st follow-up assessment enrolled on 118 trials, 302 (34.4%) pts received immunotherapy alone or in combination with chemotherapy/targeted agents across 49 trials. Of them, 15 pts (5%) with 5 females (33%) and median age of 63 years (range, 44 -72) met criteria for hyperprogression. The primary cancers included lung (5), colorectal (2), renal (2), biliary (1), pancreatic (1), esophageal (1), bladder (1), small bowel (1), and melanoma (1). The median time to hyperprogression was 67 (range 42-110) days, and the mean survival was 7.9 months from trial enrollment. We did not identify any clinical factor or specific CPI therapy that associated with hyperprogression. Exploratory biomarker analysis of genomic (gene panel assay) and immune subsets of tissue microenvironment (multiplex staining) is underway. **Conclusions:** This is the largest cohort investigated for hyperprogression across multiple cancers in literature. The rate of hyperprogression observed is less than previously reported in literature, and physicians need to be aware of this possibility while administering CPI to their patients. Research Sponsor: None.

3576 Poster Session (Board #306), Fri, 8:00 AM-11:00 AM

Targetable immune checkpoint molecules may be significantly differentially expressed in minority ethnicities. *First Author: Jacob J. Adashek, University of South Florida, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL*

Background: Studies of immune checkpoint blockade therapy (ICT) outcomes have been largely performed in melanoma and lung cancer patients, both of which are enriched for White patients. For example, a National Cancer Database study found that 97% of first-line ICT treatments in melanoma have been administered to White recipients (Patel, ASCO-SITC 2020). Given expanding indication in tumor types affecting more diverse populations, we sought to study whether minority populations might be projected to have differing checkpoint blockade response rates. **Methods:** Ethnicity information and RNAseq expression profiles and primary site information were obtained for 7087 patients from TCGA. Ethnicity was tested for association with RNA expression of targetable checkpoint genes (*PD1, PDL1, PDL2, CTLA4, IDO1, LAG3, TIM3, TIGIT, OX40, VISTA*, and *GITR*) in 5 tumor histology types by Wilcoxon methods with Benjamini-Hochberg correction for multiple hypothesis testing. A dataset of $>$ 2700 cases was obtained from NantHealth, with paired whole exome/RNAseq data. Ethnicity for 579 patients was assigned using allele-fraction from ~250 single nucleotide polymorphic sites found exclusively in 6 populations within the 1000 Genomes project. Ethnicity/checkpoint associations found in TCGA were tested within this dataset. **Results:** Within the TCGA cohort, ethnicity was not a factor in differential expression of checkpoint molecules in lung cancer. Within melanomas, in Asian patients *PDL1, CTLA4*, and *IDO1* were expressed at lower levels than in White patients (each $p = 0.04$). These associations did not remain significant after correction for multiple hypothesis testing. Breast cancers in Black patients had significantly higher *PD1, CTLA4, IDO1, LAG3, GITR*, and *OX40* expression compared to White patients, all remaining significant after correction (adj. p 3.7e-5 to 6.4e-3). Among White patients, colon cancers showed higher expression of *PDL1/2, IDO1, LAG3, TIM3*, and *GITR* (p 0.04 to 0.0017). *IDO1* was significantly higher in White patients even after correction (adj. $p = 0.03$), and lower in Black patients (adj. $p = 0.03$). **Conclusions:** Ethnicity may represent a significant factor for efficacy checkpoint blockade therapies. White breast cancer patients might be anticipated to exhibit reduced sensitivity to PD1/CTLA4 blockade, while Black colon cancer patients may exhibit reduced sensitivity to IDO1 therapies such as epacadostat. A biomarker-driven approach to patient selection may ameliorate ethnic disparities in ICT outcomes. Research Sponsor: None.

3577 Poster Session (Board #307), Fri, 8:00 AM-11:00 AM

Comparison of recurrence patterns after surgery and radiation therapy with 68Ga-PSMA-11 PET/CT in nonmetastatic castrate-sensitive prostate cancer patients: A single-center post-hoc retrospective analysis in 787 patients. *First Author: Wesley R Armstrong, Ahmanson Translational Theranostics Division, University of California, Los Angeles, CA*

Background: 20 to 50% of prostate cancer (PCa) patients undergoing radical prostatectomy (RP) or definitive radiation therapy (dRT) will experience disease recurrence. However, anatomical recurrence patterns may differ depending on the therapeutic approaches. The aim of this post-hoc retrospective analysis was to investigate if the relapse pattern as assessed by 68Ga-PSMA-11 PET/CT was different depending on the type of local pelvic therapy (RP, dRT, salvage RT (SRT), pelvic lymph node dissection (PLND), pelvic lymph node RT (PLNRT)) in patients with non-metastatic castrate sensitive (nmCS) recurrent disease after primary definitive therapy. **Methods:** Patients who underwent a 68Ga-PSMA-11 PET/CT for nmCS PCa recurrent disease after primary definitive therapy were screened from a database of 4 prospective studies (NCT02940262, NCT03515577, NCT04050215, NCT03582774). Patients who underwent primary staging ($n = 95$), without definitive therapy ($n = 68$), with known metastatic disease (M1) ($n = 68$) or with castrate resistant (CR) disease ($n = 291$) were excluded. We examined the relationship between recurrence patterns as assessed by 68Ga-PSMA-11 PET/CT (PROMISE criteria) and prior local treatments: i) RP, ii) dRT, iii) RP + SRT. **Results:** 787 patients were included in the analysis. Positive scan rates were 60%, 94% and 75% in RP, dRT and RP + SRT populations, respectively. Median pre-scan PSA levels were 0.50 (0.02-72.5) ng/ml, 4.4 (0.1-202) ng/ml, and 1.07 (0.04-33) ng/ml for patients who underwent RP ($n = 464$), dRT ($n = 109$) and post-RP SRT ($n = 214$). Median time to first recurrence was 27.7 after RP and 54.6 months after dRT ($p = < 0.0001$). Patients who underwent RP had lower local recurrence (LR) pattern (T+) rates by PSMA PET than those with dRT (99/464; 21% vs 69/109; 63%; $p = < 0.0001$). Nodal metastasis (N1) positivity rate was similar between RP and dRT (179/464; 39% vs 43/109; 39%; $p = 0.87$). Extrapelvic metastasis (M1) positivity rate was lower for RP than dRT (93/464; 20% vs 51/109; 47%; $p = < 0.0001$). Median time from post-RP SRT to second recurrence was 22.3 months. In patients who had a second recurrence after RP and SRT the positivity rate of LR (T+), N1 disease and M1 disease by PSMA PET/CT was 12% (24/214), 46% (99/214) and 44% (95/214). **Conclusions:** In this cohort of patients with nmCS PCa recurrent disease after primary definitive therapy, the patterns of failure differ based on prior local treatments. Research Sponsor: None.

3578 Poster Session (Board #308), Fri, 8:00 AM-11:00 AM

Highly accurate automated tissue classification using deep learning on digital pathology images: A novel tool for resolving conflicts in diagnosis. *First Author: Stephen Charles Benz, NantOmics, LLC, Santa Cruz, CA*

Background: Pathologist inspection of biopsy slides is the gold-standard for diagnosis and is crucial for effective therapy decisions. However, expert shortage is resulting in turnaround times exceeding College of American Pathologists' (CAP) standards (Alshieban, 2015). Further, discrepancy between diagnoses can exceed 4% (Mukhopadhyay, 2018), and 2% of cases are designated as 'carcinoma of unknown primary' (CUP) negatively affect outcomes due to difficulty selecting therapies (Rassy, 2020). Here we sought to aid in diagnosing patients from whole-slide images (WSIs) using deep neural networks. **Methods:** $>$ 6.3K high-resolution H&E-stained diagnostic WSI of formalin-fixed paraffin-embedded (FFPE) tumor block slices were selected from TCGA sources. Slide images were obtained from 30 different cancer subtypes including 368 Breast (5.6%), 324 Colon (5.12%), 287 Lung Adenocarcinoma (LUAD) (4.5%), Lung Squamous-Cell carcinoma (LUSC) (4.5%), and Stomach Adenocarcinoma (4.3%). Local regions containing tumor tissue were automatically identified by training an *Inception V3* deep-learning network as previously presented. A separate *Inception V3* network was trained to classify the primary tissue of 200mm^2 tumor regions in 60% of the images, which was validated in the remaining 40% testing cohort. **Results:** The proposed deep-learning model was 92.7% accurate in identifying the primary tissue within the test set of WSIs. As expected, most misclassification occurred in highly-related tissue-types: Rectal cancers misclassified as colon (25%) and vice versa (4.8%), uveal melanomas misclassified as cutaneous melanomas (18.6%), cholangiocarcinomas as hepatocellular carcinomas (8.6%), and LUSC misclassified as LUAD (6.0%) and vice versa (3.4%). Combining related tissues, the classifier achieves 94.6% accuracy across 24 primary types. Unexpectedly, cutaneous melanomas samples were misclassified as breast (9.1%) and LUSC (5.6%), suggestive of related molecular phenotypes. **Conclusions:** By focusing machine-vision attention on tumor regions, the automated system approaches pathologist accuracy. Used in conjunction with molecular profiling, rates of CUP or misdiagnosis can feasibly be minimized to improve patient care. This system is currently being validated in an external set of $>$ 4K unselected clinical cases from the NantHealth database. Research Sponsor: ImmunityBio.

3579 Poster Session (Board #309), Fri, 8:00 AM-11:00 AM

A phase Ib study of oral Chk1 inhibitor LY2880070 as monotherapy in patients with advanced or metastatic cancer. *First Author: Wilson H. Miller, Segal Cancer Center, Jewish General Hospital, Rossy Cancer Network, McGill University, Montreal, QC, Canada*

Background: LY2880070 (LY) is an orally-administered, selective adenosine triphosphate-competitive inhibitor of checkpoint kinase 1 (Chk1). LY blocks the checkpoint response, and Chk1 inhibition results in mitotic catastrophe to produce apoptosis. **Methods:** This 2-part, open-label multicenter study explores the safety, pharmacokinetics (PK) and anti-tumor activity of LY in patients with advanced or metastatic cancers. The primary objective of this study was to determine the maximum tolerated dose (MTD) for multiple escalating oral doses of LY. Secondary objectives were to: 1) Characterize the dose-limiting toxicities (DLTs) and overall safety profile for LY; 2) Evaluate the PK of LY; and 3) Evaluate the anti-tumor activity of LY. Patients received LY orally in 21-day cycles in two treatment arms: 1) A multiple ascending dose (MAD) arm in patients with normal/intermediate CYP2D6 metabolism; or 2) An arm with LY administered as monotherapy to CYP2D6 poor metabolizers. **Results:** The MTD in normal/intermediate CYP2D6 metabolizers was 200 mg BID daily. A dose of 400 mg QD was not tolerated even with the use of anti-emetics. However, BID administration (same total daily dose) made LY tolerable. Dose-limiting toxicities were predominantly vomiting, nausea, and fatigue, and appeared to be correlated with C_{max}. The mean half-life was 5.35 (+/- 2.3) hours. BID dosing provided maintenance of the AUC (3271.4 h•ng/mL 200 mg BID vs 3377.9 h•ng/mL 400 mg QD) while lowering C_{max} (350.0 ng/mL 200 mg BID vs 691.9 ng/mL 400 mg QD) and increasing C_{min}, compared to QD dosing of the same total daily dose. Importantly, BID administration of 200 mg LY resulted in a median C_{min} at steady-state that remains above the IC_{80} for 12 h/day and above the IC_{50} for 24 h/day. Five patients had a best response of SD for a duration of $\geq$ 6 cycles. **Conclusions:** LY was tolerated in a daily BID schedule. The toxicity profile can be modulated by changing the dosing frequency from QD to BID while administering the same daily dose. LY may be a potential combination therapy with DNA damaging agents. Study #: NCT02632448. This study is sponsored by Esperas Pharma Inc., 1255 boul. Robert-Bourassa #1610, Montreal, Qc, H3B 3X3. Clinical trial information: NCT02632448. Research Sponsor: Esperas Pharma Inc.

3580 Poster Session (Board #310), Fri, 8:00 AM-11:00 AM

Preclinical evaluation of XPO1 inhibition in Wilms tumors. *First Author: Michael Vincent Ortiz, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: XPO1 is a nuclear export protein that selectively transports tumor and growth regulatory proteins out of the nucleus, thereby effectively inhibiting their function. We previously utilized the Virtual Inference of Protein-activity by Enriched Regulon analysis (VIPER) algorithm to discover that malignant rhabdoid tumors were dependent upon XPO1 inhibition and then evaluated a preclinical cohort using selinexor (KPT-330), the first-in-class selective inhibitor of nuclear export, to demonstrate that XPO1 inhibition was sufficient to cause cell cycle arrest, apoptosis, and disease control in multiple cell line and patient derived xenograft (PDXs) models. Our subsequent analysis revealed that the most common childhood kidney tumor, Wilms tumor, has even high higher inferred activity of XPO1 than rhabdoid tumors leading to our hypothesis that XPO1 inhibition is an effective therapeutic strategy to treat Wilms tumors. **Methods:** A panel of 9 Wilms tumor cell lines and 3 Wilms tumor PDXs were genomically characterized and tested to evaluate the pre-clinical efficacy of XPO1 inhibition in Wilms tumors. **Results:** Proliferation rate, increased XPO1 protein expression, and loss of function mutations in TP53 correlated with *in vitro* Wilms tumor cell line sensitivity to selinexor. Evaluation of co-segregation of all single nucleotide variant changes using with inferred activity of XPO1 on VIPER in all TGCA tumors demonstrates a strong association with TP53 alterations. XPO1 inhibition was effective in all Wilms tumor models tested, most significantly in MSKREN-57196, a favorable histology Wilms tumor PDX with somatic 1q gain as well as WTX and MYCN mutations, as well as in MSKREN-31827, a diffusely anaplastic TP53 mutant Wilms tumor PDX. Eltanexor (KPT-8602) is an XPO1 inhibitor with decreased CNS penetration and an improved toxicity profile; this drug was tested in these in vivo models and found to be at least as effective as selinexor. **Conclusions:** Somatic 1q gain in favorable histology Wilms tumors and TP53 mutations in diffusely anaplastic Wilms tumors have a particularly poor prognosis in the relapsed setting. Our study demonstrates that XPO1 inhibition may provide a rational therapeutic option to treat such high-risk Wilms tumors. Future clinical trials evaluating XPO1 inhibitors should evaluate its efficacy in children with relapsed Wilms tumors. Research Sponsor: Cycle for Survival, Other Foundation, U.S. National Institutes of Health, Friends and family of Caroline Bhatt.

3581 Poster Session (Board #311), Fri, 8:00 AM-11:00 AM

A phase Ib study of oral Chk1 inhibitor LY2880070 in combination with gemcitabine in patients with advanced or metastatic cancer. *First Author: Quincy S. Chu, Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada*

Background: LY2880070 (LY) is an oral, selective competitive inhibitor of checkpoint kinase 1 (Chk1). Chk1 inhibitors are known to increase the antitumor efficacy of agents such as gemcitabine (GEM), which induce replication stress. Synergy between these two agents has been applied to the clinical setting. **Methods:** This two-part, open-label multi-center study explores the safety, pharmacokinetics (PK), and anti-tumor activity of LY in patients with advanced or metastatic cancers. The primary objective of this study was to determine the maximum tolerated dose (MTD) for multiple escalating oral doses of LY in combination with GEM. Secondary objectives were to: 1) Characterize the dose-limiting toxicities (DLTs) and overall safety profile for LY; 2) Evaluate the PK of LY; and 3) Evaluate the anti-tumor activity of LY. Patients received LY in a variety of different dose regimens, in combination with GEM (50 to 800 mg/m^2) on days 1, 8, and 15 (optional) of a 21-day cycle. **Results:** The combination of LY with GEM required lower doses of both LY (vs 200 mg BID monotherapy RP2D dose) and GEM (vs approved doses). The dose levels explored ranged from LY:GEM of 10 mg QD: 800 mg/m^2 to 50 mg BID:100 mg/m^2. BID dosing of LY was implemented in order to maximize the total daily dose and avoid the adverse events that appeared to correlate with C_{max}. Treatment-emergent adverse events in $>$ 40% of patients included vomiting, nausea, and fatigue. DLTs included reduced platelet count (Gr2), fatigue (Gr3), diarrhea (Gr3), and thrombocytopenia (x2, Gr2). The $t_{1/2}$ of LY was ~ 5 h, and was not significantly affected by combination with GEM. Two patients had a best overall response of SD for a duration of $\geq$ 6 cycles, and a confirmed PR was observed in an ovarian cancer patient who had failed multiple regimens. **Conclusions:** LY was tolerated in combination with lower dose GEM. The toxicity profile can be modulated by changing the dosing frequency from QD to BID while administering the same daily dose. LY may be good candidate for combination therapy with DNA damaging agents. Clinical trial information: NCT02632448. Research Sponsor: Esperas Pharma Inc.

3582 Poster Session (Board #312), Fri, 8:00 AM-11:00 AM

Preclinical evaluation of KZR-261, a novel small molecule inhibitor of Sec61. *First Author: Eric Lowe, Kezar Life Sciences, South San Francisco, CA*

Background: Secreted and transmembrane proteins play key roles in malignant transformation and growth, including in autocrine growth factor expression, receptor oncogene signaling, and immune system evasion. Biogenesis of these proteins involves translocation of the nascent polypeptides into the endoplasmic reticulum (ER) through the Sec61 channel, providing an untapped therapeutic target for a broad spectrum of malignancies. Here we describe preclinical activity of KZR-261 and related inhibitors of Sec61-dependent protein secretion. **Methods:** Sec61 inhibition with KZR-261 and related analog KZR-834 were evaluated using cell lines overexpressing proteins of interest tagged with luciferase. In vitro anti-tumor activity was assessed against a panel of 346 cell lines across 25 tumor types. Quantitative proteomic profiling by mass spec and gene expression profiling by RNAseq were conducted following treatment in multiple solid and heme tumor cell lines. Anti-tumor efficacy was evaluated in athymic nude mice implanted with the cancer cell lines H82 (SCLC), HT29 (CRC), BxPC3 (Pancreatic), 22RV1 (Prostate), H929 (Myeloma) and RL (NHL). Activity was also evaluated in a MC38 syngeneic colon tumor model. **Results:** KZR-261 and KZR-834 exhibited nanomolar potency against many therapeutic targets, including immune checkpoints, VEGF-A, VEGFR and EGFR. Broad in vitro anti-cancer activity was observed with KZR-834, which potently decreased cell viability across both solid and heme tumor types including CRC, Pancreatic, HNSCC, HCC, Lymphoma and Myeloma. Global proteomic analysis observed more than 1.5 fold downregulation of $<$ 10% of detected Sec61 client proteins following treatment, while gene expression profiling revealed upregulation of ER stress response genes in sensitive versus resistant cell lines. Analysis of the TCGA database also found these genes upregulated in a number of different tumor types. In vivo, weekly IV administration was well tolerated and induced a dose dependent anti-tumor response at doses below the MTD in solid and heme xenograft models. In the syngeneic MC38 model, administration of KZR-834 in combination with anti-PD1 antibody resulted in greater anti-tumor activity than either single agent. **Conclusions:** Novel Sec61 inhibitors potently block expression of secreted and membrane proteins, translating into anti-tumor activity against many tumor types in vitro and in vivo, suggesting broad therapeutic potential. Clinical trials are being planned with KZR-261 to understand safety and early efficacy of this novel compound and therapeutic target. Research Sponsor: Kezar Life Sciences.

3583 Poster Session (Board #313), Fri, 8:00 AM-11:00 AM

Results of a completed phase I trial of CBL0137 administered intravenously (IV) to patients (Pts) with advanced solid tumors. *First Author: John Sarantopoulos, Institute for Drug Development, Mays Cancer Center at University of Texas Health San Antonio, San Antonio, TX*

Background: The novel curaxin CBL0137 intercalates into DNA, interfering with histone/DNA binding. Consequent trapping of histone chaperone FACT leads to MYC, NF-kB, and HSF1 inhibition, p53 activation, and an IFN response. CBL0137 shows broad nonclinical antitumor activity (Gasparian et al. Sci Transl Med. 2011; 3(95):95ra74). **Methods:** This dose-ranging study assessed the CBL0137 maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) and CBL0137 safety, pharmacokinetics (PK), and efficacy in adults with advanced treatment-refractory solid tumors. CBL0137 was administered IV on Days 1, 8, and 15 of repeated 28-day cycles until progressive disease (PD) or unacceptable toxicity. Doses were escalated using a 3+3 design based on Cycle 1 dose-limiting toxicities (DLTs). PK was assessed through 168 hours after Day 1. Efficacy was evaluated every 8 weeks. **Results:** The study enrolled 83 pts (M/F [n] = 49/34; median [range] age = 64 [33-85] years; ECOG status [n] = 1/2 [32/51]), with cancer types (n) of colorectal (23), prostate (7), glioblastoma (6), liver (6), non-small-cell (5), and others (36) across 17 dose levels from 10 to 700 mg/m^2/infusion. Durations of therapy ranged to 24 months. Cycle 1 DLTs (n type) were observed at 240 mg/m^2 (1 Gr 3 photosensitivity), 400 mg/m^2 (1 Gr 3 anemia), 700 mg/m^2 (1 Gr 4 thrombocytopenia, 1 Gr 4 neutropenia/Gr 4 thrombocytopenia), and 650 mg/m^2 (1 Gr 3 thrombocytopenia, 1 Gr 4 neutropenia/Gr 3 thrombocytopenia). Nausea and vomiting were successfully prevented with dexamethasone/serotonin antagonists. Photosensitization was effectively managed with sun protection. Peripheral venous thrombosis required central vein infusion in subjects with glioblastoma. PK showed dose-proportional increases in plasma CBL0137 area under the concentration-time curve (AUC), a high mean (range) volume of distribution (Vd) of 1,030 (655-1460) L/m^2 consistent with extensive tissue distribution and DNA intercalation, and an average mean (range) half-life ($t_{1/2}$) of 24.7 (10.3-40.7) hours without dose dependence. The best response was stable disease: 2 pts with liver cancer had tumor control for 9 and 24 months and a maximum tumor regression of 10%; 2 pts with prostate cancer had tumor regressions by 11% and 22%; 1 pt with uterine cancer had a 20% tumor regression. **Conclusions:** CBL0137 administered IV was generally well tolerated with manageable toxicities The MTD and RP2D were estimated at 540 mg/m^2 due to myelosuppressive DLTs. PK were predictable. Preliminary evidence of antitumor activity supports Phase 2 testing. Clinical trial information: NCT01905228. Research Sponsor: Incuron, Inc.

3584 Poster Session (Board #314), Fri, 8:00 AM-11:00 AM

Selpercatinib (LOXO-292) in patients with *RET*-fusion+ non-small cell lung cancer. *First Author: Koichi Goto, National Cancer Center Hospital East, Kashiwa, Japan*

Background: Selpercatinib (LOXO-292) is a highly selective and potent small molecule RET kinase inhibitor. Here we report an update on the efficacy and safety of selpercatinib in *RET*-fusion+ non-small-cell lung cancer (NSCLC). **Methods:** Patients with *RET*-fusion+ NSCLC were enrolled to the Phase 1/2 LIBRETTO-001 trial (NCT03157128), a global, multicenter trial (16 countries, 89 sites). Following the Phase 1 dose escalation portion of the trial, patients received the recommended dose of 160 mg orally twice daily. Each cycle was 28 days. The primary endpoint was objective response rate (ORR) per RECIST 1.1. Secondary endpoints included duration of response (DoR) and safety. Per health authority agreement, the primary analysis set was defined as the first 105 consecutively enrolled patients previously treated with platinum-based chemotherapy. Treatment-naïve patients were analyzed separately. All analyses were based on a 16-Dec-2019 data cutoff date. **Results:** In the primary analysis set of platinum-treated patients (median of 3 prior systemic regimens; range 1-15), the ORR by investigator assessment was 70% (95% CI 59.8–78.1, n = 73/105). Responses did not differ by fusion partner or number or type of prior therapies, including anti-PD-1/PD-L1 agents and off-label multikinase inhibitor use. The median DoR was 20.3 months (95% CI 15.6–24.0) with 45 of 73 (62%) responders censored at a median follow-up of 14.8 months. Among 39 treatment-naïve patients, the ORR by investigator assessment was 90% (95% CI 75.8–97.1, n = 35/39, including 2 responses pending confirmation). Median DoR was not reached with 27 of 33 (82%) confirmed responses ongoing at a median follow-up of 7.4 months. In the safety analysis set consisting of all selpercatinib dosed patients (N = 702), the most common treatment-related adverse events (TRAEs) that occurred in ≥15% of patients were dry mouth (33.3%), increased AST (24.5%), increased ALT (23.8%), hypertension (23.2%), diarrhea (19.7%), and fatigue (16.8%). Only 2% (14 of 702) of patients discontinued selpercatinib for TRAEs. **Conclusions:** Selpercatinib achieved marked and durable antitumor activity in patients with *RET*-fusion+ NSCLC. Selpercatinib was well tolerated. Efficacy data assessed by independent review committee based on the 16-Dec-2019 data cutoff date will be presented. Clinical trial information: NCT03157128. Research Sponsor: Loxo Oncology Inc., a wholly owned subsidiary of Eli Lilly and Company.

3585 Poster Session (Board #315), Fri, 8:00 AM-11:00 AM

Activity of SY-5609, an oral, noncovalent, potent, and selective CDK7 inhibitor, in preclinical models of colorectal cancer. *First Author: Liv Johannessen, Syros Pharmaceuticals, Cambridge, MA*

Background: Colorectal cancer (CRC) is driven by genetic alterations that result in constitutive activation of oncogenic transcription factors (eg β-catenin, MYC) and of mitogenic signaling and cell cycle progression (driven by oncogenic mutations in KRAS and BRAF). CDK7 is a key regulator of transcription, through phosphorylation of the CTD domain of RNA Polymerase II, and of cell cycle progression, through phosphorylation of the cell cycle kinases CDK1, 2, 4, and 6. This dual role of CDK7 suggests inhibitors of CDK7 may be effective in the treatment of CRC. SY-5609 is an oral, noncovalent, potent and highly selective CDK7 inhibitor in phase 1 clinical development for patients with advanced solid tumors including CRC (NCT04247126). Here we report on the activity of SY-5609 in patient-derived xenograft (PDX) models of CRC. **Methods:** SY-5609 was administered once daily (QD) by oral gavage for 21 days (end of treatment, EOT) to mice bearing PDX models of CRC. The relationship between SY-5609 dose, pharmacodynamic (PD) changes in xenograft tissue, tumor growth inhibition (TGI), and mouse body weight (BW) was evaluated across a range of doses. SY-5609 TGI activity was also evaluated at sub-maximum-tolerated-dose levels across a panel of 30 independent CRC models including BRAF-, KRAS-, and non-BRAF/KRAS-mutant (wild type) models (n = 10 per group). **Results:** SY-5609 induced dose-dependent TGI in BRAF-mutant CRC PDX tumors, with tumor regressions observed at well tolerated doses (no BW loss at EOT), and no tumor regrowth for 2+ weeks after treatment was discontinued. Dose-dependent TGI was associated with dose-dependent PD changes in PDX tumor tissue. Across 30 PDX models, SY-5609 at well-tolerated doses (average BW loss of 0% at EOT across all models) induced ≥50% TGI in 67% (20/30) of models. Deep responses (≥90% TGI or regressions) were observed in 23% (7/30) of models, with enrichment for deep responses in BRAF mutant models (50%, 5/10) relative to KRAS mutant (10%, 1/10), and wild type (10%, 1/10) models. **Conclusions:** Daily oral dosing of the CDK7 inhibitor SY-5609 induces robust TGI, including regressions, in CRC PDX models at well-tolerated doses. Dose-dependent TGI is associated with dose-dependent PD changes in CRC PDX tumor tissue. These results highlight the therapeutic potential of SY-5609 in CRC and support the evaluation of SY-5609 in CRC patients in early phase clinical trials. SY-5609 is in phase 1 clinical development for patients with advanced solid tumors including CRC (NCT04247126). Research Sponsor: Syros Pharmaceuticals.

3586 Poster Session (Board #316), Fri, 8:00 AM-11:00 AM

A phase I, first-in-human, open-label, dose-escalation, safety, pharmacokinetic, and pharmacodynamic study of oral TP-3654 administered daily for 28 days to patients with advanced solid tumors. *First Author: Ignacio Garrido-Laguna, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT*

Background: TP-3654 is an oral, second generation, potent PIM-1 kinase inhibitor with activity against PIM 2, 3 and favorable selectivity against other kinases. These cytoplasmic serine/threonine kinases are highly expressed in many cancers and their oncogenic potential has been largely attributed to supressing apoptosis downstream of stimuli including inflammatory cytokines and other immune effectors. TP-3654 has efficacy in various hematologic and solid tumor models inducing stromal Pim-1 also has been shown to mediate various aspects of the tumor microenvironment. Thus, Pim kinases are attractive targets for the treatment of many human malignanices. **Methods:** A first in human, multicenter, phase 1, dose escalation study using a standard 3+3 design with a modified Fibonacci scheme to examine the safety and clinical activity of TP-3654 in patients with advanced solid tumors. **Results:** Ten patients were enrolled between 30Apr and 31Dec2019 receiving 480, 720, and 1080 mg respectively. Grade 3 AEs were scrotum wound infection, altered mental status, anemia, fall, and lower extremity edema, none were related to study drug and all were manageable with supportive care. There were no Grade 4 or 5 AEs and no DLTs. Median duration of SD was 5.5 months (6/10) and with prolonged SD > 16wks (4/10). One CRC patient with 4 lines of prior therapy had a 22% reduction in tumor volume (SD > 5+ mos). TP-3654 plasma PK values (C_{max}, AUC) continuously increased through all 3 cohorts. Average C_{max} (ng/mL) and $AUC_{0\text{-}24}$ (ng*hours/mL) were 195, 1965 (480mg); 357, 3310 (720mg); 735, 6922 (1080mg), respectively. PK values increased linearly with higher doses without reaching saturation. Peripheral Blood Mononuclear Cells were isolated from subjects prior and up to 24hours after treatment. Western Blot from protein lysates revealed a decrease in phosphorylation of BAD and p70s6K proteins, both regulated by PIM-1 kinase. **Conclusions:** These findings suggest that TP-3654 is tolerated as a monotherapy in patients with heavily pretreated, relapsed, and resistant solid tumors warranting further clinical development in selected indications. Research Sponsor: Tolero Pharmaceuticals.

3587 Poster Session (Board #317), Fri, 8:00 AM-11:00 AM

AVID200, first-in-class TGF-beta 1 and 3 selective and potent inhibitor: Safety and biomarker results of a phase I monotherapy dose-escalation study in patients with advanced solid tumors. *First Author: Timothy A Yap, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: AVID200 is a rationally designed first-in-class, selective inhibitor of transforming growth factor-beta (TGF-beta) that neutralizes TGF-beta 1 & 3 with pM potency and 4,000 fold selectivity over TGF-beta 2. TGF-beta 1 & 3 signaling has been associated with immune checkpoint inhibitor resistance and immunosuppression in the tumor microenvironment while TGF-beta 2 is required for normal cardiac function and hematopoiesis. **Methods:** NCT03834662 (AVID200-03) is a multicenter Phase 1 study following a standard 3 + 3 dose escalation to evaluate safety and tolerability of AVID200 given IV every 3 weeks to patients (pts) with advanced solid tumors. Peripheral target engagement was assessed in blood by ELISA and a cell-based functional assay, and in skin biopsies by immunohistochemistry (IHC). Pharmacodynamic markers of TGF-beta signal modulation and immune activation were evaluated in serum using the InflammationMAP v 1.0 (Myriad RBM) and in paired tumor biopsies by IHC and Imaging Mass Cytometry. **Results:** Nineteen pts (ECOG 0-1, median age 63 [range 39-77], 52.6% male) received AVID200 at 3 planned dose levels of 180 (N = 7), 550 (N = 6), and 1100 mg/m^2 (N = 6) (~5, 15, and 30 mg/kg). The maximum tolerated dose was not reached. Three Grade (G) 3 treatment-related adverse events (TRAEs) were reported in 2 pts (diarrhea and lipase elevation, anemia); no > G3 TRAEs were observed. Serum exposure was dose-proportional and AVID200 sequestered all active TGF-beta 1 & 3, but not beta 2, in blood across the entire dosing period at all dose levels, providing proof-of-mechanism of AVID200. SMAD2 phosphorylation in skin biopsies was detectably reduced on Day 4 at 15 and 30 mg/kg. Pro-inflammatory markers in serum were increased on Day 8 versus baseline in a dose-dependent manner. Tumor biopsies of pts treated at 15 mg/kg showed modulation of TGF-beta signaling and immune activation. A best response of RECIST stable disease > 12 weeks was observed in 2 pts: 1 with adenoid cystic carcinoma (5 mg/kg; 8.7 months); 1 with breast carcinoma (30 mg/kg; 3.1 months). **Conclusions:** AVID200 was safe and well tolerated at dose levels of 5-30 mg/kg, with peripheral target engagement across the entire dosing period. AVID200 led to TGF-beta target modulation and immune activation. These data provide proof-of-principle that AVID200-mediated selective and potent inhibition of TGF-beta 1 & 3 is feasible in the clinic. The AVID200 monotherapy data warrant exploration of rational combination with a PD-(L)1 inhibitor. Clinical trial information: NCT03834662. Research Sponsor: Forbius.

3588 Poster Session (Board #318), Fri, 8:00 AM-11:00 AM

Correlation between overall response rate and progression-free survival/overall survival in comparative trials involving targeted therapies in molecularly enriched populations. *First Author: Benjamin J. Solomon, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia*

Background: Randomized trials involving agents targeting oncogene addicted tumors have greatly increased over the past decade. Whether clinical response rates can predict or correlate with efficacy measures such as progression-free survival (PFS) or overall survival (OS) has not been established in molecularly enriched patient populations. In this meta-analysis, we investigated whether improvements in objective response rate (ORR) in comparative trials using targeted agents could serve as a potential surrogate endpoint for improvements in PFS or OS in populations with oncogene addicted cancer. **Methods:** CT.gov and MEDLINE databases were queried (using commercial text mining software I2E) for randomized, phase 3 clinical trials based on the following prospectively defined criteria: (1) use of agents targeting EGFR activating mutations (erlotinib, gefitinib, afatinib, dacomitinib, osimertinib), ALK and ROS1 rearrangements (crizotinib, ceritinib, alectinib), BRAF V600E or V600K mutations (dabrafenib), and BCR-ABL fusion protein (imatinib, dasatinib, nilotinib, ponatinib); (2) must include molecularly enriched trial populations (biomarker subgroup data included if available); (3) control arms should not include targeted agents directed towards those molecularly enriched populations. ORR, OS, and PFS data were manually extracted from the relevant studies and correlative analyses (weighted Pearson correlation) were performed. **Results:** 61 trials were identified with 15 ultimately meeting the prespecified criteria. ORR effect size (both the ORR difference and log odds ratio) and the log PFS hazard ratio were strongly correlated (-0.78, p-value = 0.0007). No significant correlation was found between ORR and OS. **Conclusions:** In our analyses, a strong correlation between ORR and PFS was found in randomized clinical trials investigating agents targeting oncogene-driven cancers. Establishing a correlation between ORR and OS was limited, most probably due to confounding factors such as treatment cross-over following progression, number of subsequent therapies and long post-progression survival in this setting. These findings further warrant the use of ORR as a surrogate for PFS in biomarker-driven studies. Research Sponsor: Eli Lilly and Company.

3589 Poster Session (Board #319), Fri, 8:00 AM-11:00 AM

Phase I study of the combination of alisertib (MLN8237) and gemcitabine in advanced solid tumors. *First Author: Jasmine Huynh, UC Davis Comprehensive Cancer Center, Sacramento, CA*

Background: Aurora Kinase A (AKA) is a key mitotic regulator overexpressed in multiple solid tumors. This open-label dose escalation and expansion phase I study evaluated the safety and tolerability of alisertib (MLN8237), an oral AKA inhibitor, in combination with gemcitabine. **Methods:** In dose escalation, patients (pts) > 18y with refractory solid tumors received 28-day cycles of gemcitabine on days 1, 8, 15 and alisertib twice daily on days 1-3, 8-10, and 15-17. Gemcitabine was given at 1000mg/m2. Four dose levels (DL) of alisertib (20-50mg) were given per 3+3 design to investigate dose limiting toxicities (DLT) in cycle 1, to determine maximum tolerated dose (MTD) and recommended phase II dose (RP2D). In dose expansion, advanced pancreatic adenocarcinoma pts received the MTD dose twice daily on a modified dosing schedule to allow for pharmacokinetic (PK) evaluation. Anti-tumor activity was assessed by response rate (RECIST 1.1) and progression-free survival (PFS). PK evaluation of plasma gemcitabine and alisertib was performed on all pts enrolled in the dose expansion. PK sampling was performed before treatment, immediately after gemcitabine infusion, and at other pre-specified post-infusion timepoints. **Results:** Twenty-six pts were treated in total: 21 pts in dose escalation and 5 pts in dose expansion. Overall, median age was 57y [42-82]; 50% male; 62% PS 1 (16 pts); 2 [0-7] median prior therapies. In the dose escalation phase, 9 tumor types were included and NSCLC was most common (7 pts). Maximum administered dose (DL4) achieved 900 mg alisertib per cycle and was tolerated (1 DLT in 6 pts). The dose expansion phase enrolled 5 pts with advanced pancreatic adenocarcinoma; median age 63y [48-82]; 60% male; 60% PS 1 (3 pts); 2 [1-2] median prior therapies. Grade ≥3 TRAEs were observed in 73% of all pts and were predominantly hematologic, including neutropenia (54%), leukopenia (50%), and lymphopenia (31%). Similar TRAEs were seen at DL4; all 14 pts experienced neutropenia with 64% experiencing grade ≥3 neutropenia. Fourteen of 23 evaluable pts (61%) had stable disease and 2 pts (9%) had partial response (PR) as best overall response. Median PFS was 2.9 months (95% CI 2.0-4.2). Analysis of PK data is ongoing and will be reported. **Conclusions:** Alisertib can be safely administered with gemcitabine. RP2D for alisertib is 50 mg PO BID in combination with full dose gemcitabine. Best response was at least stable disease in a majority of pts with PR observed in 9% of this heavily pretreated group of patients. Most grade ≥3 TRAEs were hematologic. Results of PK studies will also be reported. Clinical trial information: NCT01924260. Research Sponsor: Takeda.

3590 Poster Session (Board #320), Fri, 8:00 AM-11:00 AM

Phase I study of IM156, a novel potent biguanide oxidative phosphorylation (OXPHOS) inhibitor, in patients with advanced solid tumors. *First Author: Sun Young Rha, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea*

Background: IM156, a novel oral potent biguanide OXPHOS inhibitor of Protein Complex 1 (PC1) of the mitochondrial electron transport chain, causes AMPK phosphorylation, the downstream effects of which are detrimental to OXPHOS-dependent cancer cells prone to energy stress. Preclinical experiments with IM156 demonstrated activity in solid tumor and hematologic malignancy models as a single-agent and in combinations. **Methods:** This was an open label, first-in-human, multi-center, dose-escalation study (NCT03272256) using a 3+3 design. The primary endpoint was to determine the maximum tolerated dose and/or recommended Phase 2 dose (RP2D) based on dose limiting toxicities (DLT), safety and tolerability. Secondary endpoints included pharmacokinetics (PK), pharmacodynamics (PD) and preliminary signals of efficacy. Eligible patients were adults with advanced solid tumors refractory to standard therapies with ECOG Performance Status <2, adequate organ function, and measurable disease (RECIST 1.1 or RANO [gliomas]). IM156 was administered orally every other day (QOD) or daily (QD) in 28-day cycles. **Results:** 22 patients (gastric cancer: N = 8; ovarian cancer: N = 3; colorectal cancer: N = 3; endometrial cancer: N = 2; sarcoma: N = 2; other: N = 4) were enrolled in 7 dose cohorts (100, 200, 400, 800, and 1,200 mg QOD; 800 and 1,200 mg QD). The most frequent treatment-related adverse events (TRAEs) were gastrointestinal (nausea [N = 16, 73%], diarrhea [N = 12, 55%], and vomiting N = 11, 50%]). Nausea, reported in 3 (14%) patients, was the only Grade 3 TRAE. No DLTs were reported; the RP2D declared was 800 mg as 1,200 mg QD was associated with Grade 2/3 nausea requiring dose modifications. PK demonstrated dose-proportional increases in C_{max} and $AUC_{0\text{-}last}$ reaching the expected efficacious range. PD demonstrated a decrease in tumor growth rate in 3 patients (1,200 mg QOD: N = 2; 800 mg QD: N = 1), and a decrease in VEGF and tumor markers in a patient with gastric cancer with neuroendocrine differentiation treated at 800 mg QD who remains on study in Cycle 11. Best response was stable disease in 7 (32%) patients. **Conclusions:** IM156 is the first PC1 OXPHOS inhibitor to have been successfully tested in patients with cancer with the identification of a RP2D. It was well tolerated at dose levels active in preclinical models, and demonstrated modest clinical activity in an unselected population of patients. Subsequent development will focus on OXPHOS-dependent tumors and in combinations with agents in which OXPHOS metabolism is a mechanism of resistance. Clinical trial information: NCT03272256. Research Sponsor: Immunomet Therapeutics.

3591 Poster Session (Board #321), Fri, 8:00 AM-11:00 AM

TOOme: A novel computational framework to infer cancer tissue-of-origin by integrating both gene mutation and expression. *First Author: Wei Gao, Departments of Internal Medicine-Oncology, Fujian Provincial Cancer Hospital and Fujian Medical University Cancer Hospital, Fuzhou, China*

Background: Metastatic cancers require further diagnosis to determine their primary tumor sites. However, the tissue-of-origin for around 5% tumors could not be identified by routine medical diagnosis according. With the development of machine learning techniques and the accumulation of big cancer data from TCGA and GEO, it is now feasible to predict cancer tissue-of-origin by computational tools. **Methods:** Developed a computational framework to infer tumor tissue-o. **Results:** Applied TOOme to the TCGA data containing 7,008 non-metastatic samples across 20 solid tumors including BLCA, BRCA, CESC, COAD, GBM and so on. 74 genes by gene expression profile and 6 genes by gene mutation are selected by the random forest process, which can be divided into two categories: (1) cancer type specific genes, which are highly expressed or mutated only in one specific cancer and (2) those expressed or mutated in several cancers with different levels of expression or mutation rates. Function analysis indicates that the selected genes are significantly enriched in gland development, urogenital system development, hormone metabolic process, thyroid hormone generation prostate hormone generation and so on. According to the multiple-label classification method, random forest performs the best with a 10-fold cross-validation prediction accuracy of 96%. We also use the 19 metastatic samples from TCGA and 256 cancer samples downloaded from GEO as independent testing data, for which TOOme achieves a prediction accuracy of 89%. The cross-validation validation accuracy is better than those using gene expression (i.e., 95%) and gene mutation (83%) alone. **Conclusions:** TOOme provides a quick yet accurate alternative to traditional medical methods in inferring cancer tissue-of-origin. In addition, the methods combining somatic mutation and gene expressions outperform those using gene expression or mutation alone. Research Sponsor: None.

3592 Poster Session (Board #322), Fri, 8:00 AM-11:00 AM

Phase Ib/IIa study of GC1118 in combination with irinotecan or FOLFIRI in patients with metastatic solid tumors. *First Author: Keun Wook Lee, Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea*

Background: GC1118 is a novel anti-EGFR monoclonal antibody which has a unique binding epitope and superior ligand inhibition potential. It showed promising antitumor activity as a single agent in the phase I study. This study aimed to determine the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D) of GC1118 in combination with irinotecan or FOLFIRI in metastatic solid tumors and evaluate the efficacy of GC1118 plus FOLFIRI as a second line therapy for RAS and BRAF wild-type metastatic colorectal cancer. **Methods:** Phase 1b part was designed to evaluate weekly GC1118 (starting from 3 mg/kg) in combination with biweekly irinotecan (180mg/m^2) or FOLFIRI (irinotecan 180mg/m^2, leucovorin 400mg/m^2, 5-FU 400 mg/m^2 bolus, and 5-FU 2400mg/m^2 over 46hrs) in a 3+3 design. In the phase 2a part, the RP2D of GC1118 is administered in combination with FOLFIRI in a Simon's two stage design with objective response rate (ORR) as the primary endpoint. **Results:** 13 pts were enrolled in phase 1b and received 3mg/kg of GC1118 with irinotecan (N = 6) or FOLFIRI (N = 7). DLT occurred in 2 pts (G4 neutropenia, G2 rash) in irinotecan arm and 1pt (G3 neutropenia) in FOLFIRI arm with 3mg/kg of GC1118 and it was determined as MTD and RP2D. Adverse events (AE) of grade $\geq$ 3 included neutropenia (61.5 %), skin rash (15.4 %) and diarrhea (15.4%). Dose reductions due to GC1118-related AE were required in 6 (46.2%) patients. Among 10 response-evaluable pts in phase 1b, best overall response was PR in 3 and SD in 6, and median PFS was 12 months. In stage 1 of phase 2a (N = 9), 4 PR and 5 SD were observed (ORR 44.4%, 95% CI 13.7 – 78.8). We moved to stage 2, and are currently enrolling additional 20 pts. AE of grade $\geq$ 3 included neutropenia (66.7%), skin rash (22.2%) and diarrhea (11.1%). Updated data of the phase 2a part will be presented at the meeting. **Conclusions:** The MTD and RP2D of weekly GC1118 in combination with irinotecan or FOLFIRI was 3mg/kg. Preliminary results of GC1118 and FOLFIRI as a 2nd line treatment in mCRC suggests promising antitumor activity and acceptable safety profile. Clinical trial information: NCT03454620. Research Sponsor: Green Cross Corporation.

3593 Poster Session (Board #323), Fri, 8:00 AM-11:00 AM

Phase I study of regorafenib and sildenafil in advanced solid tumors. *First Author: Andrew Stewart Poklepovic, VCU Massey Cancer Center, Richmond, VA*

Background: Regorafenib (R) is an oral multikinase inhibitor with anti-angiogenic properties approved for use in several solid tumors. Sildenafil (S) is an oral phosphodiesterase-5 (PDE5) inhibitor that interacts synergistically with R in both short-term and colony formation assays to kill multiple cancer cell types. Mechanistic studies identified that PDE5 knockdown enhances R lethality, suggesting a direct target effect for S. **Methods:** A single-center, open-label, dose-escalation study was conducted in adults with advanced solid tumors. Patients (pts) took R (120 or 160 mg) and S (50 or 100 mg) once daily days 1 through 21 of each 28-day cycle. Pts remained on study treatment until progression or excessive toxicity, with response assessments every 8 wks. The maximum tolerated dose (MTD) was defined as the maximum tested dose with $\leq$1/6 pts experiencing dose-limiting toxicity (DLT), with Cycle 1 as the DLT observation period. **Results:** 32 pts were enrolled and 29 treated at 3 dose levels (DLs). Median duration of treatment was 8 (range 2 – 101) wks. One of 6 evaluable pts treated at DL2 (160 mg R + 50 mg S) experienced DLT (grade 4 lipase increase). One of 12 evaluable pts treated at DL3A (160 mg R + 100 mg S, the MTD) experienced DLT (grade 3 rash and grade 3 muscle pain). The toxicity profile was generally consistent with that seen in R monotherapy at FDA-approved doses. 10 pts had a best response of progressive disease (PD). 14 pts had a best response of stable disease (SD), 5 of whom had stable disease duration $>$ 24 wks. 5 treated pts were not evaluable for response. Notably, 2 pts with ovarian cancer and 1 with cervical cancer had stable disease $>$ 24 wks. Analyses of correlative studies to examine pharmacokinetics and drug combination pharmacodynamic effects are underway. **Conclusions:** The combination was well-tolerated. The recommended phase 2 dose is 160 mg R + 100 mg S. Objective responses were not observed, but prolonged stable disease was seen in a subset of pts. Encouraging disease control was seen in gynecologic cancers. Dosing up to 100 mg S is safe concurrently with standard doses of R, and may be considered as an adjunct to R in future trials. Evaluation of R+S in gynecologic cancers warrants further consideration. Clinical trial information: NCT02466802. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

Dose Level (mg R + mg S)	# treated pts	# DLT evaluable pts	# pts with DLTs	# Response evaluable pts	# pts with PD	# pts with SD
1 (120 + 50)	4	3	0	4	2	2
2 (160 + 50)	9	6	1	6	2	4
3A (160 + 100)	16	12	1	14	6	8

3594 Poster Session (Board #324), Fri, 8:00 AM-11:00 AM

Selpercatinib (LOXO-292) in patients with *RET*-mutant medullary thyroid cancer. *First Author: Manisha H. Shah, Ohio State University Comprehensive Cancer Center, Columbus, OH*

Background: Selpercatinib (LOXO-292) is a highly selective and potent small molecule RET kinase inhibitor. Here we report an update on the efficacy and safety of selpercatinib in *RET*-mutant medullary thyroid cancer (MTC). **Methods:** Patients with *RET*-mutant MTC were enrolled to the Phase 1/2 LIBRETTO-001 trial (NCT03157128), a global, multicenter trial (16 countries, 89 sites). Following the Phase 1 dose escalation portion of the trial, patients received the recommended dose of 160 mg orally twice daily. Each cycle was 28 days. The primary endpoint was objective response rate (ORR) per RECIST 1.1. Secondary endpoints included duration of response (DoR) and safety. Per health authority agreement, the primary analysis set was defined as the first 55 consecutively enrolled patients previously treated with multikinase inhibitors cabozantinib and/or vandetanib. Patients naïve to cabozantinib and vandetanib treatment were analyzed separately. All analyses were based on a 16-Dec-2019 data cutoff date. **Results:** In the primary analysis set of prior cabozantinib and/or vandetanib-treated patients with MTC (n = 55), the ORR by investigator assessment was 62% (95% CI 47.7–74.6, n = 34/55) and the median DoR was not reached (95% CI 18.4 months–not estimable) despite a median follow-up of 14.8 months. In cabozantinib/vandetanib treatment-naïve patients (n = 88), the ORR by investigator assessment was 69% (95% CI 58.6–78.7, n = 61/88, including 2 responses pending confirmation). Of the 59 confirmed responding patients, with a median follow-up of 8 months, responses were ongoing for 57 responders at the time of the analysis. In the safety analysis set consisting of all selpercatinib dosed patients (N = 702), the most common treatment-related adverse events (TRAEs) that occurred in $\geq$15% of patients were dry mouth (33.3%), increased AST (24.5%), increased ALT (23.8%), hypertension (23.2%), diarrhea (19.7%), and fatigue (16.8%). Only 2% (14 of 702) of patients discontinued selpercatinib for TRAEs. **Conclusions:** Selpercatinib use was associated with marked and durable antitumor activity in prior cabozantinib and/or vandetanib-treated patients and in cabozantinib/vandetanib-naïve patients with *RET*-mutant MTC, with the majority of responses ongoing in both cohorts. Selpercatinib was well tolerated. Efficacy data assessed by independent review committee based on the 16-Dec-2019 data cutoff date will be presented. Clinical trial information: NCT03157128. Research Sponsor: Loxo Oncology Inc., a wholly owned subsidiary of Eli Lilly and Company.

3595 Poster Session (Board #325), Fri, 8:00 AM-11:00 AM

IGM-8444 as a potent agonistic Death Receptor 5 (DR5) IgM antibody: Induction of tumor cytotoxicity, combination with chemotherapy and *in vitro* safety profile. *First Author: Beatrice Wang, IGM Biosciences Inc, Mountain View, CA*

Background: Death receptor 5 (DR5) is a member of the tumor necrosis factor (TNF) receptor superfamily that multimerizes when bound to its ligand, TNF-related apoptosis inducing ligand (TRAIL), to activate the extrinsic apoptotic pathway. DR5 is broadly expressed on solid and hematologic cancers and has been targeted with both recombinant TRAIL and agonistic antibodies in the clinic. However, these therapeutics have generally been unsuccessful due to toxicity or lack of efficacy. We have developed a multivalent IgM DR5 agonist, IGM-8444, that multimerizes DR5 to selectively and potently induce tumor cell apoptosis while maintaining tolerability. **Methods:** IGM-8444 is an engineered, pentameric IgM antibody with 10 binding sites specific for DR5. Human tumor cell lines or hepatocytes were evaluated *in vitro* for dose dependent IGM-8444 induced cytotoxicity. The efficacy of IGM-8444 was evaluated with or without chemotherapy, in cell line-derived xenograft (CDX) and patient-derived xenograft (PDX) mouse tumor models, with IGM-8444 administered at various dose levels and schedules when tumors reached approximately 100 mm^3. Sera and tumors were analyzed for biomarkers of tumor apoptosis. **Results:** *In vitro* cytotoxicity assays identified IGM-8444 activity across cell lines from 18 solid and hematologic malignancies. In IGM-8444 partially resistant cell lines, combination with chemotherapy or a Bcl2 inhibitor enhanced *in vitro* cytotoxicity. IGM-8444 was efficacious as a monotherapy in CDX and PDX tumor models including colorectal, lung, and gastric indications. In a gastric PDX model, IGM-8444 induced complete and durable dose-dependent tumor regressions. *In vivo*, combination of IGM-8444 with standard-of-care chemotherapies, such as irinotecan, led to enhanced efficacy. IGM-8444 administration increased markers of tumor apoptosis, identifying potential clinical pharmacodynamic biomarkers. At doses several log-fold higher than efficacious doses, IGM-8444 demonstrated a favorable single agent *in vitro* safety profile, with little to no *in vitro* cytotoxicity observed using primary human hepatocytes from multiple donors. **Conclusions:** These data support the clinical development of IGM-8444 in both solid and hematological malignancies as a single agent and in combination with standard of care therapy. IGM-8444 is projected for IND filing in 2020. Research Sponsor: IGM Biosciences Inc.

3596 Poster Session (Board #326), Fri, 8:00 AM-11:00 AM

Tumor-targeted oncolytic adenovirus demonstrates high cytotoxicity for human lung and renal cell carcinomas independently of the level of tumor PD-L1 expression. *First Author: Jia Yao, Emory University School of Medicine, Atlanta, GA*

Background: Immuno-checkpoint (IC) inhibitors targeting PD1-PD-L1 pathway have proven highly effective at extending survival of cancer patients. However, the clinical benefits of IC inhibitors are limited to only about 20% patients who have moderate to high levels of tumor PD1 and/or PD-L1 expression. To develop therapeutics that would provide clinical benefits to a larger proportion of cancer patients, we engineered oncolytic adenovirus for targeted infection of human tumor cells via CD46 and integrins of $\alpha 3\beta 1$ or $\alpha 6\beta 4$ classes, overexpressed on many epithelial human cancers. **Methods:** Here, we analyzed the infectivity and cytotoxicity of this novel oncolytic virus in a panel of human non-small cell lung cancers (NCSLC) cell lines, primary patient derived NSCLC xenografts, and tumor surgical explants from patients with renal cell carcinoma (RCC). **Results:** The in vitro analysis of NSCLC cells lines (N = 17) demonstrated that over 60% of them were highly sensitive to virus infection. The genome-wide transcriptional profiling showed that only 3 out of 12 cell lines that were sensitive to oncolytic virus infection, expressed PD-L1 ($>$ 4.5 Log2 RPMK). Furthermore, although the pre-treatment of these cell lines with IFN-I activated PD-L1 expression, IFN-I treatment did not reduce the efficacy of tumor cell infection by the oncolytic virus. The analysis of virus infectivity on primary human tumor cells from patients with NSCLC (N = 4) and RCC (N-24) demonstrated that primary tumors were highly sensitive to oncolytic virus infection. Specifically, tumor-targeted oncolytic virus demonstrated strong cytotoxicity in 22 out of 24 analyzed primary isolated RCC cell samples. Next, we subcutaneously grafted PD-L1-negative NSCLC A549 cells to NSG mice, treated them with oncolytic virus intravenously, and the kinetics of tumor growth and animal survival was monitored. This analysis showed that after intravenous administration, oncolytic virus was able to infect tumor cells and suppress tumor growth. Whereas the median survival in mock-treated group was 26 days, all mice survived up to 100 days post oncolytic virus therapy (endpoint). **Conclusions:** Our study showed that tumor-targeted oncolytic adenovirus infects human tumor cell lines independently of their PD-L1 expression status and is not sensitive to IFN-I inhibition. This novel tumor-targeted oncolytic virus has the potential to provide clinical benefits to cancer patients, who do not respond or became resistant to ICI drugs. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

3597 Poster Session (Board #327), Fri, 8:00 AM-11:00 AM

RICTOR amplification as a novel therapeutic target for lung cancer brain metastases. *First Author: Haiying Cheng, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY*

Background: Approximately 20% to 50% of patients with advanced lung cancer develop brain metastases, which are associated with debilitating neurologic impairment and a dismal prognosis. There have been very limited studies investigating the genomics of brain metastases in lung cancer. **Methods:** We comprehensively investigated the frequency of PI3K/AKT/RICTOR/mTOR pathway aberrations in primary and metastatic sites using an extensive database of 11845 cases of lung adenocarcinoma by NGS (FoundationOne). The potential roles of *RICTOR* amplification in the development of brain metastases were studied both in vitro and in vivo in orthotopic mouse models. **Results:** Compared to the primary tumor, *PI3K/AKT/mTOR* gene alterations were more frequent in metastatic sites, with particular enrichment noted in brain metastases. *RICTOR* amplification alone accounted for the observed higher frequency both in brain metastases (brain vs. primary: 9.73% vs 3.50%, P = 2.6E-14; brain vs. other mets: 9.73% vs. 7.3%, P = 0.03) and other metastatic sites (other mets vs. primary: 7.3% vs.3.5%, P = 10E-15), whereas the frequency of *PTEN, AKT1, PK3CA* or *mTOR* genetic alterations was not different in the primary tumor, brain and other metastatic sites. *In vitro*, inducible RICTOR knockdown in H23 lung cancer cells (parental line with *RICTOR* amplification) was associated with reduced cell migration and invasion, whereas upregulation of RICTOR in HCC827 lung cancer cells (parental line with normal *RICTOR* copy numbers) was associated with an increase of both processes. These results were confirmed with pharmacological inhibition using mTOR1/2 inhibitors with known CNS penetration. In vivo, both inducible ablation of RICTOR and the mTOR1/2 inhibitor TAK228 (Sapanisertinib) significantly inhibited lung cancer H23-R4-Luc tumor growth in the brain, including a number of near complete responses. Mechanistic studies suggest that RICTOR may regulate the brain metastasis process through AKT and CXCL12 chemokine-CXCR4 axis. **Conclusions:** *RICTOR* amplification is the first identified actionable target that is markedly enriched in brain metastases. Our study provides a strong rationale for the development of RICTOR-targeted therapeutic strategies for the treatment and/or prevention of these major causes of lung cancer morbidity and mortality. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

3598 Poster Session (Board #328), Fri, 8:00 AM-11:00 AM

Therapeutic drug monitoring of pazopanib: Using cost-neutral PK-guided interventions to optimize exposure. *First Author: Stefanie L. Groenland, The Netherlands Cancer Institute–Antoni van Leeuwenhoek, Amsterdam, Netherlands*

Background: Pazopanib is an approved treatment for renal cell carcinoma (RCC) and soft tissue sarcoma (STS). At the currently registered fixed dose of 800 mg QD, 20% of patients (pts) do not attain the efficacy threshold of $C_{min} \geq 20.5$ mg/L (Suttle et al, 2014), providing a strong rationale for therapeutic drug monitoring (i.e. individualizing the dose based on measured plasma drug concentrations). Previous studies provided cost-neutral alternatives to absolute dose increments to optimize exposure (i.e. splitting intake moments or concomitant intake with food (Groenland et al, 2020; Lubberman et al, 2019)). This study aimed to investigate the feasibility, tolerability and efficacy of TDM of pazopanib, using cost-neutral interventions. **Methods:** Patients starting treatment with pazopanib at the standard dose of 800 mg QD in modified fasting state were included in the prospective DPOG TDM study (www.trialregister.nl, NL6695). PK sampling occurred 4, 8 and 12 weeks after start of treatment, and every 12 weeks thereafter. Pazopanib concentrations were measured with LC-MS/MS and C_{min} was calculated. In case of $C_{min} < 20.5$ mg/L and acceptable toxicity, a dose intervention was recommended. As a first step, intake moments were split (i.e. 400 mg BID). Secondly, concomitant intake with food was recommended. **Results:** In total, 34 pts were included (19 STS, 15 RCC), of whom 158 PK samples were collected. Eleven pts (32%) were underdosed and had at least 1 PK sample below the target. In 24% of the pts a PK-guided intervention could be performed, which was successful in 6 pts (75%). Median C_{min} increased from 15 mg/L to 32 mg/L (p = 0.027). Eventually, 3 pts went back to 800 mg QD due to toxicity, after which C_{min} remained $\geq$ 20.5 mg/L in 2 pts. In pts with adequate exposure throughout the study, median C_{min} was 32 mg/L (range 23 – 65 mg/L). In 3 pts, a PK-guided intervention could not be performed, due to progression (n = 1) or logistical issues (n = 2). Twelve pts (35%) received a dose reduction due to toxicity (lowest dose was 200 mg QAD), exposure remained adequate at this reduced dose in all pts. For STS pts, median PFS was 19.8 months in pts with $C_{min} < 20.5$ mg/L who did need an intervention vs. 6.4 months in pts with all $C_{min} \geq 20.5$ mg/L (not significant). For RCC pts, this was 15.5 months vs. 7.4 months, respectively (not significant). **Conclusions:** This prospective study shows that PK-guided dose optimization of pazopanib using cost-neutral interventions is feasible in daily practice. A PK-guided intervention was performed in 24% of the patients, which was successful in 75% of these patients. Clinical trial information: NL6695. Research Sponsor: Unrestricted research grants by Novartis, Pfizer and Roche.

3599 Poster Session (Board #329), Fri, 8:00 AM-11:00 AM

Preliminary clinical pharmacokinetics and dose-response to support a phase II dose selection for CX-2009: A masked probody drug conjugate to CD166. *First Author: Mark Stroh, CytomX Therapeutics, Inc., South San Francisco, CA*

Background: PROBODY therapeutics are antibody prodrugs with cleavable peptide masks designed to reduce off-tumor, on-target toxicities. The mask blocks binding in the periphery and is removed by tumor-associated proteases resulting in intratumoral binding. CX-2009 is a PROBODY drug conjugate directed against CD166/ALCAM, which is a target overexpressed in carcinomas but not suitable for traditional ADC targeting because it is expressed in normal epithelium. CX-2009 is conjugated to DM4, a potent microtubule inhibitor. Here we report preliminary clinical pharmacokinetic (PK) and exploratory dose-response (DR) analyses for CX-2009 from the ongoing phase 1/2 PROCLAIM-CX-2009 study (NCT03149549). **Methods:** Human PK and anti-drug antibody (ADA) data were obtained at selected times post-dose following IV 0.25–10 mpk CX-2009 Q3W and of 6 mpk Q2W. Covariates were selected for population PK (POPPK) based on multivariate screening at $P < 0.01$. Preliminary exploratory DR analyses were conducted for selected endpoints including adverse events of special interest and response data (CR, PR, SD, and PD). **Results:** Preliminary CX-2009 PK data from 92 subjects were available as of October 2019. Median free DM4 levels circulated at ≤0.3% of Total CX-2009 (masked + activated CX-2009) levels across the 1–10 mpk dose levels. A two-compartment POPPK model with linear elimination was fit to the Intact (masked form) CX-2009 data. The preliminary CX-2009 POPPK model estimates for Intact CX-2009 clearance (CL), volume of distribution, and half-life were 0.47 L/day, 4.51 L, and 7.14 days, respectively, with 91% of CX-2009 circulating as Intact CX-2009. ADA was not a statistically significant covariate on Intact CX-2009 CL. Evidence of clinical activity was observed at doses of 4 mpk Q3W or higher. DR analysis suggested that the frequency of grade ≥3 ocular toxicity events increased significantly at dose equivalents ≥8 mpk Q3W. POPPK simulations suggested that the targeted 90 nM trough concentration (based on nonclinical data) would be contained within the 90% prediction interval of predicted Intact CX-2009 levels following CX-2009 7 mpk. **Conclusions:** Preliminary CX-2009 PK data following CX-2009 0.25-10 mpk suggest that CX-2009 circulates predominantly as Intact CX-2009, and that Intact CX-2009 PK is not strongly influenced by target-mediated drug disposition or ADA. Preliminary DR and POPPK simulations support further evaluation of 7 mpk CX-2009 Q3W in selected cohort expansions. Clinical trial information: NCT03149549. Research Sponsor: CytomX Therapeutics, Inc.

3600 Poster Session (Board #330), Fri, 8:00 AM-11:00 AM

Prophylactic dihydropyrimidine dehydrogenase (DPYD), and reactive cytidine deaminase (CDA) testing is feasible and reduces severe toxicity in Irish patients receiving 5-fluorouracil (5-FU) based chemotherapy. *First Author: Jake Murphy, Bon Secours Hospital, Cork, Ireland*

Background: 5-Fluorouracil (5-FU) steady state concentrations can vary up to fourfold among cancer patients. 5-FU intolerance and toxicity is associated with reduced activity of the key metabolic enzyme dihydropyrimidine dehydrogenase (DPD) due to polymorphisms of the DPYD gene, as well as mutations in cytidine deaminase (CDA). Since 2012, Bon Secours Hospital, Cork has implemented prophylactic DPYD screening to reduce toxicity. **Methods:** In this retrospective cohort study, 742 adult cancer patients who underwent reactive or prophylactic DPYD testing in our center between 2012 and 2019 were included. Reactively tested patients were screened prior to 2012. 5-FU related toxicities were graded according to Common Terminology Criteria for Adverse Events (CTCAE) and analysed. Frequencies of polymorphisms in DPYD, affecting 5-FU metabolism in patients who experienced severe toxicity are described, in both patients who were retrospectively tested, and in our larger prophylactic patient cohort. Mutations of genes encoding CDA were also analysed. Analysis of type and severity of toxicity, and survival analysis will be presented at the Annual Meeting. **Results:** 742 patients were tested for DYPD in our centre, of which 704 were prophylactic tests. 11.4% of the patients tested prophylactically were found to have polymorphisms in the DYPD gene. Expectedly, a higher proportion of patients tested reactively were found to have polymorphisms in DYPD (21.9%). 21 out of 34 patients who had severe toxicity had CDA mutations present on testing. Further data involving classification and severity of toxicities, along with survival analysis will be presented at the Annual Meeting. **Conclusions:** The prevalence of DPYD mutations in Ireland is estimated to be 7-10%, and is putatively responsible for approximately 20% of all severe 5-FU toxicities suffered by cancer patients. Implementing prophylactic DPYD screening is beneficial in reducing toxicities in this setting. Future work will focus on phenotypic measurements of uracil metabolism and pharmacokinetic 5-FU monitoring to further reduce toxicity in patients who do not have DPYD mutations. Research Sponsor: None.

3601 Poster Session (Board #331), Fri, 8:00 AM-11:00 AM

Myelodysplastic syndrome and acute myeloid leukemia as side effect of PARP inhibitors. *First Author: Samip R. Master, Louisiana State University Health Sciences Center, Shreveport, LA*

Background: Acute myeloid leukemia(AML) and myelodysplastic syndrome(MDS) have been rarely noted in patients on PARP inhibitors. The actual incidence is unknown and it has been put has warning/precaution of FDA label for olaparib, niraparib and rucaparib. **Methods:** The FDA has made the data on the adverse effects of various treatments available to the general public through the FDA Adverse Events Reports System (FAERS) public dashboard. We investigated the adverse events reported for PARP inhibitors like olaparib, niraparib and rucaparib for the years 2017-2019 to find out the number of patients who had acute leukemia or myelodysplastic syndrome reported while on those medications. **Results:** A total of 8151 adverse events were reported between 2017 and 2019 for olaparib, niraparib and rucaparib. Out of which, 6077 were serious and 1121 deaths were reported. There were 237 reports of AML and MDS, which compromise 2.9 % of total events reported. We also looked that cyclophosphamide data for comparison purposes during the same period. There were 29,162 adverse events reported for cyclophosphamide, out of which 963 i.e. 3.3% were AML and MDS. For olaparib, 2523 adverse events were reported and 173 (6.8%) were MDS/AML. For niraparib, 5496 adverse events were reported and 41(0.7%) were MDS/AML. For rucaparib, 153 adverse events were reported and 4 (2.6%) were MDS/AML. **Conclusions:** Based on this retrospective data, AML/MDS is an adverse event in pts of PARP inhibitors and needs to be monitored. Pts on olaparib seem to have high risk of AML/MDS compared to other two to PARP inhibitors. Research Sponsor: None.

3602 Poster Session (Board #332), Fri, 8:00 AM-11:00 AM

Preliminary population pharmacokinetics supports phase II dose selection for masked anti-PD-L1 antibody CX-072. *First Author: Mark Stroh, CytomX Therapeutics, Inc., South San Francisco, CA*

Background: PROBODY therapeutics (Pb-Tx) are antibody prodrugs designed to reduce off-tumor, on-target toxicities. The mask inhibits Pb-Tx binding in the periphery yet can be removed by tumor-associated proteases, restricting target engagement to the tumor. This is the first report of preliminary clinical pharmacokinetic (PK) analysis supporting selection of the phase II dose for CX-072, an anti–PD-L1 Pb-Tx, from the ongoing phase I/II PROCLAIM-CX-072 study (NCT03013491). **Methods:** A quantitative systems pharmacology (QSP) model[1] was used to project the CX-072 plasma trough level (C_{min}) corresponding to 95% intratumoral receptor occupancy (RO). Human PK and anti-drug antibody (ADA) data were obtained at selected times postdose following IV administration of 0.03–30 mpk CX-072 in PROCLAIM-CX-072. Population PK (POPPK) modeling was performed with NONMEM v7.3.0. Exploratory analysis and simulations were done with R v3.3.1 or later. Covariates were selected for POPPK using forward addition ($P<0.05$) followed by backward deletion ($P<0.01$). **Results:** The preliminary POPPK analyses were informed using available PK data as of August, 2019 from 135 subjects receiving CX-072 Q2W as monotherapy in the dose-escalation and expansion cohorts of PROCLAIM-CX-072. A mixture model was used to capture time- and dose-dependent apparent ADA effect on clearance (CL). The preliminary POPPK model estimates for CX-072 CL and volume of distribution (Vd) were 0.306 L/day and 4.84 L, respectively. Statistically significant covariate effects included body weight on the central Vd and CL, and albumin on CL. The QSP model predicted a CX-072 C_{min} of 13–99 nM would be required for 95% intratumoral RO. POPPK simulations suggested that >95% of patients receiving CX-072 10 mg/kg Q2W would meet or exceed this targeted C_{min} regardless of ADA. Additional observed data indicated that the majority of patients receiving 10 mpk CX-072 Q3W × 4 with 3 mpk ipilimumab (IPI) Q3W × 4 in the CX-072-IPI combination part of PROCLAIM-CX-072 maintained the targeted C_{min}. Simulations did not suggest there would be a clinically meaningful change in exposure following a fixed dose of CX-072 800 mg relative to the 10 mpk weight-based dose. **Conclusions:** Preliminary PK analysis supports selection of 800 mg CX-072 Q2W as the recommended monotherapy dose and 800 mg Q3W when combined with IPI. The combination of 800 mg CX-072 + 3 mpk IPI Q3W × 4 doses, followed by monotherapy administration of 800 mg CX-072 Q2W is being further explored in phase II. Reference: 1) Stroh M et al. *CPT.* 2019(9):676-84. Clinical trial information: NCT03013491. Research Sponsor: CytomX Therapeutics, Inc.

3603 Poster Session (Board #333), Fri, 8:00 AM-11:00 AM

Final results from the phase I study expansion cohort of the selective FGFR inhibitor Debio 1,347 in patients with solid tumors harboring an FGFR gene fusion. *First Author: James M. Cleary, Dana Farber Cancer Institute, Boston, MA*

Background: Debio 1347 is a selective oral inhibitor of FGFR 1-3 tyrosine kinases. It exhibited high antitumor activity in *in vitro* and *in vivo* tumor models with FGFR1-3 gene fusions. Here we report the results of the expansion portion of a Phase 1 study of advanced solid tumors patients (pts) harboring an FGFR1-3 gene fusion. **Methods:** Pts with advanced refractory solid tumors harboring an FGFR1-3 gene fusion were enrolled. Based on results from the dose escalation portion, pts received Debio1347 80 mg once daily (qd) in 28-day cycles. Pharmacokinetics (PK) and pharmacodynamics were evaluated. The data cut-off was October 8, 2019. **Results:** Among 18 pts enrolled, 5 had primary brain tumors (PBT), 5 had cholangiocarcinoma, 2 had urothelial cancer, 2 had colon cancer, 1 patient each lung neoplasm, gastric cancer, endometrial cancer and squamous cell carcinoma of the chest wall. Tumors harbored fusions with FGFR1 (n = 1), FGFR2 (n = 8), and FGFR3 (n = 9). All had prior systemic therapy (median 3 lines; range 1-4). The most common treatment emergent adverse events were fatigue (50%), hyperphosphatemia (44.4%), anemia (38.9%), alopecia (33.3%), nausea (33.3%), vomiting (33.3%), constipation (33.3%), and palmar-plantar erythrodysesthesia syndrome (22.2%). Blurred vision was reported in 1 pt. There were no findings on ocular exams compatible with retinal detachment. No grade 3 AE related to study drug were reported. One patient needed dose reduction due to grade 2 nails toxicity. In PK analysis, plasma steady-state was rapidly achieved and serum phosphate increase correlated with Debio 1347 plasma exposure, confirming target engagement at 80 mg qd. Median follow-up was 18 weeks. Partial responses were observed in 3 pts harboring an FGFR2 fusion: 1 out of 2 colon cancer and 2 out 5 cholangiocarcinoma. Median duration of response was 16.1 weeks (range: 8.4-22.8+). Overall disease control was observed in 11 out of 14 pts without PBT (79%). Median PFS was 18.3 weeks. No signs of activity were observed in the 5 patients with PBT, all with an FGFR3-TACC3 fusion. **Conclusions:** Debio 1347 at the recommended dose of 80 mg qd was generally well tolerated and showed signs of activity in solid tumors harboring an FGFR fusion. The FUZE phase 2 clinical trial of Debio 1347 is recruiting FGFR fusion-positive advanced solid tumors irrespectively of tumor histology, excluding PBT. Clinical trial information: NCT01948297. Research Sponsor: Debiopharm International SA.

3604 Poster Session (Board #334), Fri, 8:00 AM-11:00 AM

Results of a phase Ib trial evaluating the safety and clinical activity of sapanisertib (TAK 228) in combination with serabelisib (TAK 117) and paclitaxel in patients with advanced ovarian, endometrial, or breast cancer. *First Author: Casey B. Williams, Avera Cancer Institute, Sioux Falls, SD*

Background: The link between taxane resistance and activation of PI3K/AKT/mTOR signaling suggests that by inhibiting this pathway in combination with anti-microtubule agents like paclitaxel may improve treatment outcomes in many malignancies. To investigate this further we combined the TORC 1/2 inhibitor sapanisertib (TAK-228), the PI3Kα isoform inhibitor serabelisib (TAK-117), and paclitaxel in a phase I trial to determine the safety, efficacy, and RP2D. **Methods:** Open label, cohort study using a traditional 3+3 dose escalation design with a maximum of 5 dosing cohorts. A dose expansion of cohort 4, the recommended RP2D, is planned for February 2020. **Results:** Enrollment to the DLT evaluation has been completed and the clinical results are summarized in Table. Sixteen patients have been enrolled; a majority were heavily pretreated and resistant to paclitaxel. Overall, the combination was safe and tolerable. One DLT occurred due to renal dysfunction in cohort 5. 360 adverse events have been reported, but only 28 (8%) grade 3 or 4 events. The most common events were leukopenia and non-febrile neutropenia. Two patients required dose reductions as a result of pneumonitis. The ORR is currently 46% in 13 evaluable patients. CBR is 69% and PFS is currently at 10 months. Two patients achieved a CR and three patients remain on treatment. **Conclusions:** The combination proved to be well tolerated in the doses and schedules used in cohorts 1-4 and exhibited very promising clinical activity in heavily pretreated patients. This regimen could prove to be a highly effective treatment option and a phase 2 study is warranted at the RP2D. Clinical trial information: NCT03154294.Research Sponsor: Takeda.

Pt # and Diagnosis	Cohort	Previous Lines	TAK 228/117 (mg) days 2-4, 9-11, 16-18, and 23-25	Paclitaxel Dose (mg/m2) days 1, 8, and 15	Best Response
1 (Breast)	1	3*	2/100	60	PR (PFS 9 months)
2 (Ovarian	1	12*	2/100	60	SD (PFS 9 months)
3 (Endometrial)	1	2	2/100	60	PD
4 (Endometrial)	1	6	2/100	60	PR (PFS 12 months)
5 (Breast)	2	5	2/200	60	NE
6 (Breast)	2	5	2/200	60	NE
7 (Endometrial)	2	1	2/200	60	CR (Duration of CR - 15 months)
8 (Mullerian)	3	3	2/200	80	PD
9 (Ovarian)	3	3*	2/200	80	SD (PFS 6 months)
10 (Ovarian)	3	5*	2/200	80	SD/PR (29% by RECIST) (PFS 6 months)
11 (Ovarian)	4	4	3/200	80	PD
12 (Ovarian)	4	3	3/200	80	PR (PFS 12 months)
13 (Ovarian)	4	4	3/200	80	SD (Cycle 12 and ongoing)
14 (Endometrial)	5	4*	4/200	80	CR (Cycle 9 and ongoing)
15 (Ovarian)	5	4	4/200	80	PD
16 (Ovarian)	5	6	4/200	80	DLT – Still on treatment

* Received Prior Everolimus/Temsirolimus

3605 Poster Session (Board #335), Fri, 8:00 AM-11:00 AM

Efficacy and safety of entrectinib in patients (pts) with *NTRK*-fusion positive (*NTRK*-fp) solid tumors: An updated integrated analysis. *First Author: Christian Diego Rolfo, University of Maryland School of Medicine, Baltimore, MD*

Background: *NTRK* gene fusions lead to transcription of chimeric TRK proteins with overexpressed kinase function. Entrectinib is a potent inhibitor of TRKA/B/C. In phase 1/2 studies (ALKA, STARTRK-1, STARTRK-2; EudraCT 2012-000148-88; NCT02097810; NCT02568267), entrectinib was effective in pts with *NTRK*-fp solid tumors. We present updated data in a larger population with longer follow-up. **Methods:** In this integrated analysis of adult pts from 3 phase 1/2 trials (data cut-off 31 Oct 2018), tumors were assessed by blinded independent central review (BICR) with RECIST v1.1 (end of cycle 1; then every 8 wks). Primary endpoints were overall response rate (ORR) and duration of response (DOR). Secondary endpoints were progression-free survival (PFS), overall survival (OS), efficacy in pts with/without baseline CNS disease, and safety. **Results:** There were 74 evaluable pts with advanced/metastatic *NTRK*-fp solid tumors (Table). Median duration of survival follow-up in all pts was 14.2 mo (range 0.1–29.7). BICR ORR was 63.5% (95% CI 51.5–74.4), with 5 complete responses (6.8%). Median BICR DOR was 12.9 mo (95% CI 9.3–NE); median BICR PFS was 11.2 mo (95% CI 8.0–15.7); median OS was 23.9 mo (16.0–NE). In pts with no baseline CNS disease (investigator-assessed; n=55), BICR ORR was 65.5% (95% CI 51.4–77.8) and median BICR DOR in responders was 12.9 mo (95% CI 9.3–NE). In pts with baseline CNS disease (investigator-assessed; n=19), BICR ORR was 57.9% (95% CI 33.5–79.8) and median BICR DOR in responders was 6.0 mo (95% CI 4.2–NE). Safety was in line with that previously reported; the most common ≥grade 3 treatment-related AEs were weight gain (8, 7.1%), anemia (8, 7.1%), and fatigue (7, 6.2%). **Conclusions:** In this updated analysis, including more pts and longer follow-up, entrectinib continued to demonstrate clinically meaningful responses in pts with *NTRK*-fp solid tumors, with and without baseline CNS disease. Clinical trial information: NCT02097810, NCT02568267.Research Sponsor: Ignyta/F Hoffmann-La Roche.

Baseline characteristic	*NTRK*-fp tumors (N=74)
Age (yrs): mean (SD)	56.5 (14.6)
Race,* n (%): White/Asian/Black	52 (70.3)/13 (17.6)/2 (2.7)
ECOG PS, n (%): 0/1/2	30 (40.5)/34 (45.9)/10 (13.5)
CNS mets at baseline,† n (%)	19 (25.7)
Tumor type, n	
Sarcoma	16
MASC	13
NSCLC	13
CRC	7
Thyroid	7
Breast	6
Neuroendocrine	4
Pancreatic	3
Gynecological	2
Cholangiocarcinoma	1
Gastrointestinal non-CRC	1
Neuroblastoma	1

*7 not reported. †Investigator-assessed. CRC, colorectal cancer; ECOG PS, European Cooperative Oncology Group performance status; MASC, mammary analogue secretory carcinoma; NSCLC, non-small cell lung cancer; SD, standard deviation.

3606 Poster Session (Board #336), Fri, 8:00 AM-11:00 AM

Safety and efficacy of pemigatinib plus pembrolizumab combination therapy in patients (pts) with advanced malignancies: Results from FIGHT-101, an open-label phase I/II study. *First Author: Martin Gutierrez, John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ*

Background: Pemigatinib (INCB054828) is a selective fibroblast growth factor receptor (FGFR) 1–3 inhibitor with demonstrated efficacy as monotherapy in phase 1/2 (FIGHT-101) and phase 2 (FIGHT-201, -202, -203) trials in pts with advanced cancer. Here, we present preliminary safety, efficacy, and pharmacokinetic (PK) data for pemigatinib (PEMI) combined with pembrolizumab (PEMBRO), a programmed cell death protein-1 (PD-1) inhibitor, in pts with refractory advanced malignancies enrolled in the ongoing FIGHT-101 trial (NCT02393248). **Methods:** FIGHT-101 includes monotherapy (part 1 and 2) and combination therapy (part 3) cohorts. This analysis is based on pts enrolled in the PEMI + PEMBRO combination dose finding (3a) and dose expansion (3b) cohorts. Eligible adults had advanced malignancies who had progressed after prior therapy and for whom PEMBRO treatment was relevant; pts in part 3b had *FGF/FGFR* alterations. Pts received oral PEMI at 9 mg or 13.5 mg QD on an intermittent dosing (ID) schedule (21-day cycle, 14-day on/7-day off), or 13.5 mg QD on a continuous dosing (CD) schedule, plus PEMBRO 200 mg IV on day 1 of each 21-day cycle. **Results:** At data cutoff (August 30, 2019), 23 pts had received PEMI + PEMBRO; 22 (96%) had discontinued therapy (disease progression, 70%). Most frequent tumors were NSCLC (n = 3), bladder (n = 3), pancreatic, testicular, and sarcoma (each n = 2). Of 19 enrolled pts with baseline *FGF/FGFR* data; 5 had *FGFR* mutations or rearrangements. No dose-limiting toxicities occurred with PEMI + PEMBRO. The recommended PEMI dose combined with PEMBRO was 13.5 mg QD. Most frequent all-cause, all-grade (Gr) adverse events for ID (n = 17) were hyperphosphatemia (n = 14 [82%]; Gr ≥3, n = 0), anemia (n = 9 [53%]; Gr ≥3, n = 3 [18%]), and decreased appetite (n = 9 [53%]; Gr ≥3, n = 0); for CD (n = 6), hyperphosphatemia (n = 5 [83%]; Gr ≥3, n = 0), and dry mouth (n = 4 [67%]; Gr ≥3, n = 0). One pt discontinued, 2 reduced dose, and 13 interrupted dose due to AEs (none for hyperphosphatemia; dose interruption mainly for gastrointestinal AEs [n = 5]). One fatal AE occurred (suicide, not treatment-related). PK parameters for PEMI in the PEMI + PEMBRO combination were comparable with those for PEMI monotherapy. Five pts had partial response (3 had *FGFR* rearrangements or mutations); 5 pts had stable disease. **Conclusions:** PEMI + PEMBRO combination therapy was tolerable with no new safety signals, and demonstrated preliminary antitumor activity in pts with advanced malignancies including those with *FGF/FGFR* alterations. Clinical trial information: NCT02393248. Research Sponsor: Incyte Corporation.

3607 Poster Session (Board #337), Fri, 8:00 AM-11:00 AM

Results of a completed first-in-human phase Ib dose-escalation study of oral CBL0137 in patients with advanced solid tumors. *First Author: Mikhail Fedyanin, Federal State Budgetary Institution N.N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russian Federation*

Background: Curaxin CBL0137 is a novel compound with broad anticancer activity in animal models. The drug is a non-genotoxic DNA intercalator that interferes with histone/DNA binding causing decondensation of chromatin in tumor cells, functional inactivation of histone chaperone FACT, activation of p53 and IFN responses, and inhibition of pro-cancer transcriptional factors, MYC, NF-kB, HSF1, and HIF1a. **Methods:** The study enrolled adults with advanced chemorefractory solid tumors, ECOG PS ≤2, and adequate organ function. The primary objective was to find the maximum tolerated dose (MTD) and recommended dosing regimen (RDR). Secondary objectives were to evaluate CBL0137 safety, pharmacokinetics, and efficacy. CBL1037 was given orally once daily (QD) for the first 14 days of repeated 28-day cycles. A 3+3 dose escalation determined the MTD, defined as the highest dose at which ≤1 of 6 pts had Cycle 1 dose-limiting toxicity (DLT). Pharmacokinetics were assessed on Days 1 and 13. Efficacy was evaluated every 8 weeks. **Results:** 60 pts were enrolled (females/males [n]: 42/18; median [range] age 56 [25-76] years; ECOG PS [n] 0/1/2: 8/49/3); cancer types [n]: ovarian cancer [15], colorectal cancer [14], breast cancer [11], others [20]) over 16 dose levels ranging from 4 mg to 200 mg QD. Durations of therapy ranged from 6 to 342 days. Three DLTs were observed: prolongation of QTc Gr 3 (88 mg QD), neutropenia/thrombocytopenia Gr 4 (200 mg QD), and LV dysfunction Gr 3 (200 mg QD). Dose-dependent nausea/vomiting was observed and was Gr 2-4 at 200 mg QD. Gr 1/2 photosensitization occurred in 11 subjects across doses from 48 to 200 mg QD but was successfully managed with sun protection and resulted in no dose modifications or discontinuations. On Day 1, mean (range) plasma CBL0137 T_{max} values were 5.1 (1-10) hrs. Generally linear increases in AUC occurred with increasing CBL0137 dose. Mean (range) $t_{1/2}$ values were 25.6 (0.3-166) hrs, with minor dose dependency. Mean (range) Day 13/Day 1 C_{trough} ratios showed 3.6 (1.7-7.2)-fold accumulations. Disease control was registered in 11 pts who had stable disease (SD). Target lesion regressions up to 21% were documented in 4 patients with breast cancer (2), sarcoma (1), and ovarian cancer (1). Pts with breast cancer (1) and sarcoma (1) had SD for > 36 weeks. **Conclusions:** The Phase 2 RDR for oral CBL0137 was established as 180 mg QD x 14 days in 28-day cycles based on bone marrow and gastrointestinal DLTs at 200 mg QD. CBL0137 showed a manageable safety profile with efficacy signals. Further study as a component of combinations is planned. Clinical trial information: 847. Research Sponsor: Incuron.

3609 Poster Session (Board #339), Fri, 8:00 AM-11:00 AM

CTEP 9557: A dose-escalation trial of combination dabrafenib, trametinib, and AT13387 in patients with BRAF mutant solid tumors. *First Author: Meghan Mooradian, Massachusetts General Hospital Cancer Center, Boston, MA*

Background: Combination BRAF and MEK inhibitor therapy is associated with response in patients (pts) with BRAF mutant (mut) solid tumors; however critical limitations for the durable activity of these agents remains. Preclinically, the addition of heat shock protein 90 (HSP90) inhibitors improves the efficacy of BRAF inhibitor (BRAFi) therapy in both BRAFi-sensitive and resistant mutant cell lines. **Methods:** CTEP study 9557 (NCT02097225) is a phase I study designed to determine the safety and efficacy of the small molecule HSP90inhibitor, AT13387, in combination with dabrafenib (dab) and trametinib (tram) in patients with $BRAF^{V600E/K}$ mut solid tumors. Prior chemotherapy, immunotherapy, BRAF and/or MEK exposure was permitted. The primary objective was to determine the maximum tolerated dose (MTD). **Results:** From July 2015 to June 2018, 22 patients with previously treated, metastatic $BRAF^{V600E/K}$ mut solid tumors were enrolled using a 3 + 3 design at four dose levels (DL) (Table). Pts were predominantly female (59%) with a median age of 57.5yrs (37 -75). The most common tumor type was $BRAF^{V600E}$mut colon cancer (N=12). Dose limiting toxicities (DLTs) occurred in one patient in DL3 and one in DL4, specifically grade 3 myelosuppression and fatigue, respectively. The MTD was Dab 150mg [BID/PO], Tram 2mg [QD/PO] and AT1187 260mg/m2 [D1,8,15/IV]. Twenty-one of 22 pts were eligible for efficacy assessment. Best response, per RECIST 1.1, was partial response (PR) in 2 pts – one with colon ca (TKI-naïve), one with melanoma (TKI-resistant) - stable disease (SD) in 8 pts, and disease progression (PD) in 11 with a disease control rate (PR + SD) of 47.6% (90% CI: 29% - 67%). Median time to progression was significantly longer in DL3 (3.9 mths; 1.8-9.2) compared to DL1 (1.6mths; 0.9-1.7) or DL2 (1.5; 0.6-3.6). Median PFS and OS were 1.8mths (90% CI: 1.6 – 3.7mths) and 5.1 mths (90% CI: 2.5 -10.6mths), respectively. Median OS was not reached in DL3/4. Correlative data on the expression of the key signaling proteins relating to response will be presented at the meeting. **Conclusions:** HSP90 inhibition combined with BRAF/MEK inhibition was determined to be safe with evidence of disease control in a heavily pre-treated population of pts with $BRAF^{V600E/K}$ mut solid tumors. Clinical trial information: NCT02097225.Research Sponsor: U.S. National Institutes of Health.

Dose level cohorts.

DOSE LEVEL	DABRAFENIB [BID/PO]	TRAMETINIB [QD/PO]	AT13387 [D1,8,15/IV]
-1	75 mg	1 mg	180 mg/m2
1	150 mg	1 mg	180 mg/m2
2	150 mg	2 mg	180 mg/m2
3	150 mg	2 mg	220 mg/m2
4	150 mg	2 mg	260 mg/m2

3610 Poster Session (Board #340), Fri, 8:00 AM-11:00 AM

Activity and safety of larotrectinib in adult patients with TRK fusion cancer: An expanded data set. *First Author: Alexander E. Drilon, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: The highly selective TRK inhibitor larotrectinib is approved for the treatment of adult and pediatric cancers that harbor *NTRK* gene fusions; it achieves a 79% overall response rate (ORR) in this population (Hong et al., *Lancet Oncol*, 2020). The activity of larotrectinib in adults alone was further characterized in this update with a larger series of patients and more mature durability data. **Methods:** Adults (aged ≥18 y) with TRK fusion cancer treated in three larotrectinib clinical trials (NCT02122913, NCT02576431, and NCT02637687) were analyzed. Larotrectinib was administered 100 mg BID until disease progression, withdrawal, or unacceptable toxicity. ORR was investigator-assessed (RECIST v1.1). Compared to previously presented data on 74 patients, this expanded data set includes an additional 42 patients (data cutoff: July 15, 2019). **Results:** 116 adults (median age: 56 y, range 19–84 y; 53% female) with TRK fusion cancer were treated. Tumor types included thyroid cancer (22%), salivary gland cancer (19%), soft tissue sarcoma (16%), lung cancer (12%), colon cancer (7%), melanoma (5%), breast cancer (5%), GIST (3%), and 9 other types (≤2% each). *NTRK* fusions involved *NTRK1* (43%), *NTRK2* (3%), and *NTRK3* (54%). 78% of patients had received prior systemic therapy (with 68% of those receiving ≥2 prior therapies). The ORR was 71% (95% CI 62–79): 10% complete response, 60% partial response (2% pending confirmation), 16% stable disease, 9% progressive disease, 3% not determined. In patients with brain metastases, the ORR was 71% (95% CI 42–92; 10 of 14 patients, all partial responses). Median duration of response for the overall data set (n = 116) was 35.2 mo (95% CI 21.6–not estimable [NE]). Median progression-free survival was 25.8 mo (95% CI 15.2–NE). Median overall survival was not reached (range 0.5+ to 51.6+ mo) at a median follow-up of 15.8 mo. Duration of treatment ranged from 0.10 to 51.6+ mo. 12% of patients had dose reductions. One patient (1%) discontinued due to a larotrectinib-related adverse event (AE). AEs were mostly grade 1–2; no new unexpected AEs were reported. **Conclusions:** In an expanded data set of adults with TRK fusion cancer, larotrectinib demonstrated robust and durable tumor-agnostic efficacy and favorable safety, supporting *NTRK* gene fusion testing in patients with solid tumors of any type. Clinical trial information: NTC02122913, NCT02576431, NCT02637687. Research Sponsor: Bayer and Loxo Oncology (a subsidiary of Lilly).

3611 Poster Session (Board #341), Fri, 8:00 AM-11:00 AM

A phase I, first-in-human, open-label, dose-escalation, safety, pharmacokinetic, and pharmacodynamic study of oral TP-1287 administered daily to patients with advanced solid tumors. *First Author: Ben George, Froedtert & The Medical College of Wisconsin, Milwaukee, WI*

Background: TP-1287 is a an orally bioavailable phosphate prodrug of alvocidib, a cyclin dependent kinase 9 (CDK9) inhibitor. TP-1287 exhibits potent inhibition of intracellular kinases including CDK9. Inhibition of CDK9 leads to downregulation of the BCL-2 family member, MCL-1, which in turn inhibits tumor growth in preclinical animal models of prostate, breast, and lung carcinomas. **Methods:** This is a multicenter, Phase 1, dose escalation study using a standard 3+3 design with a modified Fibonacci scheme to examine the safety and clinical activity of TP-1287 in patients with advanced solid tumors. Patients will be added at the maximum tolerated dose (i.e. expansion cohort) to test TP-1287 as a single agent in patients with castrate resistant prostate cancer. **Results:** Twenty-two patients who were enrolled between December 2018 and January 2020 received a range of doses from 1 mg QD to 11 mg BID over 7 cohorts. Data are available for 20 patients as of the data cutoff date. TP-1287 plasma PK C_{max} and AUC increased in near linear fashion over cohorts 1 thru 6, reaching 80 ng/mL and 499.3 ng*h/mL in cohort 6 for C_{max} and AUC, respectively. TP-1287 treatment resulted in dose-dependent reductions of phospho-RNA Pol II, consistent with CDK9 inhibition, as measured by a flow cytometric assay assessing pharmacodynamic changes in phosphorylation state in PBMCs. The most frequently observed Grade 3 AE was unrelated anemia in 2 patients. All other events of Grade 3 (9 events/7 patients) and Grade 4 (1 event/seizure with new CNS mets) were unlikely related or unrelated. Clinical benefit was seen in one sarcoma patient with PR (15+cycles), one RCC patient with SD (7+cycles) and 2 bladder cancer patients with SD (6 and 8 cycles). **Conclusions:** These findings suggest that TP-1287 is tolerated as a monotherapy in patients with heavily pretreated, relapsed, refractory solid tumors and further clinical development in selected indications is warranted. Clinical trial information: NCT03298984. Research Sponsor: Tolero Pharmaceuticals, Inc.

3612 Poster Session (Board #342), Fri, 8:00 AM-11:00 AM

Phase II trial of the MEK 1/2 inhibitor selumetinib (AZD6244, ARRY-142886 Hydrogen Sulfate) in adults with neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas (PN). *First Author: Geraldine Helen O'Sullivan Coyne, Developmental Therapeutics Clinic/Early Clinical Trials Development Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, Bethesda, MD*

Background: NF1-related PN are locally invasive tumors characterized by increased activation of the RAS pathway causing significant morbidity including disfigurement, pain and functional limitations. Selumetinib has received breakthrough designation for NF1 PN based on phase I / II trials in children. We present results for the ongoing phase II study of selumetinib in adults with NF1 PN, which includes pharmacodynamic (PD) evaluation of serial tumor biopsies as well as functional/patient-reported outcomes (PROs). **Methods:** Open-label Simon 2-stage design. Eligibility: NF1 patients (pts) ≥18 years old with inoperable/symptomatic/progressive PN. First 2 pts received selumetinib 75 mg BID; subsequent pts received selumetinib 50 mg BID. Primary objective: response rate by volumetric MRI analysis (partial response [PR]; ≥20% volume decrease). Secondary objectives: PD studies on pre/on-treatment biopsies of PN and cutaneous neurofibromas, assessment of clinical benefit using PROs (Numeric Rating Scale-11, Pain Interference Index), and PN-specific functional assessments. Validated, fit-for-purpose, isozyme-specific measurements of pERK/ERK/pMEK/MEK performed using SOPs designed for labile phosphoproteins (PMID 27001313). **Results:** As of February 2020, 27 pts have enrolled. Outcomes are reported for 23 pts (74% male; median age 33 years, range 18-60). Most common PN-related morbidity: pain (19 pts). Sixteen pts achieved PR (69%), with 13/16 confirmed; no disease progression. Time to response: 11 months (range 5-25); median change in PN volume at best response: -22% (range -41% to +5.5%); median duration of treatment: 28 months (range 2-50). Selumetinib suppressed tumor pERK1,2/ERK1,2 but not pMEK1,2/MEK1,2 ratios from 1-10 hours following oral dosing (one $t_{1/2}$). Pt-reported target tumor pain intensity and pain interference scores significantly improved (both $p < 0.03$). Pts 1 and 2 were dose-reduced due to grade 3 intolerable rash (n = 2) and pain (n = 1). Grade ≥3 drug-related toxicities on 50 mg (21 pts) include transaminitis (5 pts), rash (1 pt) and pancreatic enzyme elevation (1 pt). Two pts were dose reduced (rash = 1 pt, transaminitis = 1 pt). Two pts discontinued by choice, 2 pts withdrawn by PI (best interest of patient), and 1 pt each removed for transaminitis, surgical resection, serious concurrent medical illness, and noncompliance. **Conclusions:** Selumetinib shrinks the majority of adult PN and results in molecular target suppression and clinical benefit. Clinical trial information: NCT02407405. Research Sponsor: U.S. National Institutes of Health.

3613 Poster Session (Board #343), Fri, 8:00 AM-11:00 AM

Phase I study of afatinib plus selumetinib in patients with KRAS mutation-positive colorectal, non-small cell lung and pancreatic cancer. *First Author: Sanne Huijberts, Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: Mutations in the *KRAS* gene result in a constitutively activated RAS-RAF-MEK-ERK (MAPK) pathway. In KRAS mutant tumors, the antitumor activity of MEK inhibitors is limited due to intrinsic resistance caused by feedback activation of upstream epidermal growth factor receptors (HER). This upstream activation not only reactivates MAPK, but also the phosphoinositide 3-kinase (PI3K)-AKT pathway in preclinical research. Based on these data, a phase I clinical trial was initiated with the combination of the orally administered pan-HER inhibitor afatinib and the MEK inhibitor selumetinib in patients with *KRAS* mutant and *PIK3CA* wildtype colorectal cancer (CRC), non-small cell lung cancer (NSCLC), or pancreatic cancer to determine the recommended phase 2 regimen (RP2R). **Methods:** In this multicentre study, patients received escalating doses of afatinib and selumetinib according to a 3+3 design starting with 20 mg afatinib once daily (QD) continuously and 25 mg selumetinib twice daily (BID) in a 21 days on/7 days off schedule. Continuous and intermittent dosing were explored to assess optimal exposure and tolerability. The primary aim was determining the RP2R. Secondary objectives included assessment of anti-tumor activity and the analyses of pharmacokinetic and pharmacodynamic parameters for target inhibition. Clinicaltrials.gov identifier: NCT2450656. **Results:** In total, 26 mostly heavily pretreated patients with CRC (n=19), NSCLC (n=6) and pancreatic cancer (n=1) were enrolled among 5 dose-levels. Dose-limiting toxicities (DLTs) occurred in 6 patients and consisted of grade 3 diarrhea (n=3), decreased appetite (n=1), nausea/vomiting (n=1), dehydration (n=2) and mucositis (n=1). Clinical efficacy was limited with no responses according to RECIST v1.1 and stable disease for 221 days in a patient with NSCLC as best response. **Conclusions:** The RP2R was determined at 20 mg afatinib QD continuously and 25 mg selumetinib BID 21 days on/7 days off for continuous dosing. The 3 patients treated in the escalation cohort of the ongoing intermittent dose-level with 20 mg afatinib QD and 25 mg selumetinib BID 5 days on/2 days off, experienced no DLTs. Pending the latest safety results of the expansion cohort for this ongoing dose-level, the RP2R of intermittent dosing has not been established at the moment. Clinical trial information: NCT2450656. Research Sponsor: Boehringer Ingelheim Inc., AstraZeneca Inc.

3614 Poster Session (Board #344), Fri, 8:00 AM-11:00 AM

Quality of life of adults and children with TRK fusion cancer treated with larotrectinib compared to the general population. *First Author: Shivaani Kummar, Stanford Cancer Institute, Stanford University, Palo Alto, CA*

Background: *NTRK* gene fusions occur in diverse tumor types in adults and children. The selective TRK inhibitor, larotrectinib, has shown high response rates, durable disease control, and a favorable safety profile in patients (pts) with TRK fusion cancer. We report an expanded quality of life (QoL) analysis for pts treated with larotrectinib. **Methods:** QoL data were collected in two trials of larotrectinib in pts with TRK fusion cancer using EORTC QLQ-C30 (adults) and PedsQL (children) questionnaires, and were analyzed descriptively and longitudinally. EORTC QLQ-C30 global health scores (GHS) and PedsQL total scores range from 0 to 100, with higher scores indicating better QoL. We calculated the proportion of pts with normal/above and below normal QoL scores compared to values in the literature for the US general population. **Results:** By July 2019, 126 pts with TRK fusion cancer (74 adults, 24 children ≥2 yrs, and 28 infants <2 yrs) had received larotrectinib and completed baseline (BL) and ≥1 post-BL questionnaire. Most pts had clinically meaningful QoL improvements that reached or exceeded the minimally important difference (Table); a positive change from BL was also seen in infants: mean best change of 12.0 (SD 13.8). Of 52 adults with BL EORTC QLQ-C30 GHS at or above the population norm, 51 remained in this category on treatment and 1 moved into the below normal category. Of 22 adults with BL scores below the population norm, 20 moved into the normal/above normal category. All 9 children aged ≥2 yrs with BL PedsQL scores at or above the population norm remained in this category on treatment. Of 15 children with BL scores below the population norm, 10 moved into the normal/above normal category. Sustained QoL improvements (change from BL ≥0) occurred by 2 months of treatment in 69% of adults and 75% of children. Median duration of sustained improvement in EORTC QLQ-C30 GHS and PedsQL total score was 12.0 months (range 1.7–20.3) and not estimable (range 1.1–23.0), respectively. **Conclusions:** Adults and children with TRK fusion cancer treated with larotrectinib had rapid, clinically meaningful, and sustained improvements in QoL. Clinical trial information: NCT02576431, NCT02637687.Research Sponsor: Bayer HealthCare and Loxo Oncology, Inc., a wholly owned subsidiary of Eli Lilly.

	EORTC QLQ-C30 GHS	PedsQL total score (≥2 yrs old)
BL and ≥1 post-BL measurement, n	74	24
Best change in total score from BL, mean (SD)	17.5 (20.0)	20.7 (17.2)
Best post-BL score above BL score, % (n)	69 (51)	88 (21)
MID* improvement, % (n)	59 (44)	79 (19)
BL and ≥2 post-BL measurements, n	64	24
Sustained improvement for ≥2 consecutive cycles, % (n)	47 (30)	75 (18)

*Minimally important difference: ≥10 points for EORTC QLQ-C30; ≥4.5 points for PedsQL

3615 Poster Session (Board #345), Fri, 8:00 AM-11:00 AM

Single-agent ONC201 in recurrent H3 K27M-mutant diffuse midline glioma. *First Author: Isabel Arrillaga-Romany, Massachusetts General Hospital, Boston, MA*

Background: Recurrent H3 K27M-mutant diffuse midline glioma is a lethal brain tumor that predominantly affects children and young adults and has no effective therapy. ONC201 is a first-in-class orally administered, anti-cancer small molecule that selectively antagonizes the dopamine receptors DRD2/DRD3 and agonizes ClpP, a mitochondrial protease. Prior studies have indicated dysregulated dopamine receptor expression and enhanced ONC201 sensitivity among H3 K27M-mutant gliomas. **Methods:** Adults with midline H3 K27M-mutant glioma patients were enrolled to a dedicated Phase II clinical trial (NCT03295396), a multi-arm Phase II clinical trial (NCT02525692), and expanded access protocols under the Sponsor's IND. Results were pooled among patients treated with ONC201 monotherapy through any of these trial with H3 K27M confirmed glioma, progressive and measurable disease by RANO, > 90 days from completion of prior radiation, no evidence of leptomeningeal dissemination, midline location other than primarily pons or spinal cord, and baseline KPS > 60. Using an enrollment cutoff of February 15, 2019 and data cutoff of July 31, 2019, there were 20 patients (NCT03295396, 12; NCT02525692, 7; expanded access, 1). Dosage was 625 mg weekly in 19 and once every 3 weeks in 1. **Results:** No DLTs or treatment discontinuations due to toxicity occurred. Midline gliomas can exhibit minimal contrast enhancement or exhibit a mixture of contrast-enhancing and non-contrast enhancing regions in the tumor. As a result, blinded independent central review (BICR) of tumor response by MRI was assessed by RANO-HGG and RANO-LGG for each patient to capture contrast-enhancing lesions by T1 post-contrast and non-contrast-enhancing assessments by T2/FLAIR, respectively, in the object response rate. The best response by RANO-HGG or RANO-LGG is 30% (95% CI, 11.9-54.3%). Duration of response by RANO-HGG is median 52.7 weeks (range 15.9-138.3). One patient with stable disease as of this data cutoff has continued on treatment beyond 12 months and recently underwent an investigator-reported PR by RANO-HGG that is pending confirmation. **Conclusions:** Single agent ONC201 is well tolerated and clinically active in recurrent H3 K27M-mutant diffuse midline glioma patients. Clinical trial information: NCT03295396, NCT02525692. Research Sponsor: U.S. National Institutes of Health.

3616 Poster Session (Board #346), Fri, 8:00 AM-11:00 AM

The next-generation RET inhibitor TPX-0046 is active in drug-resistant and naïve RET-driven cancer models. *First Author: Alexander E. Drilon, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: *RET* fusions/mutations drive oncogenesis in lung and thyroid cancers, and several other malignancies. Selective RET inhibitors (selpercatinib/pralsetinib) are active in patients with these cancers; unfortunately, resistance often occurs. On-target resistance includes the acquisition of solvent front mutations (SFMs i.e. *RET* G810 substitutions). TPX-0046 is a structurally differentiated RET inhibitor that is potent against a range of RET fusions and mutations including SFMs. **Methods:** The rationally-designed, compact, macrocyclic RET/SRC inhibitor TPX-0046 was characterized in RET-driven *in vitro* and *in vivo* tumor models. **Results:** In enzymatic assays, TPX-0046 showed low nanomolar potency against wild-type RET and 18 *RET* mutations/fusions. It was potent against SRC and spared VEGFR2/KDR. TPX-0046 inhibited RET phosphorylation ($IC_{50} < 10$ nM) in tumor cell lines (LC2/ad, *CCDC6-RET*; TT, *RET* C634W) and Ba/F3 engineered RET models (WT, G810R). In cell proliferation assays, TPX-0046 inhibited *KIF5B-RET* Ba/F3, LC2/ad, and TT cells with IC_{50} values ~1 nM. Ba/F3 RET engineered cells with SFMs (e.g. G810C/R/S) were potently inhibited by TPX-0046 (mean proliferation IC_{50} 1–17 nM). TPX-0046 demonstrated marked *in vivo* anti-tumor efficacy in RET-driven cell-derived and patient-derived xenograft tumor models. In a Ba/F3 *KIF5B-RET* xenograft model, a single dose of 5 mg/kg TPX-0046 inhibited > 80% of RET phosphorylation (corresponding mean free plasma concentration: 51 nM). At 5 mg/kg BID, tumor regression was observed in RET-dependent xenograft models, including those that harbor RET SFMs: TT, CTG-0838 PDX (NSCLC, *KIF5B-RET)*, CR1520 PDX (CRC, *NCOA4-RET*), Ba/F3 *KIF5B-RET*, and Ba/F3 *KIF5B-RET* G810R. **Conclusions:** TPX-0046 is a unique next-generation RET inhibitor that possesses potent *in vitro* and *in vivo* activity against a diverse range of *RET* alterations, including SFM-mediated resistance. A phase 1/2 trial for RET inhibitor-resistant and naïve RET-driven cancers is on-going (NCT04161391). Research Sponsor: Turning Point Therapeutics.

3617 Poster Session (Board #347), Fri, 8:00 AM-11:00 AM

Clinical efficacy of ONC201 in thalamic H3 K27M-mutant glioma. *First Author: Abed Rahman Kawakibi, Michigan Medicine, Ann Arbor, MI*

Background: Diffuse midline gliomas, H3 K27M-mutant are associated with a poor prognosis compared to H3 wild-type gliomas and have no effective therapy following first-line radiation. ONC201 is a bitopic DRD2 antagonist and allosteric ClpP agonist that has shown encouraging single agent efficacy in recurrent H3 K27M-mutant gliomas located in various midline structures of the brain. In addition to tumor and immune cells, the pharmacodynamics of ONC201 extend to stromal cells that can mediate a bystander antitumor response in preclinical models. Given this observation and that the thalamus has the highest extrastriatal expression of DRD2, we report the clinical experience of ONC201 in a subgroup of H3 K27M-mutant glioma patients with primary tumors located in the thalamus. **Methods:** We analyzed 29 thalamic H3 K27M-mutant glioma patients treated with ONC201 in clinical trials enrolled as of 5/22/19. Nineteen enrolled with recurrent disease whereas 10 enrolled following radiation prior to recurrence. Twelve patients enrolled on NCT03295396, 10 NCT03416530, 4 NCT02525692, and 3 expanded access. Median age was 22 years old (range: 5-70) and baseline KPS was 80 (range: 60-90). Median time from radiation to start of ONC201 was 1.8 months (range: 0.2-8.7) for non-recurrent patients and 7.2 months (range: 1.4-102.0) for recurrent patients. **Results:** As of 12/18/2019, PFS6 and OS12 measured relative to initiation of ONC201 are 26.3% and 36.8%, respectively, in the recurrent group. For patients initiating ONC201 post-radiation prior to recurrence, median PFS or OS have not been reached with a median follow up of 21.9 months (8.6-26.6) from diagnosis, which surpass historical OS of 13.5 months. Best response for evaluable recurrent patients by RANO: 1 CR, 3 PR, 4 SD, 8 PD, 3 not reported; for non-recurrent patients: 2 PR, 4 SD, 1 PD, 3 not reported. Median duration of response for recurrent patients is 14.0 months (2.0-33.1). ONC201 was well tolerated and no dose-limiting toxicities or treatment discontinuations due to toxicity occurred. Furthermore, H3 K27M cell-free tumor DNA in plasma and CSF correlated with MRI response. **Conclusions:** In summary, single agent ONC201 administered at recurrence or following radiation, demonstrates promising clinical efficacy in thalamic H3 K27M-mutant glioma patients. Investigations are ongoing to assess whether micro-environmental DRD2 expression correlates with responses of thalamic H3 K27M-mutant glioma to ONC201. Clinical trial information: NCT03295396, NCT03416530, NCT02525692. Research Sponsor: None.

3618 Poster Session (Board #348), Fri, 8:00 AM-11:00 AM

BET inhibitor molibresib for the treatment of advanced solid tumors: Final results from an open-label phase I/II study. *First Author: Sophie Cousin, Medical Oncology, Institute Bergonié, Bordeaux, France*

Background: Molibresib is an orally available, small molecule bromodomain and extra-terminal domain (BET) protein inhibitor under investigation for treatment of advanced solid tumors. **Methods:** This was an open-label, single- and repeat-dose, 2-part, Phase 1/2 study including patients (aged ≥16 years) with advanced solid tumors. Part 1: patients received different oral doses of molibresib (2–100mg QD; amorphous free-base formulation) to determine recommended Phase 2 dose. Part 2 (expansion cohort): patients with various tumor types received the bioequivalent besylate formulation (75mg) to explore clinical activity at recommended dose. Safety and efficacy (response rate [RR] based on RECIST 1.1 criteria, progression-free survival [PFS], and overall survival [OS]) were evaluated for the total cohort (patients from Part 1 and 2). Safety, pharmacokinetic, pharmacodynamic, and efficacy per tumor type were evaluated in Part 2. **Results:** Part 1 only data have previously been reported. Overall, 196 patients were included in the total cohort (1 patient in Part 1 was counted twice). In the all treated population, 195 patients (median age 58 years; 46% male) received ≥1 dose of molibresib (Part 1: n = 93; Part 2: n = 102). Adverse events (AEs) were experienced by 193/196 (98%) patients; 180/196 (92%) had a treatment-related AE (TRAE). AEs led to permanent treatment discontinuation in 38/196 (19%) patients. Of different tumor types in Part 2, NUT carcinoma (NC) had the lowest frequency of TRAEs (10/12 [83%]) and AEs leading to permanent treatment discontinuation (1/12 [8%]). In total cohort, 3/31 NC patients and 1/35 with castration-resistant prostate cancer (CRPC) achieved a confirmed partial response. A further 67/196 (34%) achieved stable disease (SD). In Part 2, RR in 12 NC patients was 8% (CI: 0.2–38.5); 50% had SD and median PFS was 4.8 months with median OS of 5.0 months. In CRPC patients, RR was 4% (CI: 0.1–21.9); 22% had SD; median PFS was 8.0 months with median OS of 9.1 months. Plasma concentrations for molibresib and active metabolites were similar between different tumor types. Gene expression analysis from pre- and post-dose biopsy samples collected from 10 mCRPC patients showed transcriptional downregulation of Myc target genes upon treatment with molibresib. **Conclusions:** Molibresib demonstrated a manageable safety and tolerability profile with single agent activity observed in selected patients with NC and CRPC. Clinical trial information: NCT01587703. Research Sponsor: GSK, Other Foundation.

3619 Poster Session (Board #349), Fri, 8:00 AM-11:00 AM

ONC201 in previously irradiated pediatric H3 K27M-mutant glioma or newly diagnosed DIPG. *First Author: Sharon L. Gardner, New York University School of Medicine, New York, NY*

Background: ONC201 is a first-in-class DRD2 antagonist and ClpP agonist that has demonstrated promising activity in high-grade glioma preclinical models and radiographic regressions with single agent ONC201 in recurrent H3 K27M-mutant glioma patients . The recommended phase 2 dose (RP2D) of 625mg ONC201 orally once a week has been established in adult patients as well tolerated and biologically active. ONC201 efficacy has been shown in high-grade glioma preclinical models and radiographic regressions with single agent ONC201 have been reported in adult recurrent H3 K27M-mutant glioma patients. We report results from the first Phase I pediatric clinical trial of ONC201. **Methods:** This open-label, multi-center trial for pediatric H3 K27M-mutant glioma or non-biopsied DIPG employed a 3+3 dose-escalation and dose-expansion design with 6 arms. Arms A and E, which have completed accrual, determined the RP2D of ONC201 using oral capsule and liquid formulations in post-radiation pediatric H3 K27M-mutant glioma patients ONC201, respectively. Arm B aims to determine the RP2D for ONC201 in combination with radiotherapy in patients with newly diagnosed DIPG. Arms C and D aim to measure intratumoral ONC201 concentrations in midline glioma patients and the impact of ONC201 on H3 K27M DNA levels in CSF, respectively. Arm F was recently opened to study ONC201 as a single agent in patients with progressive H3 K27M-mutant tumors (excluding DIPG and spinal cord tumors) following radiotherapy. After determining the RP2D, a dose-expansion cohort will evaluate the safety, radiographic response, and activity of ONC201. **Results:** An RP2D of weekly 625mg ONC201 scaled by body weight as a capsule or in liquid formulation was established in the primary endpoints of arms A, B and E alone or in combination with radiation, without incidence of dose-limiting toxicity (DLT). Pharmacokinetic profiles were similar to those observed in adults ($T_{1/2}$: 8.4h; T_{max}: 2.1h; C_{max}: 2.3ug/mL; $AUC_{0\text{-tlast}}$: 16.4ug/mL), with similar exposure across body weights. **Conclusions:** ONC201 was well tolerated without DLTs at the same adult RP2D scaled by body weight as monotherapy or in combination with radiotherapy in pediatric H3 K27M-mutant glioma patients. Further investigation of ONC201 to treat H3 K27M-mutant glioma and DIPG is warranted. Clinical trial information: NCT03416530. Research Sponsor: U.S. National Institutes of Health.

3620 Poster Session (Board #350), Fri, 8:00 AM-11:00 AM

Pan-cancer analysis of FGFR1-3 genomic alterations to reveal a complex molecular landscape. *First Author: Melanie A. Krook, The Ohio State University Comprehensive Cancer Center, Ohio State University, Columbus, OH*

Background: Activating genomic alterations (GAs) in the fibroblast growth factor receptor (FGFR) gene family occur in many tumor types. *FGFR1-3* mutations and rearrangements are of particular interest given evidence of clinical activity of selective FGFR inhibitors in patients (pts) with susceptible alterations. We queried *FGFR1-3* GAs in patient tumor samples analyzed using comprehensive genomic profiling (CGP) and performed *in vitro* characterization of select novel alterations. **Methods:** Tumor samples were assayed by hybrid capture based CGP on 0.8-1.2 Mb of the genome to identify GAs in exons and select introns in up to 404 genes (Foundation Medicine, Inc, Cambridge MA). Cell lines were stably transduced with alterations of interest and transformation assays and drug sensitivity assays were performed to determine oncogenic potential and sensitivity to FGFR inhibition by pemigatinib. **Results:** GAs in *FGFR1-3* were present in 6314 of 274,694 pt specimens (2.3%), of which 4091 (64.8%) were short variants and 2269 (35.9%) were rearrangements. Tumor types with the highest frequency of *FGFR1-3* alterations were bladder cancer (17.9%), cholangiocarcinoma (11.1%), endometrial cancer (7.9%), and glioma (5.5%) (Table). We identified 270 unique *FGFR1-3* short-variants, including 144 missense mutations and 94 truncating alterations. Of short variants, the most frequent were *FGFR3* p.S249C (18.3%), *FGFR2* p.S252W (9.9%) and *FGFR1* p.N546K (6.9%). Truncating alterations were largely identified in exon 18, downstream of the kinase domain. We identified 476 unique *FGFR1-3* rearrangement pairs (*FGFR1*; n=77, *FGFR2*; n=338, *FGFR3*; n=61). *FGFR3-TACC3* was the most prevalent *FGFR* rearrangement (29.0%), followed by *FGFR2-BICC1* and *FGFR2*-N/A (both 9.7%). *In vitro* analysis of the transforming potential and drug sensitivity for select alterations will be reported. **Conclusions:** *FGFR1-3* mutations and rearrangements are highly diverse and present at low to moderate frequencies across many cancers. Therefore, cataloging and characterizing these diverse alterations has the potential to facilitate precision medicine. Tumor-specific and -agnostic trials of selective FGFR inhibitors in pts with susceptible alterations are ongoing. Research Sponsor: Incyte Corporation.

Disease Group	Pts, n	Short Variant, %	Rearrangement, %	Total, %
Bladder	4338	14.6	3.6	17.9
Cholangiocarcinoma	4826	1.9	9.4	11.1
Endometrial	7055	7.4	0.5	7.9
Glioma	10072	2.7	2.8	5.5
Cancer of unknown primary	13989	2.2	2.2	4.4
Kidney	4687	3.2	0.8	3.9
Cervix	2008	2.4	1.7	3.9
Head and neck	4210	2.3	0.7	3.0
Melanoma	7097	2.2	0.1	2.3
Plasma cell neoplasm	2530	1.9	0.2	2.1

3621 Poster Session (Board #351), Fri, 8:00 AM-11:00 AM

Identifying pan-cancer transcriptomic determinants of perineural and lymphovascular invasion using machine learning. *First Author: Jimmy Guo, Broad Institute, Cambridge, MA*

Background: Tumor invasion of nerves, blood vessels, and lymphatics are a primary means of local recurrence and escape from the local microenvironment, resulting in metastases and poor clinical outcomes. However, the genetic drivers that are most pertinent to these malignant processes are not well understood, and few therapeutics successfully target perineural invasion (PNI) and lympho-vascular invasion (LVI). Identifying genetic drivers and biomarkers can be valuable for therapeutic targeting and prognostication. **Methods:** We analyzed surgical pathology reports and bulk RNA-seq data of 1,624 patients across 12 cancer types from The Cancer Genome Atlas (TCGA). Differential gene expression analysis between patients with and without PNI/LVI was performed using DEseq2 in Python while adjusting for age, sex, race, and cancer type. Genes with an adjusted p-value < 0.001 were then used to derive parsimonious signatures using random forest classifier and recursive feature selection algorithms. **Results:** To assess whether these invasive histological phenotypes have clinical ramifications, we examined outcomes data and found that patients with PNI or LVI have reduced overall (OS) and disease-free survival (DFS) ($p < 0.05$) relative to those without. In addition, patients with both PNI and LVI have the lowest DFS from our pan-cancer analysis, suggesting that each may have non-redundant contributions to poor outcomes. From the differential gene expression analysis, we identified a set of 621 and 606 genes that were highly associated with PNI and LVI, respectively ($p_{adj} < 0.001$). Many of these genes such as TEKT5 ($p_{adj} = 3.18 \times 10^{-64}$), which is canonically associated with ciliary and flagellar microtubules, and SCRIB ($p_{adj} = 1.60 \times 10^{-21}$), which helps establish apico-basal cell polarity, have not been described previously in relevance to PNI and LVI, and warrant further scientific and clinical investigation. These genes were ultimately condensed into a signature that optimizes for both model simplicity and goodness of fit with up to 90% accuracy as determined by trials on both a logistic regression and neural network model. **Conclusions:** We concluded from a pan-cancer analysis that PNI and LVI are associated with poor outcomes, and we were able to robustly identify sets of genes that characterize each invasive mechanism for further functional investigation. Research Sponsor: None.

3622 Poster Session (Board #352), Fri, 8:00 AM-11:00 AM

Increased tumor purity and improved biomarker detection using precision needle punch enrichment of pathology specimen paraffin blocks: Method validation and implementation in a prospective clinical trial. *First Author: Jonathan Keith Killian, Foundation Medicine, Cambridge, MA*

Background: While many sequencing assays may be geared for short variants (SV), more complex biomarkers such as genomic loss of heterozygosity (gLOH) score, also referred to as homologous recombination deficiency (HRD) score, require higher tumor purity for confident detection. Practical methods to increase tumor nuclei percentage (TN%) from pathology specimens are needed to achieve biomarker results to maximize patient matching to approved therapies and/or clinical trial enrollment. **Methods:** Tumor purity of specimens was determined by the computational analysis pipeline component of the FDA-approved NGS assay, FoundationOneCDx. In the validation study, specimen purities for each tissue block were compared following either no enrichment (UnE, n=46), pathologist-directed enrichment by straight razor blade (RBE, n=30) or precision needle punch (NPE, n=47). Post-enrichment H&E slides confirmed target region sampled for the NPE arm. Based upon validation data, the needle punch process was implemented for the Lung-MAP prospective clinical trial (LM-NPE). TN% was compared between the first 55 tested LM-NPE specimens and the validation study to assess performance on real-world samples outside of a controlled validation experiment. **Results:** The mean computational TN% in the 4 groups were: UnE: 33%; RBE: 30%; NPE: 52%; and LM-NPE: 48%. In the validation study, NPE had significantly higher purity than both UnE and RBE ($p<0.001$); in the trial arm, LM-NPE performed equivalently to NPE ($p=0.344$). Based upon a 30% tumor purity cutoff, gLOH could be determined for 52% UnE, 50% RBE, 89% NPE and 71% LM-NPE. Comparing NPE and LM-NPE groups reveals no statistical difference in Pass/Fail rates for gLOH determination ($p=0.883$; Fisher's Test). **Conclusions:** Precision needle punch cores from tissue blocks have elevated tumor purity, and consequently, a greater number of successful gLOH determinations. Moreover, this process is rapid and inexpensive. Precision punches may constitute best practice with respect to enriching tumor cells from low-purity specimens for biomarker detection in a routine laboratory specimen-processing setting. Research Sponsor: Foundation Medicine Inc.

Comparison	p-value Abs tumor purity	p-value gLOH Pass rate	Abs Diff in mean tumor purity	Abs Diff in gLOH Pass Rate
UnE (n=46) vs RBE (n=30)	0.491	0.853	3%	2%
UnE (n=46) vs NPE (n=47)	<0.001	<0.001	19%	37%
RBE (n=30) vs NPE (n=47)	<0.001	<0.001	22%	39%
LM-NPE (n=55) vs NPE (n=47)	0.344	0.883	4%	18%

3623 Poster Session (Board #353), Fri, 8:00 AM-11:00 AM

Targeting G1-S phase cell-cycle alterations with CDK4/6 inhibitor-based genomically matched personalized therapy approach. *First Author: Jacob J. Adashek, University of South Florida, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL*

Background: Although CDK4/6 inhibitors are established as a standard treatment option for hormone receptor-positive, HER2-negative metastatic breast cancer patients, its benefit in other solid tumors is unclear. Moreover, no clear biomarker exists that predicts the response to CDK4/6 inhibitors. Herein, we investigated the factors associated with clinical outcomes from CDK4/6 inhibitor-based therapy, used alone or in combination with other therapies targeting genomic co-alterations, among diverse cancer patients with potentially sensitizing alterations in G1-S phase cell-cycle alterations (defined as *CDK4/6* amplifications, *CCND1/2/3* amplifications or *CDKN2A/B* alterations). **Methods:** We interrogated molecular profiles of 2,457 patients with diverse solid tumors for G1-S phase cell-cycle alterations and co-altered genes using clinical-grade next generation sequencing (182-465 genes). **Results:** G1-S phase cell-cycle alterations occurred in 20.6% (507/2,457) of patients with 99% of those with cell cycle alterations (N = 501/507) harboring at least one characterized co-alteration (median, 4; range, 0-24). Significant improvement in median PFS was observed when CDK4/6 inhibitor-based therapies matched a larger proportion of tumor alterations, often by being given together with other drugs that were matched to genomic co-alterations, hence achieving a high Matching Score (high Matching Score [≥50%] vs. low Matching Score [< 50%]: all cohorts including breast cancer [N = 58]: PFS: 6.2 vs. 3.2 months, P = 0.001; non-breast cancer cohort [N = 40]: PFS 6.2 vs. 2.0 months, P < 0.001 [multivariate]). (Matching Score roughly equivalent to number of alterations targeted divided by total number of characterized alterations). In contrast, targeting CDK4/6 alone in patients harboring cell-cycle pathway alterations along with other co-alterations, without targeting the genomic co-alterations, did not improve PFS even in patients who received matched CDK4/6 inhibitors as part of a combination regimen. Representative cases that were successfully treated with a matched combination strategy will also be presented. **Conclusions:** Most patients with G1-S phase cell-cycle alterations harbored co-genomic alterations. Our current study suggests that targeting co-alterations along with cell cycle molecular alterations may be necessary to achieve better clinical outcome. Further clinical investigation with larger numbers of patients are required. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

3624 Poster Session (Board #354), Fri, 8:00 AM-11:00 AM

Tumor genomic analysis for biomarker identification in a phase I trial of the Wee 1 inhibitor adavosertib (AZD1775). *First Author: Abdul Rafeh Naqash, Developmental Therapeutics Clinic/Early Clinical Trials Development Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, Bethesda, MD*

Background: Adavosertib, a first-in-class Wee1 kinase inhibitor, abrogates G2/M cell cycle arrest causing premature mitosis and DNA replication stress, yielding enhanced DNA damage. Here we report on potential biomarkers of response from tumor genomic analysis in patients (pts) with solid tumors treated with adavosertib. **Methods:** Adavosertib was administered once daily on days 1-5 and 8-12 of a 21-day cycle. RECIST 1.1 was used to evaluate clinical response. Paired tumor biopsies were obtained for RNASeq gene expression profiling (GEP) and for whole-exome sequencing (WES) to evaluate gene mutation and copy number amplification (CNA). Fold change (FC) was calculated to define gene overexpression. To identify the frequency of CNA and mRNA overexpression for the genomic biomarkers of interest, cBioPortal analysis using TCGA and MSK-IMPACT datasets was performed. Differential GEP analysis of tumor and paired normal tissue was performed using the gene expression profiling interactive analysis (GEPIA) interface (Tang et al. 2017). **Results:** Out of 35 pts evaluable for response, 6 (17%) had partial response (PR; 4 ovarian carcinoma [OVC], 2 endometrial carcinoma [EC]). The median duration of response was 5.2 months (range 4.0-23.1). Eighteen pts (51.4%) had stable disease. Genomic analysis of tumor biopsies was available for 9 pts; 7 of these pts were evaluable for response, and 3 had PR (2 OVC, 1 EC). WES revealed TP53 mutations in 6 pts (66.6%; 3 pts with PR, 2 with progressive disease,1 not evaluable). On WES, tumor Cyclin E1 (*CCNE1*) CNA was present in 1 of 3 PR pts while tumors from all 3 PR samples showed relatively high *CCNE1* expression by RNAseq (FC = 4.07). In the MSK-IMPACT 2017 dataset, *CCNE1* CNA was identified in 1.8% of pts (194 of 10336); of which, OVC (10.3%) and EC (8.7%) had the highest incidence of *CCNE1* CNAs. In separate tumor-specific (OVC, EC) TCGA datasets having *CCNE1* overexpression and/or CNA, overlap in *CCNE1* overexpression with *CCNE1* CNA was 35.5% (OVC) and 25.2% (EC). Compared to normal ovarian/ endometrial tissues, GEPIA analysis revealed significantly higher *CCNE1* mRNA expression in OVC (FC = 3.5) and EC (FC = 3.8). **Conclusions:** *CCNE1*alterations (overexpression and/or CNA) tend to be enriched in OVC and EC with a limited fraction showing both overexpression and CNA. Tumor genomic analysis of additional OVC and EC pts treated with adavosertib is required to determine whether *CCNE1* mRNA overexpression, regardless of *CCNE1* CNA, is a potential biomarker of response to this drug in these tumor types. Funded by NCI contract No. HHSN261200800001E. Clinical trial information: NCT01748825. Research Sponsor: U.S. National Institutes of Health, Funded by NCI contract No. HHSN261200800001E.

3625 Poster Session (Board #355), Fri, 8:00 AM-11:00 AM

Therapeutic vulnerabilities among KRAS G12C mutant (mut) advanced cancers based on co-alteration (co-alt) patterns. *First Author: Maliha Nusrat, Gastrointestinal Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Oncogenic *KRAS* mut drive cancers and confer therapeutic resistance by activating MAPK signaling. Inhibiting *KRAS* has been elusive until the recent promising phase I trials with KRAS G12C inhibitors (i). We characterized frequencies of *KRAS* G12C mut and gene co-alt among advanced cancer patients (pts) to identify therapeutic vulnerabilities for combination development. **Methods:** We analyzed next generation sequencing datasets from MD Anderson Cancer Center (MDACC, n = 42,316) and AACR GENIE (n = 56,970). Genes and individual alterations were annotated for potential actionability with approved or investigational drugs and grouped into 12 oncogenic pathways. Frequencies of potential drug combinations with KRAS G12Ci were estimated per tumor type based on co-occurrence of potentially actionable alterations. **Results:** *KRAS* G12C was present in 850/34,801 (2.4%) advanced solid tumor and 22/7698 (0.3%) hematologic malignancy pts in MDACC dataset; and 1422 (2.5%) pts in AACR GENIE. Among solid tumor pts, 798 had histology data and 640 had ≥46 gene profiling. Most common cancers were non-small cell lung (NSCLC, 67%), colorectal (CRC, 24%), other gastrointestinal (oGI, 4%) and gynecologic (gyn, 2%). KRAS G12C prevalence was 19.5% (441/2265) in NSCLC and 4.2% (146/3469) in CRC. Genes most commonly co-altered were *TP53* (42%), *STK11* (17%) and *MET* (11%) in NSCLC; *TP53* (58%), *APC* (54%) and *PIK3CA* (24%) in CRC; *TP53* (42%), *APC* (21%) and *ATM* (21%) in oGI; *TP53* (56%), *PIK3CA* (25%), and *PTEN* (19%) in gyn cancers. These co-alt did not impact overall survival. In both datasets, as compared to *KRAS* wild, *KRAS* G12C was significantly co-altered with *STK11* in NSCLC; *PIK3CA* and *SMAD4* in CRC ($P < 0.05$ for all). *EGFR* mut in NSCLC and *BRAF* mut in CRC rarely co-occurred with *KRAS* G12C ($P < 0.01$). Most frequently co-altered oncogenic pathways in NSCLC, CRC, oGI and gyn cancers respectively included PI3K (27, 32, 33, 44 %), receptor tyrosine kinases (13, 16, 42, 13 %) and DNA damage repair (12, 10, 38, 19 %). Potentially actionable co-alt frequencies suggest that combining KRAS G12Ci with mTORi or PI3Ki would be indicated most frequently, in 24% and 13% of all pts respectively. **Conclusions:** KRAS G12Ci development is most relevant for NSCLC, gastrointestinal and gyn cancers. The co-alt patterns highlight relevant oncogenic pathways and candidate drugs for future combination therapies. Co-inhibition of PI3K-mTOR and MAPK pathways has shown synergism in prior pre-clinical studies but had poor tolerance in pts. There is opportunity to revisit this approach with the new KRAS G12Ci. Research Sponsor: Cancer Prevention Research Institutive of Texas (CPRIT) Precision Oncology Decision Support Core RP150535.

3626 Poster Session (Board #356), Fri, 8:00 AM-11:00 AM

The landscape of predictive biomarkers for ATR inhibition in Chinese solid-tumor patients. *First Author: Rong Shen, Department of Chemotherapy, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, China*

Background: Ataxia Telangiectasia and Rad3-related (ATR) is one of the core regulators participating in DNA damage response as a sensor of replication stress. Besides, ATR also plays a role in cell cycle checkpoint activation and DNA replication regulation. Several ATR inhibitors (ATRi) have been demonstrated in anti-cancer clinical trials. Herein, we describe the distribution of selected biomarkers, which have been shown to predict a higher sensitivity to ATRi according to preclinical data, in Chinese cancer population. **Methods:** FFPE tumor tissues and matched blood samples from 10,194 Chinese patients with 25 different types of solid tumors were collected. NGS based 450 cancer genes panel assay were performed to detect genomic alterations, including SNV, short and long insertions/deletions, CNV and rearrangements/fusions. The testing was carried out by a CAP accredited and CLIA certified laboratory. **Results:** The prevalence of *ARID1A* mutations, *ATM* mutations, *BRCA1/BRCA2* mutations, *MYC* amplification, and *CCNE1* amplification accounted for 9.5%, 4.7%, 6.0%, 3.5% and 3.3% of this cohort respectively. The most common tumors with *ARID1A* mutations were endometrial carcinoma (EC, 34.4%), gastric carcinoma (GC, 19.4%), small bowel carcinoma (SBC, 19.3%), intrahepatic cholangiocarcinoma (19.3%), extrahepatic cholangiocarcinoma (17.7%) and urothelial carcinoma (UC, 16.7%). For *ATM* mutations, the prevalence was colorectal carcinoma (CRC, 8.9%), SBC (8.8%), pancreatic cancer (7.8%), UC (7.3%), gallbladder carcinoma (GBC, 7.1%) and GC (6.8%). For *BRCA1/BRCA2* mutations, the prevalence was ovarian carcinoma (29.5%, Germline 23%), breast carcinoma (13.3%, Germline 7.1%), EC (11.5%, Germline 3.3%), UC (10.4%), melanoma (8.5%) and CRC (7.9%). For *MYC* amplification, the prevalence was breast carcinoma (10.2%), ovarian carcinoma (9.2%), esophageal carcinoma (7.2%), thymic tumor (6.1%), cancer of unknown primary (CUP, 5.8%) and gastrointestinal neuroendocrine tumor (GI-NET, 5.4%). For *CCNE1* amplification, the prevalence was GC (11.9%), GBC (8.8%), bone sarcoma (7.7%), ovarian carcinoma (6.9%), CUP (4.2%) and GI-NET (4.1%). **Conclusions:** Our study reported the prevalence of gene mutations of ATRi sensitivity determinants in a large cohort of Chinese cancer patients. The results revealed the high prevalence and different distribution of these biomarkers across a wide spectrum of cancers. The genomic profile study also provided information for ATRi sensitivity assessment and the drug combinations with ATR inhibition. Research Sponsor: None.

3627 Poster Session (Board #357), Fri, 8:00 AM-11:00 AM

Modeling differentially expressed genes in patient tumors to guide expression-based biomarker development. *First Author: Derek Liu, Dana–Farber Cancer Institute, Boston, MA*

Background: Differential gene expression (DGE) methods, initially developed for analyzing bulk RNA changes in pure tumor cell lines under experimental settings, are commonly used to identify biomarkers in and infer biological differences between patient tumor samples, which are admixtures of tumor and non-tumor components. Methods to sensitively and accurately detect cell type-specific expression differences in admixed patient samples are not well characterized but may greatly affect emerging targeted and immunotherapy biomarker strategies. To address this issue, we developed a simulation framework to benchmark our ability to detect changes in tumor-intrinsic gene expression. **Methods:** Pseudobulk RNAseq melanoma cohorts were simulated by sampling from melanoma single cell RNAseq data. Simulation parameters were optimized to maximize concordance of gene expression means and variances (Spearman r = 0.81, 0.68, respectively) between the TCGA SKCM cohort (n = 462) and matched simulated cohort, and then validated in two independent melanoma cohorts (n = 42, 129; means Spearman r = 0.80, 0.78; variances Spearman r = 0.68, 0.63). Using this simulation framework, we benchmarked the effect of sample size, magnitude of differential expression, and differences in cell type proportions on the sensitivity and positive predictive value (PPV) of detecting true differentially expressed genes in the tumor-intrinsic compartment. **Results:** Reference cohorts of 50 total tumors (n = 10) were simulated to contain a 2 standard deviation tumor-intrinsic expression change in 50 randomly selected genes and a 11% difference in mean purity between two equally sized 25-tumor subgroups. DGE analysis using DESeq2 with an FDR q-value threshold of 0.1 yielded a sensitivity of 0.37 and PPV of 0.29. DGE analysis of the same simulated cohorts using a non-parametric Mann-Whitney U test with an FDR q-value threshold of 0.1 yielded a sensitivity of 0.13 and PPV of 0.76. **Conclusions:** Commonly used DGE methods for existing expression-based biomarker strategies have poor sensitivity and PPV in admixed tumor samples, limiting our ability to find meaningful transcriptional biomarkers in clinical cohorts. We are currently developing methods to more accurately detect true differentially expressed genes in admixed bulk RNAseq samples and applying these approaches for biomarker discovery in immunotherapy-treated patient cohorts and other clinical tumor cohorts. Research Sponsor: U.S. National Institutes of Health.

3628 Poster Session (Board #358), Fri, 8:00 AM-11:00 AM

Employing RNA sequencing to enhance treatment options for cancer patients. *First Author: Gargi D. Basu, Ashion Analytics, Phoenix, AZ*

Background: Fusions and translocations account for 20% of cancer mortality globally. Maximizing their detection enhances the utility of precision medicine for various solid and hematologic cancers. Practice guidelines stress the importance of RNA sequencing. Novel assay techniques employing a comprehensive genomic profiling approach, including RNA sequencing, yield information beyond conventional DNA next generation sequencing (NGS) alone. **Methods:** Tumor samples (N = 1517) were assayed combining whole transcriptome (RNA) sequencing, whole exome (DNA) sequencing, and comparison of tumor sequence vs. paired normal DNA. Results were analyzed to determine the frequency of rare and common RNA fusion and variant detection. Findings were mapped to a knowledge-base of targeted treatment options. **Results:** Analysis detected 79 (5.2%) actionable fusions and 15 (1%) transcript variants across major solid and heme-based malignancies. Notably, we observed actionable transcript variants that are not detectable at the DNA level including: EGFRvIII, EGFRvIVa and EGFRvIVb in GBM; ARv7 in prostate, and METe14 in TNBC. Many fusion cases (42%, n = 33) had no other actionable molecular abnormalities. Novel fusions included: SLC12A/ROS1 in low-grade spindle cell neoplasm with myogenic differentiation, KANK1/NTRK2 in ganglioneuroblastoma, ETV6/NTRK3 in metastatic mammary analogue secretory carcinoma, FGFR1/SCT in germ cell tumor, ZNF33B/RET fusion in GBM, SH3BP4/ERBB4 and EML4/ALK in RCC, VTCN1/NRG1 in pancreatic cancer, and AGRN/NRG1 in cholangiocarcinoma. More common actionable fusion events included: EML4/ALK in NSCLC, KIAA1549/BRAF in pilocytic astrocytoma, FGFR2 and FGFR3 in cholangiocarcinoma and urothelial cancers and ESR1 in endocrine therapy-resistant breast cancers. The fusion events detected in heme-based malignancies included MLLT10 and MLLT4 in AML, BCR/ABL in leukemias, TCF3/PBX1 in B cell ALL, NPM1/ALK in ALCL, and novel fusion CIITA/CD274 in DLBCL. All RNA fusions and transcript variants found were matched to FDA-approved or investigational treatment options. **Conclusions:** Maximizing the rate of variant detection for targeted therapy relies on precise identification of common and rare fusion events. Without the addition of RNA sequencing, 15 transcript variants in our cohort would have been missed and 33 of the fusions may have gone undetected by conventional DNA NGS testing, resulting in zero targeted treatment options for this vulnerable population. Further use of comprehensive genomic profiling is vital to optimizing cancer care. Research Sponsor: None.

3629 Poster Session (Board #359), Fri, 8:00 AM-11:00 AM

Identifying functional loss of *ATM* gene in patients with advanced cancer. *First Author: Patrick Glen Pilie, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: *ATM* is frequently mutated in cancer, and defects may serve as a putative predictive biomarker. However, the functional impact of most *ATM* variants is not well known. In this study, we examined the relationship between *ATM* variants and ATM protein expression to better discern ATM functional defects in patients (pts) with advanced cancer. **Methods:** We retrospectively identified pts seen at MD Anderson Cancer Center who had *ATM* variants detected on CLIA-certified next generation sequencing (NGS) assays. ATM immunohistochemistry (IHC) was performed on available tumors. We then prospectively assessed ATM IHC on tumors from pts who were referred for DNA damage repair inhibitor (DDRi) trials. Functional classification of the variants was performed via published in silico tools and/or precision oncology decision support (PODS). An IHC cut-off of 100% loss in tumor cell nuclei defined ATM loss of protein (LOP). **Results:** Of 1394 *ATM*-mutant tumors identified retrospectively, *ATM* alterations were classified as 16% (N = 216) inactivating, 12% (N = 163) potentially inactivating, 71% (N = 993) variant of unknown significance (VUS), and 2% (N = 22) benign. Coding variants were seen across the *ATM* exonic structure/splice sites, and 20 individual variants were shared in > 10 pts. 263/297 available retrospective tumor samples had interpretable IHC results; 27% (N = 72) had ATM LOP. LOP was most prevalent in tumors with inactivating *ATM* variants (39/100, 39%); but, importantly, LOP was seen in 20% (N = 33/162) of potentially inactivating/VUS, thus better clarifying their functional impact. In the prospective cohort of 217 pt tumors, 17% (N = 37) had ATM LOP. 29% (N = 62/217) of this cohort also had *ATM* variants. ATM LOP was seen in 48% of tumors with inactivating variants (N = 14/29), 25% of tumors with potentially/VUS(N = 9/36), and 9% (N = 14/156) of tumors without *ATM* variants identified. ATM LOP was detected most commonly in colorectal (24%; N = 8/34), cholangiocarcinoma (20%; N = 6/30), prostate (16%; N = 16/104) and pancreatic (9%; N = 1/11) cancers among this cohort of pts referred for DDRi trials. **Conclusions:** *ATM* coding variants occurred across the gene, with certain variants shared across tumor types. The functional impact of most *ATM* variants was VUS, and ATM LOP can help clarify function in up to 25% of these VUS. Also, ATM LOP can be seen even in tumors without *ATM* variants identified, suggesting epigenetic or post-translational loss. Future prospective studies assessing predictive capability of paired DNA and protein-level profiling of ATM are warranted. Research Sponsor: MD Anderson internal departmental funding.

3630 Poster Session (Board #360), Fri, 8:00 AM-11:00 AM

Predictive value of a CLIA-approved organoid based drug sensitivity test. *First Author: Astrid Margossian, Sengine Precision Medicine, Seattle, WA*

Background: Precision medicine integrates genetic, molecular, and clinical information to optimize therapy selection for cancer patients. *Ex vivo* drug testing has the potential to match the right drug to the right patient. We developed a CLIA-certified functional drug assay for all solid tumors which provides an actionable report of organoid sensitivity to targeted, endocrine and chemotherapy agents as a tool for therapeutic decisions. Objectives: To establish the predictive power of the test in relation to well-known genomic biomarkers as well as prior treatments to identify drug sensitivity. To demonstrate that functional drug testing increases the actionability of genomic reports. **Methods:** From 2016 to 2019, 240 organoids from cancer patients were subjected to functional testing at SEngine Precision Medicine. Patients with advanced primary or metastatic cancer (solid tumors) who were treatment naïve or had previous therapies fail. Fresh samples of tumor cells from core biopsies, surgical excisions, or fluids arrived <48 hrs following collection and were cultured as 3D organoids. They were evaluated using a multi-dose response format with a library of up to 130 compounds. Drug sensitivity was quantified using a score that combines sensitivity and personalization of each patient's response relative to a reference population. Known genomic actionability from levels of evidence 1-2 from MSKCC OncoKB were queried against results for correlation. **Results:** Organoids were derived from breast (18.7%), ovarian (18.3%), colorectal (17.9%), pancreatic (6.7%), and others solid tumors (38,3%). Median age of patients was 53 (r5-83). 68 drugs on average were tested per patient with a mean turnaround time of 18 days (r9 -37). A mean of 7 drugs per patient were identified as top scoring drugs. In 75 patients with genomic data, we found high concordance of drug sensitivity with known genomic anchors (e.g., inhibitors of BRCA1/ PARP, ERBB2/HER2, FGFR1-2/FGFR, KRAS, PIK3CA/PI3K), measured as sensitivity to drugs among this targeted groups. However, several patient samples demonstrated sensitivity to targeted agents in the absence of known genomic biomarkers. Most important, analysis of previous treatments indicated >90% of retrospective concordance. **Conclusions:** Organoid based drug testing exhibits strong concordance with genomic and retrospective clinical evidence. In addition, functional testing identifies candidate therapies in patients with no known biomarkers and can identify the significance of variants currently not validated. Research Sponsor: Sengine Precision Medicine.

3631 Poster Session (Board #361), Fri, 8:00 AM-11:00 AM

Comprehensive molecular analysis of microsatellite-stable (MSS) tumors with high mutational burden in gastrointestinal (GI) cancers. *First Author: Jingyuan Wang, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA*

Background: Mutational signatures contributing to high tumor mutation burden (TMB-H) independent from microsatellite instability-high (MSI-H) status are not well-studied. We aimed to characterize specific molecular features of a large cohort of GI tumors with TMB-H & MSS. **Methods:** We sequenced23392 GI tumors, including 2707 gastroesophageal (GE), 11616 colorectal (CRC), and 9069 others. Samples were analyzed using Next-generation sequencing (NGS) and immunohistochemistry (IHC) (Caris Life Sciences, Phoenix, AZ). MMR/MSI status was evaluated by a combination of IHC, Fragment Analysis and NGS. Tumors with TMB ≥ 17 mutations/Mb were defined as TMB-H. PD-L1 was tested by IHC [22C3 (CPS score, positivity: CPS ≥ 1%) in GE tumors and SP142 (Positivity: TPS ≥ 5%) in other cancers]. Findings were compared in four groups (TMB-H/L & MSI-H/MSS) using Fisher-Exact or Chi-square and adjusted for multiple comparison by Benjamini-Hochberg. Significance was determined by adjusted (adj) $p < .05$. **Results:** Overall, TMB-H & MSS was observed in 1% of patients (pts) (n = 237, including 45 GE, 124 CRC, 68 others), while TMB-H & MSI-H, TMB-L & MSS, TMB-L & MSI-H were observed in 4% (n = 936), 94.4% (n = 22089) and 0.6% (n = 130) respectively. Compared to other groups, TMB-H & MSS showed the most prevalent amplifications (AMPs), including *CCND1* (5.6%), *FGF3/4/19* (4.9%, 4.3%, 4.4%), *MYC* (4.3%) (Top 5, adj $p < .05$), and the highest mutation rates in *POLE* (21.6%), *RB1* (13.1%), *CDC73* (10.3%), *RUNX1* (6.5%), and genes involved in PI3K & MAPK (*PIK3R1* 17%, *mTOR* 3.4%, *MAP2K1* 3.8%, *MAP2K4* 5.6%) and Wnt (*APC* 48.5%, *SMAD2* 6.5%, *TCF7L2* 3.8%) pathways (adj $p < .05$). The rates of HER2 AMP and high-expression (IHC) were the highest in TMB-H & MSS, followed by TMB-L & MSS, TMB-H & MSI-H, TMB-L & MSI-H (adj $p < .0001$); PD-L1 positive rate was similar between TMB-H & MSS and TMB-L & MSI-H, while the highest and lowest in TMB-H & MSI-H and TMB-L & MSS respectively in GE and other GI cancers (adj $p < .01$) (Table). **Conclusions:** This is the largest study to investigate the special molecular landscape of pts with TMB-H & MSS in GI cancers. Our data may provide novel insights for pt selection and more effective targeted combination immunotherapies (e.g. HER2, PI3K inhibitors) in GI cancers. Research Sponsor: National Cancer Institute (grant number P30CA014089), The Gloria Borges WunderGlo Foundation-The Wunder Project, Dhont Family Foundation, San Pedro Peninsula Cancer Guild, Daniel Butler Research Fund and Call to Cure Fund, Fong research project.

The status of HER2 and PD-L1 among four groups (TMB-H/L & MSI-H/MSS).

Moleculars	TMB-H & MSS (%)	TMB-L & MSS (%)	TMB-H & MSI-H (%)	TMB-L & MSI-H (%)	Adj *p*
HER2					
High expression (IHC)	**9.9**	4.5	0.3	0	< .0001
AMP	**3.4**	2.9	0.1	0	< .0001
PD-L1 positivity					
GE cancers (22C3)	73.9	71.4	**87.9**	73.9	< .01
Other GI cancers (SP142)	16.8	7.1	**22.9**	14.9	< .0001

3632 Poster Session (Board #362), Fri, 8:00 AM-11:00 AM

Comprehensive analysis of HER2 status through genomic, transcription, and translation among 5,305 patients with diverse malignancies. *First Author: Akram Mesleh Shayeb, University of California San Diego, Moores Cancer Center, La Jolla, CA*

Background: HER2 alterations is a predictive biomarker for anti-HER2 regimen. Success in breast and gastric cancers with anti-HER2 therapies translated to explore their efficacy in other tumors. Currently, measurement of HER2 can be done by assessing the expression of protein [e.g. immunohistochemistry (IHC)] or gene amplification of copy number variation (CNV) [e.g. fluorescence in situ hybridization or next-generation sequencing (NGS)]. But little is known about the transcription level (mRNA) of HER2. Herein, we investigated HER2 mRNA expression and its association with gene and protein expressions among diverse cancer types. **Methods:** Between 2015-2019, HER2 status was evaluated using IHC, qRT-PCR and NGS by Paradigm Diagnostics (CLIA-certified laboratory). All tumors in the database were included for analysis. Correlations between all 3 tests were done. An illustrative patient who was treated with anti-HER2 therapy base on the mRNA testing is presented. **Results:** HER2 testing was performed on 5305 patients (pts) with diverse cancers including NSCLC (n=1175), breast (n=1040) and colon (n=566); 4.1% (161/3926) had amplification through NGS, 33.3% (615/1848) had mRNA overexpression and 9.3% (236/2533) had overexpression by IHC. Of 723 pts who had all three tests performed, we found 7.5% (54/723) of pts with all three HER2 markers being positive (CNV [+]/mRNA [+]/ IHC [+]). Meanwhile, variety of amplification/ expression patterns were seen (see Table). CNV positivity translated to protein expression in 95% of cases. While only 4% of pts were IHC positive when CNV and mRNA were negative. 20% (144/723) of pts had mRNA overexpression alone among diverse cancer types. Representative case of 70yo female with metastatic cholangiocarcinoma harboring mRNA overexpression (but negative for CNV, IHC unclear due to sample insufficiency) who had near complete response to anti-HER2 therapy with progression-free survival of 24+ months is presented. **Conclusions:** HER2 status can be discordant with different assays but NGS positivity has excellent correlation with mRNA and protein expression. Of importance, HER2 mRNA can be overexpressed in 20% of pts even when gene amplification and protein expression are negative. Further studies are warranted to determine the clinical utility of mRNA as a biomarker for HER2 and potential use for anti-HER2 targeted therapies. Research Sponsor: None.

HER2 status signaling in a diverse cohort of cancers (n=723).

DNA	mRNA	Protein	Cases	%
+	+	+	54	7.5
+	+	-	1	0.1
+	-	+	1	0.1
+	-	-	1	0.1
-	+	+	41	5.7
-	+	-	144	19.9
-	-	+	26	3.6

3633 Poster Session (Board #363), Fri, 8:00 AM-11:00 AM

Olaparib monotherapy in pretreated patients with *BRCA1/2* alterations: Results of a DRUP trial cohort. *First Author: Hanneke van der Wijngaart, Department of Medical Oncology, Amsterdam UMC, Vrije Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, Netherlands*

Background: Extensive molecular profiling in cancer regularly reveals targets for which approved drugs are available in tumor types outside the registered label. Efficacy of off-label use of these drugs is unavailable. Access to these drugs for pts is challenging. In the Drug Rediscovery Protocol (DRUP, Van der Velden et al, Nature 2019), pts are treated based on their tumor molecular profile. Here, we present the results of the successful cohort "Olaparib for tumors with *BRCA1/2* alterations". **Methods:** Twenty five adult cancer patients (pts) who exhausted all treatment options and had *BRCA1/2* loss of function (LoF) mutations (found in routine diagnostics) were included. No pts were eligible for on-label treatment with PARP inhibitors. Pts were treated with olaparib until disease progression or unacceptable toxicity. The primary endpoint was clinical benefit (CB: objective response or stable disease (SD) $\geq$ 16 weeks). Pts were enrolled using a Simon-like two-stage model, with 8 pts in stage 1 and up to 24 pts in stage 2 if at least 1 pt had CB in stage 1. A fresh frozen biopsy was obtained from each pt for whole genome sequencing (WGS) and target confirmation. **Results:** Fourteen pts (56%) had CB. The objective response rate was 32%. Nine different cancer types were included: prostate (n=11), breast (n=4), ovarian (n=2), pancreatic (n=3), colorectal (n=2), biliary tract (n=2), kidney (n=1), adrenal gland (n=1) and endometrial (n=1). WGS could be performed on 58% of baseline tumor biopsies, confirming the original *BRCA1/2* mutations in 86%. CB was observed in pts with both somatic and germline *BRCA* alterations and across tumor types. CB was only observed in cases with biallelic loss of *BRCA1/2* in the tumor and when classified as HRD by a pan-cancer homologous recombination deficiency classifier (CHORD), which relies on genome-wide SNV, indel, and SV mutational footprints for HRD detection. No evidence of complete *BRCA* loss and HRD was observed in 5 pts with PD, while 4 patients with effective *BRCA* complete loss and HRD also had PD. WGS analysis of these pts suggested resistance mechanisms due to other oncogenic drivers (e.g FGFR1 amplification, CTNNB1 stabilization, KEAP1 inactivation). **Conclusions:** Olaparib seems to be an effective treatment option for pts with *BRCA1/2* LoF mutated malignancies, regardless of histology, for both germline and somatic alterations, which needs confirmation in an independent cohort. CB of olaparib was observed in malignancies showing biallelic loss of *BRCA1/2* and when classified as HRD, indicating the importance of the *BRCA*/HRD signature status. Clinical trial information: NCT02925234. Research Sponsor: KWF Cancer Society, Pharmaceutical/ Biotech Company.

3634 Poster Session (Board #364), Fri, 8:00 AM-11:00 AM

A randomized, controlled trial of structured palliative care versus standard supportive care for patients enrolled on phase I clinical trials. *First Author: Michelle Elizabeth Treasure, Cleveland Clinic Foundation, Cleveland, OH*

Background: Phase 1 clinical trials are the first step in developing new cancer therapeutics. Patients enrolled in these studies have typically exhausted standard therapies and are at a point in their disease trajectory where they often are choosing between a phase 1 clinical trial and hospice care. These patients may have significant symptom burden, which can result in early trial discontinuation and confound phase 1 trial outcomes, including toxicity profiles, which may influence further drug development. This study aimed to determine the palliative care needs of patients enrolled on phase 1 clinical trials and their caregivers (CGs), along with differences in study duration, adverse event (AE) and symptom profiles, and quality of life (QOL) between those receiving structured palliative care vs usual supportive care. **Methods:** 68 patients enrolled on phase 1 clinical trials were randomly assigned to receive structured palliative care or usual supportive care. 39 of their CGs were enrolled and assigned to the same arm as the patient. Quality of life metrics were obtained monthly: the Functional Assessment of Cancer Therapy-General and Memorial Symptom Assessment Scale -Short Form for patients, and The Quality of Life in Life Threatening Illness - Family Carer Version and Caregiver Reaction Assessment for CGs. Palliative care resources utilized were assessed for those in the palliative care arm, and referrals to supportive care services assessed in those in the usual care arm. AEs recorded on the Phase 1 trials were evaluated & compared between arms. **Results:** Mean duration on phase 1 study was 132 days in the palliative care arm vs 114 days in the usual care arm ($p = 0.55$). Total weighted AE rate (# of AE [x] AE grade per month) was 26.9 in the palliative care arm vs 34.0 in the usual care arm ($p = 0.53$). Patients in the palliative care arm experienced better QOL and lower symptom burden, as did their CGs, compared to those in the usual care arm. While the differences in outcomes were not statistically significant, all results favored structured palliative care. **Conclusions:** Phase 1 patients and their CGs have physical and psychosocial needs which warrant palliative care services. Preliminary results suggest structured palliative care is associated with increased duration on study (by nearly 3 weeks), improved patient and CG QOL, and reduced patient symptom and CG burden. A larger study is warranted to confirm these results and further develop the ideal palliative care intervention in these populations. Clinical trial information: NCT02543541. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

3635 Poster Session (Board #365), Fri, 8:00 AM-11:00 AM

Pooled safety analysis of single-agent lurbinectedin versus topotecan (Results from a randomized phase III trial CORAIL and a phase II basket trial). *First Author: Alexandra Leary, Institut de Cancérologie Gustave Roussy, Villejuif, France*

Background: Lurbinectedin (L), an inhibitor of active transcription, has shown activity in second-line (2L) small cell lung cancer (SCLC) (ASCO 2019). Topotecan (T) is the only approved drug in 2L SCLC and is also used in platinum resistant ovarian cancer (PROC). **Methods:** This pooled safety analysis includes data from 554 patients (pts) treated with L at 3.2 mg/m^2 Day 1 q3wk 1-h (no primary prophylaxis with G-CSF required): 335 with selected solid tumors (9 indications, including 105 pts with SCLC) from a phase II Basket study and 219 with PROC in the phase III CORAIL study. An indirect exploratory comparison (pooled data from CORAIL + Basket) and a direct comparison (data from CORAIL) of L *vs.* T are presented. **Results:** Most common adverse events with L were grade 1/2 fatigue, nausea and vomiting. Treatment-related (L/T): dose reductions: 22.9/48.3%, delays: 25.8/52.9%, grade $\geq$3 serious adverse events (SAEs): 15.0/32.2%, discontinuations: 3.2/5.7%, deaths: 1.3/1.5%, G-CSF use: 23.8/70.1%, and transfusions: 15.9/52.9%. **Conclusions:** Lurbinectedin has a predictable and manageable safety profile. A significant safety advantage was observed when lurbinectedin was compared with topotecan in the CORAIL trial in terms of hematological toxicities. With the limitations of indirect comparisons, in the pooled safety analysis, fewer lurbinectedin-treated pts had severe hematological toxicities, SAEs, dose adjustments, treatment discontinuations and use of supportive treatments than topotecan-treated pts. Clinical trial information: NCT02421588 and NCT02454972. Research Sponsor: PharmaMar SA.

Safety profile (L *vs.* T): grade 3/4 adverse events (related or unknown) and laboratory abnormalities (regardless of relationship).

	Lurbinectedin 3.2 mg/m^2 1-h iv q3wk		Topotecan 1.5 mg/m^2 D1-D5 iv q3wk	P-value
	L Pool (n=554)	L CORAIL (n=219)	T CORAIL (n=87)	CORAIL (L *vs.* T)
Neutropenia	40.6	32.0	78.2 [a]	<.0001
Leukopenia	29.6	23.7	57.5 [a]	<.0001
Anemia	17.1	17.8	56.3	<.0001
Thrombocytopenia	9.9	9.1	33.3	<.0001
ALT increase	6.9	6.8	3.6	0.42
Fatigue	6.7	7.3	13.8	0.08
FN	6.3	5.5	11.5 [a]	0.08
Nausea	3.2	5.9	4.6	0.79
Vomiting	2.9	5.5	3.4	0.57
Diarrhea	0.9	0.9	4.6	0.06

[a] Primary G-CSF prophylaxis allowed.

3637 Poster Session (Board #367), Fri, 8:00 AM-11:00 AM

The skin types closely related to development of the facial acneiform rash and the therapeutic effects of EGFR inhibitors in RAS wild-type metastatic colorectal cancer: Ancillary analysis of FAEISS study. *First Author: Syusuke Yoshikawa, Shizuoka Cancer Center, Shizuoka, Japan*

Background: At ESMO2019, we reported the primary results of a randomized controlled trial (FAEISS study) investigating the efficacy of topical corticosteroid treatment to facial acneiform rash (AR) by EGFR inhibitors comparing groups starting with a very strong topical corticosteroid and the standard weak topical corticosteroid. As an ancillary analysis, we investigated the association between AR and the pre-treatment skin types, as well as between the skin types and therapeutic effects of EGFR inhibitors on the primary disease. **Methods:** Utilizing pre-treatment clinical photos of the face taken according to the method determined by FAEISS study protocol, we divided the skin types into categories including enlarged pore, oiliness, xerosis, wrinkles, skin color/redness, and allocated the score (1-3) by central review. The severity of AR occurred during the study was graded and was evaluated the association with the specific skin type by Fisher's exact test. We also investigated the association between the skin types and the best overall response (RECISTv1.1) to EGFR inhibitor therapy on the primary disease using the Cochran-Armitage trend test. **Results:** Of the registered 172 cases of RAS wild-type metastatic colorectal cancer [104 men and 68 women, median age = 68 (26-79)], omitting the cases with unevaluable data, finally we analyzed 146 cases for associations between the skin types and AR and 147 cases for best overall response. Interestingly, AR developed 13.6% of enlarged pore score 1, 29% of score 2 and 45.8% of score 3, and patients with enlarged pore tended to have more AR ($p = 0.058$). Surprisingly, the response(CR/PR/SD) of the primary disease were 59.1% of the enlarged pore score 1, 70.6% of score 2 and 87.0% of score 3, and showed statistically significant trend($p < 0.038$). **Conclusions:** This study suggested that a skin type (enlarged pore) is a possible marker predicting AR risk in EGFR inhibitor therapy for RAS wild-type metastatic colorectal cancer, and better therapeutic effects of EGFR inhibitors. Research Sponsor: None.

3638 Poster Session (Board #368), Fri, 8:00 AM-11:00 AM

Safety, tolerability, and preliminary pharmacokinetic/pharmacodynamic profile of JMT103 in patients with bone metastases from solid tumors: A multicenter, open-label, dose-escalation, phase I clinical study. *First Author: Jin Li, Department of Medical Oncology, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China*

Background: Bone is one of the most common metastatic sites of malignancies. The metastatic tumor cells activate osteoclast activity and promote bone resorption via RANKL/RANK signaling pathway, and lead to osteolytic destruction. JMT103 is an innovative fully human IgG4 monoclonal antibody targeting RANKL. It can block RANKL/RANK signaling pathway, inhibit bone resorption, and protect bones from tumor metastasis. This study aimed to evaluate the safety and tolerability of JMT103 in patients with bone metastasis. **Methods:** This is a multicenter, open label, dose escalation, phase I clinical trial. The patients (ECOG score: 0-1) with bone metastasis from solid tumor who had not received bisphosphonates within 6 weeks before enrollment and were naïve to denosumab were enrolled. The initial dose was 0.5 mg/kg, sequentially escalated to 1.0, 2.0, and 3.0 mg/kg. JMT103 was injected subcutaneously by accelerated titration in 0.5 and 1.0 mg/kg dose groups, but via traditional "3+3" dose-escalation design in 2.0 and 3.0 mg/kg dose groups. Expansion study was conducted for subjects in 1.0, 2.0, and 3.0 mg/kg dose groups. Specifically, 3 additional doses (q4w) were injected after the end of 12-week single-dose study. The primary endpoints were maximum tolerated dose and safety. The secondary outcome measures included PK profile, preliminary efficacy biomarkers, immunogenicity, and bone mineral density (BMD). **Results:** From May 2018 to January 2020, 56 patients (13 males, 43 females, mean (SD) age: 55.57 (11.42) years) were enrolled, including bone metastasis from breast cancer (n = 36), gastric cancer (n = 5), lung cancer (n = 4), rectal cancer (n = 3), colorectal cancer (n = 2), or other solid tumors (n = 6). Nineteen patients participated in the dose-escalating study and 37 patients participated in the expansion study. JMT103 showed overall good safety. There were 74 drug-related AEs in all, including grade 3 (DLT hypocalcemia, n = 1; hypophosphatemia, n = 3), grade 2 (n = 15), and grade 1 (n = 55) AEs. The most common drug-related AEs were hypophosphatemia (n = 15), hypocalcemia (n = 12), and hypermagnesemia (n = 6). Median uNTx/Cr decrease from baseline was 76.6% (n = 20). **Conclusions:** JMT103 shows good safety and tolerability in patients with bone metastasis. Clinical trial information: NCT03550508. Research Sponsor: JMT-Bio Technology Co., Ltd.

3639 Poster Session (Board #369), Fri, 8:00 AM-11:00 AM

BXQ-350 to target to the lysosome and kill glioblastoma (GBM) cells via activation of apoptotic caspases in vitro. *First Author: Laura Felix, Student, Covington, KY*

Background: Apoptosis is a programmed cell death mechanism where cells respond to internal or external stimuli by initiating a cascade of events and enzymes leading to cell death. One of the hallmarks of cancer is the ability of tumor cells to resist these apoptotic stimuli. This allows tumor cells to have aberrant metabolisms, such as sphingolipid metabolism in tumor cell lysosomes, or mutations which would normally commit cells to death. Saposin C, the protein component of BXQ-350, Bexion Pharmaceuticals' proprietary biotherapeutic, is involved in normal lysosomal sphingolipid metabolism. Removing resistance, shortcutting steps leading to apoptosis, or correcting sphingolipid metabolism can result in the death of these tumor cells. **Methods:** The GBM cell line Gli36ΔEGFR was plated in 96 well plates at a density of $1x10^4$ cells per well in Dulbecco's Modified Eagle Media with 10% FBS overnight at 37°C for caspase and cytotoxicity assays. Cells were treated with 9uM to 30uM BXQ-350 in triplicate and incubated for 24 hours at 37°C. Promega's Caspase-Glo 9 or Caspase-Glo 3/7 reagent was added to appropriate wells and the plates were incubated at room temperature in the dark for 3 hours then luminescence was read. The parallel cytotoxic assay was run under the same conditions except Roche's MTT labeling reagent was added to the appropriate wells after 24 hours and incubated at 37°C for 4 hours. Solubilization solution was added to each well and the plate was incubated at 37°C overnight then absorbance was read. The GBM cell line U87 MG was used to determine lysosomal targeting. U87 MG cells were treated with 10uM BXQ-350 and incubated at 37°C overnight. They were stained with anti-SapC (RFP) and anti-LAMP1 (GFP) antibodies and images were taken. **Results:** BXQ-350 mediated cell death is correlated with a rise in Caspase 3, Caspase 7 and Caspase 9 activity. The caspase activity levels did not rise until after BXQ-350 passed its IC50 and stayed elevated. Caspases 3/7 levels showed higher activity compared to untreated than Caspase 9. In addition to this, BXQ-350 was seen to colocalize to LAMP1, a lysosomal membrane protein. **Conclusions:** BXQ-350 tracks to the lysosomal membrane where it initiates the cascade of enzymes necessary to cause apoptosis. Caspases 3/7 are the effector caspases and are necessary for the completion of the apoptotic pathway. The higher activity levels of these caspases show the cells are committed to cell death not allowing these cells to subvert apoptosis. This removes one of the major barriers to fighting cancer. Research Sponsor: Bexion Pharmaceuticals.

3640 Poster Session (Board #370), Fri, 8:00 AM-11:00 AM

Phase I dose-finding study of oral ERK1/2 inhibitor LTT462 in patients (pts) with advanced solid tumors harboring MAPK pathway alterations. *First Author: Filip Janku, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, MD Anderson Cancer Center, Houston, TX*

Background: LTT462 is an investigational small molecule inhibitor of ERK1/2, which has demonstrated preclinical activity in multiple MAPK activated cancer cells and xenograft models. This first-in-human study was designed to evaluate the safety and tolerability of LTT462 in advanced solid tumors harboring MAPK pathway alterations (NCT02711345). **Methods:** The dose-escalation part of this Phase I, open-label study, enrolled adult and adolescent pts with advanced solid tumors harboring ≥1 documented MAPK pathway alteration with progressive disease (PD) despite standard therapy, or for whom there is no effective standard treatment. Oral LTT462 was given once daily (QD) at 45–600 mg or twice daily (BID) at 150 mg or 200 mg. Objectives were to determine the maximum tolerated dose (MTD) using a Bayesian hierarchical logistic regression model guided by escalation with overdose control, and characterize safety, pharmacokinetics, pharmacodynamics, and preliminary efficacy of LTT462. **Results:** Sixty-five pts (median age 60 years) including 1 pt aged 15 were enrolled in the dose-escalation; most pts (22%) had 3 prior therapies. Most common primary sites for cancer were in the colon (n = 21; 32%), ovary (n = 9; 14%), and pancreas (n = 7; 11%). All pts discontinued, the majority due to PD (n = 44; 68%). Eleven pts experienced DLTs; 6 pts experienced Grade 3 eye disorder DLTs (4 pts retinopathy, 2 pts chorioretinopathy). Treatment-related adverse events (TRAEs) were reported for 89% of pts, most commonly (> 30%) diarrhea (n = 25; 38%) and nausea (n = 22; 34%). Grade 3/4 TRAEs were reported in 29% of pts; most common was retinopathy (n = 4; 6%). MTD of LTT462 was 400 mg QD and 150 mg BID. Overall, 8 pts (12%) had stable disease (SD) and 35 pts (54%) had PD. An unconfirmed partial response was reported in a pt with cholangiocarcinoma with *BRAF* mutation; best change in sum of target lesions per RECIST 1.1 was -33.9%. LTT462 increased plasma peak drug concentration and drug exposure at increasing doses between 45–450 mg QD. Exposure at LTT462 600 mg QD was lower than anticipated, indicating potential saturation of absorption at this dose. LTT462 inhibited ERK1/2 and reduced *DUSP6* expression relative to baseline in most pts evaluated. **Conclusions:** LTT462 is well tolerated. Limited clinical activity was reported with single agent LTT462; best overall response was SD. An ongoing study is investigating LTT462 in combination with the RAF inhibitor, LXH254, in NSCLC and melanoma. Clinical trial information: NCT02711345. Research Sponsor: Novartis.

3641 Poster Session (Board #371), Fri, 8:00 AM-11:00 AM

The incidence of myelodysplastic syndrome in patients receiving poly-ADP ribose polymerase inhibitors for treatment of solid tumors: A meta-analysis. *First Author: Roni Nitecki, MD Anderson Cancer Center, Houston, TX*

Background: Clinical trials have reported improved outcomes with PARPi (poly [adenosine diphosphate–ribose]-ADP polymerase inhibitor) therapy in ovarian, breast, pancreatic and lung cancers. There is concern that PARPi therapy may cause myelodysplastic syndrome (MDS). In this meta-analysis we seek to quantify the risk of MDS among patients treated with PARPi for solid tumor malignancies. **Methods:** We searched Medline, Embase, and Cochrane databases (up to January 6, 2020) to abstract randomized controlled trials that include a PARPi in the experimental arm in solid tumors. Combinations included PARPi versus (vs.) placebo, PARPi vs. cytotoxic treatment, and PARPi with cytotoxic treatment vs. cytotoxic treatment. We used to time-to-event curves to estimate person-time and calculated the incidence of MDS among all studies. We used random-effects Poisson regression models to estimate pooled incidence risk ratio (RR) for developing MDS. **Results:** We identified 14 studies, 10 in ovarian, 3 in breast, and 1 in pancreatic cancer patients. Of 5,646 patients, 62.3% received a PARPi alone or in combination with chemotherapy or bevacizumab, and 37.8% received treatment consisting of placebo alone or with chemotherapy or bevacizumab. PARPi were investigated as an upfront treatment in 2,827 patients, and as treatment for recurrence in 2,819 patients. The incidence of MDS was 6.73 cases vs. 3.85 per 1000 person-years in patients receiving PARPi as compared to control corresponding to a 3-year cumulative incidence of 2.0% and 1.1%. Accounting for intra-study clustering, PARPi use was associated with a 60% increase in risk (incidence RR 1.60, 95% Confidence Interval [CI] 0.89-2.87) of MDS compared to control. In the upfront setting, patients randomized to PARPi were twice as likely to develop MDS (RR 2.08, 95%, CI 1.39-3.64). Among patients treated for recurrence, the risk of MDS appeared to be similar among patient randomized to PARPi or control treatment (RR 1.13, 95% CI 0.35-3.64). In studies that compared PARPi in combination with other cytotoxic treatment vs. cytotoxic treatment alone, PARPi was associated with a large risk of MDS (RR 5.08, 95% CI 1.36-19.03). **Conclusions:** In pooled estimates from randomized controlled trials in solid tumors PARPi treatment appears to be associated with an increased incidence of MDS particularly in the upfront setting and when combined with cytotoxic treatment. Despite pooling 14 randomized trials our estimates remain imprecise due to the rarity of MDS. Research Sponsor: U.S. National Institutes of Health.

3642 Poster Session (Board #372), Fri, 8:00 AM-11:00 AM

Evaluation of a computational decision support system for molecularly targeted treatment planning by the clinical outcome data of the randomized trial SHIVA01. *First Author: Anna Dirner, Oncompass Medicine Hungary Ltd, Budapest, Hungary*

Background: Precision oncology requires the identification of individual molecular pathomechanisms to find optimal personalized treatment strategies for every cancer patient. Incorporation of complex molecular information into routine clinical practice remains a significant challenge due to the lack of a reproducible, standardized process of clinical decision making. **Methods:** To provide a standardized process for molecular interpretation, we develop a precision oncology decision support system, the Realtime Oncology Molecular Treatment Calculator (MTC). MTC is a rule-based medical knowledge engine that dynamically aggregates and ranks relevant scientific and clinical evidence using currently 26,000 evidence-based associations and reproducible algorithm scoring of drivers, molecular targets to match molecular alterations to efficient therapies. To validate this novel method and system, we used data of the SHIVA01 trial of molecularly targeted therapy (Lancet Oncol 2015 16:1324-34). Molecular profiles of participants were uploaded to MTC and aggregated evidence level (AEL) values of associated targeted treatments were calculated, including those used in the SHIVA01 trial. **Results:** The MTC output provided a prioritized list of drugs associated with the driver alterations in the patient molecular profile, where ranking is based on AEL values. Of 113 patients who received targeted therapy with available clinical best response data, disease control was experienced in 63 cases (PR: 5, SD: 58), while disease progression occurred in 50 cases. The average AEL score for the therapies applied was significantly higher in the responsive group than in the non-responsive group (1512 and 614, respectively ($p = 0.049$)). In 94 cases, drugs other than those used for therapy were ranked higher by the MTC. The average AEL difference between the top-ranked and the used drugs was in an inverse correlation with clinical response, i.e. smaller differences associated with a better outcome. **Conclusions:** Results indicate that the aggregation of evidence-based tumor-driver-target-drug associations using standardized mathematical algorithms of this computational tool is a promising novel approach to improve clinical decisions in precision oncology. Further validation based on the results of other targeted clinical trials and real-life data using more detailed molecular profiles is warranted to explore the full clinical potential of this novel medical solution. Research Sponsor: ERA PerMed, Hungarian Innovation Agency, Agence Nationale de le Recherche, Site de Recherche Intégrée contre le Cancer (SiRIC) ERA PerMed (ERAPERMED2018-078), Hungarian Innovation Agency (NVKP_16-1-2016-0005).

3643 Poster Session (Board #373), Fri, 8:00 AM-11:00 AM

Survival associated with mutations in SWI/SNF chromatin remodeling complex genes. *First Author: Michael J. Hassett, Dana-Farber Cancer Institute, Boston, MA*

Background: The SWI/SNF (SWitch/Sucrose NonFermentable) chromatin remodeling complex (CRC) - a combinatorial assembly of products from multiple genes - alters histone/DNA interactions and thereby impacts transcription, DNA replication/repair, and cell division. Studies suggest that over 20% of human cancers contain mutations in at least one SWI/SNF gene, implying that it is the most highly mutated CRC in human cancer. To address existing knowledge gaps, we sought to evaluate the association between SWI/SNF mutations and overall survival (OS). **Methods:** We identified adult cancer patients who consented to have OncoPanel testing (Dana-Farber/Brigham & Women's Hospital's next generation sequencing platform) from June 2013-August 2019. These data were merged with institutional electronic health records and National Death Index vital status. We determined mutation frequency and co-occurrence for the nine SWI/SNF genes included in OncoPanel (ARID1A, ARID1B, ARID2, BCL11B, PBRM1, SMARCA4, SMARCB1, SMARCE1, and SS18). We assessed the association between mutation and OS (from time of OncoPanel testing) for cancers with at least 500 analyzed and 20 mutated cases, controlling for age and TP53 status. Exploratory analyses were conducted using cBioPortal and SAS (no multiple comparison adjustment). **Results:** Among 25,434 samples from 24,648 patients, a mutation in at least one evaluated SWI/SNF gene was identified in 26% of cases (ARID1A 10.5%, ARID1B 7.2%, SMARCA4 5.5%, PBRM1 4.9%, ARID2 4.8%, BCL11B 3.5%, SMARCE1 1.1%, SMARCB1 1.0%, and SS18 0.7%). The most frequently mutated cancers included small bowel (52%), endometrial (49%), ampullary (48%) and bladder (45%). Co-occurrence was common (30 of 36 potential gene-pairs), with the largest associations (odds ratio; all $P < .05$) seen for SMARCB1:BCL11B (4.19), ARID1B:BCL11B (3.87), ARID2:BCL11B (3.85), and SMARCA4:BCL11B (3.78). Associations between having a mutation and OS were seen for the following cancers/genes (odds ratio; all $P < .05$): ARID1A (colorectal 0.72, pancreatic 1.46), ARID1B (melanoma 0.32), SMARCA4 (esophagogastric 1.48, non-small cell lung 1.89, ovarian 0.43), SMARCB1 (non-small cell lung 2.04), and SS18 (soft tissue sarcoma 2.06). **Conclusions:** Mutations in SWI/SNF genes are widespread, with mutation rates varying by cancer type. Co-occurrence was common, especially with BCL11B. Associations with OS were both favorable and unfavorable, with variability seen by gene and cancer type. Future research should explore the mechanisms by which mutations in SWI/SNF genes influence treatment response/OS. Research Sponsor: Institutional.

TPS3645 Poster Session (Board #375), Fri, 8:00 AM-11:00 AM

A phase I trial of aerosol gemcitabine for the treatment of patients with solid tumors and lung metastases. *First Author: Nancy Beatriz Gordon, UT MD Anderson Cancer Ctr, Houston, TX*

Background: Pre-clinical studies of aerosol gemcitabine (GCB) in mice and dogs with osteosarcoma (OS) lung metastases demonstrated therapeutic efficacy. Aerosol GCB administered once weekly proved to be safe in adults with lung cancer. Direct delivery of GCB to the lungs via inhalation may offer higher drug concentration in the tumor with fewer side effects. We initiated a Phase I study to evaluate the feasibility and safety of aerosol GCB treatment in patients>12 years with solid tumors and lung metastases (2015-0720- NCT03093909). **Methods:** Eligibility criteria: 1) Diagnosis of solid tumor with lung metastases, 2) willing to comply with protocol therapy, 3) adequate organ function, 4) patient age > 12 and < 50 years, 5) good performance status, 6) resolution of all acute toxic effects of any prior anti-cancer therapy, and 7) no radiotherapy within 2 weeks. Patients who previously received systemic GCB are eligible. Objectives: To determine the maximum tolerated dose (MTD) and toxicities of aerosol GCB, to evaluate for drug spillover into the circulation, and to preliminarily assess the anti-tumor activity. Correlative studies include effect of aerosol GCB on immune cell infiltration in the lung, autophagy, apoptosis, heat shock protein 27, evidence of DNA strand breaks (gH2AX) and expression of human equilibrative nucleoside transporter-1.Aerosol GCB is administered via a breath-induced nebulizer twice a week in 28-day cycles. A maximum of 6 dose levels will be studied; the starting dose is 0.75 mg/kg twice weekly. If no progressive disease or unacceptable treatment-related toxicity, patients may continue for 12 cycles. The study uses the accelerated titration method for the first 2 dose levels then the 3+3 design for the remaining dose levels. After determining the MTD, we will evaluate the defined MTD in an expansion cohort of 14 patients with relapsed OS. Symptoms, pulse oximetry, and pulmonary function are assessed prior to each nebulized dose using remote spirometry that allows raw numbers and flow-volume curves to be uploaded and transmitted via bluetooth to an android tablet provided to patients. Data is transmitted to a web portal and captured in a HIPAA-compliant web-based database (REDCap) that is accessible to the research team. **Results:** To date, the study enrolled 4 patients and accrual is ongoing at dose level 3. **Conclusions:** This study will provide information on the feasibility and safety of aerosol GCB. If proven to be feasible and safe, it can potentially offer a novel approach to treat metastatic OS to the lungs while minimizing systemic toxicity. Clinical trial information: NCT03093909. Research Sponsor: The Gateway for Cancer Research and Archer Charitable Foundation.

TPS3646 Poster Session (Board #376), Fri, 8:00 AM-11:00 AM

A phase I/II, two-part, multicenter, first-in-human study of DS-7300a in patients with advanced solid malignant tumors. *First Author: Johanna C. Bendell, Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN*

Background: B7 homologue 3 (B7-H3) is a protein that is overexpressed in various cancer types, including lung, head and neck squamous cell carcinoma, prostate, esophageal, and breast. B7-H3 overexpression is associated with poor prognosis because it promotes increased invasive and metastatic potential of cancer cells (Dong P, et al. *Front Oncol.* 2018;8:264). Currently, no B7-H3–targeted cancer therapies are approved. DS-7300a is an antibody-drug conjugate composed of a humanized anti–B7-H3 IgG1 monoclonal antibody (MABX-9001a) conjugated to a drug linker that releases its payload upon internalization by cancer cells. The payload, DXd, is an exatecan derivative that inhibits topoisomerase I, an enzyme that relaxes supercoiled DNA for replication and transcription. DS-7300a induced apoptosis in cancer cells in vitro and showed potent antitumor activity in xenograft models of various types of solid tumors in vivo. **Methods:** This phase 1/2, multicenter, nonrandomized, open-label, first-in-human study of DS-7300a is ongoing in the United States and Japan in patients with selected advanced solid tumors (NCT04145622). This study has 2 parts: dose escalation (part 1) and dose expansion (part 2). Primary objectives are to evaluate the safety, tolerability, and antitumor activity of DS-7300a and to determine the maximum tolerated dose or recommended dose for the expansion part. Secondary objectives include the pharmacokinetic characterization of DS-7300a, determination of the total levels of anti–B7-H3 antibody and the drug component (DXd), and assessment of the incidence of anti-drug antibodies against DS-7300a. Key inclusion criteria are age $\geq$ 18 years (United States) or $\geq$ 20 years (Japan), an ECOG performance status of 0 or 1, $\geq$ 1 measurable lesion according to RECIST 1.1 as assessed by the investigator, and consent to provide pre- and on-treatment tissue samples (mandatory if clinically allowed and not contraindicated). Key exclusion criteria include prior treatment with orlotamab, enoblituzumab, other B7-H3–targeted agents, or an antibody-drug conjugate that is conjugated with a topoisomerase I inhibitor. Dose expansion will start with 3 cohorts, including patients with selected advanced solid tumors. In both parts, DS-7300a will be administered intravenously on day 1 of each 21-day cycle. During dose escalation, the starting dose of DS-7300a is 0.8 mg/kg. This trial is currently in the dose-escalation part. Clinical trial information: NCT04145622. Research Sponsor: Daiichi Sankyo Co., Ltd.

TPS3647 Poster Session (Board #377), Fri, 8:00 AM-11:00 AM

EV-202: A phase II study of enfortumab vedotin in patients with select previously treated locally advanced or metastatic solid tumors. *First Author: Justine Yang Bruce, Carbone Cancer Center, University of Wisconsin, Madison, WI*

Background: Nectin-4, a transmembrane cell adhesion protein, is highly expressed in urothelial carcinoma (UC), breast cancer (BC), non-small cell lung cancer (NSCLC), and gastroesophageal cancers (GEC); targeting Nectin-4 on these tumors may provide a novel treatment approach. Enfortumab vedotin (EV), an investigational human monoclonal antibody-drug conjugate, binds to Nectin-4 and upon internalization releases MMAE resulting in cell cycle arrest and cell death. Recently, EV received accelerated approval by the FDA for the treatment of adults with locally advanced/metastatic UC who previously received a PD-1 or PD-L1 inhibitor, and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting. Use of EV in this study is investigational. **Methods:** This open-label phase 2 study (NCT04225117) will assess the efficacy and safety/tolerability of EV in patients (pts) with previously treated locally advanced/metastatic malignant solid tumors. Adult pts (~240) with histologically or cytologically confirmed disease and an ECOG $\leq$1 will be enrolled into 1 of 6 tumor-specific cohorts (Table), with ~40 pts each. While Nectin-4 expression is not required for enrollment, it is being tested retrospectively. Patients with active CNS metastases, grade $\geq$2 preexisting sensory or motor neuropathy, grade $\geq$3 immunotherapy-related hypothyroidism or panhypopituitarism, ongoing grade $>$3 immunotherapy-related AEs requiring high-dose steroids, or a history of uncontrolled diabetes mellitus within 3 months of the study will be excluded. All pts will receive EV 1.25 mg/kg IV on Days 1, 8, and 15 of each 28-day cycle until treatment discontinuation criteria are met; dose reductions/interruptions will be permitted. For all cohorts, the primary endpoint is investigator-assessed confirmed objective response rate (RECIST v1.1); secondary endpoints include duration of response, disease control rate, progression-free and overall survival, and safety/tolerability of EV. This study is recruiting as of February 2020. Clinical trial information: NCT04225117.Research Sponsor: Astellas Pharma, Inc.

Cohort	Tumor Type
1	Hormone receptor–positive/human epidermal growth factor receptor 2–negative BC
2	Triple-negative BC
3	Squamous NSCLC
4	Nonsquamous NSCLC
5	Head and neck cancer
6	GEC, including gastroesophageal junction adenocarcinoma

TPS3648 Poster Session (Board #378), Fri, 8:00 AM-11:00 AM

TROPiCS–03: A phase II open-label study of sacituzumab govitecan (SG) in patients with metastatic solid tumors. *First Author: Ashish Saxena, Weill Cornell Medicine, New York-Presbyterian Hospital, New York, NY*

Background: Trophoblast cell surface antigen (Trop-2) is highly expressed in many epithelial cancers (non–small-cell lung cancer [NSCLC], endometrial cancer, urothelial carcinoma [UC], and triple-negative breast cancer [TNBC]) and has been linked to aggressive disease and poor prognosis. SG is a Trop-2–directed antibody drug conjugate containing SN-38 (active metabolite of irinotecan) with a 7.5:1 drug-to-antibody ratio and unique hydrolyzable linker that allows for extracellular bystander effect. The phase 1/2 IMMU-132-01 basket study reported clinical activity with SG in patients with multiple tumor types not selected for Trop-2 expression including NSCLC (objective response rate [ORR]: 17%), TNBC (ORR: 33%), and UC (ORR: 31%).1-3 Results from the overall safety population (N=420) from this study found that SG was tolerable, with a predictable and manageable safety profile, and low discontinuation rates due to AEs. **Methods:** To test a biomarker-enrichment strategy with Trop-2, the TROPiCS-03 (TROP-2 Investigations in Cancer with SG) study was initiated. TROPiCS-03 (NCT03964727) is a multi-cohort, open-label, phase 2 study in patients with metastatic solid tumors - presently NSCLC (adenocarcinoma and squamous cell carcinoma), head and neck squamous cell carcinoma, and endometrial cancer - selected based on elevated Trop-2 expression by a validated IHC assay. Patients receive SG (10 mg/kg IV, days 1 and 8 every 21 days) and continue treatment until lack of clinical benefit or unacceptable toxicity. The primary endpoint is objective response rate (local assessment) and additional endpoints include clinical benefit rate, duration of response, progression-free survival, and safety. Females or males $\geq$18 years old who are histologically documented to have locally advanced or metastatic (M1, stage 4) solid tumors of the above types are eligible. Patients must have ECOG 0 or 1 and adequate clinical laboratory results to be enrolled. All subjects will have progressed after prior platinum-based chemotherapy and programmed death-ligand 1 (PD-L1) or programmed cell death protein 1 (PD-1) directed therapy. Patients who have previously received topoisomerase I inhibitors and those with known active CNS metastases are excluded. Approximately 160 patients will be enrolled in the trial overall; enrollment in the NSCLC cohort is currently in progress. References: Heist RS et al. *J Clin Oncol.* 2017;35:2790-7, Bardia A et al., *NEJM.* 2019;380:741-51.,Tagawa ST et al., Oral presentation; ASCO-GU 2019, San Francisco, CA. Clinical trial information: NCT03964727. Research Sponsor: Immunomedics, Inc.

TPS3649 Poster Session (Board #379), Fri, 8:00 AM-11:00 AM

Phase I study of the antibody-drug conjugate ABBV-321 in patients with non-small cell lung cancer and squamous head and neck cancer with overexpression of the epidermal growth factor receptor. *First Author: Benedito A. Carneiro, The Warren Alpert Medical School, Brown University, Providence, RI*

Background: ABBV-321 (serclutamab talirine) is an epidermal growth factor receptor (EGFR)-targeted antibody-drug conjugate that consists of a humanized immunoglobulin G1 anti-EGFR monoclonal antibody conjugated to a pyrrolobenzodiazepine (PBD) dimer via a maleimidocaproyl-valine-alanine linker. Once bound, ABBV-321 is internalized, the maleimidocaproyl-valine-alanine linker undergoes proteolytic cleavage, and the cytotoxic PBD is released, causing DNA cross-links and cell death. Preclinical studies have shown cytotoxicity in numerous human xenograft and patient (pt)-derived tumor models. This first-in-human trial is assessing the safety, pharmacokinetic (PK), and preliminary antitumor activity of ABBV-321 in pts with advanced solid tumor types likely to exhibit elevated levels of EGFR. **Methods:** This is a 2-part, multicenter phase 1 study (NCT03234712) of ABBV-321 monotherapy in pts ($\geq$18 years; Eastern Cooperative Oncology Group performance status 0–1) with advanced solid tumors associated with overexpression of EGFR. EGFR overexpression will be determined by centralized testing using an RNA-based assay. Primary objectives of the completed part 1 (dose escalation) were to determine the maximum tolerated dose (MTD)/recommended phase 2 dose (RP2D) of ABBV-321 and assess the PK and toxicity and safety profile; part 2 (dose expansion) will evaluate safety and PK profile at the RP2D in specific cohorts (NSCLC and HNSCC). Secondary objectives include assessment of preliminary antitumor activity. Pts will receive escalating doses of ABBV-321 until the MTD/RP2D is determined. Dose-limiting toxicities will be assessed during the first cycle of dosing. Adverse events (AEs) will be evaluated per National Cancer Institute Common Terminology Criteria for AEs (version 4.03). Blood samples for PK analysis (ABBV-321, total antibody, unconjugated PBD) will be collected at designated time points throughout the study. The multinational trial is active, with the first pt screened on 1 Feb 2018. The dose-escalation phase has been completed; screening and enrollment for the expansion phase of the study in NSCLC and HNSCC is underway. Clinical trial information: NCT03234712. Research Sponsor: AbbVie, Inc.

TPS3650 Poster Session (Board #380), Fri, 8:00 AM-11:00 AM

A basket trial of trastuzumab deruxtecan, a HER2-targeted antibody-drug conjugate, for HER2-amplified solid tumors identified by circulating tumor DNA analysis (HERALD trial). *First Author: Masataka Yagisawa, Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan*

Background: Trastuzumab deruxtecan, a new HER2-targeting antibody-drug conjugate, has been approved for unresectable or metastatic HER2-positive breast cancer by the Food and Drug Administration. In a phase I/II trial, trastuzumab deruxtecan showed a manageable safety profile and antitumor activity in HER2-positive various cancer types. In addition, a tissue-based HER2 test occasionally cannot identify accurate HER2 status due to spatial and temporal intratumoral heterogeneity, leading to potentially missing an opportunity for responders to receive benefit from anti-HER2-targeted therapy. Circulating tumor DNA (ctDNA) analysis can detect comprehensive somatic genome alterations by assessment of spatial and temporal intratumoral heterogeneity with minimal invasiveness. **Methods:** We designed an investigator-initiated multicenter phase II basket trial to evaluate efficacy and safety of trastuzumab deruxtecan in advanced solid tumor malignancies with *HER2* amplification identified by Guardant360, a 74-gene sequencing ctDNA panel, as a part of the Nationwide Cancer Genome Screening Project (GOZILA study, UMIN000029315). The key eligibility criteria are as follows: 1) Histopathologically confirmed advanced solid tumor malignancy; 2) Identified *HER2* amplification by Guardant360; 3) Failed prior standard therapy. The participants will receive intravenously 5.4 mg/kg of trastuzumab deruxtecan every 3 weeks. The primary endpoint is objective response rate (ORR). The planned sample size is 55-65. A Bayesian model considering the potential heterogeneity across cancer types will be applied to detect ORR of 5% versus 25% to a certain level while maintaining the false-positive error rate in each cancer type at 10%. Furthermore, tumor tissue, ctDNA and circulating tumor cells are serially collected and analyzed to investigate the predictive biomarkers and resistance mechanisms. The trial was activated in late 2019. At the time of the abstract submission, 2 patients have been enrolled. This trial is granted by AMED under Grant Number JP18lk0201084. Clinical trial information: JapicCTI-194707. Research Sponsor: Japan Agency for Medical Research and Development.

TPS3651 Poster Session (Board #381), Fri, 8:00 AM-11:00 AM

A phase I, open-label, dose-escalation trial of BI 1701963 as monotherapy and in combination with trametinib in patients with KRAS mutated advanced or metastatic solid tumors. *First Author: Eelke Gort, University Medical Center Utrecht, Utrecht, Netherlands*

Background: Activating mutations of *KRAS* drive many types of cancer. Activation of KRAS relies on guanine nucleotide exchange factors, such as SOS1, to mediate exchange of GDP for GTP. BI 1701963 is a small-molecule protein–protein interaction inhibitor that prevents the interaction between KRAS and SOS. Binding of BI 1701963 to the catalytic site of SOS1 inhibits binding of SOS1 to RAS–GDP, thereby hindering the exchange from RAS–GDP (inactive form) to RAS–GTP (active form). In preclinical studies this has been shown to lead to cytostasis in cancer cells addicted to KRAS signaling. **Methods:** NCT04111458 is a first-in-human trial of BI 1701963 in patients aged ≥18 years with tumors harboring *KRAS* mutations. Primary objectives are to determine the maximum tolerated dose (MTD) and recommended Phase II dose of BI 1701963 as monotherapy and in combination with trametinib, based on dose-limiting toxicities (DLTs). Secondary objectives are to evaluate safety, tolerability, pharmacokinetics/-dynamics and preliminary efficacy. The study will have two arms (mono- and combination therapy), and be divided into dose escalation (Part A), confirmation (Part B) and expansion (Part C, combination only) phases. Inclusion criteria include activating *KRAS* mutation, ≥1 evaluable lesion (RECIST 1.1), ECOG PS ≤1 and adequate organ function. Exclusion criteria include history of: RAS, MAPK or SOS1 targeting therapies; retinal vein occlusion; retinal pigment epithelial detachment; and decreased cardiac function. Parts B and C will be conducted in patients with advanced NSCLC. Treatment will continue until confirmed clinical benefit, defined toxicities, or withdrawal of consent. The primary endpoints are: Part A, the MTD, and the number of patients with DLTs during Cycle 1; Part B (monotherapy), the number of patients with DLTs; Part C, objective response (OR, RECIST 1.1). Starting doses of BI 1701963 in Part A will be 50 mg once daily (QD) orally (monotherapy) and 100 mg QD (combination, once proved safe as monotherapy) and will be escalated until the MTD is reached. The starting dose of trametinib will be 1 mg QD, escalated to the MTD or a max. of 2 mg QD. Dose cohorts will include ≥3 patients, with two therapeutic relevant doses (TRDs) established in each arm. In Part B, patients will be randomized to groups receiving one of the TRDs. If an OR is observed at a TRD in the combination arm, additional patients will be recruited into expansion cohorts receiving the relevant dose. As of Feb 11, 2020 three patients have been treated. Clinical trial information: NCT04111458. Research Sponsor: Boehringer Ingelheim.

TPS3652 Poster Session (Board #382), Fri, 8:00 AM-11:00 AM

SGN228-001: A phase I open-label dose-escalation, and expansion study of SGN-CD228A in select advanced solid tumors. *First Author: Amita Patnaik, START, San Antonio, TX*

Background: SGN-CD228A is an investigational antibody-drug conjugate (ADC) that targets CD228, a cell-surface oncofetal protein with prevalent expression in several types of cancer and limited expression on normal tissues. SGN-CD228A consists of a humanized IgG1 anti-CD228 monoclonal antibody conjugated to an average of 8 molecules of monomethyl auristatin E (MMAE) via a PEGylated β-glucuronidase cleavable linker. MMAE is a well-studied and highly active chemotype with an established safety profile. The proposed mechanism of action involves binding CD228 on cell surfaces, ADC internalization, and trafficking to lysosomes. MMAE is then released through β-glucuronidase cleavage of the glucuronide MMAE linker. MMAE then binds tubulin, which disrupts microtubule networks and causes cell cycle arrest and apoptosis. **Methods:** SGN228-001 (NCT04042480) is a phase 1, open label, multicenter, dose escalation, and expansion study enrolling up to 240 subjects to evaluate the safety, tolerability, PK, and antitumor activity of SGN-CD228A in select advanced solid tumors. Eligible subjects are ≥18 years of age and have metastatic cutaneous melanoma, malignant pleural mesothelioma, human epidermal growth factor receptor 2-negative metastatic breast cancer, advanced non-small cell lung cancer, metastatic colorectal cancer, or advanced pancreatic ductal adenocarcinoma. Subjects must have relapsed, refractory, or progressive disease, and should have no appropriate standard therapy available. Measurable disease per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1), Eastern Cooperative Oncology Group (ECOG) performance status score of ≤1, and adequate renal, hepatic, and hematologic function are required. The study includes dose escalation and dose expansion, with multiple disease-specific dose expansion cohorts and a biology cohort. Dose escalation will be conducted using the modified toxicity probability interval method (Ji 2010) to evaluate the safety and identify the maximum tolerated dose of SGN-CD228A. Following dose escalation, disease-specific expansion cohorts and a biology cohort (to evaluate exploratory biomarkers) are planned. Response assessments will be conducted every 6 weeks per RECIST v1.1 and all subjects will be followed for safety. Pharmacokinetics and markers of pharmacodynamics will be assessed regularly. Key efficacy endpoints include objective response rate, progression-free survival, and duration of objective response. Enrollment is ongoing in the US and planned in Europe. Clinical trial information: NCT04042480. Research Sponsor: Seattle Genetics Inc.

TPS3653 Poster Session (Board #383), Fri, 8:00 AM-11:00 AM

Randomized phase II trial of topotecan plus M6620 (VX-970) versus topotecan alone in patients with relapsed small-cell neuroendocrine cancers including small cell lung cancer. *First Author: Nobuyuki Takahashi, National Cancer Institute, Bethesda, MD*

Background: Ataxia telangiectasia and Rad3-related (ATR) is an essential kinase that senses stressed replication forks and orchestrates the multifaceted replication stress response. Cancer cells under replication stress are particularly susceptible to ATR inhibition. Small-cell neuroendocrine cancers (SCNCs) are highly aggressive and arise in multiple tissues, most commonly lung (SCLC). We hypothesized that SCNCs are under replication stress and that exacerbating this stress could selectively kill SCNC by replicative damage. Based on promising data from a single-arm study, this study seeks to evaluate the improvement of progression free survival (PFS) by adding M6620 to topotecan in patients with SCNC. **Methods:** This study is an investigator-initiated, multicenter, open-label randomized phase 2 clinical trial. Key inclusion criterion are patients at age ≥18 with SCNCs that had relapsed after at least one prior chemotherapy, ECOG PS ≤ 2, and adequate organ function. Patents with asymptomatic brain metastasis, irrespective sensitivity with prior platinum-based chemotherapy, and previously treated with immune checkpoint inhibitors are eligible. The primary cohort consists of 54 patients with SCLC randomized 2:1 to receive either topotecan in combination with M6620 or topotecan alone. Topotecan is administered 1.25 mg/m^2 intravenously over 30 minutes every 23 hours on day 1 through 5, pegfilgrastim 6 mg subcutaneously on day 6 and M6620 is administered at 210 mg/m^2 intravenously over 60 minutes on day 2 and day 5 if the patient is randomized to the combination arm, in 21-day cycles. Patients randomized to the topotecan alone arm can cross-over to the combination arm at disease progression. An exploratory cohort will enroll 20 patients with SCNC. Primary endpoint is PFS improvement with the combination compared with topotecan alone. Secondary endpoints are ORR and overall survival. To evaluate the genomic features associated with clinical outcomes and to gain insight into the underlying mechanisms of ATR inhibitor response, we require mandatory biopsy before starting treatment. Clinical trial information: NCT03896503. Research Sponsor: U.S. National Institutes of Health.

TPS3654 **Poster Session (Board #384), Fri, 8:00 AM-11:00 AM**

A phase II basket study of MCLA-128, a bispecific antibody targeting the HER3 pathway, in NRG1 fusion-positive advanced solid tumors. *First Author: Alison M. Schram, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: *NRG1* fusions are oncogenic drivers across various cancers. NRG1 fusion proteins bind to HER3, leading to HER2/HER3 heterodimerization, increased downstream signaling, and tumor growth. Clinical responses to anti-HER3 antibodies or HER2 tyrosine kinase inhibitors have been reported. In contrast to these agents, MCLA-128 is a HER2/HER3 bispecific antibody that blocks both NRG1 binding and HER2/3 dimerization. Two patients with chemotherapy-resistant *ATP1B1-NRG1*-positive pancreatic *KRAS*-wild-type adenocarcinomas who received MCLA-128 through FDA-approved single-patient Investigational New Drug (IND) applications showed significant tumor shrinkage and durable tumor marker (CA-19-9) response. These data support the evaluation of MCLA-128 in *NRG1* fusion-positive tumors using a basket approach. **Methods:** This is a global, open-label, multicenter phase 2 basket trial of MCLA-128 in patients with solid tumors harboring *NRG1* gene fusions. Main eligibility criteria are locally advanced unresectable or metastatic cancers harboring an *NRG1* fusion, and failure under prior standard therapy appropriate for the tumor type and disease stage. Genomic screening of tumor tissue is done at a local laboratory (with post-hoc central confirmation) or central laboratory (RNA sequencing). Three *NRG1* fusion-positive tumor cohorts are being evaluated: pancreatic cancer, NSCLC, and other solid tumors. The sample size for the first two cohorts is up to 25 patients; the basket group may enroll up to 40 patients. The primary endpoint for all cohorts is investigator-assessed objective response rate (RECIST v1.1). The key secondary endpoint is duration of response. Other secondary endpoints include progression-free and overall survival. Eligible patients receive a bi-weekly dosing regimen of 750 mg of MCLA-128 (2-hour infusion), every 2 weeks, in 4-week cycles. The study is actively accruing patients in North America, Europe, and Asia. *Previously presented at ESMO 2019, 685TiP, Schram et al.-Reused with permission.* Clinical trial information: NCT02912949. Research Sponsor: Merus NV.

TPS3655 **Poster Session (Board #385), Fri, 8:00 AM-11:00 AM**

BT5528-100 phase I/II study of the safety, pharmacokinetics, and preliminary clinical activity of BT5528 in patients with advanced malignancies associated with EphA2 expression. *First Author: Johanna C. Bendell, Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN*

Background: BT5528 is a Bicycle Toxin Conjugate (BTC), comprising a bicyclic peptide targeting the tumor antigen EphA2, linked to a cytotoxin (monomethyl auristatin E [MMAE]) via a tumor microenvironment cleavable linker. *Bicycles* are a novel class of chemically synthesized constrained peptides, developed by Bicycle Therapeutics. EphA2 is reported to be overexpressed in a range of solid tumors, contributes to oncogenesis, tumor-associated angiogenesis and metastasis. Intracellular EphA2 signaling converges on pathways that are integral to cell growth, proliferation, migration and invasion. Increased EphA2 expression has been identified as a resistance mechanism to EGFR Tyrosine Kinase Inhibitor based therapy. BT5528 mechanism of action is dependent on tumor penetration, target binding and release of MMAE toxin payload. BTCs offer advantages over antibody-toxin conjugates exhibiting rapid penetration of dense tumors and decreased extra-tumor exposure. BT5528 exhibited a favorable preclinical profile supporting the initiation of a first-in-human study to investigate safety and efficacy of BT5528 in indications with evidence of EphA2 expression including non-small-cell lung cancer (NSCLC), ovarian cancer, triple-negative breast cancer (TNBC), gastric/upper gastrointestinal (GI), pancreatic and urothelial cancers. **Methods:** BT5528-100 (NCT04180371) is a Ph I/II study to evaluate safety and tolerability of weekly BT5528 alone and in combination with Q4W nivolumab. Each dose escalation utilizes a 3+3 design which converts to a Bayesian design to determine MTD or MAD and RP2D for BT5528 with and without nivolumab. Eligible patients must have advanced solid tumors associated with EphA2 expression which have recurred after exhausting standard treatment options. Patients must have available tumor tissue and acceptable hematologic and organ function, with exclusions for uncontrolled brain metastases, thromboembolic events, bleeding disorders, uncontrolled hypertension, CYP3A4 inhibitors/inducers or, for the nivolumab cohorts, autoimmune disease. On-study tumor and blood samples will be collected for biomarker evaluations including tumor EphA2 expression, ADA, and candidate response biomarkers for BT5528 alone and combination with nivolumab. Pharmacokinetic data will be reported for C1D1 and D15 for BT5528 and MMAE. The expansion phase will enroll specific tumor types to evaluate clinical activity of BT5528. Enrollment is ongoing. Clinical trial information: NCT04180371. Research Sponsor: Bicycle Tx Limited.

TPS3656 **Poster Session (Board #386), Fri, 8:00 AM-11:00 AM**

An open-label, first-in-human, phase I trial of the safety and efficacy of daily PCLX-001. *First Author: Randeep S. Sangha, Cross Cancer Institute, Edmonton, AB, Canada*

Background: Myristoylation regulates numerous membrane-bound signal transduction pathways important in cancer biology. This modification is catalyzed by N-myristoyltransferases 1 and 2 (NMT1 and NMT2). PCLX-001 is an oral small molecule with high affinity for both NMT proteins (IC50 of 5nM and 8nM, respectively) with high bioavailability and drug-like pharmacokinetic properties. In *ex vivo* sensitivity screening cell lines of hematologic cancer origin were exquisitely sensitive to PCLX-001, although high sensitivities and cell killing were also seen in some solid tumor lines derived from lung, pancreas, breast, colon, and bladder carcinomas. PCLX-001 demonstrated strong preclinical single-agent antitumor activity and tolerability *in vivo* in subcutaneous tumor xenograft models derived from lymphoma cell lines, lung cancer cell lines, a breast cancer cell line, as well as in a patient derived xenograft model from a patient with refractory DLBCL. The primary objective of this study is to determine the MTD and/or recommended phase II dose, safety, tolerability, and pharmacokinetics of PCLX-001 as a single agent, in patients with refractory lymphomas and advanced solid tumors. The secondary objective of the study is to evaluate the preliminary single agent antitumor activity of PCLX-001 in the patient populations studied. **Methods:** This is a multicenter, open-label, phase I dose-escalation study of oral PCLX-001 comprised of two parts (dose escalation and dose expansion). Eligible patients will have: histologically-confirmed advanced solid tumor or B-cell lymphomas who have failed prior therapy and/or are not eligible for therapies; ages $\geq$ 18 years; adequate organ function; life expectancy of at least 12 weeks; and measurable disease. Part A (dose-escalation) patients will be accrued in cohorts of 3 to 6 patients to each dose level, starting at 20 mg daily on a 28 day cycle. Dose escalation will follow a modified Fibonacci design such that the magnitude of escalation decreases as the dose level nears the human equivalent dose of the highest non-severely toxic dose in dogs and then escalate at 1.4 times the previous dose. Dose escalation and determination of the maximum tolerated dose will be based on the occurrence of dose limiting toxicities in cycle 1. Part B will have two single agent expansion cohorts (n = 20 each) in advanced solid malignancies and relapsed/refractory B-cell lymphoma, to determine the preliminary clinical activity of PCLX-001 to determine the recommended phase II dose. The first patient on study is planned for Q3 2020. Research Sponsor: Pacylex, Other Foundation.

TPS3657 **Poster Session (Board #387), Fri, 8:00 AM-11:00 AM**

A phase I/II, open-label, dose-escalation, and cohort-expansion study evaluating the safety, pharmacokinetics, and therapeutic activity of OBI-999 in patients with advanced solid tumors. *First Author: Apostolia Maria Tsimberidou, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Aberrant glycosylation is a hallmark of cancer. Glycosphingolipids (GSLs), glycans conjugated to a lipid (ceramide) core, are essential for the recruitment of immune-related proteins to specific membrane microdomains. Globo H (GH) is a GSL found on normal cells but highly overexpressed on various epithelial tumors playing a role in tumor development and progression. GH is a promising target for immunotherapy. OBI-999 is an ADC composed of a human recombinant immunoglobulin G (IgG) monoclonal antibody that selectively and specifically binds to GH, attached by a linker to the antimitotic agent monomethyl auristatin E (MMAE). Its mechanism of action is based on tumor-selective delivery of MMAE to GH-expressing tumors with subsequent tumor cell death. Preclinical studies demonstrated that OBI-999 antibody binds specifically to the GH antigen, and antitumor efficacy was noted in breast, gastric, pancreatic, and lung cancer xenograft models. The pharmacokinetics (PK) of OBI-999 were determined in normal and tumor-bearing mice, rats, and monkeys. Exposure of OBI-999 increased proportionally with dose. No sex difference or accumulation was seen. The primary objectives are to determine dose limiting toxicities (DLTs), the maximum tolerated dose (MTD), and the phase 2 recommended dose (P2RD). The secondary objectives are to assess the rates of objective response and clinical benefit, the duration of progression-free survival, the immunogenicity of OBI-999, and the PK and pharmacodynamics (PD) of OBI-999 and MMAE. **Methods:** In Part 1, a "3+3" dose-escalation part of the study, up to 30 patients with advanced solid tumors refractory to $\geq$1 line of systemic therapy, who cannot tolerate standard therapy, or for whom no standard treatment is available, regardless of GH status will be treated. OBI-999 will be administered as a 60-minute IV infusion using a dose range of 0.4, 0.8, 1.2, 1.6, and 2.0 mg/kg on day 1 of every 21-day cycle. In Part 2, the cohort-expansion portion of the study, patients will be treated at the MTD or at a lower RP2D as determined by cumulative toxicities and tolerability profile. The study will determine the preliminary clinical activity and safety of OBI-999 in up to 155 patients with advanced solid tumors, pancreatic, gastric, esophageal, and colorectal cancer according to a Simon two-stage phase 2 design. Patients must have GH overexpression defined as an H-score of $\geq$100 according to an FDA Investigational Device Exempt (IDE) validated IHC assay. Clinical trial information: NCT04084366. Research Sponsor: OBI Pharma Inc.

TPS3658 Poster Session (Board #388), Fri, 8:00 AM-11:00 AM

A first-in-man phase I/II study of OBI-3424, an AKR1C3-selective bis-alkylating agent prodrug, in subjects with advanced cancer, including hepatocellular carcinoma (HCC) and castrate-resistant prostate cancer (CRPC). *First Author: Apostolia Maria Tsimberidou, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Aldo-keto reductase family 1 member C3 (AKR1C3) modulates cellular differentiation and proliferation through indirect regulation of ligand access to hormone and nuclear receptor signaling. AKR1C3 is expressed at high levels in various human cancers, including HCC. In prostate cancer cells exposed to anti-androgen therapies, AKR1C3 is adaptively upregulated. CRPC is a potential indication for this targeted alkylating agent. AKR1C3 tumor expression is associated with poor patient survival and resistance to cancer therapies. OBI-3424 is a nitro-benzene prodrug of a nitrogen mustard that can be selectively cleaved in the presence of AKR1C3 enzyme into a bis-alkylating agent capable of forming intra- and inter-strand crosslinks with DNA, thereby resulting in cell death. The selectivity of OBI-3424 for AKR1C3 distinguishes it from traditional alkylating agents, which are nonselective. The primary objectives of the study are to evaluate the safety and tolerability of single-agent OBI-3424. The dose-escalation phase will determine the dose-limiting toxicities (DLT), maximum tolerable dose (MTD), and recommended Phase 2 dose (RP2D) of OBI-3424 through assessment of PK of OBI-3424 and OBI-2660 in plasma and urine. After determining the maximum tolerated dose (MTD), the study will enroll subjects with advanced HCC or CRPC, two tumor types with a high likelihood of over-expression of AKR1C3, into the dose expansion portion of the study according to a Simon two-stage phase 2 design. This phase is designed to assess the objective response rate, and progression-free survival in patients with HCC and CRPC. Immunohistochemistry assays are being developed to assess tumor expression of AKR1C3 for this study. The clinical safety and relationship of efficacy to AKR1C3 tumor expression will serve to guide further clinical development of OBI-3424 in these two unmet need settings. **Methods:** Based on the toxicology and PK results in cynomolgus monkeys, the starting dose is one sixth of the human equivalent dose of the highest non-severely toxic dose observed. Doses of 1, 2, 4, 6, 8, 12, and 14 mg/m^2 will be used. OBI-3424 is administered intravenously (IV) over 30 minutes on days 1 and 8 of each 21-day cycle. Subjects without clinically significant disease progression may continue on treatment for up to 2 years, if they do not experience a DLT or other significant toxicity. Clinical trial information: NCT03592264. Research Sponsor: OBI Pharma Inc.

TPS3659 Poster Session (Board #389), Fri, 8:00 AM-11:00 AM

SKB264 ADC: A first-in-human study of SKB264 in patients with locally advanced unresectable/metastatic solid tumors who are refractory to available standard therapies. *First Author: Yongheng Liu, Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China*

Background: Elevated expression of trophoblast antigen 2 (TROP2) is often associated with invasion/aggression, progression, and metastasis of many different tumor types. Efficacies of anti-TROP2 ADC have been demonstrated both preclinically and in the clinical trials. SKB264 is being developed as a further optimized TROP2-targeting ADC with a proprietary cytotoxic, belotecan-derived payload and novel stable conjugation chemistry to achieve average DAR (Drug Antibody Ratio) of 7.4. Release of payload upon SKB264 internalization is in a TROP2 expression dependent manner. Extensive preclinical studies demonstrated antitumor activity of SKB264 in vitro, in xenograft and patient-derived xenograft (PDX) animal models. In addition, safety studies have demonstrated a good safety profile to allow SKB264 to be studied in clinical trials. **Methods:** SKB264-01 is a global open label multicenter study. The study is divided into 2 parts, the phase I is to determine the safety profile, define MTD and/or the RP2D, and characterize DLTs of SKB264. Dose escalation and MTD identification will be directed using a Bayesian logistic regression model (BLRM) with overdose control. The phase II is to evaluate efficacy and obtain clinical activity data of SKB264 as a monotherapeutic agent at the RP2D in each of the designated Phase II cohorts and overall (n = 16 per cohort; n = 48 for entire Phase II part). Objective response rate (ORR) will be continuously evaluated in each cohort using a Bayesian hierarchical model. TROP2 assessments will not be performed prior to enrollment but it will be assessed retrospectively. Confirmation of TROP2 expression by immunohistology or other methods is not required, but the Sponsor will request tissue specimens from archived materials for determination of TROP2 expression. The patient must have, in the judgment of the investigator, historically documented, incurable, locally advanced or metastatic cancer that are refractory to standard therapies of one of the following types: i. ovarian epithelial cancer, ii. gastric adenocarcinoma, iii. pancreatic adenocarcinoma, iv. triple negative breast cancer, v. bladder cancer. Patient will receive study drug as a single IV infusion at the prescribed dose level at each administration. Cycles will continue until disease progression or unacceptable toxicity. Adverse Events (AE) will be graded according to CTCAE V.5.0. Responses will be evaluated according to RECIST V1.1. The enrollment will began in Mar 2020 in USA sites. Clinical trial information: NCT04152499. Research Sponsor: KLUS Pharm Inc.

TPS3660 Poster Session (Board #390), Fri, 8:00 AM-11:00 AM

A phase Ia/Ib, dose-escalation/expansion study of BI 907828 in combination with BI 754091 and BI 754111 in patients (pts) with advanced solid tumors. *First Author: Anthony W. Tolcher, NEXT Oncology, San Antonio, TX*

Background: Preclinical data show that the combination of a murine double minute 2–tumor protein 53 (MDM2–TP53) antagonist with anti-PD-1 and anti-LAG3 antibodies produces an anti-tumor effect in multiple tumor types. This Phase Ia/Ib study aims to determine the safety, recommended dose for expansion (RDE), and preliminary efficacy of BI 907828, a MDM2–TP53 antagonist, with BI 754091, an anti-PD-1 antibody, and BI 754111, an anti-LAG-3 antibody, in a variety of *TP53* wild-type cancers. **Methods:** In Phase Ia (dose escalation), ~30 pts with a confirmed diagnosis of any unresectable, advanced/metastatic solid tumor, irrespective of *TP53* mutation status, will be enrolled. Pts will receive one dose of BI 907828 every 21 days (Q3W), at a starting dose of 10 mg orally, plus BI 754091 and BI 754111 (240 mg and 600 mg, respectively, Q3W, intravenously). Dose escalation will be guided by a Bayesian Logistic Regression Model with overdose control. The primary endpoint is the maximum-tolerated dose of BI 907828 based on dose-limiting toxicities (DLTs) during the first treatment cycle. Secondary endpoints include pharmacokinetics and DLTs in the treatment period (to determine the RDE). In Phase Ib (dose expansion), pts with previously treated, unresectable, advanced/metastatic *TP53* wild-type tumors with ≥1 measurable target lesion will be enrolled into four expansion cohorts (1: NSCLC; 2: melanoma; 3: well-differentiated/dedifferentiated liposarcoma or undifferentiated pleomorphic sarcoma; 4: hepatocellular carcinoma). The RDE of BI 907828 will be administered with fixed doses of BI754091 and BI 754111 (Q3W). In the NSCLC cohort only, pts will be randomized to one of three arms: RDE of BI 907828 + 240 mg BI 754091 + 600 mg BI 754111 (arm A, 32 pts); 240 mg BI 754091 + 600 mg BI 754111 (arm B, 32 pts); RDE of BI 907828 + 240 mg BI 754091 (arm C, 16 pts). The primary endpoint is objective response (OR, per RECIST 1.1). Secondary endpoints include OR (per iRECIST), disease control (per RECIST 1.1 and iRECIST), progression-free survival (PFS), PFS rate at 12 and 24 weeks (cohort 3), and safety. Phase Ib will include at least 140 evaluable pts (80 pts in cohort 1 and 20 pts each in cohorts 2–4). Clinical trial information: NCT03964233. Research Sponsor: Boehringer Ingelheim.

TPS3661 Poster Session (Board #391), Fri, 8:00 AM-11:00 AM

Trial in progress: A phase Ib study of AMG 510, a specific and irreversible KRAS^{G12C} inhibitor, in combination with other anticancer therapies in patients with advanced solid tumors harboring *KRAS* p.G12C mutation (CodeBreak 101). *First Author: Marwan Fakih, City of Hope National Medical Center, Duarte, CA*

Background: Kirsten rat sarcoma viral oncogene homolog *(KRAS)* p.G12C mutation has been identified as a driver oncogenic mutation in several solid tumors (eg, non-small cell lung cancer [NSCLC], colorectal cancer [CRC]). Development of therapies targeting KRAS^{G12C} has been unsuccessful. AMG 510 is a specific and irreversible small molecule inhibitor of KRAS^{G12C}. A first-in-human clinical trial of AMG 510 monotherapy in patients with *KRAS* p.G12C mutant solid tumors is currently ongoing. AMG 510 in combination with additional anticancer therapies may lead to enhanced antitumor efficacy. This study is a master protocol designed to evaluate multiple investigational regimens of AMG 510 in patients with *KRAS* p.G12C mutant solid tumors. Here, we present two combination cohorts of AMG 510 with a mitogen-activated protein kinase kinase (MEK) inhibitor and an investigational anti-programmed cell death protein-1 (PD-1) therapy, respectively. Additional combination cohorts will be presented at the meeting. **Methods:** This is a phase 1b, open-label study evaluating AMG 510 in combination with a MEK inhibitor or an investigational anti-PD-1 therapy in pts with *KRAS* p.G12C mutant solid tumors. The dose exploration phase (part 1; n=20) will evaluate the safety and tolerability of AMG 510 in combination with the MEK inhibitor or anti-PD-1 therapy; this will be followed by a dose expansion phase (part 2; n=40) to verify the safety and tolerability profile of AMG 510 combination therapies and assess antitumor efficacy. Key eligibility criteria include locally-advanced or metastatic malignancy with *KRAS* p.G12C mutation identified through molecular testing and at least one or multiple lines of prior systemic therapy (eg, ≥2 for advanced/metastatic colorectal cancer). Primary endpoints include dose-limiting toxicities, treatment-emergent or -related adverse events. Secondary endpoints include pharmacokinetic parameters of combination regimens, disease control rate, duration of response, progression-free survival, and duration of stable disease (measured by computed tomography or magnetic resonance imaging and assessed per RECIST 1.1). The study began enrolling pts in December 2019 and is ongoing. For more information, please contact Amgen Medical Information: medinfo@amgen.com. Clinical trial information: NCT04185883. Research Sponsor: Amgen Inc.

TPS3662 Poster Session (Board #392), Fri, 8:00 AM-11:00 AM

First-in-human phase I study of SY-5609, an oral, potent, and selective noncovalent CDK7 inhibitor, in adult patients with select advanced solid tumors. *First Author: Kyriakos P. Papadopoulos, South Texas Accelerated Research Therapeutics, LLC, San Antonio, TX*

Background: SY-5609 is an oral, noncovalent, highly selective and potent inhibitor of cyclin-dependent kinase 7 (CDK7), a key regulator of 2 biological processes that play critical roles in driving tumor development: transcription and cell cycle control. Evaluation of SY-5609 as a single agent in PDX models from a range of solid tumors, including breast, ovarian, lung and colorectal tumors, revealed robust antitumor activity including complete regressions, and activity in models known to be resistant to standard of care therapy. Models with genetic alterations in RB pathway genes demonstrated deep ($>$ 90% TGI) and sustained SY-5609-induced tumor regressions following treatment discontinuation, in contrast to models without genetic alteration in RB pathway genes, suggesting that tumor cells with aberrant cell-cycle control may be particularly sensitive to SY-5609 treatment. The study is designed to evaluate the safety, tolerability, and maximum tolerated dose (MTD) of SY-5609, to characterize the pharmacokinetic (PK), pharmacodynamic (PD), and preliminary antitumor activity of SY-5609, and to explore candidate biomarkers predictive of response to SY-5609. **Methods:** This is a multi-center, open-label Phase 1 trial expected to enroll approximately 60 adult patients with select advanced solid tumors for which standard treatment is no longer effective. The dose escalation phase of the trial is open to adult patients with ovarian, breast, colorectal, or lung cancer, and patients with any solid tumor histology with molecular evidence of deregulated RB cell cycle control. SY-5609 is being administered orally once daily, for each 4-week cycle. Initially, patients will be enrolled into single-patient accelerated titration cohorts; subsequent cohorts will transition to a 3 + 3 design. Following completion of DLT evaluation at a given dose level, additional patients may be enrolled at that dose to further characterize safety, PK, PD, and early clinical activity. Data from this trial will support dose selection for planned evaluations of antitumor activity of SY-5609 as a single agent and in combination. Clinical trial information: NCT04247126. Research Sponsor: Syros Pharmaceuticals.

TPS3663 Poster Session (Board #393), Fri, 8:00 AM-11:00 AM

A phase I, open-label, multicenter, first-in-human study of the safety, tolerability, pharmacokinetics, and antitumor activity of TPX-0022, a novel MET/CSF1R/SRC inhibitor, in patients with advanced solid tumors harboring genetic alterations in MET. *First Author: David S. Hong, Department of Investigational Cancer Therapeutics (Phase I Program), The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Alterations in the MET gene, including amplifications, chromosomal translocations, and activating mutations (kinase domain [KD] or exon 14 [Δex14]), occur across various tumors and may function as oncogenic drivers. SRC family kinases function as a key downstream node for MET signaling. CSF1R is a receptor tyrosine kinase associated with tumor progression and suppression of the immune response in the tumor microenvironment. TPX-0022 is a type I kinase inhibitor with a novel macrocyclic structure that potently inhibits MET, CSF1R and SRC to simultaneously target oncogenic MET signaling, its key downstream mediators, and the tumor microenvironment. **Methods:** This is a multicenter phase 1 first-in-human, open-label study to determine the safety, tolerability, PK, and preliminary efficacy of TPX-0022 in adults with advanced solid tumors harboring genetic alterations in MET. TPX-0022 will be administered orally in continuous 28-day cycles. The primary endpoint is the incidence of DLTs and determination of recommended phase 2 dose (RP2D). Secondary endpoints include ORR by blinded independent central review, intra-cranial response rate, PFS and OS (dose expansion only). In the dose escalation portion, ~30 subjects age $\geq$18 with solid tumors harboring MET gene amplifications, Δex14, fusions or KD mutations as determined by local tissue-based or liquid biopsy will be enrolled in a 3+3 design. Intrasubject dose escalation will also be allowed. Once the RP2D has been determined, a food effect sub-study will be conducted and ~80 subjects will be enrolled in a dose expansion portion of the study into the following cohorts: I: non-small cell lung cancer (NSCLC) Δex14 (MET therapy naïve), II: NSCLC Δex14 (MET therapy pre-treated), III: MET amplified NSCLC, gastric, or hepatocellular carcinoma, IV: solid tumors with MET KD mutations or fusions. Correlative studies will include analysis of circulating cell-free DNA to identify genomic alterations that may predict activity of TPX-0022 as well as circulating protein biomarkers such as s-MET, HGF, CSF1 and serum cytokines. The study is open and enrolling in the dose escalation portion at the time of submission. Clinical trial information: NCT03993873. Research Sponsor: Turning Point Therapeutics.

TPS3665 Poster Session (Board #395), Fri, 8:00 AM-11:00 AM

Masterkey-01: Phase I/II, open-label multicenter study to assess safety, tolerability, pharmacokinetics, and antitumor activity of BDTX-189, an inhibitor of allosteric ErbB mutations, in patients with advanced solid malignancies. *First Author: Erika Paige Hamilton, Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN*

Background: A significant unmet need exists for drugs targeting allosteric ErbB mutations (non-canonical mutations outside the ATP binding site). Current EGFR and HER2 tyrosine kinase inhibitors or mAbs have limited antitumor activity against allosteric mutations, resulting in toxicity before adequate drug exposure (Connell and Doherty, 2017). BDTX-189 is a potent and selective orally available irreversible inhibitor targeting unique oncogenic driver mutations of ErbB kinases in EGFR and HER2, while sparing WT EGFR. Preclinical studies demonstrated antitumor activity across a range of allosteric ErbB mutants, including extracellular domain allosteric mutations of HER2 as well as EGFR and HER2 kinase domain exon 20 insertions (Buck, 2019). This first-in-human trial (NCT04209465) is aimed to determine the recommended phase 2 dose (RP2) and schedule (Phase 1, P1), and evaluate the efficacy (Phase 2, P2) of BDTX-189. P1 primary objective is to determine the RP2 dose and schedule of monotherapy BDTX-189. Secondary objectives include assessment of safety, tolerability, pharmacokinetics (PK), pharmacodynamic (PD) effects in tumor, and preliminary efficacy. The P2 primary objective is to assess antitumor activity of monotherapy BDTX-189. **Methods:** The study will enroll patients (pts) $\geq$18 yrs with histologically or cytologically confirmed locally advanced or metastatic solid tumors with no standard therapy available or for whom standard therapy is unsuitable or intolerable. P1 dose-escalation will use a BOIN design (Yuan, 2016) and will enroll $\leq$ 88 pts with allosteric HER2 or HER3 mutation; EGFR or HER2 exon 20 insertion mutation; HER2 amplified or overexpressing tumor; or EGFR exon 19 deletion or L858R mutation. BDTX-189 will be dosed orally (PO) initially QD in 3 wk cycles. Regimen optimization will use PK, PD and safety data and may explore a BID schedule. An expansion cohort of $\leq$12 pts will further evaluate safety and preliminary efficacy of BDTX-189 prior to P2. P2, utilizing a Simon 2-stage design, will enroll $\leq$100 pts with NSCLC with EGFR or HER2 exon 20 insertion mutations (cohort 1); breast cancer with an allosteric ErbB mutation (cohort 2); tumors (except breast) with S310F/Y mutation (cohort 3); and other allosteric ErbB mutations not defined in cohorts 1-3 (cohort 4). Assessments include safety, tolerability, DLTs, evaluation of MTD, PK, PD, and preliminary antitumor activity. Enrollment began 1/2020. Clinical trial information: NCT04209465. Research Sponsor: Black Diamond Therapeutics.

4000 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A phase II, multicenter, open-label study of trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01. *First Author: Salvatore Siena, Department of Oncology and Hemato-Oncology, Università degli Studi di Milano and Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, Milan, Italy*

Background: T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and topoisomerase I inhibitor payload. Early studies have shown promising activity in advanced HER2-expressing tumors. DESTINY-CRC01 (DS8201-A-J203; NCT03384940) is a phase 2, open-label, multicenter study of T-DXd in pts with HER2-expressing mCRC. **Methods:** Pts with centrally confirmed HER2-expressing, *RAS*–wild type mCRC that progressed on ≥ 2 prior regimens received T-DXd 6.4 mg/kg every 3 weeks (q3w) in 3 cohorts (A: HER2 IHC 3+ or IHC 2+/ISH+; B: IHC 2+/ISH−; C: IHC 1+). The primary endpoint was confirmed objective response rate (ORR) by independent central review in cohort A; secondary endpoints included, disease control rate (DCR; CR + PR + SD), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and ORR in cohorts B and C. **Results:** At data cutoff (Aug 9, 2019), 78 pts (A, 53; B, 7; C, 18) had received T-DXd. Median age was 58.5 y (range, 27-79 y), 52.6% of pts were male, and 89.7% had left colon or rectum cancer; median number of prior regimens was 4 (range, 2-11); all pts had prior irinotecan. Median treatment duration was 3.5 mo (95% CI, 2.1-4.3 mo; cohort A, 4.8 mo [95% CI, 3.9-5.8 mo]); 38.5% of pts remained on T-DXd treatment. The confirmed ORR was 45.3% (24/53 pts; 95% CI, 31.6%-59.6%) in cohort A, including 1 CR and 23 PRs; median DOR was not reached (95% CI, 4.2 mo-NE). The ORR in pts with prior anti-HER2 treatment was 43.8% (7/16 pts; 95% CI, 19.8%-70.1%). The DCR was 83.0% (44/53 pts; 95% CI, 70.2%-91.9%); median PFS was 6.9 mo (95% CI, 4.1 mo-NE); median OS was not reached. No responses were observed in cohorts B or C. Grade ≥ 3 treatment-emergent adverse events (TEAEs) occurred in 61.5% of pts (48/78); the most common (≥10%) were decreased neutrophil count (21.8%) and anemia (14.1%). Seven pts (9.0%) had TEAEs leading to drug discontinuation. Five pts (6.4%) had interstitial lung disease (ILD) adjudicated by an independent committee as related to T-DXd (2 grade 2; 1 grade 3; 2 grade 5 [the only drug-related deaths]). **Conclusions:** Overall, T-DXd 6.4 mg/kg q3w demonstrated remarkable activity in pts with HER2-expressing mCRC refractory to standard therapies, with a safety profile consistent with previous results. ILD is an important risk and requires careful recognition and intervention. Clinical trial information: NCT03384940. Research Sponsor: Daiichi Sankyo Co., Ltd.

4001 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Encorafenib plus cetuximab with or without binimetinib for *BRAF* V600E metastatic colorectal cancer: Updated survival results from a randomized, three-arm, phase III study versus choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC). *First Author: Scott Kopetz, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: BEACON CRC is a randomized, phase 3 study which evaluated the triplet of encorafenib (ENCO) + binimetinib (BINI) + cetuximab (CETUX) and the doublet of ENCO + CETUX vs. investigator's choice of irinotecan + CETUX or FOLFIRI + CETUX in patients (pts) with *BRAF*V600E metastatic colorectal cancer (mCRC) whose disease had progressed after 1-2 prior regimens in the metastatic setting. Primary endpoints were overall survival (OS) and objective response rate (ORR; by blinded central review) for triplet vs control. In a previous interim analysis, triplet and doublet improved OS and ORR versus standard of care. Here we report on an updated analysis. **Methods:** Updated analysis includes 6 months of additional follow-up and response data for all randomized pts. The study is ongoing. **Results:** Pts received triplet (n=224), doublet (n=220), or control (n=221). Median OS was 9.3 months (95% confidence interval [CI]:8.2, 10.8) for triplet and 5.9 months (95% CI:5.1-7.1) for control (hazard ratio [HR] (95% CI): 0.60 (0.47-0.75)). Median OS for doublet was 9.3 months (95% CI: 8.0-11.3) (HR vs. control: 0.61 (0.48-0.77). Confirmed ORR was 26.8% (95% CI: 21.1%-33.1%) for triplet, 19.5% (95% CI: 14.5%-25.4%) for doublet, and 1.8% (95% CI: 0.5%-4.6%) for control. Retrospective subgroup analyses suggested some pts may benefit more from triplet than doublet therapy (Table). Both triplet and doublet showed improved OS compared to control in all subgroups. Adverse events were consistent with prior analysis, with grade ≥3 adverse events in 65.8%, 57.4%, and 64.2% for triplet, doublet and control, respectively. **Conclusions:** The updated analysis of the BEACON CRC study confirmed that encorafenib + cetuximab with or without binimetinib improved OS and ORR in previously treated pts with *BRAF* V600E mCRC compared with standard chemotherapy. Clinical trial information: NCT02928224. Research Sponsor: Pfizer Inc.

OS in select subgroups, triplet vs. doublet.

		Events/Patients	Triplet vs Doublet Medians (months)	HR (95% CI)*
All Patients		265/444	9.3 vs 9.3	0.95 (0.74-1.21)
CRP	**High**	139/174	6.5 vs 5.1	0.76 (0.54, 1.06)
	Normal	120/261	13.8 vs 14.0	1.09 (0.76, 1.56)
ECOG PS	**1**	153/216	8.1 vs 6.1	0.81 (0.59, 1.11)
	0	112/228	10.4 vs 13.9	1.28 (0.88, 1.86)
No. of organs	**3+**	141/214	8.5 vs 6.7	0.69 (0.49, 0.96)
	<=2	124/230	10.0 vs 12.3	1.34 (0.94, 1.91)
Tumor Status	**Partially/Not Resected**	123/188	8.5 vs 8.3	0.80 (0.56, 1.14)
	Resected	142/256	9.5 vs 12.3	1.20 (0.86, 1.68)

*HR<1 favors triplet; HR>1 favors doublet

4002 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

First-line FOLFOX plus panitumumab versus 5FU plus panitumumab in RAS-BRAF wild-type metastatic colorectal cancer elderly patients: The PANDA study. *First Author: Sara Lonardi, Veneto Institute of Oncology (IOV)-IRCCS, Padua, Italy*

Background: Data on first-line treatment efficacy in elderly patients are limited. Many analyses adopt a questionable cut-off of 65 years and specific evidence with anti-EGFRs is low. FOLFOX-panitumumab (pan) is an option for RAS wild-type (wt) untreated mCRC patients. Guidelines recommend considering fluoropyrimidine monotherapy as an option for elderly patients, but no randomized studies have ever explored the role of the combination with an anti-EGFR. **Methods:** This is a prospective, open-label, multicenter phase II randomized trial. Unresectable and previously untreated *RAS-BRAF* wt mCRC patients aged ≥70 were randomized to receive FOLFOX-pan (arm A), or 5FU/LV-pan (arm B) for up to 12 cycles followed by pan maintenance until PD. The primary EP was PFS in both arms. Stratification criteria were age (≤75 vs > 75 years), ECOG PS (0–1 vs 2) and geriatric assessment with G8 Score (≤14 vs > 14). In each treatment arm, the null hypothesis for median PFS was set at ≤6 months. Assuming an expected median PFS time ≥9.5 months with both experimental regimens, a sample size of 90 patients in each arm granted to the study a power of 90%, with a type I error rate equal to 5% (1-sided Brookmeyer-Crowley test) for rejecting the null hypothesis. No formal comparison between the two arms was planned. **Results:** From Jul 2016 to Apr 2019 a total of 394 patients were screened, 211 were deemed eligible for inclusion and 185 were randomized (92 arm A and 93 arm B). Main pts' characteristics were (arm A/B): males 66%/61%; median age 77/77y; PS≥1 49%/55%; right colon 23%/21%; G8 > 14 31%/30%. At a median follow up of 20.5 mos, 135 (arm A/B: 64/71) PD events were collected. Median PFS was 9.6 (95% CI 8.8-10.9) in arm A with FOLFOX-pan and 9.1 (95% CI 7.7-9.9) in arm B with 5FU/LV-pan. Response rates were (arm A/B): 65%/57%. Grade 3-4 toxicities were (arm A/B): neutropenia 9.8%/1.1%; diarrhea 16.3%/1.1%; stomatitis 9.8%/4.4%; neurotoxicity 3.3%/0%; fatigue 6.5%/4.4%; skin rash 25%/24.2%, hypomagnesemia 3.3%/7.7%. **Conclusions:** Large prospective randomized studies in molecularly selected elderly mCRC are feasible with multicenter collaborative efforts. Primary EP was met in both treatment arms. 5FU/LV plus panitumumab for up to 12 cycles followed by panitumumab maintenance until PD might be a reasonable option in elderly mCRC patients with RAS/BRAF wt tumors deserving further investigations in phase III trials. Clinical trial information: NCT02904031. Research Sponsor: GONO Group, Pharmaceutical/Biotech Company.

4003 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Celecoxib in addition to standard adjuvant therapy with 5-fluorouracil, leucovorin, oxaliplatin (FOLFOX) in stage III colon cancer: Results from CALGB/SWOG 80702. *First Author: Jeffrey A. Meyerhardt, Dana-Farber Cancer Institute, Boston, MA*

Background: Aspirin and cyclooxygenase-2 (COX-2) inhibitors have been associated with a reduced risk of colorectal polyps and cancer in observational and randomized studies. CALGB/SWOG 80702 tested the effect of celecoxib, a COX-2 inhibitor, on reducing the risk of recurrence in stage III CC. **Methods:** CALGB/SWOG 80702 is a 2x2 randomized controlled phase III trial of 3 v 6 months of adjuvant FOLFOX (data previously reported as part of the IDEA collaboration) with concurrent celecoxib (400 mg daily) v placebo x 3 yrs for patients (pts) with resected stage III CC. The primary endpoint of the trial is disease-free survival (DFS), defined as time from randomization to recurrence or death from any cause. The trial was designed to provide 91% power to detect a hazard ratio (HR) of 0.79 in favor of celecoxib with 2-sided alpha = 0.05 (775 events required); due to slowing accumulation of events 4 years after complete accrual, power was lowered to 85% with same HR and alpha assumptions (696 events required). The DSMB released data on February 24, 2020 at median f/u of 5.6 yrs with 689 DFS events. **Results:** Between June 2010 and November 2015, 2,526 pts were consented and randomized to the trial. Treatment arms were well balanced by patient and tumor prognostic features, as well as low-dose aspirin use. Baseline characteristics included 45% female, 18% non-White, 8% Hispanic, 15% T4, 26% N2. 3-yr DFS for celecoxib was 76.3% v 73.3% for placebo (HR 0.89 [95% CI 0.77-1.04]; P = 0.14). 5-yr overall survival (OS) was 83.9% for celecoxib v 81.7% for placebo (HR 0.87 [95% CI 0.72-1.05]; P = 0.14). When considering the 4 treatment arms separately, 3-yr DFS was 77.0% for 12 months FOLFOX + celecoxib, 74.9% for 12 months FOLFOX + placebo, 75.5% for 6 months FOLFOX + celecoxib, and 71.9% for 6 months FOLFOX + placebo (log rank P = 0.22; P interaction = 0.64). There were no significant differences in grade 3-4 toxicity with celecoxib v placebo. Compliance with protocol celecoxib treatment, defined as 3 yrs of therapy completion or recurrence/death while on treatment, was 58.1% pts on celecoxib and 60.2% pts on placebo. **Conclusions:** The addition of celecoxib to standard chemotherapy did not significantly improve DFS or OS. Clinical trial information: NCT01150045. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

4004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Overall survival (OS) and long-term disease-free survival (DFS) of three versus six months of adjuvant (adj) oxaliplatin and fluoropyrimidine-based therapy for patients (pts) with stage III colon cancer (CC): Final results from the IDEA (International Duration Evaluation of Adj chemotherapy) collaboration. *First Author: Alberto F. Sobrero, Ospedale Policlinico San Martino IRCCS, Genoa, Italy*

Background: In overall population, IDEA pooled analysis did not demonstrate non-inferiority (NI) regarding 3y DFS in pts with stage III CC receiving 3m vs. 6m of adj FOLFOX/CAPOX. However, in pts treated with CAPOX (especially in low-risk pts), 3m of therapy was as effective as 6m. Results of OS and 5y DFS are reported. **Methods:** OS was defined as time from enrollment to death due to all causes. OS NI margin was conservatively set to be Hazard Ratio (HR) = 1.11, which is equivalent to: the maximum acceptable loss of OS efficacy, by shortening treatment to 3m, was half of the OS efficacy gained in MOSAIC trial (i.e., 2.26% absolute reduction in 5y OS rate). Pre-planned sub-group analyses included by regimen and risk group for both OS and 5y DFS. NI was to be declared if the one-sided false discovery rate adjusted (FDRa) NI p-value < 0.025. **Results:** With an overall median survival follow-up of 72 m (range per study, 62 to 84 m), 2584 deaths and 3777 DFS events among 12,835 pts from six trials were observed. Across 6 studies, 39.5% of pts received CAPOX (rate by study, 0% to 75.1%). Overall, the 5y OS rate was 82.4% (3m) and 82.8% (6m), with estimated OS HR of 1.02 (95% confidence interval [CI], 0.95-1.11; FDRa NI p, 0.058) and absolute 5-y OS rate difference of -0.4% (95% CI, -2.1 to 1.3%). Overall, the 5y DFS rate was 69.1% (3m) and 70.8% (6m), with estimated DFS HR of 1.08 (95%CI, 1.01-1.15, FDRa NI p, 0.22). HRs (95% CI) within subgroups see table. **Conclusions:** 5y OS rate reported in IDEA trials was higher than historical rates, regardless of duration of therapy. While overall survival in IDEA did not meet prior statistical assumptions for NI in overall population, the 0.4% difference in 5y OS should be placed in clinical context. OS and 5y DFS results continue to support the use of 3m adjuvant CAPOX for the vast majority of stage III colon cancer pts. This conclusion is strengthened by the substantial reduction of toxicities, inconveniencies and cost associated with shorter treatment duration. Clinical trial information: NCT01150045; 2009-010384-16; NCT00749450; ISRCTN59757862; 2007-003957-10; UMIN000008543; 2007-000354. Research Sponsor: U.S. National Institutes of Health, Other Government Agency.

	OS	Long-term DFS
CAPOX	0.96 (0.85, 1.08)	0.98 (0.88, 1.08)
FOLFOX	1.07 (0.97, 1.18)	1.16 (1.06, 1.26)
Low Risk (T1-3 N1)	0.95 (0.84, 1.08)	1.04 (0.94, 1.14)
High Risk (T4 or N2)	1.08 (0.98, 1.19)	1.12 (1.03, 1.22)

4005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone for liver metastasis from colorectal cancer: JCOG0603 study. *First Author: Yukihide Kanemitsu, Department of Colorectal Surgery, National Cancer Center Hospital, Tokyo, Japan*

Background: The role of adjuvant chemotherapy after hepatectomy is controversial for liver only metastases from colorectal cancer (LM). Current recommendations for oxaliplatin-containing adjuvant regimen (FOLFOX) for LM are based on extrapolation of the results of the EORTC intergroup trial 40983, which showed that perioperative FOLFOX confirmed a progression-free survival benefit but did not affect overall survival (OS) in LM patients. We conducted a randomized controlled trial to determine if adjuvant modified FOLFOX (mFOLFOX) is superior to hepatectomy alone for LM. **Methods:** Eligible patients aged 20-75 years who had histologically proven colorectal adenocarcinoma with an unlimited number of LM were randomly assigned (1:1) to receive either adjuvant mFOLFOX6 (oxaliplatin 85mg/m^2, l-LV 200 mg/m^2, 5-FU bolus 400 mg/m^2 and 2400mg/m^2 over 48 h), for 12 cycles after surgery (CTX arm), or surgery alone (S alone arm). When treatment compliance after 9 courses of CTX was as high as expected in phase II, the registration was continued in phase III. The primary endpoint of phase III was disease-free survival (DFS), and the secondary endpoints were OS, toxicity, and sites of relapse. The planned sample size was 150 patients (pts) per arm, with a one-sided alpha of 5%, and 80% power detecting a 5y-DFS difference of 12% (25% with S alone vs. 37% with CTX). **Results:** Between Mar. 2007 and Jan. 2019, 300 patients were randomized. 151 pts were allocated to CTX, and 149 pts to S alone. When the third interim analysis of phase III was performed in Dec. 2019, the DSMC recommended the early termination of the trial because a statistically significant difference in terms of DFS but the futility in terms of OS was found. With a median follow-up period of 54 months for disease-free surviving patients, the 3y-DFS was 52.1% (95% CI 43.2 – 60.2) with CTX and 41.5% (33.2 – 49.6) with S alone (hazard ratio 0.63 [0.45 – 0.89], one-sided $p = 0.002 < 0.0163$ for the one-sided alpha level at the interim analysis). However, the 3y-OS was 86.6% (79.2-91.4) with CTX and 92.2% (86.0 – 95.8) with S alone (hazard ratio 1.35 [0.84 – 2.19]). The 5y-OS was 69.5% (59.6-77.5) with CTX and 83.0% (74.5-88.9) with S alone. Median OS after recurrence was 38.4 months in the CTX arm and 87.6 in the S alone arm. **Conclusions:** DFS did not correlate with OS for LM. Postoperative chemotherapy with mFOLFOX6 improves DFS but worsens OS over surgery alone due to more deaths after recurrence in the CTX arm. Adjuvant mFOLFOX is not beneficial to patients after hepatectomy for LM. Clinical trial information: UMIN000000653. Research Sponsor: National Cancer Center Research and Development Fund and Grants-in-Aid for Cancer Research.

4006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Short-course radiotherapy followed by chemotherapy before TME in locally advanced rectal cancer: The randomized RAPIDO trial. *First Author: Geke Hospers, University of Groningen, University Medical Center Groningen, Department of Medical Oncology, Groningen, Netherlands*

Background: Local control in locally advanced rectal cancer (LARC) has improved. However, systemic relapses remain high even with postoperative chemotherapy, possibly due to low compliance. Short-course radiotherapy (SCRT) followed by delayed surgery with, in the waiting period, chemotherapy, may lead to better compliance, downstaging and fewer distant metastases. The main objective of the international multicenter phase III RAPIDO trial is to decrease Disease-related Treatment Failure (DrTF), defined as locoregional failure, distant metastasis, a new primary colon tumor or treatment-related death, by reducing the risk of systemic relapse without compromising local control. **Methods:** MRI-diagnosed LARC patients with either cT4a/b, extramural vascular invasion, cN2, involved mesorectal fascia or enlarged lateral lymph nodes considered to be metastatic were randomly assigned to SCRT (5x5 Gy) with subsequent six cycles of CAPOX or nine cycles of FOLFOX4 followed by total mesorectal excision (TME) (experimental arm) or, capecitabine-based chemoradiotherapy (25-28 x 2.0-1.8 Gy) followed by TME and optional, predefined by hospital policy, postoperative eight cycles of CAPOX or twelve cycles of FOLFOX4 (standard arm). **Results:** Between June 2011 and June 2016, 920 patients were randomized. Pathological complete response rates were 27.7% vs 13.8% (OR 2.40 [1.70 – 3.39]; $p < 0.001$) in the experimental and standard arms, respectively. At three years, cumulative probability of DrTF was 23.7% in the experimental arm and 30.4% in the standard arm (HR 0.76 [0.60 – 0.96]; $p = 0.02$). Probability at three years of distant metastasis and locoregional failure were, in the experimental and standard arms, 19.8% vs 26.6% (HR 0.69 [0.53 – 0.89]; $p = 0.004$) and 8.7% vs 6.0% (HR 1.45 [0.93 – 2.25]; $p = 0.10$), respectively. No differences in DrTF between hospitals with or without policy for postoperative chemotherapy were found ($p = 0.37$). Overall health ($p = 0.192$), quality of life ($p = 0.125$) and low anterior resection syndrome score ($p = 0.136$) were comparable between the two treatment arms. **Conclusions:** A lower rate of DrTF, as a result of a lower rate of distant metastases, in high-risk LARC patients can be achieved with preoperative short-course radiotherapy, followed by chemotherapy and TME than by conventional chemoradiotherapy. In addition, the high pCR rate, achieved with the experimental treatment regimen can contribute to organ preservation. This treatment can be considered as a new standard of care. Clinical trial information: NCT01558921. Research Sponsor: Dutch Cancer Foundation, Swedish Cancer Society, Swedish Research Council, Spanish Ministry of Economy and Competitiveness, Spanish Clinical Research Network and European Regional Development Fund.

4007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: Final results of PRODIGE 23 phase III trial, a UNICANCER GI trial. *First Author: Thierry Conroy, Institut de Cancérologie de Lorraine, Vandoeuvre-Les-Nancy, France*

Background: PRODIGE 23 investigated the role of neoadjuvant mFOLFIRINOX before preoperative (preop) chemoradiation (CRT), with TME-surgery and adjuvant chemotherapy (CT) in resectable locally advanced rectal cancer. **Methods:** PRODIGE 23 is a phase III multicenter randomized clinical trial. Eligible pts had cT3 or cT4, M0 rectal adenocarcinomas <15 cm from the anal verge, age 18-75 years, and WHO PS ≤ 1. Randomization was stratified by center, T stage, N status, tumor location, and perirectal fat extramural extension. Primary endpoint was 3-yr disease-free survival (DFS). Main secondary endpoints were ypT0N0 rate, overall survival (OS) and metastasis-free survival (MFS). 460 pts were required to observe 136 events to show a gain in 3-year DFS from 75% to 85% (HR=0.56) with a 2-sided α=0.05 and 90% power. HR and 95% CI were estimated by a stratified Cox proportional hazard model. Arm A pts received preop CRT (50 Gy, 2 Gy/fraction [fr]; 25 fr + capecitabine), surgery, then adjuvant CT for 6 months (mos). Arm B pts received 6 cycles of mFOLFIRINOX (oxaliplatin 85 mg/m^2, leucovorin 400 mg/m^2, irinotecan 180 mg/m^2 D1, and 5-FU 2.4 g/m^2 over 46 h) every 14 days, followed by the same preop CRT, surgery and 3 mos of adjuvant CT. Adjuvant CT consisted of mFOLFOX6 or capecitabine, depending on the centre's choice for all pts. Imaging work-up, operative and pathology reports were centrally reviewed. **Results:** (ITT) Between 6/2012 and 6/2017, 230 and 231 pts were randomly assigned in Arm A/B, respectively by 35 participating centers. Pts characteristics were well balanced. Neoadjuvant mFOLFIRINOX and CRT in both arms were well tolerated. Compliance to CRT and to adjuvant CT was not hampered by neoadjuvant CT. Surgical morbidity did not differ between the 2 arms. The ypT0N0 rate was 11.7 vs 27.5% in Arm A/B ($p<0.001$). Median follow-up was 46.5 mos. 136 DFS events was reported. 3-yr DFS was significantly increased in arm B (HR 0.69, 95% CI 0.49-0.97, p=0.034): 68.5% (CI: 61.9-74.2) vs 75.7% (CI: 69.4-80.8) in arm A/B. The subgroup analysis showed no evidence of heterogeneity of the effect size of treatment on DFS. 3-yr MFS was also significantly higher in arm B: 71.7 in arm A vs 78.8% (HR 0.64, CI 0.44-0.93, $p<0.02$) in arm B. 3-yr OS was 87.7 vs 90.8% (HR 0.65, CI 0.40-1.05, p=0.077) in arm A/B, with 54.2% of the pts with recurrence being alive. **Conclusions:** Neoadjuvant mFOLFIRINOX plus CRT is safe, and significantly increased ypCR rate, DFS and MFS. OS data are not mature. Clinical trial information: NCT01804790. Research Sponsor: FRENCH CANCER INSTITUTE - INCA - PHRC, Other Foundation.

4008 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Preliminary results of the organ preservation of rectal adenocarcinoma (OPRA) trial. *First Author: Julio Garcia-Aguilar, Colorectal Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY*

Background: Organ preservation (OP) with a watch and wait strategy (WW) and total neoadjuvant therapy (TNT) are new treatment paradigms for patients with locally advanced rectal cancer. The safety and efficacy of WW and of TNT have not been studied prospectively. **Methods:** Patients with MRI stage II and III rectal adenocarcinoma were randomized to 4 months of FOLFOX or CAPEOX before (Induction) or after (Consolidation) fluorouracil or capecitabine based chemoradiotherapy (CRT). Patients were re-staged 8-12 weeks after finishing TNT with digital rectal exam, flexible sigmoidoscopy and MRI. Patients with complete or near-complete clinical response were offered WW. Those with incomplete response had total mesorectal excision. The trial was designed so that each arm served as its own single-stage study that discriminates between 3-year disease-free survival (DFS) rates of 75% (historical null) and 85%, with 86% power, and a two-sided type I error of 5%. Secondary objectives included comparing DFS, OP, and distant metastasis-free survival (DMFS) rates between the two arms using the log-rank test. **Results:** Of 324 patients enrolled, 307 (152 I, 155 C) are currently evaluable for the time-to-event analysis as of 2/1/2020. Median follow-up is 2.1 years; 52 DFS events were observed. Patient demographics and tumor characteristics were generally balanced across the two arms. Full compliance with systemic chemotherapy was 82% and 81% for the I- and C-arms, respectively. The median radiation dose was 5400 cGy for both arms. Table shows 3-y DFS, DMFS, and OP rates. **Conclusions:** A WW strategy for patients with locally advanced rectal cancer that achieve a clinical complete response to TNT results in organ preservation for a high proportion of patients without compromising survival. Up-front CRT followed by consolidation chemotherapy resulted in a numerically higher WW rate compared to induction chemotherapy followed by CRT. Clinical trial information: NCT02008656. Research Sponsor: U.S. National Institutes of Health.

3-year rates with 95% CI.

	Induction		Consolidation		p*
DFS	78%	(70%,87%)	77%	(69%,86%)	0.90
DMFS	81%	(74%,90%)	83%	(76%,91%)	0.86
OP	43%	(35%,54%)	58%	(49%,69%)	0.01

*log-rank test

4009 Poster Discussion Session; Displayed in Poster Session (Board #1), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Circulating tumor DNA to detect minimal residual disease, response to adjuvant therapy, and identify patients at high risk of recurrence in patients with stage I-III CRC. *First Author: Noelia Tarazona, Department of Medical Oncology, INCLIVA Biomedical Research Institute, University of Valencia, Instituto de Salud Carlos III, CIBERONC, Valencia, Spain*

Background: The clinical utility of tracking circulating tumor DNA (ctDNA) as a non-invasive biomarker for detecting minimal residual disease (MRD) and stratifying patients based on their risk of developing relapse has been well established in colorectal cancer (CRC). This study evaluates the detection and longitudinal monitoring of ctDNA in CRC patients pre- and post-operatively, during and after adjuvant chemotherapy (ACT). **Methods:** The prospective, multicenter cohort study recruited patients (n = 193) diagnosed with resected stage I-III CRC. Plasma samples (n = 1052) were collected at various timepoints with a median follow up of 21.6 months (4.6-38.5 months). Individual tumors and matched germline DNA were whole-exome sequenced and somatic mutations identified. Multiplex PCR assays were designed to 16 tumor-specific single-nucleotide variants to track ctDNA in plasma samples. The study evaluated the relationship between ctDNA status and clinical outcomes including radiologic imaging. Cox regression was used to calculate recurrence-free survival (RFS) in patients stratified by ctDNA status postoperatively and post-ACT. Multivariable analysis was performed with all clinical variables. Best model was selected according to Akaike Information Criterion. **Results:** Pre-operatively ctDNA was detected in 90% (n = 166/185) of the patients. Post-operative ctDNA status prior to ACT was assessed in 152 patients, of which 9.2% (14/152) were identified to be MRD-positive and 78.5% (11/14) eventually relapsed. In contrast, 10.1% (14/138) of MRD-negative cases relapsed (HR: 16.53; 95% CI: 7.19-38.02; $p < 0.001$). Longitudinal ctDNA-positive status, post-ACT (n = 84) and post definitive therapy (n = 139) was associated with a 27.92 HR (95% CI: 9.16-85.11; $p < 0.001$) and a 47.52 HR (95% CI: 17.34-130.3.; $p < 0.001$), respectively. In the multivariable analysis, longitudinal ctDNA status was the only significant prognostic factor associated with RFS (HR: 53.19, 95% CI: 18.87-149.90; $p < 0.001$). Serial ctDNA analysis detected MRD up to a median of 9.08 months (0.56-16.5 months) ahead of radiologic relapse with a sensitivity of 79.1% and specificity of 99%. **Conclusions:** Postoperative ctDNA analyses detect patients with high-risk of recurrence, with near 100% specificity. Early detection of MRD and longitudinal monitoring of ctDNA could guide treatment decisions. Intervention trials to assess the clinical benefit of ctDNA use are underway. Research Sponsor: Natera, Inc., San Carlos, CA.

4010 Poster Discussion Session; Displayed in Poster Session (Board #2), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A new prognostic and predictive tool to enhance shared decision making in stage III colon cancer. *First Author: Alberto F. Sobrero, Ospedale Policlinico San Martino IRCCS, Genoa, Italy*

Background: Survival outcomes in patients with stage III colon cancer varies widely according to T-N sub-stages. The ability to estimate the benefit of each therapeutic option (surgery alone, fluoropyrimidines alone, oxaliplatin-based doublet for either 3 or 6 months) in each T-N subgroup within stage III, may provide more accurate information helping doctors and patients in the complex shared decision-making process surrounding adjuvant therapy. **Methods:** Theoutcomedata of 12,834 patients with stage III colon cancer enrolled in the IDEA trial served as our database. Patients were categorized in 16 sub-stages, based on the T-N categories. We created a meta-regression model to predict the expected 3-year DFS within each T-N sub-stage and hence the 5-year DFS rates were projected. We then evaluated the efficacy of each therapeutic option in every sub-stage, working backward by subtraction, using an average of the HRs reported in the pertinent trials publication as conversion factor. **Results:** Large differences in 3-year DFS rate were observed among the subgroups, ranging from 95% (T1N1a) to 29% (T4N2b) in the overall population. The contribution to outcome of each therapeutic option in this setting varied widely across sub-stages. According to our model, patients with T1N1a cancers have a projected 5-year DFS of 85% with surgery alone. Adjuvant fluoropyrimidine alone results in 4.2% absolute DFS gain; an additional 1.7% and 0.6% gain is seen with oxaliplatin for 3 and 6 months, respectively. Patients with T4N2b cancers show a 4.7% 5-year DFS with surgery alone, and a 7.1%, 5.0%, 2.1% increase with the aforementioned adjuvant options, respectively. **Conclusions:** The resulting overlay bar graph gives patients and doctors the projected relative benefit of each treatment option and may substantially help the shared decision-making process. Research Sponsor: This research was partly supported by Associazione Italiana per la Ricerca sul Cancro (AIRC) IG 2018; by the National Cancer Institute at the National Institutes of Health [grant number: U10CA180882]; NCA (Institut National du Cancer) and PHRC2009 (Inst.

4011 Poster Discussion Session; Displayed in Poster Session (Board #3), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Impact of high-risk features on disease-free survival (DFS) in patients (pts) with high-risk stage II colon cancer (CC) in ACHIEVE-2 trial as part of the IDEA collaboration. *First Author: Dai Manaka, Kyoto Katsura Hospital, Kyoto, Japan*

Background: The IDEA collaboration for high-risk stage 2 colorectal cancer patients (pts) demonstrated that for CAPOX, 3 months was non-inferior to 6 months treatment, while for FOLFOX, 6 months was superior to 3 months treatment. We investigated the impact of high risk features on disease-free survival (DFS). **Methods:** ACHIEVE-2, one of the 4 IDEA studies (SCOT, TOSCA, ACHIEVE-2, HORG), was an open-label, multicenter randomized trial for high-risk stage II colon cancer. High risk features are defined as one or more: T4, inadequate nodal harvest < 12, poorly differentiated, clinical sign of obstruction and perforation or vascular invasion. The association of high risk features with DFS were measured by Cox regression analyses. **Results:** Between 2014 and 2017, ACHIEVE-2 enrolled 525 pts, out of whom 514 pts were the modified ITT (mITT) population; 432 received CAPOX (84.0%) and 82 did mFOLFOX6 (16.0%). High-risk features included 35.8% of T4, 12.8% of inadequate nodal harvest, 11.5% of poorly differentiated, 19.3% of obstruction, 6.4% of perforation and 87.5% of vascular invasion; 47.3% had one features, 35.2% had two, 14.6% had three, and 2.9% had four or more. With a median follow-up of 36.1 months, 3-year DFS rates were 88% in both arms, with a hazard ratio (HR) of 1.12 (95% CI, 0.67-1.87, p=0.67). In multivariate analysis, T4 (HR 3.77 [2.18-6.53], $p< 0.0001$) and inadequate nodal harvest (HR 2.98 [1.59-5.59], p= 0.0006) remained independent significant negative prognostic factors. The 3-year DFS rates in T4 and Non-T4 diseases were 78% and 94% ($p<0.0001$), while 3-year DFS rate in pts with inadequate and adequate nodal harvest were 77% and 90% (p=0.0059). No interaction was observed between treatment duration and T4 or inadequate nodal harvest. **Conclusions:** Our findings indicated the relative impact of high risk features on DFS varies across factors; T4 and inadequate nodal harvest < 12 were more significant than the others. Our results must be interpreted within the combined analysis as well as within the reproducibility of results across the 4 trials. Clinical trial information: 000013036. Research Sponsor: None.

4012 Poster Discussion Session; Displayed in Poster Session (Board #4), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Improving the AJCC/TNM staging classification for colorectal cancer: The prognostic impact of tumor deposits. *First Author: Oliver Peacock, Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Identification of tumor deposits (TD) currently plays a limited role in staging for colorectal cancer (CRC) other than for N1c designation. The aim of this study was to determine the prognostic impact, beyond AJCC N1c designation, of TD among primary CRC patients. **Methods:** Patients with stage 1 to 3 primary CRC diagnosed between 2010 and 2015 were identified from the Surveillance, Epidemiology and End Results (SEER) database. Cancer specific survival (CSS) stratified by TDs and nodal status was calculated, and Kaplan-Meier method and multivariable COX proportional hazards regression analyses were performed. **Results:** A total of 74,494 patients with primary CRC were identified. Mean age was 66.4 (SD+/-13.2) years, 36,988 (49.7%) were female and 40,651 (54.6%) were right-sided. TDs were present in 4,481 patients (6.0%) and 26,603 (35.7%) had lymph node metastases. The presence of TDs were significantly associated with adverse tumor characteristics including advanced pathological stage, nodal and metastasis status, higher grade and perineural invasion. Incorporating TDs into each nodal status was independently associated with worse CSS and supported reclassification of nodal status to incorporate TDs following multivariable regression analysis as outlined in the table. Following multivariable regression analysis, the proposed AJCC nodal reclassification incorporating TDs, in combination with tumor stage was a strong predictor of CSS, and also represents a new summary staging. **Conclusions:** TDs are an independent predictor of worse outcome in CRC. The presence of TDs have distinctly different CSS and these data support modification of the current N classification. This study proposes a reclassification of the AJCC system for CRC to incorporate TDs and informs an updated node and summary stage. Research Sponsor: None.

Proposed AJCC Reclassification	Includes current & modification	Adjusted HR (95% CIs)
N0	N0	1.00
N1a	N1a TD-ve	1.90 (1.78-2.05)
N1b	N1b TD-ve, N1c	2.63 (2.48-2.80)
N1c	Removed	-
N2a	N2a TD-ve, N1a-b TD+ve	3.73 (3.50-3.98)
N2b	N2a TD +ve, N2b TD-ve	6.12 (5.73-6.54)
N3	N2b TD+ve	7.91 (6.94-9.01)

4013 Poster Discussion Session; Displayed in Poster Session (Board #5), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

FOxTROT: neoadjuvant FOLFOX chemotherapy with or without panitumumab (Pan) for patients (pts) with locally advanced colon cancer (CC). *First Author: Jenny F. Seligmann, University of Leeds, Leeds, United Kingdom*

Background: FOxTROT has reported marked down-staging, reduced perioperative morbidity and a trend towards fewer recurrences with 6 wks of oxaliplatin-fluoropyrimidine neoadjuvant chemotherapy (NAC) in CC (Seymour, ASCO 2019 abstract 3504). Using updated data, we investigate the contribution of panitumumab (Pan) and tumour markers to efficacy of NAC. **Methods:** 1053 pts with radiologically-staged T3-4, N0-2, M0 CC were randomly allocated (2:1) to either 6 wks of NAC and 18 wks of postoperative adjuvant chemotherapy (AC) or 24 wks of AC. 279 pts with *RAS*-wt tumours were also randomised 1:1 to receive Pan or not with NAC. The primary endpoint was freedom from recurrence or residual disease at 2 years for NAC vs AC, and depth of extramural spread for the Pan randomisation; secondary endpoints include safety, histological downstaging, CC-specific survival and OS. **Results:** Of 699 allocated pre-and-postoperative chemotherapy, 674 (97%) started and 612 (88%) completed NAC. 684/699 (97.8%) pre-and-postoperative and 349/354 (98.6%) control patients underwent tumour resection. There was marked T- and N-down-staging and tumour regression with NAC (all $p<0.001$). There were fewer disease recurrences within 2 years in the NAC than AC group: 15.6% (109/698) vs 19.5% (69/354), RR=0.76 (95%CI 0.56-1.02), P=0.07. Response to NAC was significantly ($p<0.001$) less in MMR-deficient (dMMR) than MMR-proficient (pMMR) tumours: 7%(8/115) vs 23%(128/553) moderate or greater histological tumour regression. Reductions in 2-year recurrence were also seen only in pMMR tumours [RR=0.72 (0.52-1.00), p=0.05], with no apparent benefit in dMMR tumours: RR=0.94 (0.43 to 2.07), p=0.9]. Analyses of panitumumab will be presented. **Conclusions:** Six weeks of NAC for operable CC can be delivered safely, with marked histopathological down-staging, and may result in better disease control at 2 years in pMMR disease. Clinical trial information: 87163246. Research Sponsor: Cancer Research UK, Pharmaceutical/Biotech Company.

4014 Poster Discussion Session; Displayed in Poster Session (Board #6), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Tailored treatment strategy for locally advanced rectal carcinoma: Five-year results of the French phase II, randomized, multicenter GRECCAR4 trial. *First Author: Philippe Rouanet, Institut Régional du Cancer de Montpellier, Montpellier, France*

Background: Preoperative radiochemotherapy and total mesorectal excision are the standard-of-care for locally-advanced rectal carcinoma, but some patients are over- or undertreated. Our phase II study assessed the feasibility of tailored radiochemotherapy, based on tumor response to induction high-dose chemotherapy (FOLFIRINOX). **Methods:** We enrolled 206 patients; good responders after chemotherapy (≥75% tumor volume reduction) were randomly assigned to immediate surgery (arm A) or standard radiochemotherapy (Cap 50: 50 Gy and oral capecitabine daily) plus surgery (arm B). Poor responders were randomly assigned to Cap 50 (arm C) or intensive radiochemotherapy (Cap 60 (60 Gy irradiation), arm D) before surgery. **Results:** After induction treatment, 194 patients were classified as good (n=30, 15%) or poor (n=164, 85%) responders, and included in arms A and B (16 and 14 patients) or C and D (113 and 51 patients). The primary objective was obtained: (90% CI) R0 resection rates in the four arms respectively were 100% (74–100), 100% (85–100), 83% (72–91), and 88% (77–95). At 5 years: overall survival 90% (CI: 47.3-98.5), 93.3% (CI: 61.3-99.0), 84.3% (CI: 71.0-91.8), 86.1% (CI: 71.6-93.5); disease-free survival 80% (CI: 40.9-94.6), 89.5% (CI: 64.1-97.3), 72.9% (CI: 58.5-82.9), 72.8% (CI: 57.7-83.2); local recurrence 0, 0, 2.1% (CI: 0.3-13.9), 9.3% (CI: 3.6-23.0); metastasis 20% (CI: 5.4-59.1), 10.5% (CI: 2.7-35.9), 18% (CI: 31.8-94.6), 18.8% (CI: 10.2-33.0). Late morbidity and quality of life evaluations showed no significant difference between arms. **Conclusions:** Tailoring preoperative radiochemotherapy based on induction treatment response is safe and promising. Early tumoral response to induction chemotherapy can discriminate tumor prognosis. Clinical trial information: NCT01333709. Research Sponsor: Grant INCa-DGOS_5506: PHRC-K 2012–112.

4015 Poster Discussion Session; Displayed in Poster Session (Board #7), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

FOLFOXIRI/bevacizumab (bev) versus doublets/bev as initial therapy of unresectable metastatic colorectal cancer (mCRC): A meta-analysis of individual patient data (IPD) from five randomized trials. *First Author: Chiara Cremolini, Department of Translational Research and New Technologies in Medicine and Surgery, Unit of Medical Oncology 2, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy*

Background: Several randomized trials demonstrated that intensifying the upfront chemotherapy in combination with bev is beneficial for mCRC patients with an increased incidence of some adverse events. All trials had primary endpoints other than OS, and a proper estimation of the magnitude of the OS benefit from FOLFOXIRI/bev versus doublets (FOLFIRI or FOLFOX)/bev is currently lacking. Within each trial, subgroup analyses failed to identify predictors of benefit from the intensified therapy. To test OS with higher power compared to single trials, and to explore interaction of treatment effect with main patients' and disease characteristics, we performed an IPD meta-analysis. **Methods:** IPD were collected from 5 randomized trials: CHARTA (NCT01321957), OLIVIA (NCT00778102), STEAM (NCT01765582, only combined FOLFOXIRI/bev and FOLFOX/bev arms), TRIBE (NCT00719797) and TRIBE2 (NCT02339116). Primary endpoint was OS. Secondary endpoints included PFS, objective response rate (ORR), R0 resection rate, G3/4 adverse events, and subgroup analyses. All statistical analyses were by intention-to-treat, stratified by trial. **Results:** 1697 pts randomized to FOLFOXIRI/bev (N=846) or doublets/bev (N=851) were included. Among pts in the doublets/bev group, 595 (70%) received FOLFOX/bev and 256 (30%) FOLFIRI/bev. At a median follow up of 39.9 mos, pts assigned to FOLFOXIRI/bev reported significantly longer OS than those assigned to doublets/bev (median OS 28.9 vs 24.5 months; HR 0.81 [95%CI 0.72-0.91], $p<0.001$), with no significant heterogeneity among trials ($p=0.39$; $I^2=2\%$). The estimated 5-yr OS was 22.3% vs 10.7% ($p<0.001$). No significant interaction effect between treatment arm and OS was demonstrated in terms of metastatic spread (liver-limited vs. not liver-limited p=0.665), primary side (p=0.656), and *RAS/BRAF* status (p=0.337). Pts assigned to FOLFOXIRI/bev achieved longer PFS (median PFS 12.2 vs 9.9 months; HR 0.74 [95%CI 0.67-0.82], $p<0.001$), higher ORR (64.5% vs 53.6%, $p<0.001$), higher R0 resection rate (16.4% vs 11.8%, p=0.007), and experienced higher rates of G3/4 neutropenia ($p<0.001$), febrile neutropenia (p=0.019), mucositis (p=0.024), nausea (p=0.016), and diarrhea ($p<0.001$). **Conclusions:** FOLFOXIRI/bev determines a clinically and statistically significant improvement of mCRC patients' OS vs doublets/bev with a meaningful effect also on 5-yr OS, PFS, ORR and R0 resection rate. No significant heterogeneity among explored subgroups was found. Research Sponsor: None.

4016 Poster Discussion Session; Displayed in Poster Session (Board #8), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Consensus molecular subtypes and CRCassigner classifications in metastatic colorectal cancer (mCRC): Prognostic and predictive impact in the TRIBE2 study. *First Author: Beatrice Borelli, Department of Translational Research and New Technologies in Medicine and Surgery, Unit of Medical Oncology 2, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy*

Background: The TRIBE2 study (NCT02339116) recently demonstrated the superiority of upfront FOLFOXIRI/bevacizumab (bev) when compared to a pre-planned strategy of doublets/bev in molecularly unselected but mostly (74%) *RAS*/*BRAF* mutant mCRC patients. The Consensus Molecular Subtypes (CMS) and CRCAssigner (CRCA) demonstrated prognostic value in multiple studies, but their predictive role has not been established so far. Given the poor prognosis associated with early stage mesenchymal/stem-like subtypes, we hypothesized that the CMS/CRCA classifiers could predict benefit from the upfront intensified strategy in patients included in the TRIBE2 study. **Methods:** Untreated formalin-fixed paraffin-embedded samples were classified into CMS/CRCA subtypes using a custom nCounter assay (NanoString Technologies). The impact of subtypes on progression free survival (PFS), progression free survival 2 (PFS2, defined as the time from randomization until the second evidence of disease progression) or overall survival (OS) was evaluated in the profiled population. **Results:** 426 and 428 (63%) patients enrolled in the TRIBE2 study were profiled according to CMS and CRCA classifications, respectively. The distribution of CMS/CRCA subtypes differed according to primary tumour site (both $p < 0.001$ for CMS/CRCA) and *RAS*/*BRAF* mutational status (both $p < 0.001$ for CMS/CRCA). Significant associations of both CMS/CRCA classifiers with PFS, PFS2 and OS were demonstrated (Table). The effect of treatment intensification was independent of CMS subtypes (p for interaction for PFS/PFS2/OS: ns). Significant interaction effect between CRCA subtypes and treatment arm was reported in terms of PFS ($p = 0.017$), PFS2 ($p = 0.010$) and OS ($p = 0.008$). The benefit from the intensification of the upfront chemotherapy seemed more relevant in the stem-like (PFS, HR = 0.60; p = 0.03) and mixed subtypes (HR = 0.44; p = 0.002). **Conclusions:** CMS subtypes have a prognostic role in mCRC independently of *RAS*/*BRAF* status. CRCA classification may help identifying subgroups of patients who may derive a more substantial benefit from upfront FOLFOXIRI/bev. Research Sponsor: GONO Foundation.

	CMS1	CMS2	CMS3	CMS4	Enterocyte	Goblet-like	Inflammatory	Stem-like	Transit-amplifying	Mixed
Median PFS (months)	5.4	12.9	8.3	10.7	10.0	9.9	7.9	14.6	11.2	9.9
P unadj/adj		**0.0001** / **0.01**					**0.04** / 0.36			
Median PFS2 (months)	8.0	19.2	13.7	18.1	15.7	16.0	12.2	24.0	18.1	16.5
P unadj/adj		**0.0004** /0.09					**0.04** / 0.37			
Median OS (months)	8.9	27.0	18.3	26.2	22.3	24.9	19.8	31.3	25.6	21.0
P unadj/adj		**0.0003** / 0.08					**0.02** / 0.55			

4017 Poster Discussion Session; Displayed in Poster Session (Board #9), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

First-line biological agents plus chemotherapy in elderly patients with metastatic colorectal cancer: A retrospective pooled analysis. *First Author: Pilar Garcia-Alfonso, Hospital General Universitario Gregorio Marañón, Madrid, Spain*

Background: Biological agents, in combination with chemotherapy, are recommended as first-line treatment of metastatic colorectal cancer (mCRC); however, evidence guiding appropriate management of elderly patients with mCRC is lacking. This study compared the efficacy and safety outcomes in older versus younger patients with mCRC who received first-line biological therapy. **Methods:** This retrospective analysis used pooled data from five Spanish TTD collaborative group studies of adults with advanced CRC who received first-line treatment with bevacizumab, cetuximab or panitumumab, stratified by age (≥65 vs < 65 years). Endpoints included progression-free survival (PFS), overall survival (OS), overall response rate (ORR) and safety. **Results:** In total, 999 patients from five studies were included in the analysis; 480 (48%) were aged ≥65 years and 519 (52%) were aged < 65 years; 733 (73.37%) were treated with bevacizumab, 189 (18.92%) received cetuximab and 77 (7.71%) received panitumumab. Median PFS did not significantly differ between patients aged ≥65 versus < 65 years (9.9 vs 9.4 months; hazard ratio [HR] 1.01; 95% confidence interval [CI] 0.88–1.17). Median OS was significantly shorter in older versus younger patients (21.3 vs 25.0 months; HR 1.21; 95% CI 1.04–1.41; P = 0.0132). There was no significant difference between older versus younger patients in ORR (59% vs 62%). Older patients experienced more treatment-related grade ≥3 adverse events. **Conclusions:** Biological agents are an effective first-line treatment option for elderly patients with mCRC, with comparable efficacy in PFS and ORR to that observed in younger patients and a manageable safety profile. Research Sponsor: Roche Farma SA.

4018 Poster Discussion Session; Displayed in Poster Session (Board #10), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

CodeBreak 100: Activity of AMG 510, a novel small molecule inhibitor of $KRAS^{G12C}$, in patients with advanced colorectal cancer. *First Author: Marwan Fakih, City of Hope National Medical Center, Duarte, CA*

Background: Kirsten rat sarcoma viral oncogene homolog *(KRAS)* p.G12C mutation is associated with poor prognosis in colorectal cancer (CRC). AMG 510 is a first-in-class small molecule that specifically and irreversibly inhibits $KRAS^{G12C}$ by locking it in the inactive guanosine diphosphate-bound state. In a previous interim analysis of the phase 1, first-in-human trial of AMG 510, we observed a favorable safety profile and preliminary antitumor activity in patients (pts) with advanced solid tumors harboring *KRAS* p.G12C. Here, we present updated data in pts with CRC. **Methods:** Key inclusion criteria were *KRAS* p.G12C mutation identified through molecular testing, measurable disease, and progression on standard therapy. Primary endpoint was safety. Secondary endpoints were objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), as assessed per RECIST 1.1, and overall survival (OS). Oral daily doses of 180, 360, 720, and 960mg were tested in the dose escalation phase, and 960mg dose was selected for the expansion phase. **Results:** As of Jan 8, 2020, 42 pts with CRC (21 female [50%], median age: 57.5 years [range: 33–82]) were enrolled and dosed (25 on 960mg). All pts received prior systemic therapies; 19 pts (45.2%) received > 3 prior lines. Median follow-up was 7.9 months (mos) (range: 4.2–15.9). 13 pts (31.0%) died, and 8 pts (19.0%) remained on treatment (tx). 22 (52.4%) and 8 (19.0%) pts had remained on tx for more than 3 and 6 months, respectively. Progressive disease was the most common reason for tx discontinuation. 20 pts (47.6%) had tx-related adverse events (TRAEs): 18 (42.9%) had grade 2 or lower TRAEs; 2 (4.8%) had grade 3 TRAEs, which were diarrhea (2.4%) and anemia (2.4%). There were no dose-limiting toxicities, fatal TRAEs, or TRAEs leading to tx discontinuation. Overall, ORR and DCR were 7.1% (3/42) and 76.2% (32/42), respectively. At 960mg, ORR and DCR were 12.0% (3/25) and 80.0% (20/25). 3 pts with PR had duration of response of 1.5, 4.2, and 4.3 months, respectively, and their responses were still ongoing at data cutoff. In all pts treated with all doses, median duration of stable disease was 4.2 mos (range: 2.5[+]–11.0). PFS/OS will be reported. **Conclusions:** In pts with heavily pretreated *KRAS* p.G12C mutant CRC, AMG 510 monotherapy was well tolerated, with the majority of pts achieving disease control. Study is ongoing. Clinical trial information: NCT03600883. Research Sponsor: Amgen Inc.

4019 Poster Discussion Session; Displayed in Poster Session (Board #11), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

REGOMUNE: A phase II study of regorafenib plus avelumab in solid tumors—Results of the non-MSI-H metastatic colorectal cancer (mCRC) cohort. *First Author: Sophie Cousin, Department of Medicine, Institut Bergonié, Bordeaux, France*

Background: Regorafenib (R) has been shown to modulate anti-tumor immunity by different mechanisms including reduction of tumor-associated macrophages (TAMs). Synergy between R and anti–PD-1/PD-L1 antibodies has been shown in pre-clinical models. **Methods:** This is a single-arm open-label multicentric phase II trial assessing the efficacy and safety of R (160 mg QD 3weeks/4) + Avelumab (A) (10 mg/kg every 2 weeks) combination in non MSI-H mCRC patients (pts). The primary endpoint was the confirmed objective response rate, based on central review according to RECIST 1.1. Secondary endpoints included: 1-year progression free survival (PFS), 1-year overall survival (OS), and Safety using NCI-CTCAE v5.0. Correlative studies were planned from pts tumor samples obtained at baseline and C2D1. **Results:** Between Nov. 2018 and Oct. 2019, 48 pts were enrolled in 4 centers. Median age was 61.8 (range: 26.3-78.7). Median follow-up was: 7.2 months. Median number of previous treatment lines was: 3 (range: 1-7). 41 (87.2%) pts experienced at least 1 dose modification or treatment interruption. The most common grade 3/4 adverse events were palmar-plantar erythro-dysesthesia syndrome (29.8%), hypertension (23.4%) and diarrhea (12.8%). No death was related to the treatment. Among 40 pts who had at least one imaging tumor assessment, 12 (30%) had reduction in tumor burden. Best response was stable disease for 23 pts (57.5%) and progressive disease for 17 pts (42.5%). The median PFS and OS were 3.6 months ($CI_{95\%}$: [1.8 – 5.4]) and 10.8 months ($CI_{95\%}$: [5.9 – NA]) respectively. Baseline tumor samples and paired biopsies were available for 24 and 15 pts respectively. High infiltration by TAMs at baseline was significantly associated with adverse outcome (PFS: 1.9 vs 3.7 months, p=0.045; OS: 4.8 months vs NR, p=0.027). Increased tumor infiltration by CD8+ at C2D1 compared to baseline was significantly associated with better PFS (p=0.011). Combining low TAMs infiltration and low tumor cells to CD8+ T cells distance enabled the identification of a subgroup of pts (n= 6/24, 25%) more likely to benefit from R+A combination: median PFS: 5.3 vs 1.9 months (p=0.037); median OS: NR vs 5.3 months (p=0.02). **Conclusions:** The R+A combination achieved PFS and OS that compared favourably with historical data of R alone in this clinical setting. High-resolution analysis of tumor samples identified a composite score based on TAMs infiltration and tumor cell to CD8+ T cells distance which could be used as a biomarker in further studies investigating this approach in mCRC pts. Clinical trial information: NCT03475953. Research Sponsor: Bayer and Merck.

4020 Poster Discussion Session; Displayed in Poster Session (Board #12), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Pembrolizumab for previously treated advanced anal squamous cell carcinoma: Pooled results from the KEYNOTE-028 and KEYNOTE-158 studies. *First Author: Aurelien Marabelle, Gustave Roussy, Université Paris-Saclay, Villejuif, France*

Background: Patients (pts) with anal squamous cell carcinoma (ASCC) have poor outcomes and few treatment options. We report a pooled analysis of pembrolizumab (pembro) antitumor activity and safety in the ASCC cohorts of the multicohort studies KEYNOTE-028 (NCT02054806; phase 1b) and KEYNOTE-158 (NCT02628067; phase 2), providing a robust sample size and longer follow-up. **Methods:** Eligible pts were aged ≥18 y with histologically/cytologically confirmed metastatic/unresectable ASCC, had prior failure of/intolerance to standard therapy or no standard therapy options, measurable disease (RECIST v1.1), ECOG PS 0/1, and a tissue sample evaluable for PD-L1/biomarkers (KEYNOTE-028 required PD-L1 positivity). Baseline PD-L1 expression was assessed using a prototype IHC assay (QualTek) in KEYNOTE-028 and the PD-L1 IHC 22C3 pharmDx assay (Agilent Technologies) in KEYNOTE-158. Pts received pembro 10 mg/kg Q2W (KEYNOTE-028) or 200 mg Q3W (KEYNOTE-158) for 2 y or until PD/unacceptable AEs. The primary endpoint in both studies was ORR (per RECIST v1.1). Secondary endpoints were duration of response (DOR), PFS, OS, and safety. **Results:** 137 pts with ASCC were treated in KEYNOTE-028 (n = 25) or KEYNOTE-158 (n = 112) and were included in this analysis (median age, 61 y; 83.2% women; 73.0% had PD-L1–positive tumors). Median follow-up was 11.7 mo; 124 pts (90.5%) had discontinued treatment. ORR (95% CI) was 10.9% (6.3%–17.4%). 8 pts had CR and 7 had PR. ORR (95% CI) by PD-L1 status was 14.0% (7.9%–22.4%) in the PD-L1 positive group and 3.3% (0.1%–17.2%) in the PD-L1 negative group. Among all treated pts, median DOR was not reached (range, 6.0+ to 57.5+ mo). By Kaplan-Meier estimation, 84.6% of responders had a DOR ≥24 mo. Median PFS was 2.1 mo (95% CI, 2.0–2.1) and median OS was 11.7 mo (95% CI, 8.8–14.5). The 12-mo PFS and OS rates were 14.5% and 47.4%. 85 pts (62.0%) had +1 treatment-related AE, 24 pts (17.5%) with grade 3–4 events (no grade 5 events). 32 pts (23.4%) had immune-mediated AEs; 2 pts (1.5%) had infusion related reactions. **Conclusions:** In pts with previously treated advanced ASCC, pembro showed durable antitumor activity, particularly in pts with PD-L1–positive tumors, and manageable toxicity. Clinical trial information: NCT02054806 (KEYNOTE-028), NCT02628067 (KEYNOTE-158). Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

4021 Poster Session (Board #13), Fri, 8:00 AM-11:00 AM

Pre- versus postoperative CAPOX plus bevacizumab (CAPOX-Bev) for resectable liver metastases from colorectal cancer (CLM): A randomized phase II/III trial (HiSCO-01). *First Author: Yuji Takakura, Department of Gastroenterological and Transplant Surgery, Hiroshima University, Hiroshima, Japan*

Background: The role of neoadjuvant chemotherapy, particularly for those with initially resectable CLM, is controversial. And the optimal regimen and duration to be used in the neoadjuvant setting is not established. We conducted prospective, multicenter, randomized phase II/III study to assess pre-operative 8 cycles of CAPOX-Bev (arm A) plus radical surgery compared with post-operative 8 cycles of CAPOX-Bev (arm B) for patients (pts) with resectable CLM. **Methods:** The primary endpoint in the Phase II was completion rate of protocol treatment (more than 6 cycles of CAPOX-Bev plus R0 surgical resection) and PFS in the Phase III. The secondary endpoints were OS, ORR (arm A), liver damage (arm A), safety. The Phase III part was terminated due to slow enrollment. **Results:** 81 pts were enrolled from 10 centers between November 2010 and November 2017. The full analysis set consisted of 76 pts who started protocol treatment (arm A 37 vs. arm B 39). 76 pts had the following characteristics: median age 66 (27-80), median number of liver metastases 2 (1-14), 69.7% male, 67.1% synchronous and 94.7% primary resected. Completion rate of protocol treatment was 89.2% in arm A and 71.8% in arm B (p = .06). ORR was 63.9%, including 2 pts who had pathologically complete response (5.6%). Only 1 pts in arm A could not undergo surgery due to progression of disease. In the chemotherapy safety population, arm B was associated with more grade 3 neutropenia and grade 3 gastrointestinal disorder than arm A. The most frequent surgical adverse event was biliary fistula, with an incidence of 0% in arm A and 10.3% in arm B (p = .02). No patient died from treatment-related adverse events. The median follow-up time was 40 months. The rate of PFS at 3 years was 32.2% in arm A versus 38.5% in arm B (p = .99). **Conclusions:** Pre-operative 8 cycles of CAPOX-Bev is compatible with radical surgery, but may have no impact on progression-free survival compared with post-operative chemotherapy. Clinical trial information: UMIN000003783. Research Sponsor: None.

4022 Poster Session (Board #14), Fri, 8:00 AM-11:00 AM

Impact of empirically eliminating 5-fluorouracil (5-FU) bolus and leucovorin (LV) in patients with metastatic colorectal cancer (mCRC) receiving first-line treatment with mFOLFOX6. *First Author: Alexa Basilio, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Systemic chemotherapy with a 5-FU-based regimen, such as mFOLFOX6, is the preferred first line treatment option for mCRC. Due to hematologic toxicities associated with the 5-FU bolus component, providers may choose to eliminate it empirically in patients receiving palliative therapy. This study aimed to assess the impact of empirically eliminating the 5-FU bolus and LV from first line treatment with mFOLFOX6 in mCRC. **Methods:** This was a retrospective chart review of patients ≥ 18 years old with mCRC receiving palliative first line mFOLFOX6 chemotherapy with (bolus) or without (non-bolus) the 5-FU bolus and LV components from January 1, 2015 through August 31, 2019 at Moffitt Cancer Center. The primary endpoint was progression-free survival (PFS). Secondary endpoints included overall survival (OS), disease control rate (DCR) defined as partial response and stable disease at first scan, utilization of growth factor support and safety. **Results:** Data analysis cutoff was December 31, 2019, with 61 patients included in the bolus arm and 72 in the non-bolus arm. Median follow-up time was 21.8 months. No difference was found in median PFS (8.12 vs. 6.64 months, p=0.787) or OS (29.36 vs. 21.6 months, p=0.395) between the bolus and non-bolus arms, respectively. Observed DCR at first scan was similar between both arms (47.3% vs. 52.7%, p=0.44). Utilization of growth factor support was significantly higher in the bolus arm (73.7% vs. 26.3%, p=0.012). Fewer grade ≥ 3 treatment-related hematologic adverse events (AE) were seen in the non-bolus arm (37.7% vs. 22.2%, p=0.058) (table). **Conclusions:** This is the only study to date that analyzed the impact of empirically eliminating 5-FU bolus and LV from first line palliative therapy with mFOLFOX6 in mCRC. Results showed no significant difference in median PFS or OS. Despite reduced growth factor utilization, the non-bolus arm demonstrated a favorable safety profile with less treatment-related hematologic grade ≥ 3 AE. The results of this study warrant consideration of empirically eliminating 5-FU bolus and LV from the mFOLFOX6 regimen to avoid additive toxicities without negatively impacting efficacy. Research Sponsor: None.

Hematologic AE grade ≥ 3, n (%)	Bolus (n=61)	Non-bolus (n=72)
Neutropenia	12 (20)	9 (13)
Anemia	12 (20)	8 (11)
Thrombocytopenia	3 (5)	2 (3)

4023 Poster Session (Board #15), Fri, 8:00 AM-11:00 AM

Differential association of proton pump inhibitors with efficacy of capecitabine and 5-fluorouracil in metastatic colorectal cancer: A post-hoc analysis from AXEPT phase III trial. *First Author: Sun Young Kim, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea*

Background: Proton pump inhibitors (PPIs) reportedly can impair the absorption of oral anticancer agents by potent acid suppression. Concomitant use of a PPI with capecitabine (Cap) was suggested to be associated with poor outcome in gastrointestinal cancers, however, the potential interaction has not been studied yet in a prospective randomized clinical trial comparing Cap with 5-fluorouracil (FU). We analyzed the differential impact of PPI use on Cap and FU using dataset from AXEPT trial, a phase III randomized trial that demonstrated non-inferiority of a modified XELIRI (mXELIRI; Cap plus irinotecan) with FOLFIRI (FU, leucovorin and irinotecan), both either with or without bevacizumab in patients (pts) with metastatic colorectal cancer (mCRC). **Methods:** From the per-protocol set (n = 620), pts with available information on concomitant medications (n = 482) were eligible for this sub-study. PPI use was defined as concomitant exposure of Cap and any PPI for 20% or more of the study period. The treatment-by-PPI-use interaction was examined adjusting to stratification factors including age, sex, country, performance status, number of metastatic sites, previous use of oxaliplatin, and concurrent bevacizumab treatment. **Results:** 49 (10.1%) pts were PPI users. Clinical characteristics were well balanced between the two groups differing in PPI use. In PPI users, the mXELIRI group tended to have poorer OS (hazard ratio [HR], 1.83; 95% confidence interval [CI], 0.96–3.48; p = 0.0644) compared with the FOLFIRI group. In contrast, within PPI non-users, OS of mXELIRI was better than that of FOLFIRI (HR, 0.76; 95% CI, 0.61- 0.95; p = 0.0162). Similarly, a trend of worse PFS with mXELIRI than with FOLFIRI was observed in PPI users (HR, 1.73; 95% CI, 0.94-3.21; p = 0.0798), but not in PPI non-users (HR, 0.90; 95%CI, 0.73 – 1.10; p = 0.2871). Treatment-by-PPI-use interaction was significant for OS (p = 0.0116) and PFS (p = 0.0415). No significant interactions were found between treatment and PPI use in terms of treatment failure, overall response, disease control, and grade 3–4 toxicities. **Conclusions:** There was a significant interaction between PPI use and treatment (Cap vs FU) in terms of OS and PFS in AXEPT dataset. This suggests that PPI use could impair the efficacy of Cap, but not that of FU. PPIs should be used with caution in pts with mCRC taking Cap. Clinical trial information: NCT01996306. Research Sponsor: Chugai Pharmaceutical and Hoffmann-La Roche.

4024 Poster Session (Board #16), Fri, 8:00 AM-11:00 AM

Cetuximab/irinotecan/5-FU +/-oxaliplatin or FOLFOXIRI +/- bevacizumab in patients with colorectal cancer and nonresectable liver metastases (AIO CELIM2-study). *First Author: Gunnar Folprecht, University Hospital Carl Gustav Carus, Dresden, Germany*

Background: EGFR based combinations and the triplet combination FOLFOXIRI are known to increase response rates compared to doublet combinations. **Methods:** Patients with colorectal cancer and non-resectable liver metastases were enrolled into the trial. RAS wild type patients were randomised to cetuximab/FOLFIRI or cetuximab/FOLFOXIRI, RAS/BRAF mutant patients were randomised to FOLFOXIRI with or without bevacizumab. The primary endpoint was response. Secondary endpoints included progression free and overall survival. The trial was closed early due to poor recruitment. **Results:** Between 2014 and 2018, ninety-two pts were enrolled into the study. 54 wild type pts were randomised into cetuximab based treatment with (28 pts) or without (26 pts) oxaliplatin, 38 RAS/BRAF mutant pts were randomised to receive FOLFOXIRI alone (18 pts) or plus bevacizumab (16 pts). Objective response was achieved in 21/26 pts (81 % [95 CI: 61 – 93 %]) with cet/FOLFIRI, 24/28 pts (86 % [95 CI: 67 – 96 %]) with cet / FOLFOXIRI, 13/1 8 pts (72 % [95 CI: 46 – 90 %]) with FOLFOXIRI and 14/ 20 pts (70 % [95 CI: 46 – 88 %]) with bev/FOLFOXIRI. Two pts with cet/ FOLFOXIRI and one pat with FOLFOXIRI achieved CR according to imaging. The median PFS was 12.7 [95 % CI: 7.2 – 18.2], 15.0 [95 % CI: 11.3 – 18.7], 17.5 [95 % CI: 8.0 – 27.1] and 15.0 [95 % CI: 11.4 – 18.5] months with cet/FOLFIRI, cet/FOLFOXIRI, FOLFOXIRI and bev/FOLFOXIRI. The median overall survival was 42 mo. [95 % CI: 28 – 55], 55 [95 % CI:41 – 68], 28 [95 % CI: 22 – 36] and 44 [95 % CI: 0 – 94] months with cet/ FOLFIRI, cet/FOLFOXIRI, FOLFOXIRI and bev/FOLFOXIRI. The frequency of grade $\geq$ 3 toxicity per arm (cet/FOLFIRI, cet/FOLFOXIRI, FOLFOXIRI and bev/FOLFOXIRI) was 29 %, 46 %, 56 %. 45 % for neutropenia/leukopenia, 11 %, 12 %, 28 %, 25 % for diarrhea and 29 %, 19 %, 6 % and 5 % for skin toxicities. **Conclusions:** High response rates were observed in patients with colorectal liver metastases with all regimens. The numerically highest response rate was observed in RAS wild type patients treated with cetuximab/ FOLFOXIRI. Clinical trial information: NCT01802645. Research Sponsor: Merck-Serono.

4025 Poster Session (Board #17), Fri, 8:00 AM-11:00 AM

Skeletal muscle loss under chemotherapy and its association with survival and systemic treatment toxicity in metastatic colorectal cancer: An AGEO prospective multicenter study. *First Author: Claire Gallois, Hopital Européen Georges Pompidou, Paris, France*

Background: We showed in a previous work that "Patient Generated-Subjective Global Assessment" (PG-SGA) was independently associated with survival and treatment toxicities in non-pretreated metastatic colorectal cancer (mCRC) patients. We have evaluated here if muscle mass in these patients can provide useful additional information for clinical practice. The objective of the present work was to evaluate the association between baseline sarcopenia, and the variation of the Skeletal Muscle Index (SMI) under treatment with survival and chemotherapy-related toxicities in our population of non-pretreated mCRC patients. **Methods:** This prospective multicenter observational study enrolled non-pretreated mCRC patients. Measurement of SMI was performed on routine CT scan at day 0 (D0) and day 60 (D60). PG-SGA score and other nutritional factors were collected at D0. Progression-free survival (PFS) and overall survival (OS) were calculated from treatment start. Treatment related toxicities were registered according to the NCI CTCAE v4.0. **Results:** 149 patients were included in eight French centers from 7/2013 to 11/2016. Sarcopenia at baseline was not significantly associated with survival outcomes or chemotherapy-related toxicities. The best cut-point value of SMI variation (between D0 and D60) for OS prediction obtained with a log-rank maximisation method was -14%. The decrease in SMI $>$ 14%, with a median follow-up of 23 months, was significantly associated with shorter PFS (6 vs 9 mo; HR 1.8, 95%CI 1.1-3.1, p = 0.02) and OS (8.5 vs 26 mo; HR 2.4, 95%CI 1.3-4.4, p = 0.004), independently of hypoalbuminemia and malnutrition defined by PG-SGA, in multivariate analysis. 40% of patients with a SMI decrease $>$ 14%, and 22% of patients with a SMI increase or stable or decrease $<$ 14% developed grade $\geq$ 2 clinical toxicities (OR 3.0, 95%CI 1.2-7.7, p = 0.02), but the difference was not statistically significant in multivariate analysis (OR 2.3. 95%CI 0.8-6.7, p = 0.1). **Conclusions:** To our knowledge, this study is the first study assessing the association of skeletal muscle loss with survival and treatment toxicities in patients with mCRC prospectively. In our population of non pre-treated mCRC patients, baseline sarcopenia was not associated with poor survival outcomes, but the decrease in SMI $>$ 14% during the first two months of treatment was significantly associated with decreased PFS and OS, independently of other prognostic and nutritional factors. Research Sponsor: Nutricia.

4026 Poster Session (Board #18), Fri, 8:00 AM-11:00 AM

High amphiregulin mRNA expression is a strong prognostic biomarker with response to cetuximab in FIRE-1, CIOX, and FIRE-3. *First Author: Arndt Stahler, Department of Medicine III, University Hospital, LMU Munich, Munich, Germany*

Background: Amphiregulin (*AREG*) and epiregulin (*EREG*) were discussed as biomarkers for treatment of metastatic colorectal cancer (mCRC). Data from randomized controlled trials (RCT) are limited. **Methods:** *AREG* and *EREG* mRNA expression by RTqPCR in relation to housekeeping genes were available from 688 patients of three RCT (FIRE-1, n = 192, FUFIRI vs. mIrOx; CIOX, n = 113, cetuximab + CAPIRI/CAPOX; FIRE-3, n = 383, FOLFIRI+cetuximab/bevacizumab) and were normalized to their respective range of each trial with median and 3rd quartile as threshold values. Kaplan-Meier estimated overall survival (OS) and progression-free survival (PFS). Cox regression analysis calculated hazard ratio (HR) and 95% confidence interval (95% CI). Overall response rate (ORR) was compared by chi square test. **Results:** Across all trials, high *AREG* mRNA expression appeared as strong prognostic biomarker for OS, PFS and ORR for all threshold values. In *RAS* wildtype patients, high *AREG* expression was associated with better OS and PFS for cetuximab but not bevacizumab treatment. (Table) No effects were seen for epiregulin when all trials were analysed together. **Conclusions:** High *AREG* mRNA expression appeared as strong prognostic biomarker in mCRC. Positive predictive information might exist for cetuximab treatment. Research Sponsor: None.

Outcome according to AREG mRNA expression in FIRE-1, CIOX, FIRE-3.

	< median	> median	< 3rd quartile	> 3rd quartile
All patients				
n FIRE-1	103	89	152	42
n CIOX	60	53	86	27
n FIRE-3	181	202	279	104
OS, months	21.5	26.2	22.6	28.6
HR [95% CI], p	0.80 [0.68 – 0.94] p = 0.007		0.76 [0.63 – 0.92] p = 0.005	
PFS, months	8.1	10.0	8.9	10.6
HR [95% CI], p	0.74 [0.63 – 0.86] p = 0.001		0.79 [0.68 – 0.94] p = 0.009	
ORR, %	51.6	63.1	52.6	71.5
P (Chi sq.)	0.004		< 0.0001	
RAS WT & bevacizumab treated patients				
n FIRE-3	66	68	99	35
OS, months	23.8	27.5	23.8	28.6
HR [95% CI], p	0.93 [0.65 – 1.33] p = 0.71		0.96 [0.65 – 1.43] p = 0.85	
PFS, months	10.3	11.3	10.7	11.5
HR [95% CI], p	0.92 [0.65 – 1.30] p = 0.63		1.03 [0.70 – 1.53] p = 0.87	
RAS WT & cetuximab treated patients				
n CIOX	34	32	47	19
n FIRE-3	51	70	76	45
OS, months	23.5	36.6	24.5	37.1
HR [95% CI], p	0.60 [0.43 – 0.63] p = 0.002		0.61 [0.43 – 0.87] p = 0.006	
PFS, months	7.8	10.6	8.6	11.2
HR [95% CI], p	0.66 [0.49 – 0.88] p = 0.006		0.77 [0.56 – 1.05] p = 0.10	

4027 Poster Session (Board #19), Fri, 8:00 AM-11:00 AM

Prognostic characteristics of patients with benign mesenteric lymph node enlargement after surgical resection for colorectal cancer. *First Author: Fei Tian, Massachusetts General Hospital, Boston, MA*

Background: Patients with lymph node metastasis of colorectal cancer (CRC) have a greater risk of recurrence. However, the characteristics of benign mesenteric lymph node enlargement (BLNE) are not well documented. The aim of this study is to assess clinical and prognostic significance of BLNE in patients with CRC. **Methods:** 601 patients who underwent surgery for stage 0, I, II CRC from January 2010 to April 2014 were included and separated into two groups by presence of BLNE. Univariate and multivariate analyses were constructed to demonstrate prognostic factors between BLNE group (n = 275) and control group (n = 326). **Results:** The risk of recurrence in BLNE group after curative resection was significantly lower than control group, with the 1-, 3-, and 5-year disease-free survival rates being 98.2, 91.6, and 86.9 %, in BLNE group and 95.7, 86.2, and 78.2 %, in control group respectively (p = 0.004). The mortality in BLNE group was lower compared with non BLNE group (mean overall survival: 95.7$\pm$1.2 vs. 89.5$\pm$1.4 months, p = 0.001). Patients of BLNE group also had a higher percentage of younger age, family tumor history, left sided tumors and tumor size $\geq$4cm. Adjusted Cox regression showed BLNE was an independent prognostic factor for both disease free survival and overall survival (P= 0.003 and 0.001). **Conclusions:** The study indicates that BLNE can be a useful positive factor in predicting recurrence and long-term survival concerning CRC patients. This conclusion offers a new viewpoint about CRC genesis and progression. Research Sponsor: None.

4028 Poster Session (Board #20), Fri, 8:00 AM-11:00 AM

Fruquintinib combination with sintilimab in refractory metastatic colorectal cancer patients in China. *First Author: Miaomiao Gou, PLA General Hospital, Beijing, China*

Background: Fruquintinib, a vascular endothelial growth factor receptor (VEGFR) inhibitor, is a new anti-cancer targeting drug independently developed in China for refractory metastatic colorectal cancer (mCRC). Because Regorafenib combined with nivolumab has a promising future in patients with refractory mCRC, we aim to evaluate the efficiency of combination of Fruquintinib with Sintilimab (a highly selective, fully human monoclonal antibody PD-1 mAb) in these patients. **Methods:** Fifty-two patients with refractory mCRC were given fruquintinib (3mg orally, once daily for 3 weeks, followed by 1 weeks off in 4 weeks cycles) and sintilimab (200mg intravenously, once every 3 weeks). Before treatment, peripheral blood samples were collected and next-generation sequencing was performed to detect the gene profile of patients. **Results:** The ORR was 15.38% (8/52), DCR was 57.6% (30/52), and mPFS was 108 days. The patients was divided into two groups according to their PFS: PFS $\geq$ 90 days and PFS $<$ 90 days. PFS was significantly worse in patients with the following mutations: AMER1 (p=0.0073), DNMT3A (p=0.0075), ETV5 (p=0.012), EWSR1 (p=0.016), FANCA (p=0.019), IKBKE (p=0.0073), NOTCH1 (p=0.015), STAG2 (p=0.012) and TCF7L2 (p=0.0073). It was also significantly worse in the patients had the abnormalities of complexity and coagulation cascades (p = 0.026) and pancreatic cancer pathway (p = 0.0098). **Conclusions:** Fruquintinib combined with Sintilimab seemed not resulted in a significant increase in ORR, DCR and OS in refractory mCRC. Certain mutational genes and abnormal pathway caused by some frameshift mutations may affect the efficacy. It is suggested that targeting these mutational genes and signaling pathway may be helpful to improve the efficacy of Fruquintinib combination with Sintilimab. Research Sponsor: None.

4029 Poster Session (Board #21), Fri, 8:00 AM-11:00 AM

Sex differences in efficacy and toxicity of first-line treatment of metastatic colorectal cancer (CRC): An analysis of 18,399 patients in the ARCAD database. *First Author: Anna Dorothea Wagner, Lausanne University Hospital, Lausanne, Switzerland*

Background: The clearance of 5-FU differs significantly between men (M) and women (W). Adjuvant chemotherapy (CT) for CRC has a higher toxicity in W. The impact of sex on efficacy and toxicity in first-line trials of metastatic CRC (mCRC) is unknown. **Methods:** We analyzed patient (pt) and tumor characteristics, toxicities (nausea (AE1), vomiting (AE2), diarrhea, neutropenia (AE3)) and efficacy (overall survival (OS), progression-free survival (PFS)) according to sex in the following treatment groups: A: CT alone, B: CT + bevacizumab, C: CT + EGFR-antibodies, with subgroup analyses in the CT alone group for single-agent, doublets and triplets, as well as irinotecan- and oxaliplatin-based regimens. Pts from trials with treatments still used today and all relevant data available were eligible. OS and PFS were assessed using Kaplan-Meier and Cox models adjusted for primary tumor location and performance status (PS). **Results:** We included 28 trials with 18.399 pts (11.352 M and 7.047 W). W were younger (61 vs. 63 years), had more often a PS of 1 (49 vs 45%), BRAF mutations (10 vs. 7%), right-sided tumors (42 vs. 35%) and less often rectal tumors (26 vs. 32%). Significant differences in toxicity are reported in table. Rates of diarrhea were similar. There was no sex disparity in OS in the predefined subgroups except for pts receiving triplets where OS was better in M (HR_{adj}=1.39 (1.05 - 1.85)). Median (interquartile range) OS in months for M and W was 16.7 (9.2-27.4) and 16.2 (8.9-27.2) in group 1, 21.9 (12.7-37.5) and 22.3 (12.9 – 39.0) in group 2, and 26.8 (14.6-45.3) and 24.8 (12.3-49.2) in group 3. HRs_{adj} (W vs M) (95% CI), p values for OS were 1.02 (0.96-1.09), .557, 0.92 (0.83-1.03), .142, 0.99 (0.85-1.14), .866. **Conclusions:** M and W with mCRC differ significantly regarding patient and tumor characteristics. The significant higher toxicity in W does not translate in a higher treatment efficacy. Apart from known sex differences in pharmacokinetics of 5-FU, differences in pharmacodynamics must be postulated. Research Sponsor: Fondation ARCAD.

	Toxicity Gr 1-4 n (%)		Toxicity Gr 3-4 n (%)	
CT alone	**M**	**W**	**M**	**W**
AE	1745 (62.2)	1098 (70.3)	157 (5.6)	130 (8.3)
AE 2	1149 (39.3)	802 (48.8)	154 (5.3)	120 (7.3)
AE 3	1519 (48.1)	993 (54.8)	607 (19.2)	506 (27.9)
CT + bev				
AE 1	1237 (58.9)	1037 (73.6)	77 (3.7)	96 (6.8)
AE 2	782 (37.3)	728 (51.6)	99 (4.7)	96 (6.8)
AE 3	536 (29.8)	455 (37.7)	282 (15.7)	290 (24.0)
CT + anti-EGFR antibodies				
AE 1	941 (59.4)	627 (71.6)	77 (4.9)	63 (7.2)
AE 1	618 (29.1	509 (42.1)	63 (3.0)	63 (7.2)
AE 3	1080 (50.6)	754 (62.3)	439 (20.6)	428 (35.4)

4030 Poster Session (Board #22), Fri, 8:00 AM-11:00 AM

Real-world outcomes of patients with BRAF-mutated mCRC treated in the United States. *First Author: Matthew Braithwaite, University of Utah, Salt Lake City, UT*

Background: BRAF mutations portend a poor prognosis in metastatic colorectal cancer (mCRC). Recent trials have hypothesized that using more aggressive triplet-based chemotherapy regimens such as FOLFOXIRI in the frontline setting may improve outcomes in this patient population. In this study, we utilized real-world data to assess whether FOLFOXIRI is being used in the United States (US) and compared survival outcomes in BRAF mutated (BRAFmt) mCRC stratified by first line (1L) therapy. **Methods:** The nationwide Flatiron Health EHR-derived de-identified database was reviewed for patients diagnosed with mCRC between 2013 and 2018. Patients who had documented BRAF mutation testing and received a standard 1L therapy were included for analysis. Patients who did not have a visit or medication order within 90 days of metastatic diagnosis were excluded to ensure patients were engaged with care at the data-providing institution. Kaplan-Meier and Cox proportional hazard modeling were used to compare survival outcomes stratified by BRAF mutation status and 1L therapy received. **Results:** A total of 4,454 patients with documented BRAF mutational status were included, of which 3,988 (89.5%) were BRAF wild type (BRAFwt) and 466 (10.5%) were BRAFmt. Median OS was 15.4 months (mo) in the BRAFmt group compared to 28.1 mo in the BRAFwt group (HR 0.48, 95% CI 0.41- 0.56, p $<$ 0.001). Only 3% (n = 16) of BRAFmt patients received 1L FOLFOXIRI +/- bevacizumab with a median OS of 13.8 mo compared to 15.5 mo in patients receiving a chemotherapy doublet (FOLFOX, CAPEOX, or FOLFIRI) +/- bevacizumab (95% CI 4.9 – not reached vs 14.3 – 19.0, p = 0.38). In BRAFmt patients, multivariate analysis (MVA) did not detect a significant improvement in OS with the use of FOLFIRI plus bevacizumab (HR 0.88, 95% CI 0.50-1.56, p = 0.67) or FOLFOX/CAPEOX plus bevacizumab (HR 0.89, 95% CI 0.59 – 1.34, p = 0.58) when compared to chemotherapy doublet alone. A MVA comparing 1L therapies in the BRAFwt group did not detect a significant improvement in OS with bevacizumab plus chemotherapy doublet compared to chemotherapy doublet alone. When stratified by 1L treatment regimen, similar proportions of BRAFmt patients received second line therapy. **Conclusions:** This analysis of real-world data confirms the negative prognostic impact of BRAF mutations in mCRC and suggests that FOLFOXIRI has not been widely adopted in the management of these patients in the US. We were unable to demonstrate any significant difference in OS of patients with BRAFmt mCRC based on type of 1L therapy received. Research Sponsor: None.

4031 Poster Session (Board #23), Fri, 8:00 AM-11:00 AM

Results from the safety lead-in for a phase II study of pembrolizumab in combination with binimetinib and bevacizumab in patients with refractory metastatic colorectal cancer (mCRC). *First Author: Christopher Hanyoung Lieu, University of Colorado Comprehensive Cancer Center, Aurora, CO*

Background: The majority of pts with mCRC have microsatellite stable (MSS) tumors with minimal response to PD-L1/PD-1 blockade. MEK inhibition and VEGF inhibition have immunomodulatory effects (upregulation of tumor major histocompatibility complex-I expression, enhanced T-cell infiltration, reduced MDSCs and Tregs in tumors) supporting clinical evaluation of combined MEKi (B), anti–PD-1 (P), and anti-VEGF (BV) in pts with mCRC. We hypothesize that the combination of binimetinib, pembrolizumab, and bevacizumab (BPBV) will result in greater clinical benefit than pembrolizumab alone. **Methods:** Patients with chemotherapy-refractory mCRC were evaluated (20 planned in the safety lead-in and 50 planned for total accrual). B was dosed at 45mg PO BID, P was administered at 200mg IV Q21 days, and BV was administered at 7.5mg/kg IV Q21 days. Primary objectives were safety, tolerability, and investigator-assessed ORR by RECIST 1.1. Clinical benefit rate (CR+PR+SD) and progression-free survival were secondary endpoints. Descriptive statistics were used to summarize safety and clinical activity. **Results:** As of January 9, 2020, 21 pts (10 KRAS/NRASmt, 11 RASwt, 21 MSS) were enrolled into the safety lead-in and were evaluable. The median number of prior therapies was 6. The BPBV combination was tolerable. Treatment-related Gr 1-2 and Gr 3-4 AEs occurred at 60% and 38%, respectively. The most frequent related Gr 3-4 AEs were aceniform rash, diarrhea, and hypertension (19%, 14%, 14% respectively). No treatment-related Gr 5 AEs occurred. A total of 17 patients were evaluable for response. Confirmed PR was observed in 2 pts (12%). SD was noted in 14 patients (82%) leading to a clinical benefit rate of 94%. 1 patient had PD as the best response to treatment. Median PFS was 6.4 months (95% CI 4.2-8.9). Molecular determinants, immune biomarkers, and updated tumor assessments of response will be presented. **Conclusions:** B + P + BV demonstrated a tolerable safety profile and improvements in ORR and clinical benefit rate compared to those reported with SOC in heavily pretreated pts with mCRC. Objective responses observed in pts were durable, suggesting benefit of this novel combination in a patient population refractory to immune therapies. Clinical trial information: NCT03475004. Research Sponsor: Merck, U.S. National Institutes of Health.

4032 Poster Session (Board #24), Fri, 8:00 AM-11:00 AM

Pembrolizumab monotherapy for patients with advanced MSI-H colorectal cancer: Longer-term follow-up of the phase II, KEYNOTE-164 study. *First Author: Luis A. Diaz, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Pembrolizumab provides effective antitumor immunity and durable responses in patients (pts) with advanced, colorectal cancer (CRC) with microsatellite instability-high (MSI-H) tumors. We present data on antitumor immunity with pembrolizumab in pts from the phase 2, KEYNOTE-164 study who had approximately 3 years of follow-up, and in pts re-treated after disease progression. **Methods:** KEYNOTE-164 enrolled pts with metastatic MSI-H CRC, MSI-H status confirmed locally by IHC or PCR, and ≥2 (cohort A) or ≥1 (cohort B) prior lines of therapy (fluoropyrimidine, oxaliplatin, irinotecan, or anti VEGF/EGFR). Eligible pts received pembrolizumab 200 mg Q3W for 2y (35 administrations) or until progression, unacceptable toxicity, or withdrawal. Pts who stopped pembro due to a confirmed CR or after completing 2y of treatment and who progressed after stopping were eligible for re-treatment with up to 17 administrations in the second-course phase, at investigator discretion. Tumor response was assessed Q9W per RECIST v1.1 by independent review. The primary endpoint was ORR. Secondary endpoints included DOR, PFS, OS, and safety. The data cutoff date was Sep 9, 2019. **Results:** At data cutoff, the median follow-up was 31.4 mo (range, 0.2-47.8) for 61 pts in cohort A and 36.1 mo (0.1-39.3) for 63 pts in cohort B. ORR was 32.8% (3CR, 17PR; 95% CI% 21.3-46.0) for cohort A and 34.9% (8CR, 14PR; 95% CI 23.3-48.0) in cohort B. Median DOR was not reached (NR [range, 6.2-41.3+]) and not reached (range, 3.9+ to 37.1+), respectively. Fifteen pts in cohort A and 17 in cohort B had ongoing responses at data cutoff. Median PFS was 2.3 mo (95% CI 2.1-8.1) with 3-yr PFS rate of 31% in cohort A and was 4.1 mo (2.1-18.9) with 3-yr PFS rate of 34% in cohort B. Median OS was 31.4 mo (21.4-NR) with 3-yr OS rate of 49% in cohort A and was not reached (19.2-NR) with 3-yr OS rate of 52% in cohort B. Nine pts (6 in cohort A, 3 in cohort B) had a second course of treatment. The best response in second course was PR in 1 patient each in cohort A and B. Grade 3-4 drug-related adverse events occurred in 10 (16%) pts in cohort A and 8 (13%) pts in cohort B. No grade 5 drug-related events occurred. **Conclusions:** After approximately 3 y of follow-up, pembrolizumab continues to provide effective long-term antitumor immunity with durable responses, with small numbers of drug-related adverse events and no drug-related deaths in pts with advanced, MSI-H CRC. Clinical trial information: NCT02460198. Research Sponsor: Merck & Co., Inc.

4034 Poster Session (Board #26), Fri, 8:00 AM-11:00 AM

Outcomes and prognostic factors of patients (pts) with metastatic colorectal cancer (mCRC) who underwent pulmonary metastasectomy (PM) with curative intent. *First Author: Gustavo Cartaxo de Lima Gössling, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil*

Background: Indications for PM in pts with mCRC are often based on the presence of favorable prognostic factors. We aimed to analyze the prognostic factors and outcomes of pts treated with PM for mCRC. **Methods:** We retrospectively identified pts with mCRC who underwent PM with curative intent between Jan 1985 and Dec 2019 at Hospital de Clínicas de Porto Alegre. Demographics, clinicopathological features and previously described prognostic factors were collected. Univariate Cox regression was performed and followed by Kaplan-Meier (KM) curves with log-rank test when significant. **Results:** Fifty-eight pts underwent PM. Demographics are described in Table. Wedge resection was performed in 87.9% and margins were negative in 89.1%. Mean number of lesions was 2.4 ± 1.7, with the largest measuring 1.7 ± 0.9 cm. Two or more resections were performed in 36.2%, nodal sampling in 27.3%, and nodal disease was found in 5.2%.Thirty-day readmission rate was 5.2%. One pt had a Clavien-Dindo grade IIIb complication. RAS/RAF/MMR and CK20/CDX2 were available for 13.8% and 58.6% of the sample. Median PFS 14 months (m) (95% CI 10.4 - 17.5), median OS 58 m (95% CI 33.5 - 82.4) and 5-year survival 49.8%. Unfavorable prognostic factors for OS included disease-free interval (DFI) < 24 m (40 m, 95% CI 31.8 - 48.1 vs 85 m, 95% CI 75.7 -96.2; P < 0.005), synchronous presentation (33 m, 95% CI 23.9 - 42.0 vs 77 m, 95% CI 50.7 - 103.2; P < 0.001), largest lesion size ≥ 2cm (37 m, 95% CI 22.9 - 51.0 m vs 81 m, 95% CI - 33.7 - 128.2, P = 0.019) and lack of CK20 expression (19 m, 95% CI 12.1 - 27.2 vs. 83 m, 95% CI 46.9 - 119.0; P < 0.001). More than one lesion at presentation was prognostic for PFS (11 m, 95% CI 7.6 - 14.3 vs 23 m, 95% CI 0.1 - 59.2; P = 0.003) but not OS (P = 0.11). Grade was significant at Cox regression but showed no effect in further analysis. Neither CEA at baseline or relapse, resection margins, Charlson comorbidity index (CCI) or adjuvant chemotherapy were prognostic. **Conclusions:** Our results suggest a benefit for select pts and PM. Lack of CK20 expression may be associated with more aggressive disease and shorter OS. Additional molecular prognostic factors after PM should be further explored. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

Demographics.	
Age (years, median ± SD)	**64 ± 8.3**
Sex (men, %)	55.2%
Primary site (rectum, %)	56.9%
Laterality (left, %)	89.7%
CEA at diagnosis (median ± SD)	27.9 ± 81.2
Stage*:	
I	3,5%
II	28.1%
III	49.2%
IV	19.2%
DFI (months, median ± SD)	17.7. ± 17.5
CEA at relapse (median ± SD)	6.4 ± 15.1
Synchronous resectable liver disease (%)	25.9%
CCI (relapse)	
0-1	25.9%
2-3	55.2%
≥ 4	18.9%

*1 missing

4035 Poster Session (Board #27), Fri, 8:00 AM-11:00 AM

Genomic aberration of chromatin regulatory BAF complex as predictive biomarker for immunotherapy in gastrointestinal adenocarcinoma. *First Author: Changsong QI, Department of Gastrointestinal Oncology, Beijing Cancer Hospital, Beijing, China*

Background: SNF/SWI, a large ATP-dependent chromatin remodeling complex, is required for transcriptional activation of genes normally repressed by chromatin, and critical to tumor initiation and progression. Here, we analyzed the predictive utility of the mutations of the SNF/SWI members involved in BAF and PBAF complexes, and sought to explore the potential mechanisms. **Methods:** Clinical, genomic, transcriptional, and immunohistochemical data from immunotherapeutic cohort (MSKCC, n=185), Cancer Cell Line Encyclopedia (CCLE, n=92), The Cancer Genome Atlas (TCGA, n=925), and 3D Medicines database (3DMed, n=1812) were analyzed to explore the predictive effect of genomic aberration of BAF complex on the benefit from immunotherapy in patients with gastrointestinal adenocarcinoma. **Results:** In the MSKCC cohort involving 185 patients with gastrointestinal adenocarcinoma, the mutation of any member involved in BAF complex (*ARID1A*, *ARID1B*, *SMARCA4*, *SMARCB1*, and *SMARCD1*) was significantly associated with prolonged OS of ICI treatment (HR 0.53, 95%CI 0.31-0.90, P=0.019), instead of the mutations of PBAF members including *PBRM1* and *ARID2*. In addition, BAF mutation was not linked with better prognosis in TCGA database, indicating its predictive, not prognostic efficacy of immunotherapy. BAF-mutated samples exhibited higher tumour mutational burden (TMB, P<0.05, Table), and increased mRNA expression of immune-related genes including chemokines and granzyme A. In the 3DMed cohort where tumour samples received both genomic sequencing and PD-L1 immunohistochemical staining, BAF mutation was associated with higher PD-L1 positive rate in tumour cells (P<0.05, Table). **Conclusions:** Genomic aberration of members in chromatin regulatory BAF complex may serve as a predictive, not prognostic biomarker of ICI benefit in patients with gastrointestinal adenocarcinoma, partially underlying the mechanisms including higher mutational burden, transcription of immune-related genes, and protein-level PD-L1 expression. Research Sponsor: Beijing Cancer Hospital.

			Mutational count						
Database	**Tumour site**	**n**	**BAF-mutant (median)**			**BAF-wildtype (median)**			**P value**
CCLE	GC	36	680			324			<0.001
	CRC	56	584			117			<0.001
TCGA	GC	532	247.5			91			<0.001
	CRC	393	469.5			98			<0.001
Mutational burden									
3DMed	GC	679	8.07			5.65			<0.001
	CRC	1133	11.12			7.26			<0.001
MSKCC	GC	75	7.02			5.27			0.026
	CRC	110	6.14			59.79			<0.001
PD-L1 expression									
Database	Tumour site	n	BAF-mutant			BAF-wildtype			P value
			TPS≥10	TPS≥1	TPS<1	TPS≥10	TPS≥1	TPS<1	
3DMed	GC	679	23	37	137	30	83	369	0.040
	CRC	1133	24	42	157	37	119	754	<0.001

4036 Poster Session (Board #28), Fri, 8:00 AM-11:00 AM

Trifluridine/tipiracil or regorafenib in refractory metastatic colorectal cancer patients: An AGEO prospective "real life" study. *First Author: Clélia Coutzac, Centre Léon Bérard, Lyon, France*

Background: Regorafenib (R) and trifluridine/tipiracil (T) have proved their efficacy in patients (pts) with metastatic colorectal cancer (mCRC) refractory to standard chemotherapy and targeted therapies. However, it remains unclear which drug should be administered first. **Methods:** This observational study was prospectively conducted in 13 centers between 6/2017 and 9/2019 in France. All consecutive pts with chemoresistant mCRC and receiving T and/or R were eligible. The aim of this study was to describe efficacy and tolerability of T and/or R. Overall survival (OS) and progression-free survival (PFS) of pts receiving T then R (T/R) and the opposite sequence (R/T) were also assessed. **Results:** A total of 237 pts (25% R and 75% T) were enrolled (109 male, median age: 67 years (32-91), mean previous lines of treatment: 2.5 (1-7)). Baseline ECOG PS was 0-1 in 77% of pts. As compared to R pts, T pts were significantly older (68 years vs 63; p = 0.033) and with > 3 metastatic sites (44% vs 30%, p = 0.018). Median OS were 6.6 and 6.2. months in the T and R group, respectively (NS). Median PFS were 2.4 and 2.1 months in the T and R group, respectively (NS). After matching 46 paired pts according to primary tumor resection, age and number of metastatic sites, a trend to a longer OS (9.5 vs 6.8 months; p = 0.17) and a significantly longer PFS (2.8 vs 2 months; p = 0.048) were observed in the T group. Among the overall population, 24% of pts received R/T or T/R sequence. Median OS from first treatment were 10.7 months in the R/T group and 9.8 months in the T/R (NS). Treatment sequence was not an independent prognostic factor for OS or PFS in multivariable analysis. Tolerability profiles were similar to previously published data, but dose reductions were more frequent in the R group (44 vs 27%, p = 0.008). **Conclusions:** Efficacy and safety results in this real life prospective study are in line with those published phase III trials. Both treatments seem similar in term of efficacy favoring T for clinical use as shown by the higher number of patients receiving this drug. Research Sponsor: None.

4038 Poster Session (Board #30), Fri, 8:00 AM-11:00 AM

FOLFIRI versus irinotecan monodrug as second-line treatment in metastatic colorectal cancer patients: An open, multicenter, prospective, randomized controlled phase III clinical study. *First Author: Weijian Guo, Shanghai Medical College, Fudan University Shanghai Cancer Center, Shanghai, China*

Background: The most commonly used treatment methods for metastatic colorectal cancer (mCRC)are systemic chemotherapy, molecular targeted therapy and local treatment. The main chemotherapy drugs for mCRC include Irinotecan, Oxaliplatin and 5-Fu. V308 Research shows that FOLFOX and FOLFIRI can be standard first or second-line of each other in the treatment of metastatic colorectal cancer. However if the first-line treatment regimen containing 5-FU fails, whether it is necessary to re-challenge 5-FU when Irinotecan is applied in the second line is unknown. There is no head-to-head comparative study to answer whether the FOLFIRI regimen is better than the Irinotecan monodrug. Therefore, it is necessary to carry out a comparative study of FOLFIRI Versus Irinotecan monodrug to observe whether adding 5-Fu on the basis of Irinotecan can improve the therapeutic effect. **Methods:** This was a randomized phase III trial. Patients from 5 centers in China with metastatic colorectal adenocarcinoma, for whom first-line of chemotherapy including oxaliplatin combined with fluorouracil drugs (combined or not combined with targeted therapy) had failed, were enrolled. 172 patients with mCRC were randomly treated with FOLFIRI or Irinotecan monodrug were included in this study. FOLFIRI group : Irinotecan 180mg/m^2 ; Lecovorin 400mg/m^2 ; 5-Fu 400mg/m^2 ; 5-Fu 2400mg/m^2 CIV 46h. Irinotecan monodrug group 180mg/m^2, The regimen was repeated every 2 weeks. The primary endpoint is PFS , and this clinical trail is a superiority trial. **Results:** ITT (Intention-To-Treat) analysis: Among 172 patients, 10 had PR, 93 had SD, and 63 had PD , 6 patients have not received efficacy evaluation yet. The ORR was 5.68% VS. 5.95%, and the DCR was 61.36% and 54.76% in FOLFIRI group and Irinotecan monodrug group, respectively. Adverse reactions included neutropenia, stomatitis, diarrhea, fatigue, abnormal liver enzymes, pyrexia, arrhythmia, nausea and most of these were grade 1-2. The dose reduction rate induced by drug tocixity of was 13.64% and 7.14% in FOLFIRI group and Irinotecan monodrug group, respectively. **Conclusions:** These data show that Irinotecan monodrug has the similar ORR and DCR with FOLFIRI regimen in second-line treatment of mCRC. Irinotecan monodrug has lower adverse effect. Clinical trial information: NCT02935764. Research Sponsor: None.

4039 Poster Session (Board #31), Fri, 8:00 AM-11:00 AM

Encorafenib plus cetuximab with or without binimetinib for *BRAF* V600E-mutant metastatic colorectal cancer: Quality-of-life results from a randomized, three-arm, phase III study versus the choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC). *First Author: Scott Kopetz, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: In the BEACON CRC study, the triplet regimen of encorafenib (ENCO) + binimetinib (BINI) + cetuximab (CETUX) significantly improved overall survival (OS, HR:0.52, $P < 0.0001$) and objective response rates (ORR, 26% vs 2%, $P < 0.0001$) in patients (pts) with *BRAF*V600E metastatic colorectal cancer (mCRC) compared with current standard of care. This analysis focuses on the patient-reported quality of life (QOL) assessments from this study. **Methods:** The BEACON CRC study was a randomized, open-label, 3-arm, phase 3 global study which evaluated triplet (ENCO+BINI+CETUX) or doublet (ENCO+CETUX) vs. investigator's choice of irinotecan + CETUX or FOLFIRI + CETUX in pts with *BRAF*V600E mCRC. QOL assessments (secondary endpoints in the trial) included the EORTC QOL Questionnaire (QLQ C30), Functional Assessment of Cancer Therapy Colon Cancer (FACT C), EuroQol 5D 5L, and Patient Global Impression of Change (PGIC). The primary assessment for the QOL variables was the time to definitive 10% deterioration. The study is ongoing. **Results:** 665 pts were randomly assigned to receive either triplet (n = 224), doublet (n = 220), or control (n = 221). Reduction in the risk of QOL deterioration was an estimated 45% (HR 0.55, 95% CI: 0.43, 0.70) and 52% (HR 0., 9485% CI: 0.38, 0.62) in EORTC QLQ C30 and FACT C assessments, respectively, in favor of the triplet regimen over control. For the doublet vs. control, reduction in risk of QOL deterioration was an estimated 46% (HR 0.54, 95% CI: 0.43, 0.69) and 54% (HR 0.46, 95% CI: 0.36, 0.59) in EORTC QLQ C30 and FACT C, respectively in favor of the doublet. Similar results were observed in EuroQol 5D 5L and PGIC assessments. There were no overall differences in QOL between triplet and doublet across the 4 instruments. **Conclusions:** In BEACON CRC, triplet and doublet demonstrated substantial improvement in patient-reported QOL assessments over the current standard of care in pts with *BRAF*V600E-mutant metastatic CRC whose disease had progressed after 1 or 2 prior regimens. Clinical trial information: NCT02928224. Research Sponsor: Pfizer Inc.

4040 Poster Session (Board #32), Fri, 8:00 AM-11:00 AM

Nivolumab (NIVO) + low-dose ipilimumab (IPI) as first-line (1L) therapy in microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Two-year clinical update. *First Author: Heinz-Josef Lenz, USC Norris Comprehensive Cancer Center, Los Angeles, CA*

Background: In the phase 2 CheckMate 142 trial, NIVO + low-dose IPI had robust, durable clinical benefit and was well tolerated as 1L therapy for MSI-H/dMMR mCRC (median follow-up 13.8 months [mo; range, 9–19]; Lenz et al. *Ann Oncol* 2018;29:LBA18). Longer follow-up is presented here. **Methods:** Patients (pts) with MSI-H/dMMR mCRC and no prior treatment for metastatic disease received NIVO 3 mg/kg Q2W + low-dose IPI 1 mg/kg Q6W until disease progression or discontinuation. The primary endpoint was investigator-assessed (INV) objective response rate (ORR) per RECIST v1.1. **Results:** In 45 pts with median follow-up of 29.0 mo, ORR (95% CI) increased to 69% (53–82) (Table) from 60% (44.3–74.3); complete response (CR) rate increased to 13% from 7%. The concordance rate of INV and blinded independent central review was 89%. Median duration of response (DOR) was not reached (Table). Median progression-free survival (PFS) and overall survival (OS) were not reached, and 24-mo rates were 74% and 79%, respectively (Table). Nineteen pts discontinued study treatment without subsequent therapy. An analysis of tumor response post discontinuation will be presented. Ten (22%) pts had grade 3–4 treatment-related adverse events (TRAEs); 3 (7%) had grade 3–4 TRAEs leading to discontinuation. **Conclusions:** NIVO + low-dose IPI continued to show robust, durable clinical benefit with a deepening of response, and was well tolerated with no new safety signals identified with longer follow-up. NIVO + low-dose IPI may represent a new 1L therapy option for pts with MSI-H/dMMR mCRC. Clinical trial information: NTC02060188. Research Sponsor: Bristol-Myers Squibb.

Efficacy (INV)[a].

	NIVO + low-dose IPI (N = 45)
ORR,[b] n (%) [95% CI]	31 (69) [53–82]
Best overall response, n (%)	
CR	6 (13)
PR	25 (56)
SD	7 (16)
PD	6 (13)
Not determined	1 (2)
Disease control rate,[c] n (%) [95% CI]	38 (84) [70.5–93.5]
Median time to response (range), mo	2.7 (1.2–27.7)
Median DOR (range), mo	NR (1.4+ to 29.0+)
Median PFS, mo (95% CI)	NR (NE)
24-mo rate, % (95% CI)	74 (57.2–84.5)
Median OS, mo (95% CI)	NR (NE)
24-mo rate, % (95% CI)	79 (64–89)

[a]Median follow-up = time on study from first dose to data cutoff (29.0 mo [range, 24.2–33.7]).
[b]Pts with CR or PR divided by number of treated pts.
[c]Pts with CR, PR, or SD for ≥ 12 weeks divided by number of treated pts.
NE, not estimable; NR, not reached; PD, progressive disease; PR, partial response; SD, stable disease.

4041 Poster Session (Board #33), Fri, 8:00 AM-11:00 AM

Metastases resection in colorectal cancer patients with mutation in oncogene BRAF or tumors located on the right side: Experience at the HGUGM. *First Author: Laura Ortega, Hospital General Universitario Gregorio Marañón, Instituto De Investigación Sanitaria Gregorio Marañon, Madrid, Spain*

Background: Approximately 25% of patients with colorectal cancer (CRC) debut with metastatic disease. In addition, 25-35% of patients with localized disease at diagnosis develop metastatic lesions during the evolution of their disease. Consequently, approximately 50-60% of patients with CRC will present metastatic lesions at some point in their lives. Metastasis resection has improved the prognosis of these patients, achieving overall survival (OS) that exceed 40 months. However, there are doubts about the benefit of this approach in patients with mutations in oncogene BRAF or tumors located on the right-side, due their poor prognosis. The aim of the study is to analyze the impact of metastases resection on OS of these populations. **Methods:** We conducted a retrospective analysis of patients with mCRC attended in the Medical Oncology Department of the Hospital General Universitario Gregorio Marañón (Spain) between January 2010 and 2018. **Results:** 487 patients were identified and included in the analysis. Median age was 71 years (62-81). Most patients were males (62.4%). 55.2% had metastatic lesions at diagnosis. Most patients had ECOG 0-1 at diagnosis of metastatic disease (91.0%). 8.9% of patients had BRAF mutations (n = 21) and 31.8% of patients had primary tumors located on the right-side (n = 152). 474 patients received first-line chemotherapy (97.3%). OS of the entire cohort was 29.67 months; 30.69 months in BRAF mutated patients vs 35.89 in wild-type patients (p = 0.161); 25.29 months in right-side tumors vs 31.02 in left-side tumors (p = 0.044). 306 patients (62.8%) underwent metastases resection. Most common location was liver (51.4%). 147 patients (30.2%) underwent a second metastases resection. Mean number of metastases surgeries was 1.35 (+/-1.40). OS since metastases resection was 24.83 months in BRAF mutated patients vs 41.55 months in wild-type patients (p = 0.020). According to location, it was 35.49 months in right-side tumors vs 43.78 months in left-side tumors (p = 0.106). In BRAF mutated patients, OS was 38.19 months in patients underwent metastases resection vs 18.52 months in non-surgical patients (p = 0.043); 41.51 months vs 16.18 months respectively in patients with tumors located on the right-side ($p < 0.001$). **Conclusions:** Metastases resection has a positive impact on overall survival of patients with mutations in oncogene BRAF or right-side tumors, even though their prognosis is still poor compared to patients without these alterations. Research Sponsor: None.

4042 Poster Session (Board #34), Fri, 8:00 AM-11:00 AM

Rectal cancer in young patients: Clinicoepidemiologic profile and treatment outcomes. *First Author: Pankaj. Goyal, Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India*

Background: Colorectal cancers are 3rd most common cause of cancer globally however studies of rectal cancers alone in younger patients are scarce. Rectal cancers in Asian patients present at a younger age and has an aggressive tumor biology. This study looks at rectal cancer in young patients, ≤30 years old, with the aim to report clinico-epidemiologic profile and treatment outcomes in this subgroup. **Methods:** Retrospective analysis was conducted at a tertiary care centre. Of total 845 rectal cancer patients between 2012-2017, 103 patients of young rectal cancers were enrolled. Kaplan Meier method was used for survival analysis and cox regression analysis was done to identify factors affecting survival. **Results:** Young rectal cancer patients constituted 12.2% of the total rectal cancer patients. Male: Female ratio was 2.3:1 and the mean age was 24.7 ± 3.9 years. Around 73.8 % patients had locoregional disease (stage I/II/III) at presentation.CEA levels were elevated in 36.9% of patients, while most common histology was signet ring cell histology which was present in 51.5% of patients. Of 76 patients with locoregional disease, 75% received neoadjuvant chemo-radiotherapy, 7.9% received neoadjuvant chemotherapy alone while 3.9% received neoadjuvant radiotherapy alone. Of 76 patients with locoregional disease, 55 patients underwent surgery of which 53.9% underwent low anterior resection while 18.4% underwent abdomino-perineal resection. Pathologic CR rates were seen in 13.3%, while recurrences were seen in 55.4% of non-metastatic patients. Overall 5-year survival for the whole study group was 19.5%, while 1-year PFS and 3-year DFS for metastatic and non-metastatic disease were 5% and 43.8% respectively. On regression analysis elevated CEA levels and not achieving a pathologic CR (pCR) with neo-adjuvant therapy had a trend towards worse overall survival (HR 2, 95% CI 1-4, p = 0.063), (HR 4.7, 95% CI 0.64-35.1, p = 0.125) respectively. **Conclusions:** Rectal cancers in Asia present at younger age and this younger population is associated with advanced stage, increased CEA at presentation, aggressive histology and poor survival. CEA raise and not achieving pCR were associated with trend towards worse survival. Research Sponsor: None.

4043 Poster Session (Board #35), Fri, 8:00 AM-11:00 AM

Recurrence after surgery for concurrent metastatic colorectal cancer: The perspective of bioinformatics and machine learning. *First Author: Zhiwen Luo, Department of Hepatobiliary Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: Recurrence of concurrent metastatic colorectal cancers (mCRCs) after surgery is still a challenge. But mCRCs' outcomes are heterogeneous, and no clinicopathological methods can predict its recurrence and guide postoperative treatment from an intrinsic cell activities and extrinsic immune microenvironment perspective. We aimed to identify such gene models. **Methods:** Gene expression analysis on CRCs. Based on metastasis-related genes, a metastatic evaluation model (MEM) was developed, dividing mCRCs into high and low recurrence risk clusters. Machine learning tested MEM's importance to predict recurrence. Further investigating MEM's two clusters made an immune prognostic model (IPM) with immune genes differentially expressed between MEM clusters. The predictive performance of MEM and IPM on prognosis was comprehensively analyzed and validated. The mechanism of IPM on the immune microenvironment and response to immuno/chemotherapy was analyzed extensively. **Results:** RNA data of 998 CRCs were analyzed. High postoperative recurrence risk in mCRCs was owing to immune response's down-regulation, which was influenced by 3 MEM genes (*BAMBI, F13A1, LCN2*) and their related 3 IPM genes (*SLIT2, CDKN2A, CLU*). MEM and IPM were developed and validated on 239 mCRCs to differentiate a low and high recurrence risk (AUCs > 0.7). Functional enrichment analysis showed immune response and immune system diseases pathway represented the major function and pathway related to IPM gene. IPM high-risk group (IPM-high) had higher fractions of Tregs (P= 0.04), lower fractions of resisting memory CD4+ T cells (P= 0.02) than IPM-low. And stroma and immune cells in IPM-high samples were scant (P= 0.0002, 0.001, respectively). In IPM-high, MHC class II molecules all down-expressed, and DNA methylation disordered. TIDE algorithm and GDSC analysis discovered IPM-low was more promising to respond to both anti-CTLA4 therapy (P= 0.005) and common FDA targeted drugs (P< 0.05), while IPM-high had nonresponse to both of them. But anti-CDKN2A agent with activation of MHC class II response might reverse the dilemma of this refractory mCRCs subgroup. **Conclusions:** Postoperative recurrence of mCRC is strongly related to immune microenvironment. Our two relative gene models could identify subgroups of mCRC with different recurrence risk, and stratify mCRCs sensitive to immune/chemotherapy, even highlight the ignored importance of MHC class II molecules on immunotherapy in mCRCs for the first time. Research Sponsor: Capital's Funds for Health Improvement and Research [grant number 2018-1-4021].

4044 Poster Session (Board #36), Fri, 8:00 AM-11:00 AM

TAS-116, an oral HSP90 inhibitor, in combination with nivolumab in patients with colorectal cancer and other solid tumors: An open-label, dose-finding, and expansion phase Ib trial (EPOC1704). *First Author: Akihito Kawazoe, National Cancer Center Hopital East, Kashiwa, Japan*

Background: Regulatory T cells (Tregs) potentially induce the resistance of anti-PD1/PD-L1 inhibitors (A-PD1). TAS-116, a novel HSP90 inhibitor, enhanced antitumor immunity via reducing Tregs *in vitro* and *in vivo*. Combination of TAS-116 plus A-PD1 showed a superior tumor growth suppression compared with either treatment alone *in vivo*. Based on the above, we investigated safety and efficacy of TAS-116 in combination with nivolumab in patients with solid tumors. **Methods:** Enrolled patients received TAS-116 plus nivolumab in a dose-finding part to estimate the maximum tolerated dose and the recommended phase 2 dose (RP2D). Additional patients were enrolled in a dose-expansion part. TAS-116 monotherapy (orally once daily, 80mg on level 1, 120mg on level 2, and 160mg on level 3) was administrated for 2 weeks followed by the combination with nivolumab (intravenously every 2 weeks, 3 mg/kg). The primary endpoint was dose-limiting toxicities (DLTs) during the first cycle (4 weeks). PD-L1 combined positive score (CPS) and tumor mutation burden (TMB) were assessed. We also conducted biomarker research using paired samples from repeated tumor biopsies and blood collections. **Results:** A total of 44 patients with colorectal cancer (CRC, n = 29), gastric cancer (GC, n = 8), sarcoma (n = 5), non-small cell lung cancer (NSCLC, n = 1) and melanoma (n = 1) after standard of cares were enrolled. One patient had MSI-H CRC, but all other patients had MSS tumors. No DLTs were observed at all levels and TAS-116 160 mg was determined as RP2D. The common grade 3 or worse treatment-related adverse included AST/ALT increased (7%), creatinine increased (5%) and platelet count decreased (5%). Objective tumor response was observed in 6 patients including 4 MSS CRC, 1 MSI-H CRC and 1 sarcoma, resulting in objective response rate (ORR) of 16% in MSS CRC without prior A-PD-1. PD-L1 CPS and TMB could be evaluated in 18 and 17 MSS CRC without prior A-PD-1, respectively. ORR was 27% in patients with CPS ≥1 and 0% in patients with CPS < 1. ORR was 33% with TMB-high (median as the cut-off) and 12% with TMB-low. Analysis of tumor-infiltrating lymphocytes before treatment and after TAS-116 monotherapy demonstrated reduction of $FoxP3^{hi}CD45RA^{-}$Tregs fraction in the tumor microenvironment. **Conclusions:** The combination of TAS-116 160mg plus nivolumab had manageable safety profiles and anti-tumor activity especially for MSS CRC patients, which warrants further investigations in a large cohort. Clinical trial information: UMIN000032801. Research Sponsor: Taiho, Ono.

4045 Poster Session (Board #37), Fri, 8:00 AM-11:00 AM

Inpatient outcomes and predictors of mortality in patients with gastrointestinal malignancies presenting with sepsis: A nationwide analysis. *First Author: Parth Desai, John H. Stroger, Jr. Hospital of Cook County, Chicago, IL*

Background: Sepsis is a frequent cause of morbidity and mortality in patients with malignancy. However, there is paucity of literature on mortality, hospital charges and overall healthcare utilization among patients with GI malignancy, which we hope to characterize in this study. **Methods:** We queried retrospective data from the Nationwide Inpatient Sample (NIS) database for the year 2016. Sepsis (Dx1) was identified using ICD-10 code as primary diagnosis in patients with known GI malignancies (Dx2). Univariate and multivariate Poisson regression analysis was done to study outcomes. Propensity score matching was done to minimize confounding factors. Primary outcome was inpatient mortality. Secondary outcomes were Length of Stay (LOS), Total Charge (TOTCHG) and ICU admission. **Results:** A total of 43,240 patients with GI malignancy were admitted in 2016 with sepsis. Two most common GI malignancies admitted with sepsis were colorectal (35%) and hepatocellular cancer (HCC) (28.2%). Overall mortality in GI cancer was 19.8% vs 10.2% in all cancers (p<0.01). There was male (59%) and Caucasian (63%) preponderance. Out of all hospital admissions for GI malignancy, 41.4% were secondary to sepsis. E. coli (31%) infection and gram-negative bacteremia (15%) were the most common causes of sepsis. Sepsis with GI malignancy was associated with length of stay of 7.4 days vs 5.4 days (coef 2.44, 95% CI 2.3-6.7 p=0.04) and a mean hospital charge of $88,728 vs $ 54, 668 (coef 34,140, 95% CI 44,264-90,646, p<0.01) as compared to without sepsis. After adjusting for demographic and patient related variables, independent predictors of mortality were old age, uninsured, African Americans, septic shock requiring pressor support, AKI, inpatient hemodialysis, metabolic encephalopathy and acute respiratory failure. **Conclusions:** Sepsis poses a substantial healthcare burden in patients with GI malignancy and is a major cause of mortality. Early antibiotic treatment is necessary for sepsis control in patients with GI malignancy. Research Sponsor: None.

Multivariate analysis for mortality in patients with GI malignancy admitted with sepsis.

Predictor	Adjusted HR (95% CI)	P-value
Colorectal cancer	Reference	
Esophageal	1.40 (1.13-1.74)	***0.02**
Gastric	1.31 (1.03-1.66)	***0.03**
HCC	1.49 (1.27-1.74)	***<0.01**
Age > 70	1.74 (1.56 – 1.89)	***<0.01**
Uninsured	2.06 (1.56-2.72)	***<0.01**
Encephalopathy	2.54 (1.61- 4.02)	***<0.01**
ICU admission	5.42 (4.61-6.37)	***<0.01**
AKI requiring HD	6.33(5.17-7.74)	***<0.01**

*P value less than <0.05 was considered statistically significant

4046 Poster Session (Board #38), Fri, 8:00 AM-11:00 AM

Pembrolizumab (Pem) in combination with stereotactic body radiotherapy (SBRT) for resectable liver oligometastatic MSS/MMR proficient colorectal cancer (CRC). *First Author: Dustin A. Deming, University of Wisconsin Carbone Cancer Center, Madison, WI*

Background: SBRT is used to treat liver metastatic CRC, causing an increase in immunogenic antigen release and influx of responding immune cells. We hypothesize that radiation enhances the immunogenicity of MSS CRC and potentiates the effectiveness of PD-1 blockade. This phase Ib study examines the safety and efficacy of the sequential combination of SBRT and Pem in patients (pts) undergoing resection of their disease. **Methods:** Eligibility criteria include MSS CRC with resectable liver-confined metastatic disease. Prior surgery and systemic chemotherapy are allowed. Subjects receive sequential SBRT and cycle 1 of Pem prior to operative management and adjuvant Pem. The primary objectives are to determine the safety/tolerability of this regimen and the recurrence free survival (RFS) at 1 year following clearance of metastatic disease. Correlative studies examined tumor infiltrating CD8+ T lymphocytes (TILs) and the accumulation and proteolysis of versican (VCAN), an immunoregulatory tumor matrix proteoglycan. Proteolysis of VCAN results in the release of an immunostimulatory fragment, versikine. Cancers with low VCAN and high versikine (VCAN proteolysis predominant (VPP)) are hypothesized to respond better to immunotherapies. **Results:** 15 pts (median age 58.2 [range 38-69]) have been enrolled. All pts had prior FOLFOX. SBRT median dose was 50 Gy (40-60 Gy) to a single lesion targeted in all pts. No DLTs were observed. AEs included one case of biliary tract injury and biloma, not related to immunotherapy. No grade 3/4 immunotherapy-related AEs have occurred. 10 pts have completed a minimum follow-up of 1 year post resection. In the intention to treat analysis, the 1 year RFS was 70% (historic control 50%). 2 of 3 pts with BRAF V600E mutations have had early recurrences. 2 pts had VCAN high tumors and both recurred prior to 1 year. 4 pts had VPP cancers and all were recurrence free at 1 year. TILs in the radiated lesions were $>$ 2 times as abundant as in the pre-treatment (tx) tissue for 50% of pts. 3 of 4 pts who had non-radiated lesions available for analysis had TILs $>$ 2 times pre-tx in the non-radiated lesions indicating a potential abscopal effect. **Conclusions:** The combination of SBRT with Pem and surgical resection is well tolerated with no signal of increased immunotherapy-related toxicity and preliminary evidence of potential enhanced efficacy. Clinical trial information: NCT02837263. Research Sponsor: Merck.

4047 Poster Session (Board #39), Fri, 8:00 AM-11:00 AM

Clinical and pathologic factors associated with survival in BRAFV600E colorectal cancers. *First Author: Van K. Morris, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: $BRAF^{V600E}$ mutations occur in fewer than 10% of all patients (pts) with metastatic colorectal cancer (mCRC) and arise from sessile serrated adenomas. Despite efficacy with targeted therapies against MAPK signaling and with immunotherapies in this population, survival outcomes for pts with $BRAF^{V600E}$ mCRC in general are poor. Characteristics distinguishing pts with $BRAF^{V600E}$ mCRC with favorable versus unfavorable outcomes have not been well annotated. **Methods:** Records of 188 pts with $BRAF^{V600E}$ mCRC evaluated at MD Anderson Cancer Center between 3/2010-1/2020 were reviewed. Pts with the shortest and longest metastatic survival (N = 25 for each group) were compared. Associations between prognostic group and clinical/pathologic features were measured by odds ratio and for median survival by log-rank testing. **Results:** Median metastatic survival differed between the 2 $BRAF^{V600E}$ mCRC populations (8.6 vs 84 months, $p < .0001$). Pts with poor survival more commonly had primary tumors arising from the hepatic flexure/proximal transverse colon (44% vs 16%, p = .04) and more frequent hepatic involvement (75% vs 28%, p = .001). Pts with favorable survival were more likely to develop metachronous metastases (52% vs 16%, p = .01), have fewer distant organ involvement (median 1 vs 2, p = .02), and undergo definitive locoregional therapy to metastatic disease (44% vs 0%, p = .01). Microsatellite instability (36% vs 4%, p = .008) and a history of tobacco use (44% vs 16%, p = .04) were associated with a favorable prognosis. Durable responses to MAPK-targeted therapies (5/25) and immunotherapy (3/25) were noted in the favorable group. **Conclusions:** Pts with $BRAF^{V600E}$ mCRC can achieve excellent long-term survival which belies conventional context and is driven by locoregional and systemic treatment options alike. Anatomic localization of the primary tumor and prior exposures may highlight environmental influences on tumor biology which account for the clinical heterogeneity of pts with $BRAF^{V600E}$ mCRC. Research Sponsor: None.

4048 Poster Session (Board #40), Fri, 8:00 AM-11:00 AM

Evaluation of safety, immunogenicity, and preliminary efficacy of PolyPEPI1018 off-the-shelf vaccine with fluoropyrimidine/bevacizumab maintenance therapy in metastatic colorectal cancer (mCRC) patients. *First Author: Joleen Marie Hubbard, Mayo Clinic, Rochester, MN*

Background: PolyPEPI1018 is an off-the-shelf, multi-peptide vaccine containing 12 immunogenic epitopes derived from 7 cancer testis antigens (CTAs) frequently expressed in patients with CRC. Here we report the final results of the phase I study of PolyPEPI1018 vaccine as an add-on to maintenance therapy in mCRC patients. **Methods:** 11 patients with MSS mCRC were vaccinated with PolyPEPI1018 just after the transition to maintenance therapy with fluoropyrimidine/bevacizumab after first-line combo chemotherapy and bevacizumab. Part A: n = 5, single dose; Part B: n = 6, 3 doses, Q12W. Primary endpoint was safety. Immunomonitoring was performed at both blood and tumor levels, as well as prospectively predicted. **Results:** The vaccine was well tolerated; most common side effects were transient skin reactions. No vaccine-related SAE occurred. Pre-existing immune responses were boosted by the vaccine for 7/10 patients. *De novo* responses were also induced, overall, 80% of patients had CD8+ T cell responses against at least 3 CTAs. The magnitude of immune responses as well as the density and the ratio of CD8+/CD3+ tumor infiltrating T cells increased with multiple vaccine doses. Three patients had objective tumor response according to RECIST v1.1: one of them in the single dose group and two of them in the 3 doses group. Both patients in the 3 doses group qualified for curative surgery. One of them had no viable tumor cells in his primary tumor at the time of surgery. Post-trial follow-up revealed PFS of at least 12 months for 3 patients. mPFS was longer for patients receiving multiple doses (9.9 months) compared to single dose (6.1 months). Both measured and predicted multiantigenic immune responses tend to correlate with PFS and tumor volume reduction. **Conclusions:** PolyPEPI1018 was effective in restoring immunological responses to CTAs in patients' with spontaneous immunity against. Treatment with PolyPEPI1018 vaccine and maintenance therapy was safe and demonstrated evidence of early clinical activity in MSS mCRC tumors. Data support further randomized trials with PolyPEPI1018. Clinical trial information: NCT03391232. Research Sponsor: Treos Bio.

4049 Poster Session (Board #41), Fri, 8:00 AM-11:00 AM

Sequencing of treatment matters in synchronous liver or lung only metastatic colon cancer. *First Author: Saurabh Parasramka, University of Kentucky, Lexington, KY*

Background: Per SEER database, approximately 21% of patients have synchronous metastatic disease at presentation with a median 5 year survival of 14%. Liver is by far the most common site of metastatic disease followed by lung. Metastatectomy of appropriate lesions have achieved a 5 year survival ranged between 40%-70% depending on the extent of the metastasis. For liver or lung only metastatic disease, practice varies from surgery followed by adjuvant chemotherapy to perioperative chemotherapy. Benefit of one approach versus the other has not been demonstrated. We decided to study this using the National Cancer Database (NCDB) database available from the 2010-2015 period. **Methods:** Adults $>$ 20 years with primary colon cancer (excluding rectal and recto sigmoid junction) with single organ metastatic disease to liver and/or lung at diagnosis were identified. All patients had received surgery to the primary site, resection of the distant site and chemotherapy in the neoadjuvant setting (NAC) or adjuvant setting (AC) within 1 year of diagnosis. Histology except for adenocarcinoma and variants were excluded. Patients who died within 90 days of surgery were excluded. Descriptive analysis, Kaplan-Meier plots, Log-Rank tests for univariate and proportional hazards models for multivariate survival analyses were performed. To reduce biases, a sensitive analysis was also performed based on the intention to treat principle by including additional surgery only and chemotherapy only cases. **Results:** A total of 3175 colon cancer patients with liver or lung only metastatic disease were identified. 2487 (78%) had AC and 688 (22%) had NAC. Approximately 54% were males with 90% less than 75 years of age. More patients had private insurance and were treated in academic centers in the NC group (62 Vs 51%) and (58 Vs 42%) respectively. Both groups had similar Charlson comorbidity index. NC approach had better OS with HR of 0.75 (CI 0.65-0.85; $p < 0.0001$) on univariate analysis and 0.86 (0.74-0.98; $P < 0.0281$) on multivariate analysis. On multivariate analysis, age group $>$ 75 years, black race, treatment outside academic research program had worse survival ($p <$ 0.0001, 0.0139, 0.0001) respectively. The sensitive analysis showed the similar effects. **Conclusions:** Within the limitations of database review, our analysis suggests survival advantage of neoadjuvant chemotherapy approach over surgery first. Research Sponsor: None.

4050 Poster Session (Board #42), Fri, 8:00 AM-11:00 AM

Prognostic effect of specific *RAS/BRAF* mutations in patients (pts) with metastatic colorectal cancer (mCRC). *First Author: Ben George, Froedtert & The Medical College of Wisconsin, Milwaukee, WI*

Background: Somatic mutations in *KRAS, HRAS, NRAS* (extended *RAS*) and *BRAF* have prognostic and predictive impact in pts with mCRC. We analyzed the prognostic impact of specific somatic mutations in extended *RAS* and *BRAF*. **Methods:** We retrospectively reviewed the electronic medical records of pts with mCRC at our institution who underwent comprehensive genomic profiling (CGP) utilizing the Foundation One assay. DNA was extracted from clinical specimens and CGP was performed on hybrid-capture, adaptor ligation-based libraries for up to 315 genes plus 47 introns from 19 genes frequently rearranged in cancer. BRAF mutations were classified as class I, II and III according to accepted nomenclature. Fisher's exact test and Kaplan Meier estimates were used for statistical analyses. This project was approved by the Medical College of Wisconsin Institutional Review Board. **Results:** 273 pts were identified - median age at diagnosis was 57, 48% were male. Somatic mutations in extended RAS were found in 138 (50%) pts, majority being mutations in *KRAS* (46%). Among pts with *KRAS* mutations, codon 12, 13, 61 and 146 mutations accounted for 73%, 11%, 4% and 6% respectively while *KRAS* G12C mutations accounted for 9%. *BRAF* mutations were detected in 22 (8%) pts - *BRAF* V600E and non–V600E mutations accounting for 4.4% and 3.6% respectively. Among pts with BRAF mutations, 17 (77%) were kinase domain mutations, 16 of which could be further classified as class I (12/16), II (1/16) and III (3/16). Median overall survival (mOS) for the entire cohort was 26.4 months (mo). *KRAS* mutated pts had a mOS of 25.8 mo; pts with *KRAS* G12C mutation had a mOS of 23 mo compared to 27.1 mo for pts with other *KRAS* mutations ($p < 0.001$).Pts with *BRAF* mutation had a mOS of 26.2 mo; pts with *BRAF* V600E mutation had a mOS of 14.1 mo compared to 30.6 mo for pts with *BRAF* non-V600E mutations ($p = 0.1$). **Conclusions:** The poor prognosis of pts with *KRAS* G12C and *BRAF* V600E mutations compared to pts with other *KRAS* and *BRAF* mutations merit further biologic characterization with functional assays. Individualized therapeutic strategies must be conceptualized for mCRC pts with specific *RAS/BRAF* mutations, considering their widely disparate prognosis and putative downstream signaling mechanisms. Dynamic molecular simulation to understand conformational changes in proteins associated with specific mutations will be pivotal to optimizing precision therapeutic strategies. Research Sponsor: None.

4051 Poster Session (Board #43), Fri, 8:00 AM-11:00 AM

Randomized phase II trial of avelumab alone or with cetuximab for unresectable, locally advanced or metastatic squamous cell anal carcinoma progressed to at least one line of treatment: The CARACAS study. *First Author: Sara Lonardi, Veneto Institute of Oncology (IOV)-IRCCS, Padua, Italy*

Background: Advanced squamous cell anal carcinoma (advSCAC) is a rare disease with poor prognosis. No standard therapies beyond first line are currently available, yet a promising activity was documented for the anti-EGFR cetuximab (CET) and for anti-PD-1 agents in previous retrospective case series and phase I-II studies, respectively. In experimental models combination of EGFR and PD-L1 blockade was synergistic as PD-L1 blockade led to NK cells activation enhancing cetuximab ADCC. In this trial we aimed to evaluate safety and activity of the anti-PD-L1 avelumab (AVE) alone or in combination with CET in pretreated advSCAC. **Methods:** This was an open-label, prospective, multicenter randomized phase 2 trial (NCT03944252). Patients (pts) with advSCAC progressed after at least 1 line of treatment were randomized 1:1 to receive either AVE 10 mg/kg (arm A) or AVE + CET 500 mg/sqm (arm B) as bi-weekly regimens. A Simon's two-stage Mini-Max design was used. The null hypothesis of a true response rate 5% was tested against the one-sided alternative of a true response rate 20% in each arm. Setting type I error at 0.05 and power at 80%, 30 pts per arm had to be randomized. No formal comparison between the two arms was planned. Primary endpoint was overall response rate (ORR); secondary endpoints were Progression-Free Survival (PFS), Overall Survival (OS) and safety. **Results:** Sixty pts were enrolled, 30 in each arm. All baseline characteristics were well balanced between the two arms. Median age was 63 years; M/F was 19/41; 12 out of 30 pts in each arm had distant metastases; 7 in arm A and 10 in arm B received > 1 previous lines of treatment. At a median follow up of 8.7 months, 3 out of 30 pts in each arm obtained PR (ORR 10%); SD was observed in 12 pts in arm A (40%) and 14 in arm B (47%). Disease control rate was thus 50% in arm A and 57% in arm B. Duration of disease control was 6.1 (95%CI 3.7–11.0) and 6.1 (95%CI 4.1–9.6) months in arm A and B, respectively. Median PFS was 2.1 (95%CI 1.8–4.0) in arm A and 3.9 months (95%CI 2.1–5.6) in arm B. Grade 3-4 adverse events were 13.3% in arm A and 33.3% in arm B: anemia 10% vs 13.3%, fatigue 0 vs 6.7%, skin toxicity 0 vs 6.7%. Treatment interruption due to AE occurred in 3 pts, 1 in arm A and 2 in arm B. Translational analyses will be performed on tissue and blood samples for exploratory purpose. **Conclusions:** The CARACAS trial was the first clinical study to test dual EGFR and PD-L1 blockade in advSCAC. Both AVE monotherapy and AVE-CET showed promising activity with manageable safety profile. Clinical trial information: NCT03944252. Research Sponsor: Veneto Institute of Oncology IRCCS, Pharmaceutical/Biotech Company.

4052 Poster Session (Board #44), Fri, 8:00 AM-11:00 AM

Characterization of sociodemographic and clinicopathological features and associated outcomes of patients (Pts) with anal squamous cell cancer (ASCC): Analysis of 44,084 pts in the National Cancer Database (NCDB). *First Author: Joanna Alyse Young, Levine Cancer Institute, Atrium Health, Charlotte, NC*

Background: ASCC incidence is rising. There are limited data on the relationships between sociodemographic & clinicopathological features and outcomes of ASCC pts. **Methods:** Pts diagnosed with ASCC between 2004 and 2016 were retrospectively reviewed. Data obtained from the NCDB were used to examine the impact of sociodemographic status on clinicopathological features and outcomes. Pts were categorized based on low (median $<$ \$38,000) or high ($\geq$\$68,000) income and low ($>$ 21% with no high school diploma) or high ($<$ 7% with no high school diploma) education areas based on zip code at time of diagnosis. Logistic regression and chi-square were used to examine differences between groups. **Results:** In total, 44,084 pts with ASCC were identified: median age, 59 yrs, 86% white; 11% black; 64% female. Most pts (84%) resided in metro areas; 29.7% vs 19.8% lived in high vs low income areas; 22.9% vs 17.8% lived in high vs low education areas. Seven percent were uninsured, 50% had government (Gov), and 43% had private insurance. Male gender (HR 1.62, CI 1.41-1.85, $p < 0.001$), low income area (HR 1.28, CI 1.19-1.37, $p = 0.014$), and insurance status (Gov, HR 1.55, CI 1.32-1.82, $p < 0.001$ and uninsured, HR 1.37, CI 1.37-1.85, $p = 0.039$) were associated with a higher risk of death. After adjusting for age, sex, race, stage, grade, insurance status, and comorbidity, pts from low income/education (n = 6695) vs high income/education (n = 4316) areas had a 33 % increased risk of death (HR: 1.33, $p < 0.001$). Pts with stage IV ASCC in the low income/education (n = 227) vs high income/education (n = 295) groups had worse overall survival (mOS, 1.4 vs 1.9 yrs, $p < 0.020$). Of the 44,084 pts, 5461 (12.4%) had confirmed HPV status. Of these, 2658 (48.7%) were HPV+ (high risk subtypes) and 2803 (51.3%) were HPV-. Compared to the HPV- pts, HPV+ pts were more likely to be women (71.8% vs 67.8%, $p = 0.001$), have stage 3 (38.1% vs 33.6%) or 4 (7.9% vs 5.9%, $p < 0.001$) cancer, and have poorly differentiated (29.5% vs 25.6%, $p < 0.001$) tumors. There were no significant differences in race, education, income, metro area, insurance status, or comorbidity between the HPV+ and HPV- pts. Moreover, HPV status did not impact OS (HR 0.92, CI 0.81-1.04, $p = 0.195$). **Conclusions:** HPV status was not correlated to income, education or insurance status, and did not impact OS in ASCC pts. Male gender and insurance status were associated with increased risk of death. Pts living in low income and low education areas were associated with worse survival. Research Sponsor: None.

4053 Poster Session (Board #45), Fri, 8:00 AM-11:00 AM

Prospective study of biomarkers in squamous cell carcinoma of the anal canal (SCCAC) and their influence on treatment outcomes: Five-year long-term results. *First Author: Camila Motta Venchiarutti Moniz, Instituto do Câncer do Estado de São Paulo, Universidade de São Paulo, São Paulo, Brazil*

Background: Chemoradiation (CRT) is a curative treatment for SCCAC. However, some patients (pts) present primary CRT resistance. As a rare tumor, there is a lack of prospective studies of prognostic factors in this setting. **Methods:** This prospective cohort study was aimed to evaluate predictive biomarkers (Ki-67, PD-L1, Human papillomavirus (HPV), HIV status, and tumor DNA mutations) in SCCAC. We published the 6 months (m) response rate (RR) of this cohort showing that HIV- were 5.7 times more likely to achieve response 6m post CRT (OR 5.72, CI 95% 2.5-13.0, $P < 0.001$). Now we report the long-term follow-up results of 5-year progression-free survival (PFS) and overall survival (OS). Eligible pts had T2-4/N0-3/M0 disease and were candidates to standard CRT. DNA mutations were analyzed by next-generation sequencing (NGS). HPV positivity was tested by PapilloCheck Test. KI-67 and PD-L1 were evaluated by immunohistochemistry. **Results:** 78 pts were recruited from Jan/2011 to Dec/2015. 75 were evaluable for PFS and OS. The median age was 57 years; 49 (65%) were stage III, and 9 (12%) were HIV+. HPV was evaluated in 67 and found in 47 (70.1%); HPV16 was the most common. PD-L1 was tested in 61; 10 (16.4%) had positive expression $> 1\%$. Ki-67 was performed in 65, with a median of 50% (range 1-90%). The median follow up is 66m. 5-year PFS and OS rates were 63.3% (95% CI 51.2-73.2%) and 76.4% (95% CI 64.8-84.6%), respectively. In a multivariate analysis, age (HR 1.06, P = 0.022, IC 95% 1.01-1.11) and absence of complete response at 6m (HR 3.36, P = 0.007, IC 95% 1.39-8.09) was associated with inferior OS. The OS rate was 62.5% in HIV+ group (95% CI 22.9-86%) in comparison with 78% (95% CI 65.7-86.3%) among HIV- pts, although this difference was not statistically significant (P = 0.400). A tendency to inferior OS was observed among pts with p53 codon 72 polymorphism (HR 2.83, P = 0.181, 95% CI 0.61-13.02). Other tumor mutations, HPV, Ki-67 expression, and PD-L1 expression, were not associated with PFS and OS. **Conclusions:** HIV- pts were 5.7 times more likely to achieve response 6m post CRT. The absence of complete response at 6m was the main factor associated with poor 5-year OS. New strategies of follow up and complementary treatment should be studied in late responders and HIV+ pts to ensure the success of curative treatment. Clinical trial information: 36211. Research Sponsor: FAPESP- Fundação de Amparo a Pesquisa do Estado de São Paulo (Sao Paulo State Research Support Foundation).

4054 Poster Session (Board #46), Fri, 8:00 AM-11:00 AM

PDL1 expression predicts therapeutic outcome in non metastatic anal squamous cell carcinoma (NMASCC). *First Author: Ilma Soledad Iseas, Oncology Unit, Hospital de Gastroenterologia Bonorino Udaondo, Buenos Aires, Argentina*

Background: NMASCC is a rising incidence disease with up to 30% of treatment failure to achieve complete response (CR) after standard chemoradiotherapy (CRT) leading to severe morbidity and death. Stage III-TNM, p53 mutations, HPV negativity, HIV infection are linked to treatment failure. We investigated the predictive/prognostic role of TNM, CR, HPV, PDL1 positivity and CD3/CD8 densities in NM-ASCC from a single institution. **Methods:** All 79 eligible consecutive NMASCC pts (available FFPE pre-treatment samples) seen from October-2009 to April-2019 having completed definitive CRT (50.4 Gy Pelvic Radiotherapy with Mitomycin-C 12mg/m2/IV/d1-5 / FU 1000mg/m2/d1-4 d29-32 (28%), Mitomycin-C/Capecitabine 825 mg/m2/bid (38%), Cisplatin 60 mg/m2/IV d1-29 and 5FU (34%) were analyzed. Mean age: 59 (range 26-87), 72% female, Stage III: 59%, HPV positive: 86% (HPV-16: 80%);14% HIV positive. IHC assessed by two pathologist for PD-L1 expression (ClonSP263) and CD3-CD8+ TILS densities (Clone 2GV6, Clone SP57). HPV-DNA assessed by PCR (BSGP5+/6+ multiplexed with beta-globin). Kaplan-Meier survival, CR, DFS, OS and Univariate analyses were performed using Cox proportional hazard model. **Results:** CR achieved within 6 months of treatment completion was 68%(53pts). Median follow-up after treatment completion: 35 months (range 6 –149). As of February 2020, 82% (65 pts) are alive, no evidence of disease:(57%) 46 pts, recurrence rate: 26%(22 pts), cancer death: 18% (14 pts). PDL1+ tumors ($>$ 1% positivity-CPS score): 56%, expression levels: 1-5% (57%,26p), $>$ 10%-100% (43%,19p). PDL1+ had a strong association with CR (p = 0.021); higher PDL1+ levels had 8-fold of CR-likelihood than PDL1 negative.(OR 8.50 vs. 1.12). Significative Spearman correlation between PDL1 tumors with CR and CD3-CD8 TILS density was observed (R = 0.43,p = 0.0017 and R = 0.36,p = 0.00094 respectively), albeit CD3-CD8 failed to reach significance as prognostic factors for either CR, DFS or OS. Only CR and PDL1 positive were strongly significantly associated to DFS (HR 0.10 [IC 95% 0.04-0.28] p $<$ 0.001 and HR 0.28 [IC 95% 0.11-0.73] p = 0.006) and OS (HR 0.12 [IC 95% 0.03-0.45] p $<$ 0.001 and HR 0.15 [IC 95% 0.03-0.68] p $<$ 0.004). Low prevalence of HPV negative, early tumors, HIV positive cases in our series probably impacted in statistical power for prognosis correlation. **Conclusions:** PDL1 positivity was the strongest predictive/prognostic factor in NM-ASCC. Alternative therapeutics options to standard CRT should be explored on poor-risk patients as HPV-negative, P53-mutated and PDL1 negative patients. Research Sponsor: None.

4055 Poster Session (Board #47), Fri, 8:00 AM-11:00 AM

Patient-reported gastrointestinal outcomes in patients with anal cancer. *First Author: Ramez Kouzy, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Among patients with anal cancer, chemoradiotherapy tends to offer an excellent prognosis but is often associated with undesirable toxicities that diminish quality of life. We sought to quantify the gastrointestinal-related patient-reported outcomes (PROs) of anal cancer patients receiving chemoradiotherapy in order to improve patient-physician communication and shared decision making. **Methods:** We prospectively followed patients with non-metastatic squamous cell carcinoma of the anal canal who received definitive chemoradiotherapy. Patients reported outcomes were collected using the bowel subdomain of the Expanded Prostate Cancer Index Composite (EPIC) questionnaire before treatment and at 4 subsequent timepoints. We used descriptive statistics to summarize the patients' characteristics and EPIC scores, then used the paired Wilcoxon test to compare EPIC scores at different timepoints. **Results:** The study included 21 patients (16 women and 5 men), whose median age was 57 years. Most patients (52%) had T2, and either N0 (38%) or N1 (43%) disease. Most patients (91%) received standard of care chemoradiotherapy. Compared with the patients' median overall summary score at baseline (66), their median score at 1 week (82) was significantly higher (p = 0.009), whereas their median score at 5 weeks (54) was significantly lower (p = 0.025). However, the patients' median overall summary score at baseline and at 3 months did not differ significantly (p = 0.919). Three months after radiotherapy, most patients (73%) reported rarely or never having bloody stools, and most (82%) reported rarely or never being bothered by bloody stools. Overall, EPIC scores show initial improvement of all domains, followed by some worsening of symptoms before returning to baseline levels. **Conclusions:** Anal cancer patients' gastrointestinal-related PROs tend to fluctuate during radiotherapy but return to baseline by 3 months, at which time most patients report few or no residual side effects. Our data provide a clear timeline of gastrointestinal acute toxicity using sequential PRO measurements that will improve patient-physician communication regarding expectations for cancer treatment and help in shared decision making. Research Sponsor: None.

4056 Poster Session (Board #48), Fri, 8:00 AM-11:00 AM

Socioeconomic status based on race in early-stage anal squamous cell carcinoma undergoing locoregional therapy. *First Author: Suleyman Yasin Goksu, The University of Texas Southwestern Medical Center, Dallas, TX*

Background: Anal Squamous Cell Cancer (ASCC) is a highly curable cancer. Underserved and vulnerable populations are particularly at risk of developing this disease. We aimed to study racial disparities and overall survival (OS) in patients with ASCC who received radiation therapy (RT) or chemo-RT (CRT) using the National Cancer Database. **Methods:** We identified adult patients with early-stage (stage I-II) ASCC diagnosed between 2004-2016 who underwent RT or CRT. We compared the clinical and treatment characteristics of white and black patients. The chi-square test was used for categorical variables. Kaplan-Meier and Cox regression method performed for survival analyses. We used 1:1 nearest neighbor propensity score matching to eliminate selection bias. **Results:** A total of 10,014 patients; 90.2% were white and 9.8% were black. White patients were more likely to be female, older age, have higher rate high-school education, private insurance, higher income, and travel a longer distance (all $p < .001$). Black patients were more likely to be higher comorbidity score and be treated at an academic/research facility. White patients had a higher rate of CRT and significantly better overall survival (OS) as compared to black patients (5-year survival 76% vs. 70%, $p < .001$) which persisted after propensity score matching (5-year survival 76% vs. 70%, $p = .002$). This difference continued after adjusting for clinically important factors, including HPV status (unmatched $p < .03$, matched $p = .008$). In the patients who received CRT, white patients were associated with improved OS versus black patients (unmatched 77% vs. 71%, $p < .001$; matched 77% vs. 71%, $p = .011$), and even after multivariate Cox analysis (unmatched $p < .001$; matched .014) (Table). **Conclusions:** White patients had significantly better OS as compared to black patients with early-stage ASCC as well as in the patients who received CRT. White patients were associated with high education level, higher income, and private insurance. The rate of HPV positive was similar among groups. Further investigations are needed to enlighten these disparities and target the increase education of the population at risk. Research Sponsor: None.

	Unmatched			Matched		
	White	Black	*p-value*	White	Black	*p-value*
5-year survival (%)	76	70	*< .001*	76	70	*.002*
HR (95% CI)	Ref	1.15 (1.01-1.32)	*.03*	Ref	1.27 (1.06-1.52)	*.008*
CRT received						
5-year survival (%)	77	71	*< .001*	77	71	*.011*
HR (95% CI)	Ref	1.77 (1.01-1.36)	*.02*	Ref	1.26 (1.04-1.53)	*.014*
HPV (%)	8	9	*NS*	9	9	*NS*

4058 Poster Session (Board #50), Fri, 8:00 AM-11:00 AM

17-year incidence trends of anal squamous cell carcinoma. *First Author: Khushali Jhaveri, MedStar Washington Hospital Center, Washington, DC*

Background: Anal Cancer is a rare neoplasm with 9 out of 10 cases being Anal Squamous Cell Carcinoma (SCCA). We did a population-based analysis to assess the incidence trends in patients with SCCA and identify any significant change in the direction of trends using the Surveillance, Epidemiology, and End Results (SEER) database. **Methods:** Data was extracted from SEER database for the years 2000-2016 for the US population, across all gender, ages, and races. Joinpoint regression models of SCCA incidence were fitted to identify any discrete joints (year) that represent statistically significant changes in the direction of the trend. The average annual percentage change (APC) in the age-adjusted incidence rate in the pre- and post-joinpoint era were measured. Subgroup analysis for gender, ages, and races was also done. **Results:** 27,721 new adult cases of SCCA were identified from 2000 to 2016. The incidence was higher amongst females (62.44%) compared to males (37.56%) with the white population contributing 85.41% to incidence compared to black (11.84%) and other (2.75%) population. The age-based incidence rate for different groups has been mentioned in Table. A significant jointpoint for SCCA incidence was observed in 2009. The APC was 4.6% (3.5-5.6 95% CI) in 2000-2009 which reduced to 2.1% (0.7-3.4 95% CI) in 2009-2016 indicating a 54% relative reduction in the average annual APC in the US population after 2009. Subgroup analysis revealed significant joinpoints for incidence decrease in Ages 40-59, 80 and above and females of all ages. No significant changes in APC were seen when stratified by race (Refer to Table). **Conclusions:** Our study, in our knowledge, is the first study assessing incidence trends of SCCA over 17-years. The overall incidence of SCCA is increasing but a statistically significant trend towards decreasing rate of growth in incidence was observed in 2009 and later. Further studies are needed to analyze the causality of such changes in the trend of SCCA. Research Sponsor: None.

Gender	Age	Race	Incidence(N)	Joinpoint year	APC pre-joinpoint year (95% CI)	APC post-joinpoint year (95% CI)	APC reduction
Both	All	White	23,677(85.41%)	No trend change			
Both	All	Black	3,281(11.84%)	No trend change			
Both	All	Other	763(2.75%)	No trend change			
Both	20-39 years	All	1,056(3.81%)	No trend change			
Both	40-59 years	All	12,705(45.83%)	2009	5.7% (4.3- 7.0)	-0.3% (-1.8- 1.3)	105%
Both	60-79 years	All	11,100(40.04%)	No trend change			
Both	80+ years	All	2,860(10.32%)	2010	5.1% (3.9-6.3)	1.0% (-0.9-3.0)	80%
Male	All	All	10,411(37.56%)	No trend change			
Female	All	All	17,310(62.44%)	2009	5.2% (4.3- 6.1)	2.8%(1.8- 3.7)	46%

4059 Poster Session (Board #51), Fri, 8:00 AM-11:00 AM

Utilization and trends in palliation-directed treatments for stage II-IV anal squamous cell carcinoma patients. *First Author: Srinidhi Radhakrishnan, UT Southwestern, Dallas, TX*

Background: Anal squamous cell carcinoma (ASCC) is associated with significant symptom burden including pain, bleeding, and obstructive symptoms. However, the proportion of patients requiring palliation-directed treatments in ASCC is unknown. Palliation-directed treatments can control and improve symptoms and affect quality of life. We aimed to study trends, factors, and outcomes associated with utilization of palliation-directed treatment in ASCC. **Methods:** Using the National Cancer Database (NCDB), adult patients with stage II-IV ASCC diagnosed 2004-2015 were identified and stratified by receipt of palliation-directed treatments. Using chi-square test and logistic regression, we evaluated the associations of demographic, clinical, and pathological factors with palliation-directed treatment utilization. **Results:** Out of 17,988 ASCC patients in this study, palliation-directed treatments were used by 504 patients (2.8%) with stages II-IV ASCC as first line treatment. Two percent received palliation-directed surgery, chemotherapy, and radiotherapy, 0.3% received pain management, and 0.4% utilized combination therapy approach. On univariable analysis, palliation-directed treatments were associated with older age, lower income level ($p=0.004$), Medicare insurance, and higher comorbidity score (*all other* $p<0.001$). Palliation-directed treatments were also more frequent in academic/research facilities ($p=0.01$), in East North Central USA ($p=.001$), and in stage 4 versus stage 2/3 ASCC ($p<.001$). Palliation-directed treatments have increased in recent years (2004-06 vs. 2013-15; $p=.005$) and were more frequently used within 6 months of patient death ($p<.001$). On multivariable analysis stage 4 disease and life expectancy $<$ 6 months were the only variables that maintained significance. **Conclusions:** In our study, palliation-directed treatments were used by 2.8% of the patients as codified by NCDB. Its use was higher in stage 4 ASCC and within the last six months of life. Palliation-directed treatment utilization has incrementally increased in recent years. Additional research is warranted in determining the phase of care wherein palliation-directed treatments are utilized in ASCC. Research Sponsor: None.

4060 Poster Session (Board #52), Fri, 8:00 AM-11:00 AM

The role of fibroblast growth factor receptor 4 (FGFR4) signaling in anti-EGFR resistance in colon cancer. *First Author: Sang Hee Cho, Department of Hematology-Oncology, Chonnam National Univeristy Hwasun Hospital, Hwasun, South Korea*

Background: Anti-EGFR therapy has been used as a standard treatment for metastatic colon cancer, but the innate resistance is still issues of increasing significance. Fibroblast growth factor receptor 4 (FGFR4) plays an important role in cell proliferation, invasion and anti-apoptosis, through the pathway of MAPK-ERK and PI3K-AKT. We investigated potential crosstalk between FGFR4 and EGFR signaling to identify new resistant mechanism of anti-EGFR therapy and how to overcome it in colon cancer. **Methods:** RNA-Seq was used to identify the associated signal pathway and down targets induced by FGFR4. Molecular studies including RTK array, RT-qPCR, western blotting were performed to validate the interaction between FGFR4 and EGFR signaling *in vitro* and *in vivo*. Next, the effect of FGFR4 in cetuximab resistance was investigated *in vitro* and in colon cancer patients. **Results:** FGFR4 overexpression in colon cancer cells activates downstream signaling, such as, PI3K/Akt and RAS/RAF/Erk pathway. Gene Ontology (GO) analysis from RNA-seq revealed that differentially expressed genes (DEGs) altered by expression of FGFR4 were related to biological functions, including cell proliferation, epidermal growth factor receptor signaling, NIK/NF-kB signaling, interferon-gamma signaling, wound healing. RT–qRCR showed that FGFR4 promotes the EGFR and ErbB3 by inducing the expression of EGFR ligands such as AREG, BTC, EREG, HBEGF. In vivo tumorigenesis, we found that FGFR4 promotes tumor growth and high expression of AREG in xenograft tumors. FGFR4 expression reduced the sensitivity to cetuximab in colon cancer cells and synergistic effect was shown when treated with FGFR4 inhibitor with cetuximab. A positive correlation between FGFR4 and AREG expression was observed in cancer, but not in normal tissues and high FGFR4 or AREG expression showed significantly inferior overall survival than low expression in patients treated with cetuximab for metastatic colon cancer. **Conclusions:** We demonstrated a pivotal mechanism of FGFR4 in colon cancer progression and cetuximab resistance through inducing AREG. Our data point to FGFR4 as a new biomarker to predict cetuximab response and dual targeting of FGFR4 and EGFR may be a promising treatment modality for colon cancer. Research Sponsor: National Research Foundation of Korea (NRF) grants (NRF-2017R1A2B4005003, NRF-2018R1A5A2024181), grant (HCRI17904-21) Chonnam National University Hwasun Hospital Institute for Biomedical Science.

4061 Poster Session (Board #53), Fri, 8:00 AM-11:00 AM

Consensus molecular subtypes in colorectal cancer differ by geographic region. *First Author: Krittiya Korphaisarn, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkoknoi, Thailand*

Background: The consensus molecular subtypes (CMS) have emerged as a novel classification in colorectal cancer (CRC). However, these subtypes, were mostly derived from a US/European population, and have scant data in other ethnic groups. This study aimed to demonstrate molecular subtypes of CRC across geographic regions. **Methods:** Formalin fixed paraffin embedded (FFPE) tissue from untreated patients with stage II-III colon cancer from Brazil, Canada, Mexico, Thailand, and the US were evaluated. Gene expression profiling was performed at the University of Texas MD Anderson Cancer Center using NanoString's nCounter technology and an optimized classifier for FFPE. **Results:** A total of 366 samples were included in this study, evenly distributed between the 5 international sites. While the US population matched previously reported distributions, the distribution of CMS subtypes varied substantially by region ($P < 0.0001$). While CMS1 was still associated with right-sided tumors ($P < 0.001$) and deficient mismatch repair (dMMR) ($P < 0.001$), the prevalence varied between 8% in Brazil to 30% in Mexico. CMS2 was found vary from 14% in Mexico to 47% in Brazil. The metabolic CMS3 subtype was present in only 3% in Thailand, but as high as 19% in Brazil. CMS4 was confirmed to be associated with higher stage ($P = 0.047$), and the prevalence was lowest in Brazil (14%) compared to 44% and 49% in US and Mexico, respectively. Expansion of study cohort is ongoing. **Conclusions:** CMS subtype prevalence differs substantially by geographic region in CRC. These variations suggest that transcriptomic-defined disease biology in international populations may be more heterogeneous than previously appreciated. Further studies in global populations are required to validate and extend these findings, which may have important impact for novel therapeutic development. Research Sponsor: Moon Shot funding.

4062 Poster Session (Board #54), Fri, 8:00 AM-11:00 AM

Initial correlative studies from a trial of cetuximab and pembrolizumab in metastatic colorectal cancer (mCRC). *First Author: Patrick M Boland, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ*

Background: Cetuximab is an EGFR-targeting IgG1 mAb. Pre-clinical data suggests cetuximab induces $CD8^+$ cytotoxic T-cell (CTL) infiltration of tumors. We hypothesized that augmentation of CTLs in the tumor microenvironment (TME) may provide the proper milieu for effective PD-1 inhibition in metastatic colorectal cancer (mCRC). We conducted a phase Ib/II study of cetuximab with the PD-1 antibody, pembrolizumab, in mCRC. Correlative blood and tissue samples were collected to assess the impact of this treatment on CTLs, as well as potential compensatory alterations in regulatory T-cells (Tregs) and suppressive MDSCs (NCT02713373). **Methods:** 3 week treatment cycles included pembrolizumab at 200 mg on day 1 and cetuximab 250 mg/m2 following the 400 mg/m2 loading dose. Tumor biopsies were obtained at baseline and at c4d1 (Day 64). Peripheral blood (PB) was drawn at baseline, c2d1 (day 22) and c4d1 (Day 64). Flow cytometry was performed within 24 hours with additional samples stored for future analysis. In the present analysis, we assessed changes in levels of the cellular populations of interest between cycle 4 and cycle 1. **Results:** Forty-two RAS-wt patients were enrolled through October 2019. Paired tumor tissues were successfully analyzed for 16 patients and PB for 38. Intratumoral CTLs ($CD3^+CD8^+$) increased significantly (+47%, $p < .05$). In PB, there was a slight overall decrease in PB CTLs (-5%, p = NS) and a significant decrease in $CD8^+CD45RO^+PD1^+$ cells (-42%, $p < .05$). We saw simultaneous decreases in PD-1^+ CTLs in the tumor and PB. There was a trend for increase in Tregs (CD4+ Cd25+ FoxP3+) in PB (+11%, p = NS), but an overall increase in the Teff:Treg ratio (+30%, p = NS). $CD4^+CTLA4^+$ cells significantly increased (+37%, $p < .05$). Granulocytic MDSCs ($CD11b^+CD14^-CD33^+HLADR^-$) in PB decreased significantly on-treatment (-30%, $p < 0.5$). The sample size and tissue limitations prohibited meaningful evaluation of tissue Tregs and MDSCs via the present methods. **Conclusions:** Cetuximab and pembrolizumab induced dynamic changes in the TME and PB. The treatment associated increase in intratumoral CTLs was particularly pronounced, consistent with their local expansion and/or influx. This was accompanied by a decrease in PB CTLs. Decreases in multiple PD-1^+ lymphoid populations were observed in both tumor and PB, notably PD-1^+ CTLs. Of note, we saw a synchronous increase in immunosuppressive $CD4^+CTLA4^+$ T-cells in PB. Patient outcomes are pending maturation. Further analyses are planned, coupled with integration of clinical data. Clinical trial information: NCT02713373. Research Sponsor: Merck.

4063 Poster Session (Board #55), Fri, 8:00 AM-11:00 AM

Development of drug resistance in colon cancer patients following chemotherapy, a contributing factor in the failure of oxaliplatin-based HIPEC to improve survival in the Prodige 7 trial. *First Author: Robert Alan Nagourney, Nagourney Cancer Institute, Long Beach, CA*

Background: Numerous studies suggest benefit for heated intra-peritoneal chemotherapy (HIPEC) in colon cancer but the Prodige 7 trial in 265 colon cancer patients randomized to HIPEC or observation after neo-adjuvant chemotherapy (NACT) didn't confirm benefit with median OS of 41.7 vs. 41.2 mos. (p = 0.99) (Proc. ASCO, 2018). One concern is that prior drug exposure selects for drug resistance blunting HIPEC effect. To test the hypothesis we examined the impact of prior chemotherapy on drug resistance in human tumor organoids isolated from colon cancer patients. **Methods:** Data query identified 111 colorectal cancers (87 colon & 24 rectal) tested for Oxaliplatin sensitivity by ex vivo analysis of programmed cell death (EVA/PCD), a primary culture platform that examines drug induced cell death (apoptotic & non-apoptotic) by morphology, metabolism & histology. Five-point dose response curves interpolated to provide lethal concentration 50% (LC50) were compared by Z score to distribute Oxaliplatin LC50 values around the mean using standard deviation units as the metric of sensitivity or resistance. Of 87 colon 54(62%) were untreated and 33 (38%) treated with 21/33 (64%) having received FOLFOX. To approximate Prodige 7, treated patients were separated by having received FOLFOX $< 2 >$ months before EVA/PCD analysis and also compared Mitomycin (14 vs 41), Irinotecan (18 vs 47) & 5-FU (19 vs. 52) activity to assess cross-resistance. **Results:** Compared to chemo-naïve, FOLFOX-treated patients were significantly more resistant to Oxaliplatin ($P < 0.01$) with the degree of resistance increasing significantly for patients who received treatment < 2 months prior to EVA/PCD compared to those with chemotherapy > 2 months prior to EVA/PCD ($P < 0.01$). Activity for Mitomycin & Irinotecan was not significantly different for chemo-naïve vs. treated patients, but 5 FU was more resistant (P = 0.048) in previously treated. **Conclusions:** The failure of Prodige 7 to improve survival with HIPEC following NACT may reflect diminished Oxaliplatin activity in patients whose residual disease has been selected for Oxaliplatin & 5FU resistance. Resistance was not observed for Mitomycin or Irinotecan. This suggests that those using HIPEC may i) examine other classes of drugs or drug combinations for IP administration ii) improve the selection of candidates for HIPEC administration or iii) consider HIPEC administration earlier in the course of therapy when chemotherapy-induced drug resistance may be less evident. Research Sponsor: None.

4064 Poster Session (Board #56), Fri, 8:00 AM-11:00 AM

The landscape of DNA damage response (DDR) pathway in colorectal cancer (CRC). *First Author: Hiroyuki Arai, Chiba Cancer Center, Chibashi, Japan*

Background: Abnormal DDR is a hallmark of cancer, relating to genome instability, anti-tumor immunity, and sensitivity to chemotherapeutic agents and radiation. We conducted a large-scale investigation to clarify the alteration of DDR pathway in CRC. **Methods:** Tumor samples from 9321 CRC patients were retrospectively reviewed. Next-Generation Sequencing (NGS) on a custom-designed panel enriching 592 gene targets was performed. Samples with mutations detected in any of 29 DDR-related genes were deemed DDR-mutant (DDR-MT); the rest DDR-wild type (DDR-WT). Microsatellite instability (MSI) status was tested with a combination of immunohistochemistry (IHC), fragment analysis and NGS. Tumor mutational burden (TMB) was calculated based on somatic nonsynonymous missense mutations. PD-L1 was tested by IHC (SP142). Consensus molecular subtype (CMS) was developed using RNA sequencing data. **Results:** Of 9321 cases, 1290 (13.8%) were DDR-MT. DDR-MT frequency was higher in right vs. left sided (20.9% vs 10.8%, $p < 0.001$) and MSI-H vs. MSS (76.4% vs 9.5%, $p < 0.001$) cases. In the MSS cases, right-sided had marginally higher frequency of DDR-MT than left-sided (10.6% vs 9.1%, p = 0.055), with much higher frequency of Fanconi anemia pathway alteration in right-sided (1.5% vs 0.7%, $p < 0.01$). CMS1 subtype had the highest frequency of DDR-MT (34.8%); CMS2 had the lowest (7.1%). DDR-MT cases (vs. DDR-WT) had higher mutation rate of *ARID1A* (55.0% vs 19.1%, $p < 0.0001$), *PIK3CA* (22.6% vs 15.8%, $p < 0.0001$) and *BRAF* (20.4% vs 7.3%, $p < 0.0001$), and lower mutation rate of *TP53* (48.2% vs 76.1%, $p < 0.0001$), *APC* (60.5% vs 74.5%, $p < 0.0001$) and *KRAS* (44.0% vs 49.8%, $p < 0.001$). Mean TMB was much greater in DDR-MT than DDR-WT (All: 20.9/Mb vs 7.7/Mb, $p < 0.0001$; MSS: 13.7/Mb vs 7.6/Mb, $p < 0.05$). *PD-L1* positivity was also higher in DDR-MT compared to DDR-WT (All: 10.1% vs 2.7%, $p < 0.0001$; MSS: 4.8% vs 2.4%, $p < 0.0001$). **Conclusions:** Alteration of the DDR pathway was strongly associated with MSI status in CRC. The primary tumor sidedness might also be related, as DDR-MT was more prevalent in right-sided tumors. Elevated TMB and PD-L1 expression in DDR-MT CRC indicate more activated anti-tumor immune profiles compared to DDR-WT, regardless of MSI status, suggesting possible therapeutic benefit from immune checkpoint inhibitors in DDR-MT CRC. Research Sponsor: None.

4065 Poster Session (Board #57), Fri, 8:00 AM-11:00 AM

Tumor-infiltrating lymphocytes and tumor budding refine prognostication in patients with low- and high-risk stage III colon cancers (NCCTG N0147) [Alliance]. *First Author: Dan Sha, Mayo Clinic, Rochester, MN*

Background: Tumor infiltrating lymphocytes (TILs) and tumor budding (linked to epithelial mesenchymal transition) may influence metastatic potential and patient prognosis. We analyzed these features and their relative contribution to survival among low ($T_{1\text{-}3}$ N_1) and high (T_4 and/or N_2) risk groups, defined by the IDEA study, used to inform the duration of adjuvant chemotherapy in stage III colon cancer. **Methods:** Among 1,532 patients (low risk n=804; high risk n=728) treated in a phase III adjuvant trial of FOLFOX + cetuximab (x 6 months), intraepithelial TIL densities and tumor budding were quantified at microscopy in routine histologic sections. Optimal cutpoints were determined in association with 5-yr disease-free survival (DFS). Relative contribution of variables to DFS was calculated using $\chi 2$ from Harrell's rms R package based on multivariable Cox regression models. **Results:** In the overall cohort, the tumor budding/TILs combined variable was more robust for predition of DFS than either alone. Budding/TILs was significantly associated with DFS in both low (HR_{adj}, 1.59; 95% CI, 1.02-2.48; p=.0273) and high (HR_{adj}, 2.82; 95% CI, 1.72-4.63; p<.0001) risk patients. We then determined its relative contribution (%) to DFS (Table). Among low risk, budding/TILs ranked second (24.4%) behind *KRAS* status (45.5%) and ahead of treatment arm (7.2%) and mismatch repair (MMR) status (6.1%). Among high risk, budding/TILs contributed the most to DFS (45.4%) followed by primary tumor sidedness (13.0%), performance status (12.0%), and MMR (10.4%). **Conclusions:** Tumor budding/TILs provides robust prognostic stratification by risk group to improve anatomic tumor staging. The relative contribution of budding/TILs to DFS was second only to *KRAS* status in low risk patients, and was the most important predictor of DFS in high risk patients. Evaluation in patients treated with 3 vs 6 mos of adjuvant chemotherapy is warranted. Research Sponsor: U.S. National Institutes of Health.

Relative contribution to patient DFS.

Low Risk (T1-3N1)	Percent (%)	High Risk (T4 and/or N2)	Percent (%)
KRAS	45.5	Budding/TILs	45.4
Budding/TILs	24.4	Sidedness	13.0
Treatment	7.2	Performance Status	12.0
MMR	6.1	MMR	10.4
Performance Status	5.0	*KRAS*	9.1
BRAF	5.0	Treatment	5.1
Age	3.8	Histologic Grade	2.8
Sidedness	2.3	Other	2.2
Histologic Grade	0.8		

4066 Poster Session (Board #58), Fri, 8:00 AM-11:00 AM

Somatic alterations of *NF1* in colorectal cancer. *First Author: Hiroyuki Arai, Chiba Cancer Center, Chibashi, Japan*

Background: *NF1* encodes neurofibromin, which is a key GTPase-activating protein that downregulates RAS activation. Inactivating mutations in *NF1* result in sustained activation of RAS signaling, a key driver for development of colorectal cancer (CRC), and have been suggested to be a potential mechanism of resistance to EGFR inhibition in *RAS*-wild type (WT) CRC. Little is known about molecular characteristics of *NF1*-mutated (MT) CRC. **Methods:** Tumor profiles from 8150 CRC patients (pts) with available *NF1* mutation status were retrospectively reviewed. NextGen sequencing by a customized 592-gene panel was performed. Microsatellite instability (MSI) / mismatch repair (MMR) status, tumor mutational burden (TMB) and PD-L1 expression were tested. Molecular profiles between *NF1*-MT and *NF1*-WT pts were compared. **Results:** Out of 8150 pts, 176 (2.2%) had somatic *NF1* mutations with pathogenic or presumed pathogenic function. A higher *NF1*-MT frequency was observed in MSI-H/dMMR vs MSS/pMMR (13.5% vs 1.4%, $p < 0.0001$), in right-sided vs left sided (2.9% vs 1.8%, $p < 0.01$), and in *RAS*-WT vs *RAS*-MT (3.0% vs 1.4%, $p < 0.0001$). In MSS/pMMR tumors, no association with sidedness was observed (right: 1.3% vs left: 1.2%, NS). The most prevalent co-mutations with *NF-1* were *APC* (63.2%), *ARID1A* (57.5%), *TP53* (51.5%), *KMT2D* (32.9%) and *KRAS* (32.4%) in all cases, and *APC* (76.2%), *TP53* (69.5%), *KRAS* (38.8%), *ARID1A* (34.4%) and *FBXW7* (21.5%) in MSS/pMMR cases. *POLE* mutation was observed in 18.4% of *NF1*-MT/MSS/pMMR pts. Compared to *NF1*-WT pts, *NF1*-MT pts had more frequent mutations in *ARID1A* (All: 57.5% vs 23.3%, $p < 0.0001$; MSS/pMMR: 34.4% vs 15.2%, $p < 0.05$), and less frequent mutations in *KRAS* (All: 32.4% vs 49.0%, $p < 0.0001$; MSS/pMMR: 38.8% vs 50.3%, $p < 0.05$). Also, *NF1*-MT pts had more frequent alterations in homologous recombination pathway compared to *NF1*-WT pts (All: 39.8% vs 7.5%, $p < 0.0001$; MSS/pMMR: 17.5% vs 4.4%, $p < 0.0001$). Mean TMB was significantly greater in *NF1*-MT than *NF1*-WT (All: 48.9/Mb vs 10.0/Mb, $p < 0.0001$; MSS/pMMR: 48.3/Mb vs 8.2/Mb, $p < 0.0001$). Also, PD-L1 positivity was higher in *NF1*-MT compared to *NF1*-WT (All: 12.9% vs 3.6%, $p < 0.0001$; MSS/pMMR: 7.1% vs 2.6%, $p < 0.05$). **Conclusions:** While more frequent than in *RAS*-MT pts, *NF1*-MT CRC was a small subset in *RAS*-WT pts. *NF1*-MT was associated with alterations in chromatin remodeling and DNA damage response pathways, as well as elevated TMB and PD-L1 expression, which may provide alternative therapeutic strategies beyond EGFR inhibition. Research Sponsor: None.

4067 Poster Session (Board #59), Fri, 8:00 AM-11:00 AM

Prognostic differences of RAS mutations: Results from South Australian (SA) metastatic colorectal (mCRC) registry. *First Author: Timothy Jay Price, Queen Elizabeth Hospital, University of Adelaide, Adelaide, Australia*

Background: Effective targeting of RAS mutations has proven elusive until recently. AMG 510, a novel agent which targets KRAS G12C mutations (G12C MT), has shown promise in early phase clinical trials that included patients with mCRC. Prior reports have suggested that G12C MT may be predictive of poor outcome. **Methods:** We aimed to assess the prognostic implications of individual RAS in a population-based registry. The SAmCRCR collects data from all patients diagnosed with mCRC in South Australia prospectively. Individual RAS mutation data from patients entered into the SAmCRCR between February 2006 and December 2018 was reviewed. Survival was analysed for the more frequent mutations using Kaplan Meier method. **Results:** 1605 (33%) of the 4905 patients entered onto the registry had RAS mutation results available. Of these, 658 (41%) had RAS MT. The nature of the RAS MT was available in 563 (85.7% of those with RAT MT). Patient characteristics, frequency of individual RAS MT and median overall survival (OS) per RAS MT are noted in table. Low frequency MT made up an additional 16.3%. There were numerical differences in survival however there was no statistical difference in survival when comparing the various RAS MT, including the comparison of G12C to G12S (p = 0.38). **Conclusions:** Whilst the G12S mutation was associated with the longest survival numerically, the observed survival for patients with the most common RAS mutations (G12C, G12V, G12A, G12D and G13D) did not significantly differ. Research Sponsor: None.

RAS MT (percentage)	G12C (9.6%)	G12A (10.7%)	G12D (22%)	G12S (4.4%)	G12V (23.6%)	G13D (13.3%)
Median age (yrs)	64.6	65.7	65.5	65.2	66.7	64.6
Female	28%	39%	37%	27%	34%	43%
Stage 2/3/4 at diagnosis(%)	11/9/76	13/13/74	12/20/67	19/30/50	14/17/67	12/28/59
Right primary	17%	23%	38%	19%	40%	41%
Site liver or lung only (%)	35/9	55/9	37/6	42/15	32/11	28/16
Poorly diff path	11%	17%	27%	11%	20%	21%
Chemotherapy	80%	71%	82%	73%	80%	81%
Liver resection	18.5%	15.6%	12%	11.5%	12.7%	9.3%
Median OS (mths)	21.6	20.6	20.8	29.7	21.4	22.3

4068 Poster Session (Board #60), Fri, 8:00 AM-11:00 AM

Impact of tumor side on clinical outcomes in stage II and III colon cancer with known microsatellite instability status. *First Author: Katerina Mary Zakka, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: Microsatellite instability high (MSI-H) status indicates better prognosis in early stage colon cancer (CC) compared to microsatellite stable (MSS). However, the impact of tumor side, left side (L) versus right side (R), is not described on clinical outcomes based on MSI status. **Methods:** Patients with pathological stage II and III primary adenocarcinoma of the colon between 2010 and 2015 were identified in the National Cancer Database (NCDB) using ICD-O-3 morphology and topography codes: 8140-47, 8210-11, 8220-21, 8260-63, 8480-81, 8490 and C18.0, 18.2,18.3, 18.5,18.6, 18.7. Univariate (UVA) and multivariable (MVA) survival analyses were conducted, and Kaplan-Meier Curves were used to compare overall survival (OS) based on tumor location and treatment received with Log-rank test. **Results:** A total of 35,071 patients with stage II (n = 17,629) and III (n = 17,442) CC were identified. 51.3% female; 81.5% Caucasian; median age 66 (range, 18-90). Majority of stage II and III tumors were R, 61.2% (n = 10,794) and 56.0% (n = 9,763). MSI-H was more common in stage II compared to III, 23.3% (n = 4,115) vs 18.2% (n = 3,171) ($p < 0.0001$). Survival was better in stage II MSI-H compared to MSS, 5 year-OS 75.1% vs 71.8% (p = 0.0057). However, stage III CC survival was better in MSS compared to MSI-H, 5-year OS 60.5% vs 58.0% ($p < 0.001$). In stage II MSI-H CC R was more common than left, 78.3 % (n = 3223) vs 21.7% (n = 892). There was no significant difference in survival between stage II MSI-H L vs R (5-year OS 76.2% vs 74.7%, p = 0.1578). Stage II MSS CC R was more common than L, 56.0% (n = 7571) vs 44.0% (n = 5943), and survival was better in L vs R (5-year OS 73.2% vs 70.8%, p = 0.0029). Stage III MSI-H CC was more common in R than L, 75.6% (n = 2397) vs 24.4% (n = 774) and survival was better in L (5-year OS 62.5% vs 56.5%, p = 0.0026). Stage III MSS CC was more common in R than L, 51.6% (n = 7366) vs 48.4% (n = 6905), and survival was better in L vs R (5-year OS 67.0% vs 54.4%, $p < 0.001$). **Conclusions:** Survival was better in left sided tumors compared to right in stage II MSS, stage III MSS and stage III MSI-H CC. Research Sponsor: None.

4069 Poster Session (Board #61), Fri, 8:00 AM-11:00 AM

Association of postoperative serum carcinoembryonic antigen (CEA) with disease-free survival in patients with stage III colon cancer: ACHIEVE phase III randomized clinical trial. *First Author: Masahito Kotaka, Gastrointestinal Cancer Center, Sano Hospital, Kobe, Japan*

Background: ACHIEVE, as part of the IDEA collaboration, was a multicenter trial randomizing patients with stage 3 resected colon cancer to either 3 versus 6 months of adjuvant FOLFOX/CAPOX. We previously reported that the hazard ratios (HRs) in disease-free survival (DFS) of 3 versus 6 months duration according to risk stage (low-risk [T1-3 and N1] or high-risk [T4 or N2]) and regimen (FOLFOX or CAPOX) as well as in overall population were consistent with those observed in the whole IDEA. This study aimed to clarify the significance of post-operative serum carcinoembryonic antigen (CEA) on DFS in stage 3 colon cancer. **Methods:** Eligibility included post-operative serum CEA value of ≤10 ng/ml at registration in the ACHIEVE trial, which enrolled 1313 patients between 2012 and 2014, out of whom 1291 pts were the modified ITT (mITT) population and used in this study. The cutoff values of CEA analyzed for prognostic analyses were the median value (1.8 ng/ml) in the mITT, the upper limit of normal (ULN) level (5.0 ng/ml), and the half of ULN (2.5 ng/ml). The association of post-operative CEA with DFS were measured by Cox regression analyses. **Results:** Of the 3 cutoff values, the ULN (5.0 ng/ml) was associated with DFS more strongly than the median (1.8 ng/ml) or half of ULN (2.5 ng/ml), with a HR of 1.75 (95%CI, 1.24-2.46) (Table). The 99 patients (7.7%) were identified as the CEA > ULN and 1192 (92.3%) as < ULN. In univariate analysis, regimen (CAPOX or FOLFOX), ECOG PS (0 or 1), T factor (T1-3 or T4), N factor (N1 or N2-3) and CEA (< ULN or > ULN) were significantly associated with DFS. Multivariate Cox regression identified CEA > ULN as an independent poor risk factor (HR = 1.45; 95%CI, 1.03-2.05). Shorter DFS in patients with CEA > ULN than in those with CEA < ULN was consistently observed in each subgroup of baseline factors, including treatment duration, regimen, age, gender, PS, T-stage, N-stage, no of lymph nodes examined, and tumor location; no interaction was observed between CEA and these factors. **Conclusions:** Post-operative serum CEA is also a strong prognostic factor for DFS in stage 3 colon cancer. Clinical trial information: 000008543. Research Sponsor: Japanese Foundation for Multidisciplinary Treatment of Cancer.

cut-off value		EVENT/N	3-year DFS (95% CI)	5-year DFS (95% CI)	HR (95% CI)	p value
1.8ng/ml	≤	185/668	77% (74-80% j	72% (68-75%)	1.29 (1.04-1.61)	0.0226*
		138/623	81% (77-84%)	78% (74-81%)		
2.5ng/ml	≤	129/426	75% (70-79%)	69% (65-74%)	1.41 (1.13-1.76)	0.0026*
		194/865	81% (78-83%)	77% (74-80%)		
5.0ng/ml	≤	37/99	64% (54-73%)	62% (52-71%)	1.75 (1.24-2.46)	0.0014*
		286/1192	80% (78-82%)	76% (73-78%)		

4070 Poster Session (Board #62), Fri, 8:00 AM-11:00 AM

Prognostic importance of primary tumor resection and synchronous metastasis on overall survival in metastatic colorectal cancer: Data from the FIRE-3 (AIO KRK-0306) study. *First Author: Jobst C. von Einem, Department of Medicine, Division of Hematology, Oncology, and Tumor Immunology (CCM), Charité Universitaetsmedizin Berlin, Berlin, Germany*

Background: The FIRE-3 study (AIO KRK-0306) was designed as a randomized multicenter trial to compare the efficacy of FOLFIRI plus cetuximab (cet) to FOLFIRI plus bevacizumab (bev) as first-line treatment in KRAS WT mCRC patients. FOLFIRI plus cet as first-line treatment of KRAS WT mCRC patients resulted in comparable overall response rates (ORR) and progression free survival (PFS) when compared to FOLFIRI plus bev. Overall survival (OS) was significantly longer in the FOLFIRI plus cet arm. **Methods:** In the present analysis of the FIRE-3 trial we explored the impact of primary tumor resection on outcome in relation to anti-EGFR vs. anti-VEGF treatment. Furthermore, we investigated the prognostic value of synchronous versus metachronous metastases. **Results:** In patients with synchronous disease no significant difference in OS was detected when comparing resected (n=339) vs. non-resected (n=97) patients (p-value: 0.29, HR: 1.17, 95%-CI: 0.88 – 1.55). In the cetuximab arm, resection (n=167) showed no significant benefit in OS when compared to non-resection (n=52) (p-value: 0.51, HR: 1.15, 95%-CI: 0.77 – 1.71). Treated with bevacizumab, similar results were present, when comparing resection (n=172) vs. non-resection (n=45); (p-value: 0.29, HR: 1.25, 95%-CI: 0.83 – 1.9). A strong trend was seen when comparing OS in treatment arms cet. (n=219) vs. bev. (n=217)) for patients with synchronous disease; (p-value: 0.05, HR: 1,26, 95%-CI: 1.0 - 1.59). 436/592 pts suffered from synchronous, 153/592 from metachronous disease (in 3/592 pts the information was not given). Median OS in pts with synchronous disease was 24.5 months and 29.5 in pts with metachronous disease (p-value: 0.02, HR: 0.76, 95%-CI: 0.6 - 0.96). In pts treated in the cetuximab arm metachronous disease (n=77) was associated with a trend towards longer OS when compared to synchronous disease (n= 219) (p-value: 0.13, HR: 0.76, 95%-CI: 0.54 – 1.1). The same effect was present in the bevacizumab arm (p-value: 0.05, HR: 0.73, 95%-CI 0.53 – 1.0) when comparing pts with synchronous disease (n=217) vs. pts. with metachronous disease (n=76). **Conclusions:** In the FIRE-3 study, metachronous disease was associated with superior OS compared to synchronous disease. This finding was accentuated in the bevacizumab arm. The role of resection of the primary tumor had no impact on survival. Clinical trial information: NCT00433927. Research Sponsor: Merck KGaA, Darmstadt, Germany.

4071 Poster Session (Board #63), Fri, 8:00 AM-11:00 AM

Utility of circulating tumor DNA (ctDNA) versus tumor tissue genotyping for enrollment of patients with metastatic colorectal cancer (mCRC) to matched clinical trials: SCRUM-Japan GI-SCREEN and GOZILA combined analysis. *First Author: Yoshiaki Nakamura, National Cancer Center Hospital East, Kashiwa, Japan*

Background: We recently reported that ctDNA genotyping had advantages compared with tumor tissue testing in terms of enrollment to matched clinical trials across a wide range of GI cancers (Nakamura Y, et al. ASCO-GI 2020). Here, we investigated the utility of ctDNA genotyping in mCRC in a SCRUM-Japan GI-SCREEN and GOZILA combined analysis. **Methods:** In GI-SCREEN, tumor tissue genotyping was performed using a next generation sequencing (NGS)-based assay, Oncomine Comprehensive Assay since Feb 2015. In GOZILA, NGS-based ctDNA genotyping was performed using Guardant360 since Feb 2018. All tests were conducted centrally in a CLIA-certified and CAP-accredited laboratory. Patients with actionable alterations were enrolled into matched company-sponsored or investigator-initiated interventional clinical trials. **Results:** As of Apr 2019, 2,791 mCRC patients (2,754 eligible for analysis) in GI-SCREEN and 470 (464 eligible for analysis) in GOZILA were enrolled. There were no significant differences in baseline patient characteristics between GI-SCREEN and GOZILA. Most of trials affiliated with GI-SCREEN (81%) or GOZILA (78%) targeted the RTK/RAS/RAF pathway. Compared with tumor testing, ctDNA genotyping significantly improved turnaround time (median, 12 vs. 34 days, $P < 0.0001$), sequencing success rate (96.1 vs. 92.3%, $P = 0.002$), and detection rate of actionable alterations (73.3 vs. 62.2%, $P = 0.02$). Among patients with actionable alterations, enrollment to matched clinical trials was achieved in 5.0% in GI-SCREEN and 12.1% in GOZILA ($P < 0.0001$). Median time from enrollment in the respective screening study to enrollment in a matched clinical trial was 6.5 months in GI-SCREEN and 0.9 months in GOZILA, respectively ($P < 0.0001$). Objective response rate and progression-free survival were similar in both groups (tissue vs. ctDNA; ORR: 18.8 vs. 17.1%, $P = 1.00$; median PFS: 2.2 vs. 2.2 months, HR=1.05 [95% CI, 0.71–1.55], $P = 0.79$). **Conclusions:** For patients with mCRC, ctDNA genotyping had advantages over tissue genotyping with shorter turnaround time and higher sequencing success and actionable alteration detection rate, which were associated with improved clinical trial enrollment without compromising the efficacy. Funding: SCRUM-Japan Funds. Clinical trial information: UMIN000029315. Research Sponsor: SCRUM-Japan Funds.

4072 Poster Session (Board #64), Fri, 8:00 AM-11:00 AM

Colorectal cancer under the age of 50 years in U.S. Department of Veterans Affairs: Is there a role of early screening? *First Author: Abdul Moiz Khan, Albany Medical Center, Albany, NY*

Background: While the overall incidence of colorectal cancer (CRC) is decreasing, the rate has increased in population under 50, with higher stages at diagnosis and a greater proportion of African Americans (AA). Hence, there is an ongoing debate about the age of CRC screening. These trends have not been studied in the VA population. **Methods:** ICD-10 codes C18-C20 were used to identify the cases of colon and rectal cancer in National VA Cancer Cube Registry. 43,544 cases of colon cancer, 1,278 below and 42,254 above age 50, and 19,815 cases of rectal cancer, 862 below and 18,948 above age 50 were identified between 2003-17. Younger age group was defined as patients less than 50 years old. IRB approval was obtained. **Results:** Our data comprised > 97% of male patients. In younger group, in the 5 year periods, 2003-07, 2008-12 and 2013-17, colon cancer rate increased from 2.59% to 2.79% to 3.59%, while for rectal cancer it increased from 3.5% to 4.3% to 5.3% ($p < .0001$). Blacks comprise 31.6% cases of colon cancer and 27.15% cases of rectal cancer in under 50 group, compared to 18.5% and 15.9% of cases in above 50 group respectively ($p < .0001$). For under 50 group, 48.6% cases of colon and 42.2% cases of rectal cancer were diagnosed in stage III or IV compared to 35.7% and 34.05% cases in above 50 group respectively ($p < .0001$). For colon cancer, 51.87% of patients in the younger group have a < 5 year survival, worse compared to 45.05% in 50-60 group ($p < .0001$) and similar to 49.3% in 60-70 group ($p = .08$). For rectal cancer, 5 year survival showed no difference between these groups. Stage specific survival shows no difference for either colon or rectal cancer across < 50, 50-60 and 60-70 age groups. **Conclusions:** Rate of CRC is rising in < 50 age group with more advanced stage at diagnosis and higher proportion of African Americans. For colon cancer, < 50 group has a worse 5 year survival as compared to 50-60 age group likely due to increased proportion of patients in stage III or IV, as there is no difference in stage specific survival. For rectal cancer, the 5 year survival or stage specific survival shows no difference in < 50, 50-60 and 60-70 groups. These results add to our understanding of the trends of CRC and should be accounted for in the screening guidelines. Research Sponsor: None.

4073 Poster Session (Board #65), Fri, 8:00 AM-11:00 AM

Translational research of voltage-A1: Efficacy predictors of preoperative chemoradiotherapy and subsequent nivolumab monotherapy in patients with microsatellite-stable locally advanced rectal cancer. *First Author: Koji Inamori, Department of Colorectal Surgery, National Cancer Center Hospital East, Kashiwa, Japan*

Background: In VOLTAGE-A1, after 5 cycles of nivolumab (240 mg q2 weeks) plus radical surgery following chemoradiotherapy (CRT; 50.4 Gy with capecitabine 1,650 mg/m^2), a major pathologic response is observed in 38% (AJCC tumor regression grade 0-1) of 37 patients with microsatellite-stable locally advanced primary rectal cancer. Here, biomarkers for predicting the efficacy of this treatment were investigated. **Methods:** Serial tumor biopsies and blood collections were performed at 4 time points; before CRT, after CRT, after 3 cycles of nivolumab, and before surgery. Tumor-infiltrating lymphocytes (TILs) and DNA/RNA were extracted from tumor samples, and peripheral blood mononuclear cells (PBMCs) were extracted from blood samples. We analyzed the immune status of the patients by flow cytometry using the collected TILs and PBMCs. Whole exome and RNA sequencing analyses were conducted using the extracted DNA and RNA, respectively. The PD-L1 status of tumor samples was also evaluated by *in vitro* diagnostic immunohistochemistry staining. **Results:** Among the 24 patients whose samples were serially collected, 11 (46%) were AJCC grade 0-1 and 13 were 2-3. Before CRT, effector regulatory T (eTreg) cells in TILs were higher in patients with AJCC grade 2-3, and both the CD8$^+$ T cell/eTreg cell ratio in TILs and PD-L1-positive tumor cells (≥1%) were higher in patients with AJCC grade 0-1 ($p = 0.047$, $p = 0.083$, respectively). Ki67 expression by CD8$^+$ T cells in TILs was higher before CRT in patients with AJCC grade 0-1 ($p = 0.037$) and increased after CRT in all patients. Patients with consensus molecular subtype (CMS) 1 and CMS3 achieved AJCC grade 0-1 at rates of 100% (2/2) and 60% (4/6), respectively. In contrast, patients with CMS2 and CMS4 achieved AJCC grade 0-1 at rates of 43% (3/7) and 29% (2/7), respectively. The tumor mutation burden of pre-CRT samples was significantly higher in patients with AJCC grade 0-1 (median 1.45/MB) than in patients with AJCC grade 2-3 (0.84/MB) ($p = 0.016$). **Conclusions:** A higher CD8$^+$ T cell/eTreg cell ratio, PD-L1-positive, Ki67 expression by CD8$^+$ T cells in TILs, CMS1 or 3, and higher tumor mutation burden are good predictors of the efficacy of the sequential combination of CRT and nivolumab. Further results will be reported in the meeting. Clinical trial information: NCT02948348. Research Sponsor: Ono phrmaceutical Co.,Ltd.

4074 Poster Session (Board #66), Fri, 8:00 AM-11:00 AM

Neoadjuvant chemoradiation (CRT) for locally advanced rectal cancer (LARC) with or without oxaliplatin (OX): Individual patient data (IPD) meta-analysis of three randomized controlled trials (RCTs) with subgroup analyses of age cohorts. *First Author: Elisa Fontana, Sarah Cannon Research Institute, London, United Kingdom*

Background: Neoadjuvant CRT with fluoropyrimidine (FP) is standard treatment for LARC, which is increasing in younger patients (pts). RCTs examining the addition of OX are still controversial. A *post hoc* analysis of the CAO/ARO/AIO-04 trial showed significant benefit in pts < 60y. We hypothesised that younger pts with LARC might have improved outcomes with OX-CRT. **Methods:** Systematic review and IPD meta-analysis were performed. Data from 3 RCTs (CAO/ARO/AIO-04, ACCORD-12, PETACC-6) testing the addition of OX to standard FP-based CRT in LARC were available (of 9 RCTs identified). Primary endpoint: disease-free survival (DFS), secondary endpoints: pathologic complete response (pCR), overall survival (OS). Analyses were by intention to treat (ITT), stratified by trial. Age cut-offs were 60y and 50y. Given the focus on young age a multivariate analysis evaluating all possible confounders was not intended in the current work. **Results:** IPD from 2914 pts were included (48.5% of available literature). Median age was 63; 70% were male; 79% had a performance status = 0; 72% were stage ≥III. In ITT (Hazard Ratio [HR] 0.88, 95%CI 0.77-1.01, p = 0.06), DFS was not significantly improved by the addition of OX (Table). In < 60y (n = 1166, 40% total), DFS was significantly improved by OX (HR 0.77, 95%CI 0.62-0.96, p = 0.02). In < 50y (n = 350, 12% total) there was a numerically better DFS, although not significant (HR 0.73, 95%CI 0.49-1.08, p = 0.12). Interaction test between age and DFS was non-significant (60y p = 0.11; 50y p = 0.44). In ITT, OX increased pCR from 13% to 16% (Odds Ratio [OR] 1.28, 95%CI 1.04-1.57, p = 0.024 [stratified by trial]), without significant interaction with age (60y p = 0.11, 50y p = 0.74). No OS benefit was demonstrated (HR 0.97, 95%CI 0.82-1.15, p = 0.75). **Conclusions:** This first IPD meta-analysis of three RCTs evaluating the addition of OX to CRT did not show significant interaction of OX with age. However, we confirm a signal for DFS benefit in pts < 60y and a non-significant increment in DFS in < 50 y although this analysis may be underpowered. Stage-stratified analyses and feasibility/toxicity data in age cohorts will be presented. Research Sponsor: None.

ITT - DFS	HR	0.88	95%CI	0.77-1.01	p-value	0.06
< 60 - DFS		0.77		0.62-0.96		0.02
< 50 - DFS		0.73		0.49-1.08		0.12
> 60 - DFS		0.95		0.80-1.12		0.54
> 50 - DFS		0.90		0.78-1.04		0.14
ITT pCR	OR	1.28		1.04-1.57		0.02
< 60 - pCR		1.04		0.75-1.44		0.89
< 50 - pCR		1.17		0.65-2.11		0.72
> 60 - pCR		1.47		1.12-1.93		0.01
> 50 - pCR		1.30		1.04-1.62		0.02

4075 Poster Session (Board #67), Fri, 8:00 AM-11:00 AM

Duration of FOLFOX adjuvant chemotherapy in high-risk stage II and stage III colon cancer with deficient DNA mismatch repair. *First Author: Zehua Wu, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: In the IDEA collaboration, noninferiority was not confirmed for 3 months versus 6 months of FOLFOX adjuvant chemotherapy among patients with high-risk stage II and stage III colon cancer (CC). Patients with deficient DNA mismatch repair (dMMR) have a good prognosis, but for whom, whether limiting the duration of adjuvant therapy will compromise oncologic outcomes remains undefined. We evaluated the impact of 3 months of FOLFOX adjuvant chemotherapy or surgery alone in comparison with 6 months of FOLFOX on disease-free survival (DFS) in dMMR CC patients. **Methods:** This retrospective study included all consecutive patients who underwent curative surgical resection for high-risk stage II or III dMMR CC between May, 2011 and July, 2019. Prognostic factors were analyzed using Cox models, and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. **Results:** A total of 242 dMMR CC patients were included (43.4% high-risk stage II, 56.6% stage III). The patients received 6 months of FOLFOX adjuvant chemotherapy (n = 66; median cycles [rang] = 12 [10-12]), 3 months of FOLFOX (n = 87; median cycles [rang] = 6 [4-8]), or surgery alone (n = 89). Three groups were generally well balanced, although more patients with stage III were in the 6-month therapy group (74.2%), compared with the 3-month therapy group (57.5%) and the surgery alone group (42.7%). As compared with 6 months of FOLFOX adjuvant chemotherapy in the overall population, 3 months therapy reduced DFS in multivariable analysis (HR, 2.78; 95CI, 1.18 to 6.47; P = 0.02), similar to surgery alone (HR, 2.30; 95CI, 0.99 to 5.38; P = 0.05). In the subgroup analysis, a therapy duration of 6 months was statistically superior to a duration of 3 months only in the patients with stage III, with a 3-year rate of DFS of 86.2% versus 70.8% (HR, 3.06; 95% CI, 1.14 to 8.19; P = 0.026). **Conclusions:** This study supports the 6-month duration of FOLFOX adjuvant chemotherapy in stage III dMMR CC. Research Sponsor: None.

4076 Poster Session (Board #68), Fri, 8:00 AM-11:00 AM

The mutation of homologous recombination repair genetics is a potential biomarker for immunotherapy in microsatellite stable colon cancer. *First Author: Xueying Wu, Genecast Precision Medicine Technology Institute, Beijing, China*

Background: Patients with microsatellite instability-high (MSI-H) colonic adenocarcinoma (COAD) are always immunotherapy-sensitive for the use immune checkpoint inhibitors, however, the vast majority of COAD patients (85%) are microsatellite stable (MSS). Homologous recombination deficiency (HRD) is demonstrated to be a response predictor to immunotherapies in gynecologic cancers, while limited studies were reported in colon cancer. We focus herein on the mutational pattern of HRR related genes in a large Chinese COAD cohort and further analyze the relationship between HRR-gene mutations and clinical response to immunotherapy in MSS COAD. **Methods:** The genomic profiling of Genecast cohort which is consisted of 406 Chinese patients with COAD were analyzed in a panel of 543 cancer related genes via next generation sequencing (NGS). The correlation between HRR-gene mutations and tumor immunity or clinical outcome using two COAD genomics datasets (TCGA and MSK-COAD) by the bioinformatic approach. **Results:** In Genecast Cohort, seventy of 406 (17.2%) patients were identified genomic alterations in HRR-gene, the most frequently mutated genes were *ATM* (9%), *BRCA2* (4%), *ATR* (3%), *RAD50* (3%) and *BRIP1* (3%). In MSK-COAD cohort (treated with immune checkpoint inhibitors), HRR-mut group (n = 34) had a significantly better OS than HRR-wt group (n = 50) (log-rank test, $P = 0.0087$). From the analysis of TCGA cohort, we found that mutations of HRR-gene could increase immune activity in MSS COAD, including increased cytotoxic cells infiltration ($P = 0.035$), increased exhausted CD8 T cells infiltration ($P = 0.0098$) and higher IFN-g score ($P = 0.03$). In contrary, similar results were not found in MSI-H COAD (all $P > 0.05$). **Conclusions:** Mutations of HRR-gene could significantly increase immune activity in patients with MSS COAD, implying the feasibility of using HRR-mut as a response predictor of immunotherapy in MSS-COAD. Research Sponsor: None.

4077 Poster Session (Board #69), Fri, 8:00 AM-11:00 AM

Tumor mutational load, microsatellite instability and actionable mutations in metastatic colorectal cancer: Results from the TRIBE2 study. *First Author: Carlotta Antoniotti, Department of Translational Research and New Technologies in Medicine and Surgery, Unit of Medical Oncology 2, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy*

Background: In the TRIBE2 study molecularly unselected and untreated mCRC patients were randomized to receive FOLFOXIRI/bevacizumab (bev) followed by the same agents after disease progression (PD) or FOLFOX/bev followed by FOLFIRI/bev after PD. We performed a comprehensive NGS analysis of samples from randomized patients in order to investigate the prognostic impact of tumor mutational load (TML), its additional value with respect to the assessment of microsatellite instability (MSI), and the overall prevalence of potentially actionable alterations. **Methods:** Tumor DNA was obtained from formalin-fixed, paraffin-embedded blocks from primary tumors of 296 (44%) out of 679 randomized patients and underwent NGS analysis using the Caris MI TumorSeek panel, assessing 592 genes. TML was defined low, intermediate or high if < 7, 7-16 or > 16 mutations/Mb were found. MSI status was determined both by NGS and by IHC. **Results:** TML and MSI were successfully determined by NGS in 224 (76%) cases. NGS and IHC results were concordant in 221 (99%) cases. TML was low, intermediate or high in 56 (25%), 157 (70%) and 11 (5%) cases, respectively. When compared with TML low and intermediate tumors, TML high were more frequently right-sided ($p = 0.013$), mucinous ($p < 0.001$) and MSI-high ($p < 0.001$). TML high tumors were MSI-high or MSS in 8 (73%) and 3 (27%) cases, respectively. Two out of 3 TML high and MSS tumours showed a pathogenic *POLE* mutation (p.S459F and p.P286R). The other TML high, MSS and *POLE* wt tumor was dMMR at IHC (loss of MSH6 expression) and showed a pathogenic *MSH6* mutation (p.F1040fs). As compared with low and intermediate TML, high TML was associated with longer PFS (median PFS: 17.3 vs 10.6; HR: 0.54 [95%CI: 0.35-1.09], $p = 0.098$) and OS (median OS: not reached vs 23.7: HR: 0.45 [95%CI:0-28-1.13], $p = 0.106$). No interaction effect between TML and treatment arm was observed, and no difference between TML low and intermediate tumors was reported in terms of baseline characteristics and prognosis. Actionable alterations (*HER2* mutations [N = 2] and amplifications [N = 4], KRAS G12C [N = 10] and BRAF V600E mutation [N = 39]) were found in 55 (19%) out of 296 cases. No *NTRK/ROS/ALK* or *MET* amplification was found. **Conclusions:** TML high tumors are not limited to MSI-high ones but showed *POLE* or *MSH6* somatic mutation and shower longer PFS and OS. No differences are reported between TML low and intermediate tumors. Molecular alterations predictive of benefit from targeted strategies currently available are detectable only in a small percentage of mCRCs. Research Sponsor: GONO foundation.

4079 Poster Session (Board #71), Fri, 8:00 AM-11:00 AM

Circulating tumor DNA as a promising biomarker of relapse risk for stage II-III colorectal cancer. *First Author: Gong Chen, Department of Colorectal Surgery, Sun Yat-Sen University Cancer Centre, Guangzhou, China*

Background: About 30-50% colorectal cancer patients undergoing a curative resection will experience disease recurrence ultimately. Early detection of recurrence is of great significance for improving the prognosis of colorectal cancer patients. Circulating tumor DNA (ctDNA) has been suggested to be a promising biomarker for postoperative surveillance and prognosis prediction in various cancers including colorectal cancer. However, its performance in predicting early recurrence of colorectal cancer as well as appropriate testing procedures still needs large-scale prospective studies to evaluate. **Methods:** A total of 246 patients with stage II-III colorectal cancer and underwent curative resection from three clinical centers of China were enrolled in this multicenter prospective cohort study. Tissue samples as well as serial plasma samples before surgery, 7 days and 6 months after surgery and 3 months interval afterwards until recurrence were collected, and subjected to deep targeted-panel sequencing containing 425 cancer-related genes. ctDNA baseline genomic alterations and dynamic changes were analyzed. Its performance in predicting early recurrence was evaluated and compared with other clinical routine investigations, including serum biomarkers CEA and CA199, and CT examination. **Results:** The ctDNA positive rates at baseline (before surgery) and 7 days after surgery were 72.9% and 18.1% respectively. Among 199 patients with complete survival data, 18 patients were recurrent during follow up period with a median disease-free survival of 280.5 days (114-461 days). At baseline, high clinical stage ($p = 0.035$), and *PTEN* mutation ($p = 0.009$) were significantly associated with increased recurrent risk; while *APC* mutation ($p = 0.04$) predicted a decreased recurrent risk. Detection of ctDNA 7 days after surgery [HR: 5.9 (1.94-17.97); $p = 0.0004$] or any time point before clinical recurrence [HR: 6.14 (2.3-16.38); $p < 0.0001$] was associated with a significantly higher recurrent risk, and the HR increased accordingly with ctDNA mutation level. In multivariate analyses, ctDNA status was independently associated with relapse after adjusting for known clinicopathological risk factors. CEA status was not significantly ($p > 0.4$) associated with disease-free survival. A risk scoring model comprising of clinical variables and ctDNA detection after surgery was constructed and can predict 18-month recurrence with an AUC of 0.77. **Conclusions:** ctDNA is a promising marker of risk stratification, and early relapse detection in resected stage II/III CRC patients. Clinical trial information: NCT03312374. Research Sponsor: None.

4080 Poster Session (Board #72), Fri, 8:00 AM-11:00 AM

Mutation of DNA damage repair genes confers an immune-privileged tumor microenvironment in colorectal cancer with a prognostic value. *First Author: Dandan Liang, Genecast Precision Medicine Technology Institute, Beijing, China*

Background: Microsatellite instability high (MSI-H)/mismatch-repair-deficient (dMMR) has been proved as a validated biomarker in solid tumors receiving immune checkpoint inhibitors (ICIs). Recently, mutational status of the DNA damage repair (DDR) genes has been linked to anti-tumor immune response in bladder cancer. Therefore, it would be of great interest to unravel the implications of DDR in shaping the immune responsiveness in CRC. **Methods:** The genomic correlates were examined in a publicly available cohort from Memorial Sloan Kettering Cancer Center (MSK ICI cohort). To explore the associations between DDR mutation and immune features, the genomic data of The Cancer Genome Atlas (TCGA) colorectal adenocarcinoma (COADREAD) dataset was analyzed. Further, we determined DDR mutation and MSI status in a Chinese CRC cohort via a 543-gene panel sequencing. **Results:** First, we observed that DDR pathway was commonly mutated (21.79%) in the multi-cancer MSK ICI cohort, with the highest frequency of 36.36% in CRCs. Second, survival analysis revealed that the median overall survival (mOS) in patients with DDR mutations was significantly longer than that in the DDR wild-type subgroup, in both pan-cancer (P = 0.0008; mOS 31 vs 16 months) and CRC patients (P = 0.016; mOS 34 vs 13 months) in the MSK ICI cohort. However, in the TCGA COADREAD dataset, there was no significant difference in OS or progression free survival (PFS) between DDR mutant and DDR wild-type subgroups. These observation indicated a specific prognostic value for DDR mutation in patients with ICI treatment while not conventional treatment. Third, in the TCGA COADREAD dataset, DDR mutations were associated with increased TMB, enrichment of immune cell infiltration and immune checkpoint molecule expression, suggesting an improvement of various steps of the cancer immunity cycles in DDR mutant CRCs. Lastly, we investigated the DDR mutational pattern, and its associations with MSI-H and other genomic features in a Chinese CRC cohort. Notably, MSI-H and DDR mutation account for 5.7% and 13.4% respectively, suggesting that DDR may identify a higher proportion of potential responders than MSI-H. **Conclusions:** Our data suggest that DDR mutation is a potential prognostic biomarker for ICI-treated CRCs. Functional analysis in TCGA dataset revealed that DDR mutation might be an indication of enhanced cancer immunity. The higher incidence of DDR mutation in Chinese CRCs emphasized the future utility of panel-based DDR evaluation in guiding ICI treatment. Research Sponsor: None.

4081 Poster Session (Board #73), Fri, 8:00 AM-11:00 AM

The role of primary tumor (PT) site as prognostic factor after resection of colorectal (CRC) liver metastases (LM): A mono-institutional cohort study. *First Author: Maria Bensi, Oncologia Medica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli–IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy*

Background: Radical resection of LM is the only chance of cure for liver-only mCRC pts. Besides the evaluation of technical resectability, several factors must be taken into account for the evaluation of recurrence risk. Among them we should consider the Fong Risk Score and its modified version, including RAS/BRAF status (Brudvik's score). Tumor sidedness is an important prognostic factor in CRC. The impact of PT site on the outcome of LM resection is still debated. Hence, we retrospectively analysed mCRC pts, underwent to radical LM resection at our Institution, investigating the impact of PT site on DFS and OS. **Methods:** Liver-only mCRC pts underwent to radical LM resection were included. The association of PT site with DFS and OS was evaluated. The following variables were collected: gender; age ($\geq$ vs $<$ 75 years); ECOG PS; CEA baseline level; PT site; RAS and BRAF status; mucinous histology; grading (G1-2 vs G3); RECIST response during preoperative treatment; resected PT; synchronous vs metachronous; number of LM; bilobar vs unilobar LM; LM diameter $\geq$ 5 cm; R0 vs R1 resection. Univariate and multivariate analyses for DFS and OS were performed. **Results:** A total of 463 liver-only mCRC pts underwent to radical LM resection were included. Seventy (15%) pts had a right-sided (r-s) tumor and 393 (85%) pts a left-sided (l-s) tumor. R-s CRC pts more often had RAS/BRAF mutations in comparison to l-s tumors (76% vs 37%; $p < 0.0001$). Median DFS and OS was 13.1 and 41.6 months, respectively, in r-s CRC vs 16.0 (p = 0.65) and 62.2 months (p = 0.033), respectively, in l-s tumors. At the multivariate analysis no significant association with survival parameters was shown for tumor sidedness. At the multivariate analysis, R0 resection was independently associated both with better DFS and OS; RAS/BRAF wt CRC and resected PT were significantly associated with improved OS. Considering all wt CRC pts (N = 237), 14 (6%) pts had r-s tumor and 223 (94%) l-s tumor. No significant association of tumor sidedness with survival was shown (DFS r = 10.0 vs l = 16.0 months, p = 0.62; OS r = 40.3 vs l = 66.2 months, p = 0.12). **Conclusions:** Our results showed that a significant smaller proportion of r-s CRC underwent to radical LM resection, indirectly confirming its worse prognosis. Among radically resected pts, r-s CRC was associated to a shorter OS (significant) and DFS (not significant) compared to l-s CRC, but it was not confirmed at the multivariate analysis. We can conclude that right PT site should not be considered as a contraindication for radical LM surgery, when feasible. Research Sponsor: None.

4082 Poster Session (Board #74), Fri, 8:00 AM-11:00 AM

Efficacy of third-line anti-EGFR-based treatment (tx) versus (vs) Regorafenib/TAS-102 (R/T) according to primary tumor site in RAS/BRAF wild-type (wt) metastatic colorectal cancer (mCRC) patients (pts). *First Author: Raffaella Vivolo, Oncologia Medica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli–IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy*

Background: Right- (R) and left-sided (L) mCRCs exhibit different clinical and molecular features. Several retrospective analyses showed that the survival benefit of anti-EGFR-based tx is limited to *RAS/BRAF* wt L-sided mCRC pts, which a larger effect in the first-line setting. Few data are available concerning the anti-EGFR efficacy according to primary tumor site in third line. **Methods:** Pts affected by *RAS/BRAF* wt mCRC treated with third-line anti-EGFR-based tx or R/T were retrospectively collected. The objective of the analysis was to compare tx activity and efficacy according to tumor site. Primary endpoint was PFS; secondary endpoints were OS and RR. PFS and OS analyses were performed using Kaplan-Meier method, and survival curves were compared using the log-rank test. RR was evaluated according to RECIST criteria and it was compared in the two groups using Fisher's exact test. Statistical significance was set at p = 0.05 for a bilateral test. Univariate and multivariate analyses for PFS and OS were performed. **Results:** A total of 76 *RAS/BRAF* wt mCRC pts, treated with third-line anti-EGFR-based tx or R/T, were enrolled. Of those, 19 (25%) pts had R-sided tumor (9 pts received anti-EGFR tx and 10 pts received R/T) and 57 (75%) pts had L-sided tumor (30 pts received anti-EGFR tx and 27 pts received R/T). As shown in the table, a significant PFS and OS benefit in favor of anti-EGFR tx vs R/T was observed in L-sided pts, while no difference both in PFS and OS was observed in R-sided pts. RR was significantly higher in L-sided pts treated with anti-EGFR vs R/T, no difference was shown in R-sided pts. At the multivariate analysis, tx regimen was indipendently associated with PFS in L-sided pts, but not in R-sided pts. **Conclusions:** Our study confirmed the results deriving from the retrospective analysis of the phase III study 20020408. Our results demonstrated a different benefit from third-line anti-EGFR tx according to primary tumor site, confirming the role of L-sided tumor in predicting benefit from third-line anti-EGFR vs R/T, while no difference was observed in R-sided tumors. Research Sponsor: None.

	R-sided	R-sided	L-sided	L-sided
	Anti-EGFR (N = 9)	R/T (N = 10)	Anti-EGFR (N = 30)	R/T (N = 27)
Median PFS (months)	3.5 HR = 1.4 (95%CI 0.53-3.75), p = 0.49	3.8	7.3 HR = 0.47 (95%CI 0.26-0.85), p = 0.0028	3.6
Median OS (months)	9.3 HR = 0.83 (95%CI 0.30-2.26), p = 0.696	9.2	15.2 HR = 0.58 (95%CI 0.31-1.08), p = 0.0428	11.0
RR	11% p = 0.99	10%	43% $p < 0.0001$	0%

4083 Poster Session (Board #75), Fri, 8:00 AM-11:00 AM

Intra-tumoral microbes and overall survival in colorectal cancer patients. *First Author: Pannaga G. Malalur, The Ohio State University/Wexner Medical Center, Columbus, OH*

Background: The presence of certain bacteria among or adjacent to tumor cells may contribute to colorectal cancer (CRC) development. However, the effect of the tumor microbiome on survival in CRC patients undergoing treatment is poorly understood. We hypothesize that intra-tumoral microbes correlate with overall survival (OS) in CRC patients. **Methods:** We obtained RNA-seq data from CRC tumor biopsies from patients treated at The Ohio State University Comprehensive Cancer Center as part of the Oncology Research Information Exchange Network (ORIEN). Reads were aligned to human and exogenous genomes using TopHat2 and Kraken2/Bracken, respectively. **Results:** The analyzed cohort included 99 CRC patients with an age range from 31-83 years, 62% female, and 44% with metastatic CRC. Therapies received prior to sample collection were grouped into chemotherapy with or without radiation (37%), antiVEGF/EGFR therapies (33%), no systemic therapy (23%), immunotherapy (3%); 3% were unknown. Overall, eleven bacteria were significantly associated with shorter OS, including a species in the genus Clostridium and Vibrio. Conversely, five other bacteria including several commensal gut microbes, were associated with longer OS. In patients who received chemotherapy with or without radiation (n = 38), several microbes were significantly associated with shorter OS, including a member of the genus *Streptomyces*. Only three bacteria were significantly associated with longer OS. In the patients who received antiVEGF/EGFR therapies (bevacizumab, cetuximab, panitumumab) (n = 33), several bacterial taxa were associated with shorter OS. In addition, bacteria including a member of the genera Bacillus and Staphylococcus were significantly associated with metastatic CRCs. ($p < 0.05$ for all, Fisher's Exact tests). **Conclusions:** This study suggests that demonstrating the presence or absence of certain microbes in tumor biopsies could have important therapeutic implications for CRC patients. Only bacteria (no fungi, viruses, archaea, etc.) were found to significantly associate with OS across the entire cohort and within treatment subsets. The presence of bacteria was mostly, but not always, associated with worse OS. Antibiotics targeted towards bacterial species associated with negative outcomes could have the potential to improve OS in CRC patients. Research Sponsor: Award Number UL1TR002733.

4084 Poster Session (Board #76), Fri, 8:00 AM-11:00 AM

Consensus molecular subtype (CMS) as a novel integral biomarker in colorectal cancer: A phase II trial of bintrafusp alfa in CMS4 metastatic CRC. *First Author: Amir Mehrvarz Sarshekeh, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Consensus Molecular Subtype 4 (CMS4) colorectal cancer (CRC) features increased TGFβ signaling, which may account for de novo resistance to immunotherapy for patients (pts) with microsatellite stable mCRC. To date, no prior trial has incorporated CMS status as an integral biomarker. Bintrafusp alfa (M7824) is a dual PD-L1 antibody/TGFβ trap with acceptable safety. **Methods:** Primary tumors from pts with metastatic CRC underwent CMS testing in a CLIA setting. In this Simon two-stage phase II trial (Ho: $p < .05$; Ha: $p \geq .25$) for CMS4 mCRC, pts received bintrafusp alfa 1200mg IV every 14 days. RT (8Gy/day x 3 days) to a single metastatic lesion with abscopal intent was administered between doses 2 and 3. The primary objective was to estimate response rate (RR) per iRECIST. Correlative studies including RNA sequencing were performed on pre- and on-treatment biopsies. **Results:** 53 of 137 tested pts (39%) between June 2018-December 2019 had CMS4 mCRC. 13 of 15 treated pts received the agent with RT. All pts were evaluable for toxicity, and 13 for response. Median number of doses was 3 (IQR, 2-4). There was one grade 3 immune-related adverse event (colitis) requiring study discontinuation. There were 2 pts with stable disease and 11 with progressive disease as best response (RR 0%, 95% CI 0-22%). Enrollment was stopped after first stage for futility. Median PFS and OS were 1.6 months and 5.0 months, respectively. In paired samples, treatment with bintrafusp alfa resulted in an increase in the expression of IFNγ signature in nonirradiated metastatic lesions ($p < .001$, $q < .001$). Updated results will be presented. **Conclusions:** This is the first reported clinical trial to utilize CMS status as an integral biomarker for pts with metastatic CRC and capitalizes on treating CRC subpopulations with targeted agents based upon validated RNA-based signatures. Although the efficacy for bintrafusp alfa and RT is low, changes in IFNγ signature provides a potential signal for refining therapeutic strategies based upon TGFβ enrichment in pts with mCRC. Clinical trial information: NCT03436563. Research Sponsor: EMD-Serono.

4085 Poster Session (Board #77), Fri, 8:00 AM-11:00 AM

The effect of aspirin on colorectal cancer incidence in African Americans. *First Author: Oluwadunni Emiloju, Albert Einstein Medical Center, Philadelphia, PA*

Background: From 2011 to 2016, the incidence and mortality rate of colorectal cancer(CRC) were highest among African Americans(AA), compared to other US racial/ethnic groups. Long-term aspirin use is recommended as a strategy to reduce the risk of CRC. Yet, there is scant information on the chemopreventive effect of aspirin among AA. It is imperative to assess whether the reported chemo-preventive effect also occurs in AA. Our central hypothesis is that aspirin use in AA is associated with a lower incidence of CRC, irrespective of race/ethnicity. **Methods:** We conducted a secondary analysis, using data from AA participants in the Atherosclerosis Risk in Communities(ARIC) longitudinal study, who did not have CRC at enrollment, from 1987 to 1998. We extracted demographic, clinical and mortality data to compare the incidence of CRC among participants taking aspirin compared to those who were not taking aspirin, stratified by age, tobacco use, and body mass index. All-cause mortality and CRC mortality will also be assessed, and we will use Cox proportional hazard regression to determine the relationship between aspirin use and CRC incidence, and mortality. **Results:** At baseline in 1987, 15,026 participants enrolled in the ARIC study, 25% of whom were AA, median age 54(range 44-66), including 46.7% who reported using aspirin. We analyzed follow-up data from 10,960 participants in 1996-1998, 20% of whom were AA, and 56.9% of whom were taking aspirin. Non-AA participants were more likely to report using aspirin at baseline and follow-up, compared to AA, 53% vs 30% and 59% vs 50% respectively. After 10years, the total incidence of CRC in AA participants was 1% compared with 1.1% in non-AA($p = 0.7$). There was no difference in CRC incidence by aspirin use among all participants, and when stratified by race(among all participants $p = 0.81$, amongAA $p = 0.68$, among non-AA $p = 0.94$). **Conclusions:** We found no difference in the incidence of CRC among AA compared to Caucasians, by aspirin use. Investigation of consistency and/or dose of aspirin use by race may provide further insights on the relationship between aspirin use and CRC incidence, comparing AA to Caucasians. Research Sponsor: None.

4086 Poster Session (Board #78), Fri, 8:00 AM-11:00 AM

Predictive and prognostic value of *HER2* gene expression and *HER2* amplification in patients with metastatic colorectal cancer (mCRC) enrolled in CALGB/SWOG 80405 (Alliance). *First Author: Francesca Battaglin, University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA*

Background: The randomized phase III CALGB/SWOG 80405 trial found no difference in overall survival (OS) in first-line mCRC pts treated with either bevacizumab (Bev) or cetuximab (Cet) combined with the same chemotherapy. We investigated the potential prognostic and predictive value of *HER2* amplification and *HER2* gene expression using NGS and Nanostring data. **Methods:** Primary tumor DNA from 559 patients (pts) was profiled for *HER2* amplification by NGS (Foundation One). Tumor tissue from 925 pts was tested for Nanostring gene expression using an 800 gene panel. OS and progression free survival (PFS) were the endpoints as time-to-event variables. Cox proportional hazard models with gene expression fitted with linear spline (one internal knot at median) were used, adjusting for pts baseline characteristics, treatment assignment, and molecular features (microsatellite instability, *BRAF*, all *RAS*). **Results:** Of 505 tumors with both NGS and Nanostring data, 16 harbored *HER2* amplification (copy number variation > 6), limited to microsatellite stable tumors and significantly associated with *HER2* expression ($P < 0.001$) and wild-type *RAS* ($P = 0.036$). *HER2* amplification was neither prognostic nor predictive for OS or PFS. Conversely, *HER2* expression higher than median was associated with longer PFS ($P = 0.018$) but not OS ($P = 0.13$). Among pts with *HER2* not amplified, higher *HER2* expression was associated with better OS (hazard ratio [HR], 0.83; 95%CI, 0.72-0.97; $P = 0.016$) and PFS (HR, 0.85; 95%CI, 0.74-0.98; $P = 0.027$) when the expression was less than median. Additionally, in pts with no *HER2* amplification and *HER2* expression lower than median, treatment with Cet was associated with worse PFS compared to Bev (HR, 1.46; 95%CI, 1.12-1.90; $P = 0.005$). This effect was not observed with expression higher than median regardless of *HER2* amplification status. **Conclusions:** To our knowledge, this is the largest analysis of *HER2* amplification and gene expression in mCRC pts treated with standard therapy. Our results provide novel insight on the predictive and prognostic value of *HER2* gene expression in pts treated with Cet- and Bev-based regimens. Upon validation, these findings could inform pts selection and the design of more effective treatment options for pts with low *HER2* expression. Clinical trial information: NCT00265850. Research Sponsor: U10CA180821, U10CA180882; U10CA180888, UG1CA180830 (SWOG); BMS, Genentech, Pfizer, Sanofi; https://acknowledgments.alliancefound.org.

4088 Poster Session (Board #80), Fri, 8:00 AM-11:00 AM

Novel methylated DNA markers in plasma detect distant recurrence of colorectal cancer. *First Author: Hao Xie, Mayo Clinic, Rochester, MN*

Background: Methylated DNA markers (MDMs) are broadly informative for early detection of colorectal cancer (CRC) but have not been extensively studied for post-treatment surveillance and disease monitoring. We aimed to assess the feasibility of novel CRC-associated MDMs for detection of distant recurrent CRC (rCRC) in plasma. **Methods:** A panel of 13 MDMs previously identified to be discriminant for primary CRC was selected. In a cross-sectional analysis of plasma samples, MDMs were assayed blindly (by target enrichment long-probe quantitative amplified signal assay) from 160 age/sex-balanced patients (60 healthy controls, 60 with resected CRC and no evidence of disease (NED), and 40 rCRC after primary tumor resection). Plasma-derived carcinoembryonic antigen (CEA) was measured on all patients. Random forest modeling was used to derive a prediction algorithm of MDMs (with and without CEA) for the endpoint of rCRC relative to healthy controls. The accuracy of the algorithm was summarized as sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) with 95% confidence intervals (CI) in the test set. **Results:** Median patient age was 55 (interquartile range: 49-64) years. As shown in the Table below, a single MDM with the highest AUC was significantly better than CEA ($p = 0.02$). On cross validation, CEA provided no additional improvement to the performance of the panel of 13 MDMs ($p = 0.2$). The cross-validated panel of MDMs detected rCRC liver metastases with 96% (79-100%) sensitivity, lung metastases with 78% (40-97%) sensitivity, and peritoneal/nodal metastases with 57% (18-90%) sensitivity. Lesions with Response Evaluation Criteria in Solid Tumors sum > 4 cm were detected with 94% (73-100%) sensitivity and ≤ 4 cm with 78% (52-94%) sensitivity. **Conclusions:** Novel MDMs in plasma detect rCRC with promising accuracy. The clinical utility of MDMs for non-invasive post-treatment surveillance and treatment monitoring in CRC warrants further evaluation in longitudinal studies with sufficient follow-up to exclude sub-clinical recurrence in those with NED. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology, Exact Sciences provides the LBgard (Biomatrica) blood tubes and provided the TELQAS assays at no cost.

Modeling	Marker	AUC (95% CI)	rCRC Sensitivity (95% CI)	NED Sensitivity (95% CI)	Healthy controls Specificity (95% CI)	P
No cross-validation	A single MDM	0.93 (0.87-1)	88% (73-96%)	13% (6-25%)	95% (86-99%)	0.02
	CEA (cutoff: 3 ng/ml)	0.79 (0.69-0.9)	65% (48-79%)	12% (5-23%)	87% (75-94%)	
2:1 cross-validation	13 MDM algorithm	0.96 (0.91-1)	85% (70-94%)	22% (12-34%)	95% (86-99%)	0.20
	13 MDM+CEA algorithm	0.96 (0.91-1)	85% (70-94%)	22% (12-34%)	95% (86-99%)	

4089 Poster Session (Board #81), Fri, 8:00 AM-11:00 AM

Consensus molecular subtypes (CMS) as a marker for treatment and disease biology in metastatic colorectal cancer (CRC). *First Author: Michael Lam, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Consensus molecular subtypes (CMS) categorize colorectal cancer (CRC) into groups based on gene transcription and are prognostic in early-stage and first-line metastatic settings. Their impact on treatment history is unknown. We hypothesized that the best prognosis CMS2 would have higher utilization of liver-directed therapies and maintenance chemotherapy over the worst prognosis CMS4. **Methods:** Primary surgical resection specimens were annotated for CMS on a translational protocol in a 5FU-refractory metastatic CRC population. Specimens that had neoadjuvant chemotherapy or radiation were excluded. CMS1, CMS3 and indeterminate CMS were also excluded. Liver-directed therapies were defined as any surgery, direct injection of cytotoxics or microspheres, radiation or radiofrequency ablation. Multiple occurrences of liver-directed therapies or maintenance chemotherapy in the same patient were recorded once for statistical tests of association. **Results:** CMS1 (7.4%), CMS3 (8.2%) and indeterminate calls (4.1%) accounted for 20% of all samples tested. There were 43 (44%) CMS2 and 55 (56%) CMS4 patients eligible. Age, stage at diagnosis, mismatch repair and RAS mutational status were similar in both groups. Left-sided tumors were more common in CMS2 (79%) than CMS4 (42%), p = .001. The median overall survival (OS) from stage IV diagnosis was 40 [34 - 51] versus (vs) 28 [21 – 33] months ($p < .0001$) for CMS2 vs CMS4 respectively. Liver-directed therapy was greater in CMS2 (53%) vs CMS4 (31%), p = .024. The number further increased when multiple treatments in a single patient were taken into account. Microsphere injection, radiation and liver surgery combined with RFA were the most skewed towards CMS2 over CMS4. No difference in median OS was seen from first liver-directed therapy in CMS2 vs CMS4 (29 vs 27 months, p = .31). There was a trend towards greater maintenance chemotherapy in CMS2 (47%) vs CMS4 (29%), p = .076. **Conclusions:** Better prognosis with CMS2 is consistent with other studies. Significantly increased liver-directed therapy was observed in CMS2. Selection criteria for liver-directed therapy such as slowly progressing, oligometastatic and hepatic-confined disease may be enriching for CMS2 and gives insight into the natural history of this subtype. Research Sponsor: U.S. National Institutes of Health.

4090 Poster Session (Board #82), Fri, 8:00 AM-11:00 AM

Treatment effects (TEs) of EGFR monoclonal antibodies (mAbs) in metastatic colorectal cancer (mCRC) patients (pts) with KRAS, NRAS, and BRAF mutation (MT) status: Individual patient data (IPD) meta-analysis of randomized trials from the ARCAD database. *First Author: Christos Stelios Karapetis, Flinders Medical Centre, Flinders University, Adelaide, SA, Australia*

Background: EGFR mAbs have become incorporated into clinical practice for the management of mCRC over the last decade. KRAS and NRAS mutations are used as predictive biomarkers and BRAF V600E mutations are associated with an adverse prognosis. The observed TE within biomarker subpopulations has varied between studies. **Methods:** IPD from randomized trials with head-to-head comparison between EGFR mAb versus no EGFR mAb (chemotherapy alone or BSC) in mCRC, across all lines of therapy (first, second and later), were pooled. Biomarker subpopulations are defined in the table. Overall survival (OS) and progression-free survival (PFS) were compared between groups by Cox model, stratified by studies and adjusted by age, gender, and performance status. TEs were estimated by adjusted hazard ratio (HR_{adj}) and 95% confidence interval (CI). Within each biomarker subgroup, EGFR mAb efficacy was explored according to multiple exploratory factors, including line of therapy, type of backbone chemo, gender, sidedness and site of metastasis. Interaction tests were performed. P-values < 0.01 were considered statistically significant to account for multiple comparisons. **Results:** 5729 pts from 8 studies with data available for ≥ 1 biomarker were analysed. PFS benefits (median 9.2 mos in EGFR mAbs, 8.0 mos in no EGFR mAbs) were confirmed in triple-WT pts, but not for OS (refer to table). No OS/PFS benefits were observed for pts with any of the MT tumors. Exploratory analyses showed a potential detrimental TE of EGFR mAbs in KRAS MT mCRC with liver metastasis (OS: HR_{adj} 1.22, p = .003, $p_{interaction}$ .0056; PFS: HR_{adj} 1.24, p = .0009, $p_{interaction}$ .0008). These results were confirmed within the subgroup of pts with all 3 biomarkers available. **Conclusions:** This is the largest IPD analysis to explore the predictive value of RAS/BRAF biomarkers in mCRC. Our findings demonstrate that there is no evidence of efficacy of EGFR mAbs in KRAS, BRAF and/or NRAS MT mCRC. EGFR mAbs might have a detrimental effect in KRAS MT mCRC with liver metastases. Research Sponsor: National Health and Medical Research Council of Australia Project Grant.

		OS		PFS	
	N of trials (N of pts)	HR_{adj} (95% CI)	p	HR_{adj} (95% CI)	p
KRAS MT	8 (2397)	1.07 (.98, 1.16)	.13	1.05 (.96, 1.14)	.30
NRAS MT	3 (88)	1.35 (.81, 2.24)	.24	1.61 (.97, 2.65)	.062
BRAF MT	6 (232)	.94 (.70, 1.25)	.65	.90 (.67, 1.21)	.49
Triple WT	3 (1039)	.93 (.81, 1.07)	.30	.75 (.66, .85)	< .0001

4092 Poster Session (Board #84), Fri, 8:00 AM-11:00 AM

The development and validation of a novel targeted methylation sequencing technology detecting 0.003 percent tumor signal in early-stage cancer plasma. *First Author: Grace Q. Zhao, Avida Biomed Inc., Fremont, CA*

Background: Methylation analysis in cell-free DNA holds great potential for early cancer detection. In the plasma of early stage cancer patient, the tumor content is estimated to be less than 0.1%, therefore demands a highly sensitive assay. Targeted Methylation Sequencing (TMS) is the most promising approach; however, the current sensitivity and specificity are compromised by low efficiency and low recovery of target enrichment, and further hampered by background noise associated with large panels. The ideal solution would be an in-depth analysis using a focused small cancer-specific methylation biomarker panel, but is not supported by existing technologies. **Methods:** Here we present a new technology designed for TMS analysis in cfDNA: Point-n-Seq, featuring an enrichment of target molecules directly from cfDNA before bisulfite conversion and amplification. Particularly, this technology enables small focused panel that interrogates the methylation status of 1 to ~1000 markers. We designed a CRC panel covering 100 methylation markers in 3 steps: identify ~1000 CRC-specific markers from public databases; eliminate makers with high background signal in baseline cfDNA of healthy population; finalize the list with the most differentiating markers between patient and healthy cfDNA. **Results:** The capture of Point-n-Seq CRC panel is highly efficient resulting in high uniformity (94% > 0.5X) and on-target rate (> 80%). For 20 ng cfDNA input, more than 1000 deduped informative reads were obtained for each marker on average, despite the high GC content (> 80%). The output of informative reads was linear to the cfDNA input ranging from 1 ng to 40 ng. In titration studies, 0.6 pg (0.2X genome equivalent) methylated DNA in 20 ng cfDNA (0.003%) was reliably detected over cfDNA background. Using plasma samples from patients with CRC - early stage (I, n = 7; II, n = 7), late stage (III, n = 11; IV, n = 3), and control individuals (n = 105), the average fractions of methylated signal are 0.0034%, 0.013%, 0.09%, 0.17%, 0.29% for control, stage I, II, III, IV accordingly. With a simple cut-off using methylation fraction, Point-n Seq CRC panel achieved a sensitivity of 86% for stage I, 100% for stage (II-IV) at a specificity of 91%, with AUC = 0.96. **Conclusions:** Point-n-Seq TMS is the first hybridization based NGS technology enables the small focused methylation panel (e.g. 100 markers) sequencing using cfDNA, and it will greatly facilitate the development of practical and cost-effective methylation assays for clinical use. Research Sponsor: Avida Biomed seed fund.

4093 Poster Session (Board #85), Fri, 8:00 AM-11:00 AM

Can FIT rule out colorectal cancer in symptomatic patients? Diagnostic test accuracy results from 9,822 patients in the NICE FIT study. *First Author: Theo Georgiou Delisle, Croydon University Hospital, London, United Kingdom*

Background: The faecal immunochemical test (FIT) is a non-invasive quantitative test that measures occult blood in faeces (faecal haemoglobin, FHb). FIT is already used worldwide in colorectal cancer (CRC) screening programmes. Bowel symptoms have low specificity for CRC; to diagnose one patient with CRC, a large number of symptomatic patients require investigation. A negative FIT test, when blood is not detected, could be used to rule out CRC in symptomatic patients without invasive investigations such as colonoscopy. We report on the largest diagnostic accuracy study to date of FIT in symptomatic patients. **Methods:** Patients were eligible for recruitment if they experienced bowel symptoms meeting national high-risk criteria and were triaged to investigation with colonoscopy. Patients were excluded from analysis if they did not provide a valid FIT or did not undergo complete colonoscopy. Colonoscopy results were compared to FIT measurements of FHb, and the conduct of the tests was double-blinded. Quality assurance of endoscopy and clinical data was performed by senior clinicians. External statisticians analysed anonymised data. **Results:** 9822 patients from 50 sites across England participated in the study between October 2017 to March 2019. The most common colonoscopy finding was absence of any colorectal disease (31%). The prevalence of CRC at colonoscopy was 3.3%. The sensitivity of FIT at FHb thresholds of 2, 10 and 150 μg/g significantly decreased from 97.0% to 90.9% and 70.8% respectively ($p < 0.01$). FIT positivity rate at these thresholds increased from 7.6%, to 19% and 37.2% respectively ($p < 0.01$). The positive predictive value of FIT for CRC at FHb thresholds of 2, 10 and 150 μg/g was 8.7%, 16.1% and 31.1% respectively and the negative predictive value of FIT at these thresholds was 99.8%, 99.6% and 98.9% respectively. **Conclusions:** The results of this study support the use of FIT at the threshold of detectable blood (2μg/g) as an initial CRC rule-out test to triage patients with high risk CRC symptoms, reducing the number of unnecessary investigations. This is the first study to report that at the lowest threshold of detectable blood, FIT sensitivity is equivalent to the current gold standard investigation of colonoscopy. Clinical trial information: ISRCTN49676259. Research Sponsor: RM Partners, the West London Cancer Alliance hosted by The Royal Marsden NHS Foundation Trust and sponsored by Croydon University Hospital NHS Trust. The study was also supported by the National Institute for Health Research.

4094 Poster Session (Board #86), Fri, 8:00 AM-11:00 AM

APC and TP53 as potential biomarkers for EGFR sensitivity in colorectal cancer. *First Author: Ramya Thota, Intermountain Healthcare, Murray, UT*

Background: The Consensus Molecular Subtypes (CMS) of colorectal cancer (CRC) have prognostic and predictive value in identifying patients that derive benefit from EGFR targeted therapies. The CMS2 cohort was specifically noted to predict response to cetuximab. Besides CMS classification, we recently reported a two-gene mutation signature of APC and TP53 (AP) that predicts potential response to cetuximab. In this study, we hypothesize AP mutations, in addition to CMS cohorts, predict cetuximab sensitivity. **Methods:** A prespecified and validated 203 gene expression signature score measuring cetuximab sensitivity (CTX S-score) was used as a surrogate for response to cetuximab sensitivity. A cohort of 458 patients with colorectal cancer was accrued between October 2006 and September 2011. The population classified into CMS cohorts, and CTX-S scores were determined across each of the cohorts based on AP mutation status. **Results:** Among 458 tumor samples sequenced, AP mutations were identified as significantly associated with higher CTX-S scores. Among the CMS 1-4 cohorts identified, AP mutations were noted in 13 of 77 (17%) patients in CMS1 cohort, 87 of 116 (75%) patients in CMS2 cohort, 15 of 64 (23%) patients in CMS3 cohort, 46 of 112 (41%) patients in CMS4 cohort, indicating that AP mutations are dominant in CMS2 cohort. Further CTX-S score comparisons across CMS cohorts based on AP status show that AP mutated tumors have higher CTX-S scores than non-AP mutated tumors—irrespective of the CMS cohorts ($p<0.05$ unpaired, two-tailed t tests). **Conclusions:** In our study, we noted CMS2 cohort has high predicted sensitivity to cetuximab. Across other CMS cohorts, AP mutations were associated with higher CTX-S scores compared to those with AP wild-type tumors, suggesting both CMS2 and AP mutations contribute to CTX sensitivity. Research Sponsor: U.S. National Institutes of Health.

4095 Poster Session (Board #87), Fri, 8:00 AM-11:00 AM

A population-based study of young-onset colorectal cancer patients: Effect of knowledge gaps among patients and providers on stage at diagnosis and quality of life. *First Author: Ronit Yarden, Colorectal Cancer Alliance, Washington, DC*

Background: Colorectal cancer (CRC) is one of the leading cause of cancer-related death in the US. Despite a decrease in overall incidence and mortality, there has been an alarming increase in CRC diagnosis among young adults (20-49 years old) and causes remain unknown. To explore the unique challenges and unmet needs of the young-adult patients many still establishing their life-long goals, the Colorectal Cancer Alliance launched a comprehensive survey for young-onset CRC patients and survivors via social media to track the self-reported pre-diagnosis awareness, path to diagnosis, and post-diagnosis quality of life experiences of this often overlooked group. **Methods:** A cross-sectional study, conducted in the form of an online survey, was launched via multiple channels of social media. The questionnaire was based on established instruments including PROMIS, EORTC-QOL-30, and EORTC-CR-29 and EORTC-SHC-22. **Results:** The survey was completed by 885 patients and survivors. The median age at diagnosis was 42 +/-7, significantly lower than the recommended screening age. Only 6% of respondents were diagnosed with Lynch syndrome although 29% reported some family history. Most respondents (63%) indicated they were not aware that CRC can affect people younger than 50, which may explain why the majority of patients waited more than 3 months and 23% waited over 12 months after noticing their symptoms to visit their doctor. The majority, 75%, of all patients visited 2+ doctors and 11% of those patients visited 10+ doctors before their doctor suspected colorectal cancer. A significant number of patients felt their doctors were dismissive of their symptoms. 77% of patients were diagnosed with advanced disease and were subjected to aggressive therapies that substantially affected their quality of life including neuropathy, anxiety, clinical depression, sexual morbidity, unemployment, and financial toxicity. Many young patients indicated that their doctors did not inform them about fertility preservation. **Conclusions:** Our survey indicates that medical professionals and young adults need to be aware of the increasing incidence of young-onset CRC, and the importance of timely screening when signs and symptoms are present, regardless of age. Research Sponsor: Colorectal Cancer Alliance.

4096 Poster Session (Board #88), Fri, 8:00 AM-11:00 AM

Adjunctive local therapy in metastatic colorectal cancer in an unselected cohort: Improved patient-survival in comparison to systemic therapies. *First Author: Jan Schroeder, Praxis für Hämatologie und Onkologie, Mülheim, Germany*

Background: Patients with distant metastases in colorectal cancer have a poor prognosis and a low overall survival (OS). In addition to systemic treatments and irradiation, the tumor burden can be reduced by loco-regional therapeutics, including microwave ablation (MWA), radiofrequency therapy (RFA) and trans-arterial chemoembolization (TACE) available. To evaluate the benefit of such local therapies, we compared OS of a single-centre study population to a reference population of patients who underwent no loco-regional treatment within the German Tumor Registry Colorectal Cancer (TKK). **Methods:** The study population consists of a cohort of 51 patients (n = 51) treated loco-regionally in addition to systemic therapy. The patients were recruited in a single cancer centre in Mülheim, Germany during the years 2006 to 2015. A reference population of 788 patients was chosen from a prospective, longitudinal registry of the TKK. Time to event data analysis included the estimation of Kaplan-Meier cumulative survival probabilities and hazard ratios (HR) with corresponding 95% confidence intervals (95% CI) from Cox proportional hazards regression. **Results:** The median OS was 31.3 months (95% CI 26.8 - 41.6) in the study population, as compared to the reference population, where it was 21.9 months (95% CI 20.1 – 24.6). Patients with liver and lung metastases in the study population had an OS of 41.6 months (95% CI 30.5 – 78.2), the corresponding patients from the reference population 21.7 months (95% CI 16.7 – 24.6). Furthermore, patients in the reference group had a 1.79-fold death-rate, as compared to patients treated with additional loco-regional therapy (HR = 2.02; 95% CI: 1.29-3.16). **Conclusions:** Additional treatment with loco-regional therapies of distant metastases in patients with metastatic colorectal cancer appears to be associated with improved OS by nearly 10 months compared to systemic treatments only. Research Sponsor: None.

Overall survival	Liver metastases only	Liver and lung metastases only	Total
Study population	N = 20	N = 23	N = 51
Events, n (%)	12 (60.0%)	14 (60.9%)	32 (62.7%)
Censored, n (%)	8 (40.0%)	9 (39.1%)	19 (37.3%)
Median OS (months)	26.9	41.6	31.3
95% Confidence interval	19.2 - 33.4	30.5 - 78.2	26.8 – 41.6
Reference population	N = 583	N = 168	N = 788
Events, n (%)	298 (51.1%)	96 (57.1%)	416 (52.8%)
Censored, n (%)	285 (48.9%)	72 (42.9%)	372 (47.2%)
Median OS (months)	23.0	21.7	21.9
95% Confidence interval	20.4 - 26.2	16.7 - 24.6	20.1 – 24.6

4097 Poster Session (Board #89), Fri, 8:00 AM-11:00 AM

Phase II trial of adjuvant mFOLFOX6 after metastasectomy for pulmonary metastasis of colorectal cancer: WJOG5810G. *First Author: Nozomu Machida, Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Japan*

Background: Resection of pulmonary metastasis (PM) is widely accepted to improve the prognosis in selected patients (pts) with metastatic colorectal cancer (CRC). However, the clinical implication of adjuvant chemotherapy after metastasectomy of PM is unknown. We conducted a multi-center phase 2 trial of adjuvant chemotherapy with mFOLFOX6 after metastasectomy of PM-CRC. **Methods:** Main eligibility criteria were first curative metastasectomy of 4 or less PMs and no prior chemotherapy except for adjuvant chemotherapy with fluoropyrimidine monotherapy after curative resection of primary or extrathoracic CRC metastasis. The study treatment was 12 courses of mFOLFOX6 (oxaliplatin 85 mg/m^2, l-leucovorin 200 mg/m^2, 5-fluorouracil 400 mg/m^2 bolus followed by 2400 mg/m^2 continuous infusion, every 2 w). The primary endpoint was overall survival (OS). The secondary endpoints included disease-free survival (DFS), adverse events (AEs), and recurrence sites. The sample size was determined to be 93 expecting 5-year OS rate of 50% with threshold 35% (90% power, alpha error 5%). **Results:** Fifty-two pts from 34 institutions were enrolled between July 2011 and July 2014. Patient enrollment was closed prematurely because of slow accrual. Four patients were ineligible after enrollment and the safety and efficacy cohort comprised 52 and 48 patients, respectively. Patient backgrounds were as follows: gender (male/female) 31/21, median age (range) 63 (42-75) years, ECOG PS (0/1) 48/4, primary site (colon/rectum) 18/34, number of PM (1/2/3/4) 36/9/5/2, synchronous/metachronous PM 11/41, and unilateral/bilateral PM 40/12. With the median follow-up time of 6.0 (1.8-7.7) years, 5-year OS rate was 86% (95% CI: 72-93) and 5-year DFS rate was 59% (95% CI: 43-71). Tumors recurred in 19 patients (13 lung, 3 liver and 7 others). Total 41 pts (79%) completed 12 courses of mFOLFOX6 (reasons for discontinuation: AEs in 3, refusal due to AEs in 8). AEs (> Grade 3) were neutropenia 50%, fatigue 8%, peripheral sensory neuropathy 8%, appetite loss 4%, diarrhea 4%, febrile neutropenia 2% and allergic reaction 2%. There was no treatment related death. **Conclusions:** Adjuvant mFOLFOX6 is feasible and may be effective after metastasectomy for PM-CRC, considering much better OS than we had expected. Clinical trial information: UMIN000005693. Research Sponsor: None.

4098 Poster Session (Board #90), Fri, 8:00 AM-11:00 AM

Is there a benefit of oxaliplatin in neoadjuvant treatment of locally advanced rectal cancer? An updated meta-analysis. *First Author: Gaetan Des Guetz, CH Delafontaine, St Denis, France*

Background: Neoadjuvant fluoropyrimidine (5FU or capecitabine)-based chemoradiotherapy (CRT) has been considered the standard of care for locally advanced rectal cancer (LARC). Whether addition of oxaliplatin (OXP) will further improve clinical outcomes is still unclear. **Methods:** To identify clinical trials combining oxaliplatin in preoperative CRT or perioperative chemotherapy for LARC published until December 2019, we searched PubMed, the Cochrane Library. We also search for relevant ASCO conferences. Primary endpoint was Disease-Free-Survival (DFS). Data were extracted from every study to perform a meta-analysis using Review Manager (version 5.3). **Results:** A total of 7 Randomized Clinical Trials (ACCORD-12, CARO-AIO-04, FOWARC, JIAO, NSABP, PETACC-6 and STAR-01) with 5782 stage II or III rectal cancer patients were analysed, including 2727 patients with OXP + 5FU regimen and 3055 patients with 5FU alone regimen. Compared with 5FU-based regimen group, OXP-based regimen group improved DFS (HR = 0.90, 95% CI: 0.81−0.99, P = 0.03) and increased pathologic Complete Response (OR = 1.21, 95% CI: 1.07−1.37, P = 0.002). Patients treated with OXP-regimen had significantly less metastatic disease (OR = 0.79; 95% CI, 0.67 to 0.94; p = 0.007). Considering Adverse Events (AEs), there was more grade 3-4 diarrhoea with OXP (OR = 2.41, 95% CI: 1.74−3.32, P < 0.00001). However, there were no significant differences grade 3-4 haematologic AEs (OR = 1.16, 95% CI: 0.87−1.57, P = 0.31). **Conclusions:** Combining oxaliplatin with capecitabine or 5FU in preoperative chemoradiotherapy or perioperative chemotherapy seems beneficial significantly and improved DFS. It remains necessary to identify which patients benefit most from the addition of oxaliplatin. Research Sponsor: None.

4099 Poster Session (Board #91), Fri, 8:00 AM-11:00 AM

Clinicopathological and molecular biological characteristics of early-onset stage II/III colorectal adenocarcinoma: An analysis of 25 studies with 47,184 patients (pts) in the adjuvant colon cancer end points (ACCENT) database. *First Author: Zhaohui Jin, Mayo Clinic, Rochester, MN*

Background: Colorectal cancer (CRC) incidence and mortality has decreased since the 1970s but the incidence is increasing in young adults (age 20-49). The incidence of early onset CRC (eoCRC) will keep increasing significantly based on the trends of the SEER CRC registry data. There is limited data suggesting eoCRC may have different behaviors compared to traditional CRC (tCRC, age ≥ 50). **Methods:** Individual pt data of 47184 stage II/III CRC pts from 25 randomized studies in the ACCENT database were pooled. The distributions of demographics, clinicopathological features, biomarker status, and treatment-related data were summarized by age group. Overall survival (OS), disease-free survival (DFS), recurrence-free rate (RFR), and survival after recurrence (SAR) were assessed by Kaplan-Meier curves and Cox models stratified by treatment arms within studies, adjusting for stage, performance status (PS), BMI and grade. **Results:** Using 5% difference between age groups as clinically meaningful cutoff, eoCRC had similar gender, race, ethnicity, PS, risk group, disease sidedness and T stage as tCRC. eoCRC were less likely overweight (30 vs 36%) and more pts had ≥ 12 lymph nodes resected (63 vs 51%). eoCRC had more frequent dMMR status (18 vs 12%), less BRAF mutations (5 vs 13%), and more dMMR/BRAF wild type (WT) status (17 vs 7%). Overall, eoCRC had better OS, DFS, and SAR, with the most significant differences between the < 30 and > = 70 age groups. Similar results were observed within pMMR pts. eoCRC experienced less hematological side effects, diarrhea, and stomatitis, but had more nausea and/or vomiting. **Conclusions:** eoCRC have unique characteristics; although statistically significant, the clinical differences in outcomes between eoCRC and tCRC are potentially due to the difference seen in extremely young and old pts. eoCRC have a different adverse events panel compared to tCRC. Research Sponsor: U.S. National Institutes of Health.

	eoCRC	tCRC	Adjusted Hazard Ratio	95% Confidence Interval
Overall				
n	8242	38942		
5-y OS,%	78.9	74.4	0.75	0.69-0.82**
5-y DFS, %	68.9	65.2	0.87	0.81-0.93**
5-y RFR, %	70.2	68.8	0.94	0.88-1.01
median SAR, mos	25.2	21.6	0.81	0.74-0.89**
pMMR				
n	2121	9710		
5-y OS,%	81.3	78.8	0.76	0.66-0.88**
5-y DFS, %	70.8	67.9	0.86	0.76-0.97*
5-y RFR, %	72.2	70.8	0.95	0.83-1.07
median SAR, mos	30.0	25.2	0.87	0.75-1.02
dMMR				
n	471	1364		
5-y OS,%	86.7	80.7	0.62	0.41-0.93*
5-y DFS, %	80.0	75.9	0.74	0.53-1.04
5-y RFR, %	81.2	80.6	0.86	0.60-1.23
median SAR, mos	27.6	15.6	0.78	0.48-1.28

4100 Poster Session (Board #92), Fri, 8:00 AM-11:00 AM

Short-term results of VOLTAGE-A: Nivolumab monotherapy and subsequent radical surgery following preoperative chemoradiotherapy in patients with microsatellite stable and microsatellite instability-high locally advanced rectal cancer. *First Author: Satoshi Yuki, Department of Gastroenterology and Hepatology, Hokkaido University Hospital, Sapporo, Japan*

Background: Chemoradiotherapy (CRT) followed by radical surgery (S) is standard therapy for patients (pts) with locally advanced rectal cancer (LARC). Sequential use of an anti-PD-1 antibody after radiation demonstrates synergistic effects in *in vivo* models, and an anti-PD-1 antibody is effective in pts with microsatellite instability-high (MSI-H) metastatic colorectal cancer (mCRC). We studied nivolumab (nivo) and radical S following CRT (50.4 Gy with capecitabine 1,650 mg/m^2) in T_{3-4} $N_{any}M_0$ LARC. **Methods:** After the quality-assured CRT, 240 mg q2 weeks x 5 cycles of nivo and radical S were investigated. In cohort A-1, for pts with microsatellite stable (MSS) LARC, the primary endpoint was a centrally confirmed pathological complete response (pCR) rate using AJCC tumor regression grading. The estimated required sample size assuming null and alternative hypotheses pCR = 10% and 30% was 37 pts, with a 1-sided alpha of 5% and power of 90%. In Cohort A-2, 5 pts with MSI-H LARC were included in an exploratory manner. **Results:** From Jan/2017 to Oct/2019, a targeted number of pts was included and assessed. In cohort A-1, 30% (11/37; 90% CI 18-44%) of pCR (AJCC grade (gr) 0) rate and 38% (14/37) of major pathological response (MPR) (AJCC gr 0+1) rate were observed. Clinical CR was observed in one additional pt (3%) refusing S after nivo. In cohort A-2, 60% (3/5) of pCR rate and 60% (3/5) of MPR rate were observed. As of Jan/2020, only 2 pts (1 local and 1 metastatic) in cohort A-1 and none in cohort A-2 recurred. Immune-related severe adverse events were observed in 3 pts (gr 3 myasthenia, gr 3 interstitial nephritis, and gr 2 peripheral motor neuropathy); all fully recovered and received radical S. During the follow-up period, one additional pt with gr 2 colitis was observed. No treatment-related deaths were observed. **Conclusions:** Promising pCR rates of 30% and 60%, with mild toxicities, were shown in MSS and MSI-H LARC pts treated with nivo plus radical S after CRT, suggesting the candidate therapy for the future non-surgical approach. Clinical trial information: NCT02948348. Research Sponsor: ONO Pharmaceutical.

4101 Poster Session (Board #93), Fri, 8:00 AM-11:00 AM

ARISTOTLE: A phase III trial comparing concurrent capecitabine with capecitabine and irinotecan (Ir) chemoradiation as preoperative treatment for MRI-defined locally advanced rectal cancer (LARC). *First Author: David Sebag-Montefiore, University of Leeds, Leeds, United Kingdom*

Background: Phase II studies reported high pathological complete response (pCR) rates and acceptable toxicity using irinotecan and fluoropyrimidine chemoradiation in LARC (ISRCTN:09351447). **Methods:** This phase III, multicentre, open-label trial funded by Cancer Research UK, randomly assigned (1:1) patients with MRI defined LARC threatening or involving resection margins without metastases, to pre-operative radiotherapy (RT) 45Gy/25 fractions combined with either capecitabine 900mg/m^2(CRT) or 650 mg/m2 bd weekdays with Irinotecan iv once-weekly 60mg/m2 weeks 1-4 (IrCRT). The primary endpoint is disease-free survival (DFS). Secondary endpoints include treatment compliance, safety and pCR. **Results:** 75 UK sites randomised 564 eligible patients from Oct/11 to July/18; 284 to CRT and 280 to IrCRT. 370 (66%) male; median age 61 years (range:29-83). Staging in both arms was similar: mrT3 (432/564(77%), mrT4 (89/564(16%); mrCRM involved (275/564(49%); threatened ≤1mm (215/564(38%). Compared with CRT, IrCRT patients were less likely to receive 45Gy RT (207/276(75%) vs 251/283(89%), p < 0.001) or receive ≥90% capecitabine dose in 188/276(68%) vs 253/283(89.4%)p < 0.001). A total of 204/276(74%) received ≥90% irinotecan dose. The grade 3-4 gastrointestinal adverse event rate was 21%(58/276) with IrCRT and 12%(34/283) with CRT (p = 0.004). Patients receiving IrCRT had significantly more diarrhoea 38/276(13.8%) vs 10/283(3.5%)p < 0.001) and neutropenia 27/276(9.8%) vs 3/283 (1.1%) p < 0.001). Two CRT and three IrCRT patients experienced a treatment related death. 237/276(86%) IrCRT and 241/283(85%) CRT patients had surgery. The median time from end of RT to surgery(10.6 weeks), the surgical procedure APE 262/478(55%), AR 189/478(40%), Hartmann's 10/478(2%); and the surgical complications(any event) 38%(181/478) were similar in both arms. The pCR rate is available in > 95% patients and is 20.2%(46/228) for IrCRTvs.17.4%(40/230) for CRT (p = 0.45), A > 84% CRM-ve resection rate is similar in both arms. **Conclusions:** For patients with MRI defined high risk LARC low rates of CRM involvement were observed in both arms reflecting high quality multidisciplinary care. The addition of irinotecan did not significantly improve the pCR rate, was associated with a decrease in the RT and capecitabine compliance and a higher rate of adverse events. Surgical procedure or complications were unaffected. Longer follow-up is required to assess DFS and translational data. Clinical trial information: 09351447. Research Sponsor: Cancer Research UK.

4102 Poster Session (Board #94), Fri, 8:00 AM-11:00 AM

Randomized phase II trial of modified (m) FOLFOX6 induction chemotherapy with or without aflibercept before standard chemoradiotherapy (CRT) and total mesorectal excision (TME) in patients with high-risk rectal adenocarcinoma (HRRC): Final results of the GEMCAD 1402, and by molecular subtypes. *First Author: Carlos Fernandez-Martos, Hospital Quironsalud, Valencia, Spain*

Background: Neoadjuvant chemotherapy (CT) followed by CRT and TME is a treatment option for clinically staged HRRC. The goal of the GEMCAD 1402 trial was to evaluate the benefit of adding an antiangiogenic drug to the neoadjuvant CT. The analysis of primary endpoint showed a better response rate in the experimental arm (Fernandez-Martos et al. Jama Oncol 2019). Here we present 3-year disease-free survival (DFS) and a retrospective analysis of consensus molecular subtypes by Immunohistochemistry (CMSs-IHQ). **Methods:** Patients (p) with middle or distal third, mrT3/T4/N2 rectal adenocarcinoma were randomly assigned (2:1), to mFOLFOX6 with (arm 1, n=115) or without Aflibercept (arm 2, n=65) prior to CRT (capecitabine with 50.4 Gy in 28 fractions) and TME. Tissue microarrays from 90 (58 arm1, 32 arm 2) p were stained for nine markers (CDX2, FRMD6, HTR2B, ZEB1, KER, MSH2, MSH6, PMS2 and MLH1) by IHQ using both semiquantitative and quantitative approaches. Cases were classified as CMS1-IHQ1, CMS-IHQ2/3 or CMS-IHQ 4 (immune, epithelial or mesenchymal subtypes). **Results:** In the intention-to-treat population after a median follow-up time of 38 months, 29 p (25%) in arm 1 had a DFS-related event, as compared with 14 p (21%) in arm 2 (HR 1.2063, 95% confidence interval 0.6374 to 2.2829, P=0.5644. The rate of DFS at three years was 75.2% (95% confidence interval, 66.1% to 82.2%) in arm 1 and 81.5% (95% confidence interval, 69.8% to 89.1%) in arm 2 (P=0.5638 by the exact stratified log-rank test). Overall 0/80/10 p were classified as CMS-IHQ1, CMS-IHQ2/3 or CMS-IHQ4 respectively. The pathological complete response (pCR) rate (ypTON0) was achieved in 27.5% and 0% in epithelial and mesenchymal subtypes respectively. A trend towards worse survival for the mesenchymal subtype was observed. **Conclusions:** Adding aflibercept to induction mFOLFOX6 is not associated with an improvement in DFS. Our findings suggest that CMSs-IHQ subtypes could be predictive for pCR with this treatment strategy. Clinical trial information: NCT02340949. Research Sponsor: SANOFI.

4103 Poster Session (Board #95), Fri, 8:00 AM-11:00 AM

Utilization of adjuvant chemotherapy in "ideal candidates" with stage III colon cancer. *First Author: Mohsin Soleja, UT Southwestern Medical Center, Dallas, TX*

Background: Prior studies have observed under-utilization of adjuvant chemotherapy (ACT) in stage III colon cancer. Our aims were to observe the rate of utilization of ACT in very healthy or "ideal candidates", identify reasons for omission and socioeconomic factors associated with ACT use, and observe patient outcomes. **Methods:** We queried patients from the National Cancer Database (NCDB) with stage III colon cancer, age<65, and Charlson-Deyo score of 0 who underwent resection in the United States between 2004-2015. Patients who received ACT were compared to patients who had surgery only (SO). We used chi-square test for categorical variables, Kaplan-Meier and Cox regression method for survival analyses. **Results:** Out of 243,388 stage III colon cancer patients during the study time, a total of 49,046 patients met the specific criteria of "ideal candidate". Out of these, 88.5% received ACT and 11.5% underwent SO. The primary reason for chemotherapy omission was: no reason given (54.2%), patient/guardian refusal (26.7%), physician recommended against (9.3%), patient died (3%), unknown (6.7%). Patients who received ACT were more likely to be female, non-Hispanic white, have a higher level of education, travel shorter distance for cancer treatment, have private insurance or higher income as compared to counterpart (*all p<.001).* Patients who received ACT had significantly better overall survival (5-year survival rate 74% vs. 54%, *p<.001*). This persisted after multivariable Cox regression analysis [HR:0.48 (CI:0.45-0.50), *p<.001].* **Conclusions:** We observed a high rate of utilization (88.5%) of ACT in patients with stage III colon cancer who were under age 65 and without comorbidities. However, the omission of chemotherapy in this population remains a problem, partially due to patient refusal. Socioeconomic factors associated with lower utilization were primarily related to insurance status (private vs non-private). Patients who received ACT had significantly improved survival as compared to SO group. Research Sponsor: None.

Rate of utilization of adjuvant chemotherapy in "ideal candidates" from 2004-2015.

Characteristics	Adjuvant Chemotherapy	Surgery Only	p value
Total Population	43,382 (88.5%)	5,664 (11.5%)	
Private Insurance	32,426 (90%)	3,280 (9.2%)	*<0.001*
Medicaid/Uninsured	6,868 (83%)	1,371(17%)	*<0.001*
Distance > 50 miles	3,094 (84%)	605 (16%)	<0.001
Income<$40,227	8,230 (86%)	1,336 (14%)	*<0.001*
5-year survival rate %	74	54	*<0.001*

4104 Poster Session (Board #96), Fri, 8:00 AM-11:00 AM

Pharmacokinetically-guided preoperative FOLFOX chemotherapy for locally advanced colon cancer patients. *First Author: Lucia Ceniceros, Department of Medical Oncology, Gastrointestinal Oncology Unit, Clínica Universidad de Navarra, University of Navarra, Madrid, Spain*

Background: Preliminary results from ongoing randomised trials suggest that neoadjuvant chemotherapy (NAC) may be an alternative approach to conventional adjuvant therapy. We assessed the feasibility and activity of incorporating a pharmacokinetically (PK) guided dose adjustment of 5-FU within preoperative Folfox. **Methods:** Radiologically staged LACC pts, T4 or T3 with extramural depth >5mm beyond the muscularis propia, were planned to receive 4-6 biweekly cycles of Oxalipatin (85mg/m^2), Leucovorin (400 mg/m^2), bolus 5-FU (400 mg/m2) and infusional 5-FU (initial dose of 2400mg/m^2 in 46h and subsequent cycles tailored according to PK monitoring in order to reach a target 5-FU area under the curve (AUC) between 20-30 mg•h•L-1). Dihidrouracil deshidrogenase was determined before the first cycle in order to detect pts with 5-Fu intolerance. Three serum samples were obtained during the 5-Fu infusion in the first two cycles. Pathological tumor regression was graded according to the MSKCC classification and toxicity to the NCI-CTCAE 4.0. **Results:** From June 2012 to August 2017, 45 pts (M/F: 35/10; median age 63) with LACC (T3: 66.7%; T4: 31.1%; T2: 2.2%; N+:66.6%) were evaluated. Median dose of 5-FU was 4500 mg. 48.9% of the pts required a 5-FU dose increase to reach the target AUC. Side effects profile included G3 neutropenia (3 pts), G2 diarrhea (2 pts) and G2 asthenia (9 pts). NAC was discontinued in 3 pts due to small bowell obstruction requiring surgery (no progressive disease during NAC). R0 resection rate was 100% (93.3% laparoscopy-assited). MSKCC score included grades 4, 3+ and 3 in 11.1%, 26.7% and 28.9% of pts, respectively. A complete pathological response was found in 5 pts (11.1%). Median number of harvested nodes was 16 (7-51), 80% ypN0. Those pts with AUC 25-30 had a 3-fold higher likelihood of achieving a MSKCC 3, 3+ and 4 responses. Median time to hospital discharge was 7 days (range 4-22). After a median follow-up of 60 months (44-66), 5-year actuarial PFS is 88.8%. **Conclusions:** Preoperative PK-adjusted FOLFOX in LACC pts is safe and well tolerated, achieving remarkable rates of major pathological responses and R0 resections. Research Sponsor: None.

4105 Poster Session (Board #97), Fri, 8:00 AM-11:00 AM

Immunoscore as a parameter predicting time to recurrence and disease-free survival in T4N0 stage II colon cancer patients. *First Author: Jerome Galon, HalioDx, Marseille, France*

Background: Risk assessment is particularly important to decide when to propose an adjuvant treatment for Stage II Colon Cancer (CC) patients. However, the current tumor risk features are imperfect and additional risk factors are needed to guide treatment decisions. The consensus Immunoscore is an alternative and powerful approach that could be used in the T4N0 Stage II colon cancer population. Immunoscore is an *in vitro diagnostic* test that predicts the risk of relapse in patients with CC by measuring the host immune response at the tumor site. **Methods:** From the international Immunoscore consortium study (n = 2681) (Pagès et al. *The Lancet* 2018), a subgroup analysis was performed on T4N0 Stage II colon cancer patients (n = 208). **Results:** In stage II T4N0, Int+Hi Immunoscore represented 65.4% of the population and low-Immunoscore only 34.6%. T4N0 patients with Int+Hi Immunoscore presented a significantly prolonged survival for TTR compared to low Immunoscore patients (5 years recurrence rate Int+Hi: 84.6% (78.3-91.5), Lo: 46.3% (35.1-61); unadjusted HR [Int+Hi *vs* Lo] = 0.21; (95% CI 0.11-0.4); *P*< 0.0001), representing a restricted mean survival time (RMST) difference of 80.9 months (95% CI 51.1-110.6) (*P*< 0.0001). The DFS was significantly different between Int+Hi and Low Immunoscore (5 years recurrence rate Int+Hi: 70.5% (95% CI 62.7-79.1), Lo: 38.5% (95% CI 28.2-52.5); unadjusted HR [Int+Hi *vs* Lo] = 0.31; (95% CI 0.19-0.49); *P*< 0.0001). Using restricted mean survival time (RMST) a significant (*P*< 0.0001) difference of 60.4 months (95% CI 32.6-88.1) was observed between the 2 groups Importantly, Cox multivariate analysis in Stage II T4N0 colon cancer patients, revealed that Immunoscore was the only remaining significant parameter (HR [Int+Hi *vs* Lo] = 0.15; (95% CI 0.05-0.46); *P*= 0.0009). In contrast, all other parameters, gender, sidedness, mucinous, grade, T-stage, VELIPI, MSI were not significant in multivariate analysis. Finally, Immunoscore showed the highest relative contribution to predict relapse (76.2% chi2 relative contribution), stronger than all the other parameters, MSI (16.1%), Grade (5%), sidedness (2%), gender (2%), VELIPI (1%). **Conclusions:** Immunoscore is the most powerful parameter to predict the risk in T4N0 population, and could be a good tool for adjuvant treatment decision in Stage II patients. Research Sponsor: French National Institute of Health and Medical Research, the LabEx Immuno-oncology, the Transcan ERAnet Immunoscore European project, Association pour la Recherche contre le Cancer, CARPEM, AP-HP, Institut National du Cancer, Italian Association for Canc.

4106 Poster Session (Board #98), Fri, 8:00 AM-11:00 AM

Impact of antibiotics (ATB) on the recurrence of resected colorectal cancer (CRC): Results of EVADER-1 a nation-wide pharmacoepidemiologic study. *First Author: Benoit Rousseau, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Recent studies suggest that ATB increase the overall risk of CRC incidence through disruption of gut microbiota. Impact of ATB on the risk of CRC recurrence after curative resection remains unknown. **Methods:** Using the French nation-wide *Institut National du Cancer* (INCa – Système National des Données de Santé) database of cancer patients, all newly diagnozed localized CRC patients resected between 01/2012 and 12/2014 were involved. The perioperative ATB intake (6 month before until 1 year after surgery) was classified according to the spectrum, doses and period of use. The primary endpoint was 3-year Disease-Free Survival (3-DFS), stratified on chemotherapy (chemo) administration (yes/no), and assessed using multivariate Cox models. **Results:** Out of 219,884 CRC patients, the present study included 36,640 patients: male 53%, age≥75 years 39%, left colon/rectal 59%, exposure to chemo 44%, at least one ATB intake 74%. At 3-years, 29% of patients had recurred and 18% had died. In multivariate analysis, in patients not receiving chemo, ATB intake as an out-patient was significantly associated with better 3-DFS [HR (one ATB only) = 0.88 (0.82-0.94)]. This effect remained in the same range whatever the number of ATB or cumulative exposure to ATB. In patients receiving chemo, ATB intake as an out-patient had a significant detrimental effect on 3-DFS [HR (one ATB only) = 1.15 (1.08-1.23)], increasing with the number of ATB [HR (≥5 ATB) = 1.54 (1.39-1.71)] and longer exposure [HR (> 30 days) = 1.39 (1.31-1.48)]. Penicillin A, quinolones and ATB combinations were associated with worse 3-DFS. The timing of ATB intake related to chemo revealed that the strongest deleterious effect was observed when ATB were taken during chemo [HR = 1.64 (1.53-1.75)]. No difference in the mean number of chemo cycle was observed comparing patients receiving ATB or not. **Conclusions:** This nation-wide study is the first to suggest that ATB modulate 3-DFS in resected CRC with a differential impact according to chemo exposure. Importantly, ATB intake with chemo is detrimental in a dose- and time-dependent manner suggesting that dysbiosis of gut microbiota during adjuvant chemo might increase risk of recurrence. Research Sponsor: None.

4107 Poster Session (Board #99), Fri, 8:00 AM-11:00 AM

Total mesorectal excision compared to local excision in locally advanced rectal cancer achieving complete pathological response with neoadjuvant therapy: A National Cancer Database Analysis. *First Author: Ahmed Abdalla, Ascension St John, Grosse Pointe Woods, MI*

Background: Total mesorectal excision (TME) is the standard surgical intervention for patients with locally advanced rectal cancer (LARC) regardless of response to neoadjuvant therapy. In this study, we perform a comprehensive review of the National Cancer Database (NCDP) to compare the clinical and surgical outcomes of TME to local excision (LE) in patients with LARC. **Methods:** NCDP was systematically researched to abstract all patients with stage II and III rectal adenocarcinoma between the years 2004 and 2015. We subsequently excluded all the patients who did not achieve complete pathological response (pT_0) after neoadjuvant therapy. The patients were then divided into two groups; those who underwent TME and those who underwent LE. Data were analyzed using SPSS v. 26.0, SAS v. 9.4. **Results:** A total of 4,705 were included in the study; 4,589 in the TME group and 116 in the LE group. Baseline characteristics were similar between the groups except for age. A total of 81(1.8%) of patients in the TME group and 8(6.9%) of patients in the LE group did not receive radiation (p=0.006) and 19(0.4%) of patients the TME group and 4(3.4%) of patients in the LE group did not receive chemotherapy. There was no difference in median overall survival between TME and LE groups. The median length of hospital stay was remarkably shorter in the LE group compared to the TME group (1 day vs 6 days, p<0.0001). The rate of 30-day and 90-day postoperative mortality were similar between the two groups (p-value=0.334 and 0.06, respectively). In the LE group, 4 (3.4%) of patients were readmitted within 30 days of the resection compared to 374 (8.5%) in the TME group but was not a statistically significant difference (p=0.059). **Conclusions:** In this study, TME and LE had similar overall survival and time to 25% mortality in patients with LARC who achieved complete pathological response after neoadjuvant therapy. Also, LE had a shorter hospital stay compared to the TME group. This study is limited by its retrospective nature, however these interesting observations warrant further investigation in randomized clinical trials. Research Sponsor: None.

	Local excision (N=116)	TME	P
Age (years)	64.6	59.7	0.00
Sex			0.92
Male	70 (60.3%)	2788(60.8%)	
Female	46 (39.7%)	1801 (39.2%)	
Race			
White	103 (88.8%)	3944 (85.9%)	0.397
Black	9 (7.8%)	342 (7.5%)	
Other	4 (3.4%)	303 (6.6%)	
Readmission within 30 days of surgical discharge	4/115 (3.5%)	376(8.4%)	0.059
90 day mortality after surgery	1 (0.9%)	44 (1.%)	0.06
Median duration of surgical admission	1 days	6.0 days	<0.001

4108 Poster Session (Board #100), Fri, 8:00 AM-11:00 AM

Tumor-informed assessment of molecular residual disease and its incorporation into practice for patients with early and advanced-stage colorectal cancer (CRC-MRD Consortia). *First Author: Pashtoon Murtaza Kasi, Mayo Clinic, Jacksonville, FL*

Background: Circulating tumor DNA (ctDNA) testing can be used for the assessment of molecular residual disease (MRD) in patients with early-stage or advanced colorectal cancer (CRC). Prospective evaluation of this methodology in clinical practice has been limited to-date. **Methods:** A personalized and tumor-informed multiplex PCR assay (Signatera 16-plex bespoke mPCR NGS assay) was used for the detection and quantification of ctDNA for MRD assessment. We analyze and present results from an ongoing early adopter program of ctDNA testing across the spectrum of CRC management. **Results:** Here we present a total of 250 patients with colon (n=200), rectal (n=40), and other lower gastrointestinal cancers (n =10; anal, appendiceal, small bowel). MRD positivity rates and ctDNA quantification (mean tumor molecules/mL) are shown in Table. ctDNA detection was significantly associated with stage of disease (p<0.0001 Chi-square: 70.33). Additionally, in patients with radiologically measurable active metastatic disease, ctDNA detection rate was 100%. On the contrary, patients with advanced/metastatic disease who had partial response to treatment or no evidence of disease (NED) showed 28.5% and 19.2% of ctDNA-positivity, respectively. **Conclusions:** This is the first large, real-world study reporting on the results from a clinically validated MRD assay. For the first time we delineate MRD rates and quantify ctDNA concentration in patients with early-stage and advanced CRC. Furthermore, we provide an initial readout that effective ongoing treatment in patients with CRC may be correlated with ctDNA clearance. Ongoing analysis expanded to a cohort of 1200 clinical cases including correlation with genomic and serial testing will be presented. Research Sponsor: Natera, Inc.

MRD rates and quantity of ctDNA detected in patients with early-stage and advanced CRC.

Stages	MRD rates	Quantity of ctDNA (MTM/ml)
Stage I (T1-2N0)	0/6 (0%)	Mean: 41.91.8 Median: 0.63 Range: 0.11-673.01
Stage II (T3N0)	2/28 (7.1%)	
Stage II (T4N0)	2/6 (33%)	
Stage III, low-risk (T1-3N1)	2/18 (11%)	
Stage III, high-risk (T4, N1-2, T Any, N2)	7/19 (37%)	
Stage IV (Oligo-metastatic S/P resection/ablation MRD setting)	14/31 (45.2%)	
Stage IV (Metastatic)*	22/49 (44.9%)	Mean 1858 Median: 2.95 Range: 0.17 – 27,077

* Breakdown of ctDNA-positivity by clinical scenario is described in results

4109 Poster Session (Board #101), Fri, 8:00 AM-11:00 AM

Inpatient mortality, healthcare resource utilization, and complications of elective laparoscopic versus open colectomy in colon cancer patients: A nationwide inpatient sample analysis. *First Author: Ishaan Vohra, John H. Stroger, Jr. Hospital of Cook County, Chicago, IL*

Background: Laparoscopic colectomy (LC) has become an accepted safe and alternative technique to open surgical colectomy (OC) as a treatment option for colon cancer. We compared inpatient mortality, hospital resource utilization and complications in patients who underwent LC vs OC. **Methods:** All patients with known diagnosis of colon cancer who underwent elective colonic resection were identified using Nationwide Inpatient Sample (NIS) 2017. Univariate and multivariate linear and logistic regression was performed to compare the outcomes of patients who underwent LC vs OC. **Results:** In our cohort, 171, 480 adult patients with colon cancer were identified. The number of males and females were equal. The mean age was 67.2 years. They were predominantly Caucasians (67.6%). OC was performed on 3,869 patients. Of 1,345 patients who underwent LC, 385 were converted to OC. As compared to OC, LC was associated with lower postoperative complications including anastomotic leak, stricture, intestinal obstruction(1% vs 10.8%, p<0.01), blood transfusion(2.2 % vs 11.2% p=0.01), malnutrition(0.2% vs 4.4% p=0.02), shock(0.7% vs 1.8%,p=0.04), ICU care(1.9% vs 5.3%), mean length of stay (5.9 days vs 8.7 days, p=0.01), lower hospital charge (88,642$ vs 106,315 $,p<0.01) and lower mortality(0.3% vs 1.9%(p=0.02). There was a trend towards decreased venous thromboembolism (0.3% vs 1.7 %, p=0.9) and post-operative ileus (0.1% vs 0.7% p=0.60) in LC as compared to OC. On multivariate analysis, independent predictors of undergoing LC were younger age, teaching and large bed-sized hospital and lower Charlson comorbidity index. Race, insurance status and income had no significant association with selection of operative approach (Table). **Conclusions:** In our cohort, laparoscopic colectomy was found to have better peri and post-operative clinical outcomes including decreased inpatient mortality and hospital resource utilization. It should be promoted as the curative surgical option for colon cancer whenever clinically indicated. Research Sponsor: None.

Multivariate analysis for patients undergoing laparoscopic colectomy.

Variables	Adjusted OR (95% CI)	P value
Age (>70 years)	1.21(1.04-1.73)	**<0.01**
Teaching hospital	1.71 (0.95-2.53)	**<0.01**
Charlson Comorbidity score (<=1)	1.87 (1.77-2.99)	**0.029**
Large bed-size hospital	1.17 (1.11-2.46)	**<0.01**
Medicaid insurance	1.03 (0.04-1.29)	>0.05
Private insurance	1.36 (1.00-1.54)	>0.05
African American	0.78 (0.70-1.94)	>0.05
Hispanic	0.66(0.22-1.84)	>0.05

4110 Poster Session (Board #102), Fri, 8:00 AM-11:00 AM

Does neoadjuvant FOLFOX chemotherapy improve the oncological prognosis of high-risk stage II and III colon cancers ? Three years' follow-up results of the Prodige 22 phase II randomized multicenter trial. *First Author: Medhi Karoui, La pitié Salpetrière Hospital, Paris, France*

Background: Neoadjuvant chemotherapy in a perioperative setting has proven valuable in locally advanced resectable colon cancer (CC) in terms of toxicity, postoperative morbidity and downstaging, but its effect on oncological outcomes remains uncertain. **Methods:** Prodige 22 was a randomized multicenter phase II trial in patients with resectable high-risk T3, T4 and/or N2 CC on baseline CT-scan. Patients were randomized to receive either 6 months of adjuvant FOLFOX after colectomy (control) or perioperative FOLFOX for 4 cycles before surgery and 8 cycles after (FOLFOX peri-op). In RAS wild-type (wt) patients a third arm testing perioperative FOLFOX-cetuximab was added. Primary endpoint was the Tumor Regression Grade. Secondary endpoints were 3-years overall (OS), disease-free survival (DFS) and time to recurrence (TTR). **Results:** 120 patients were enrolled. At interim analysis, the FOLFOX-cetuximab arm was stopped for futility. The remaining 104 patients (control, n = 52; FOLFOX peri-op n = 52) represented our intention-to-treat population. In the FOLFOX peri-op group, 96% received the schedule 4 cycles prior to surgery and all but one underwent adjuvant FOLFOX for a total of 12 cycles. In the control arm, 38 patients received adjuvant FOLFOX (1 postoperative death and 13 low-risk stage II patients). Median follow-up was 54.3 months [48.5-57.2]. Nineteen deaths and 26 disease recurrences were observed leading to a 3 years-OS of 90.3% in both arms (p = 0.7) and to a 3-years DFS of 76.8% and 69.2% in the peri-op and control arm respectively (p = 0.6). A trend to a better TTR in the peri-op arm was observed with a 3-years TTR of 82% as compared to 72% in the control arm (p = 0.3). No benefit from adding Cetuximab was observed in the 16 RAS-wt treated patients. **Conclusions:** In this pilot randomized study, perioperative FOLFOX chemotherapy has no detrimental effect on long term oncological outcomes and may be an option for some patients with locally advanced CC. A pooled analysis of randomized trials testing peri-operative strategies in this setting is warranted. Clinical trial information: NCT01675999. Research Sponsor: PHRC 2010, Pharmaceutical/Biotech Company.

4111 Poster Session (Board #103), Fri, 8:00 AM-11:00 AM

Early ileostomy closure is safe and feasible during adjuvant chemotherapy after total mesorectal excision surgery for rectal cancer. *First Author: Xiaodong Gu, Department of General Surgery, Huashan Hospital, Fudan University, Shanghai, China*

Background: The aim of this study was to evaluate the comparative clinical and oncological outcomes of temporary ileostomy closure during or after adjuvant chemotherapy in patients with total mesorectal excision (TME) for rectal cancer. **Methods:** This randomized controlled trial investigated 87 patients (51 males, 36 females) with rectal cancer undergoing TME surgery with temporary ileostomy from January 2016 to December 2018. Patients were randomized divided into 2 groups: early group (43 patients, mean age: 60.35) who underwent stoma closure during adjuvant chemotherapy (3 months after primary surgery) and late group (44 patients, mean age 61.80) who underwent stoma closure after adjuvant chemotherapy (6 months after primary surgery). Both clinical and oncological outcomes were analyzed. **Results:** No significant differences were observed in operative time, blood loss, postoperative hospital stay, postoperative complications or hospital costs in ileostomy closure between the 2 groups. Stoma-quality of life (QOL) of patients in early group was significantly better than late group (52.02 ± 5.68 vs 46.91 ± 5.68, $P < 0.05$). No significant difference in overall survival (P = 0.702) or progression-free survival (P = 0.638) was observed between the 2 groups. **Conclusions:** Ileostomy closure during adjuvant chemotherapy was clinically safe, and interruption of chemotherapy due to ileostomy closure did not change oncologic outcomes. Early ileostomy closure can improve QOL in those patients. Clinical trial information: NCT02665026. Research Sponsor: None.

4112 Poster Session (Board #104), Fri, 8:00 AM-11:00 AM

Patient and tumor characteristics as determinants of overall survival (OS) in *BRAF* V600 mutant (mt) metastatic colorectal cancer (mCRC) treated with doublet or triplet targeted therapy. *First Author: Javier Ros Montañá, Vall d'Hebron University Hospital, Barcelona, Spain*

Background: *BRAF* V600 mt mCRC is an aggressive disease with poor OS under standard chemotherapy. Treatment with doublet and triplet targeted combinations, such as *BRAF* inhibitor+ antiEGFR+/- *MEK* inhibitor, has been shown to improve outcomes. Prognostic factors in this targeted treated population remain to be studied. **Methods:** Prospective international cohort of patients who received doublet or triplet anti-BRAF combinations in clinical trials or as compassionate use. Univariate Cox models for OS were constructed and the strongest predictors in stepwise variable selection were used to develop a prognostic score. The final multivariate model with selected predictors was stratified by prior lines. **Results:** In total, 42 patients were enrolled. Median age 60.7 y (33-83), 61% female, 61% right-sided tumors, 26% received 2 or more prior chemotherapy lines. One patient (2.6%) achieved complete response and 36% had partial response with median follow-up of 14.3 months. Median progression-free survival was 5.5 months (CI95% 4.4-10.4) and median OS (mOS) was 10.7 months (CI95% 8.4-22.1). In univariate models, ECOG performance status (1 vs 0), CEA levels (high - > 3.5 ng/mL- vs low - < 3.5 ng/mL), CA 19.9 (high vs. low), LDH (high vs. low), number of metastatic sites and presence of liver metastasis were significant prognostic factors. On the other hand, MSI status and peritoneal or nodal metastasis did not associate with outcome. In multivariable model, strongest determinants of OS were ECOG and baseline CEA levels. If high-risk for both factors (ECOG 1 and CEA high, 46% of the patients), mOS was 5.6 months (CI95% 4.2-NA); if intermediate-risk (either ECOG 1 or CEA high, 33%), mOS was 13.5 months (CI95% 10.6-NA); if low-risk (ECOG 0 and CEA low, 21%), mOS not reached (CI95% 16.5-NA). Differences between intermediate- and high-risk prognostic groups compared to low-risk were significant (HR = 5.9, p = 0.03; and HR = 25.9, p < 0.001, respectively). **Conclusions:** Patients characteristics such as ECOG and surrogates of tumor burden like CEA levels remain important OS determinants in *BRAF* V600 mt mCRC treated with doublet or triplet targeted therapy. In fact, there are not prognostic scores regarding BRAF mt mCRC treated with targeted therapies. Our study suggests that these prognostic factors may be considered as stratification factors in future clinical trials. Research Sponsor: None.

4113 Poster Session (Board #105), Fri, 8:00 AM-11:00 AM

The landscape of *MAP3K1/MAP2K4* alterations in gastrointestinal (GI) malignancies. *First Author: Matthew K Stein, West Cancer Center, U Tennessee, Memphis, TN*

Background: Inactivating alterations in *MAP3K1/MAP2K4* occur in various solid tumors, sensitize cancer models to MEK inhibitors, and have co-mutation partners which may enable therapeutic targeting. **Methods:** We retrospectively reviewed 20290 GI malignancy patients (pts), comprised of 9986 colorectal carcinoma (CRC) and 10304 non-CRC, whose tumors were profiled with Caris Life Sciences from 2015-2019. Profiling included immunohistochemistry (IHC) with programmed death ligand-1 (PD-L1), next-generation sequencing (NGS), tumor mutational burden (TMB) and deficient mismatch repair or microsatellite instability-high status (dMMR/MSI-H). **Results:** *MAP3K1/MAP2K4*-alteration (*MAP3K1/MAP2K4*-MT) was more frequent in CRC than non-CRC pts (2.0% v. 1.2%, $p<0.0001$), with truncating mutations representing the majority of lesions along both genes. While *MAP3K1/MAP2K4*-MT CRC pts were similar in age and gender to wild-type (WT), mutated non-CRC pts were older (median age 69 v. 65 years) and more likely female (51% v. 42%) compared to WT (both $p<0.05$). *MAP3K1/MAP2K4*-MT CRC (25% v. 7%) and non-CRC (30% v. 3%) were more frequently dMMR/MSI-H than WT pts (both $p<0.0001$). *MAP3K1/MAP2K4*-MT CRC cases were affiliated with higher TMB and similar rate of PD-L1 expression compared to WT. A higher rate of *MAP3K1/MAP2K4*-MT CRC pts were right-sided (36% v. 22%, $p<0.0001$) and transverse (8% v. 4%, $p<0.05$) compared to WT, whereas a higher frequency of WT cases were left-sided (20% v. 28%, $p<0.05$) and rectal (15% v 23%, $p<0.05$). Of microsatellite stable (MSS) CRC pts, those with *MAP3K1/MAP2K4*-MT were more likely *PIK3CA* (26% v. 17%) and *APC* (85% v. 78%) and less-likely *TP53* (64% v. 77%) co-mutated versus WT MSS pts (all $p<0.05$); no difference was seen in *BRAF* V600E, *ERBB2/ERBB3* or *KRAS* co-mutation rate in MSS pts. In both all-comers and MSS CRC, *MAP3K1/MAP2K4*-MT pts were more frequently co-mutated than WT with *ARID1A*, *POLE*, *ATM*, *BRCA2* and *PIK3R1* (all ≥7% of *MAP3K1/MAP2K4*-MT pts, $p<0.0001$). A higher frequency of all-comer non-CRC GI malignancy pts with *MAP3K1/MAP2K4*-MT were co-mutated with *PIK3CA* (13% v. 6%), *ERBB2/ERBB3* (8% v. 3%) or *APC* (13% v. 5%) compared to WT (all $p<0.01$). For MSS non-CRC GI cases, *ARID1A* (50% v. 30%) and *SMAD4* (21% v. 12%) were more frequently co-mutated in *MAP3K1/MAP2K4*-MT versus WT pts (all $p<0.05$). **Conclusions:** Truncating *MAP3K1/MAP2K4* alterations occur in nearly 2% of GI malignancy pts and are more commonly associated with dMMR/MSI-H than WT. Potentially targetable co-mutation partners implicated in MAPK and PI3K pathways as well as *POLE*, *BRCA2* and *ATM* warrant further evaluation. Research Sponsor: None.

TPS4114 **Poster Session (Board #106), Fri, 8:00 AM-11:00 AM**

A phase I/II study of PI3Kinase inhibition with copanlisib combined with the anti-PD-1 antibody nivolumab in relapsed/refractory solid tumors with expansions in MSS colorectal cancer. *First Author: Christopher Jakubowski, Johns Hopkins Oncology, Baltimore, MD*

Background: Certain somatic mutations are thought to promote immune evasion and resistance to immunotherapy. PIK3CA was identified in an *in vivo* genomic screen for mechanisms of resistance to anti-PD1 therapy. MC38 cells (murine colon adenocarcinoma) were engineered to express a library of human cancer-associated mutations from TCGA. Resultant tumors *in vivo* were exposed to immune pressure with anti-PD1 therapy. Cells that proliferated were then analyzed for mutations that impart immune resistance. Multiple activating mutations in *PIK3CA* conferred resistance to anti-PD1 therapy. Coadministered PI3K inhibition reversed this resistance. Multiple studies have shown the impact of the phosphatidylinositol 3-kinase (PI3K) pathway on the tumor microenvironment, and 20% of colorectal cancer (CRC) tumors have an activating mutation of PI3K. **Methods:** A multi-center, open-label, phase I/II study with the combination copanlisib and nivolumab, a PD1 inhibitor, in relapsed/refractory solid tumors with expansions in relapsed/refractory microsatellite-stable (MSS) CRC was developed. Copanlisib is an inhibitor of PI3K and exhibits its most potent inhibitory effect on the isoforms PI3Kα and PI3Kδ. The first phase seeks to determine the maximum tolerated dose (MTD) of copanlisib with fixed dose nivolumab of 480 mg given every 4 weeks. Following determination of the MTD the second phase seeks to determine the 6-month objective response rate of the combination in MSS CRC patients and contains two cohorts 1) PIK3CA wildtype, 2) PIK3CA mutated. The study is planned with 21 evaluable subjects per cohort and allows early termination for lack of efficacy. Tumor assessments will be made using RECIST 1.1. Patients will have a pre-treatment biopsy followed by nivolumab on Day 1 of each 4 week cycle and copanlisib on Day 1, 8 and 15. A second biopsy will occur after six weeks. Eligibility criteria includes completed NGS for PI3K status, and patients must have received at least 2 prior lines of standard therapy. Patients can not have received a prior checkpoint inhibitor or PI3K inhibitor. Secondary and exploratory objectives, in addition to survival and safety outcomes, include exploring immune cell subsets in the local tumor microenvironment and in the peripheral circulation, as well as investigating immune activation and suppressive pathways through RNA expression and additional NGS techniques. The clinical study was activated in January 2019 (NCT03711058). Clinical trial information: NCT03711058. Research Sponsor: American Association for Cancer Research (AACR), Stand Up To Cancer (SU2C), Pharmaceutical/Biotech Company.

TPS4115 **Poster Session (Board #107), Fri, 8:00 AM-11:00 AM**

A phase III study of comparing FOLFOX+/-bevacizumab with FOLFOX+/-bevacizumab+ high-dose intravenous vitamin C as first-line therapy in patients with advanced colorectal cancer. *First Author: Feng Wang, Department of Medical Oncology, Sun Yat-sen University Cancer Centre, Guangzhou, China*

Background: Previous studies showed that high dose vitamin C especially when administered intravenously might have anti-cancer effect. A recent preclinical study found that human colorectal cancer cells harboring KRAS or BRAF mutations are selectively killed by high dose vitamin C. Our phase I dose-escalation and expansion study has shown that high dose (up to 1.5g/kg) intravenous vitamin C with FOLFOX or FOLFIRI is well tolerated in patients with colorectal or gastric cancer. This trial is a randomized, multicenter, phase III study of high dose vitamin C infusion combined with FOLFOX +/- bevacizumab versus FOLFOX +/- bevacizumab as first-line therapy in patients with advanced colorectal cancer. **Methods:** This study has enrolled patients with histologically confirmed metastatic adenocarcinoma of colorectum, normal G6PD status and no prior treatment for metastatic disease. 432 patients are randomized 1:1 into one of two groups. Patients in the control group are treated with mFOLFOX6 (oxaliplatin 85 mg/m^2 d1 concurrent with leucovorin 400 mg/m^2, followed by bolus 5FU 400 mg/m^2 d1, followed by infusional 5FU 2400 mg/m^2 over 46 hours) with or without bevacizumab (5mg/kg, d1) every 2 weeks. Patients in the experimental group are treated with vitamin C intravenously (1.5g/kg/day, d1-3) in combination with mFOLFOX6 with or without bevacizumab every 2 weeks. Randomization is stratified by the location of primary site (left-sided or right-sided) and treatment with bevacizumab (with or without). The primary endpoint is progression free survival (assessed by investigator per RECIST v1.1). Secondary endpoints are overall survival, response rate, assessment of treatment-related adverse events, progression free survival and overall survival in RAS or BRAF mutant patients. Genome, microbiome and metabolome are also assessed. Clinical trial information: NCT02969681. Research Sponsor: Sun Yat-Sen University Clinical Research 5010 Program.

TPS4116 **Poster Session (Board #108), Fri, 8:00 AM-11:00 AM**

A phase Ib/II study of the polo-like kinase 1 (PLK1) inhibitor, onvansertib, in combination with FOLFIRI and bevacizumab for second-line treatment of patients with KRAS-mutated metastatic colorectal cancer (mCRC). *First Author: Daniel H. Ahn, Ohio State University Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH*

Background: Chemotherapy in combination with targeted agents are standard-of-care options for patients for mCRC with response rates >50% in first line. In the second line setting, efficacy of chemotherapy and targeted agents are much lower with response rates of 5% for FOLFIRI (5-fluorouracil, leucovorin, irinotecan) + bevacizumab (anti-VEGF). New treatment options are urgently needed in particular for the 50 % of patients harboring a KRAS mutation. PLK1 is a serine/threonine kinase, master regulator of the mitotic checkpoint and cell division. PLK1 is overexpressed in CRC and its overexpression is associated with poor prognostic. A genome wide RNAi screen identified PLK1 as a synthetic lethal target in KRAS mutant CRC cells, inducing cell cycle arrest and apoptosis upon inhibition. Onvansertib is an oral, highly selective PLK1 inhibitor that demonstrates single agent and synergistic activity with irinotecan in preclinical CRC models. Additionally, KRAS mutated vs wild-type cells showed higher sensitivity to onvansertib. PLK1 inhibition is a potential target in KRAS-mutated mCRC, and the combination of onvansertib + FOLFIRI + bevacizumab may provide a new second-line treatment option. **Methods:** The primary objective of this single-arm Phase 1b/2 study is to assess the safety and preliminary efficacy of onvansertib in combination with FOLFIRI and bevacizumab in the second line setting for KRAS-mutated mCRC patients. For the Phase 1b segment, a standard 3 + 3 dose-escalation design is used to determine the maximum tolerated dose or recommended phase 2 dose (RP2D) of onvansertib. As of January 24, 2020, enrollment in the second dose level is ongoing. Efficacy will be determined by objective response rate (ORR) according to RECIST v1.1 (primary endpoint), progression-free survival and reduction in KRAS allelic burden in liquid biopsies (secondary endpoints). In the phase 2, based on a one-sided one sample log-rank test with 10% Type I error, there will be at least 90% power to detect an improvement in ORR from 5% to 20% with 26 patients. Exploratory endpoints include genomic studies of circulating tumor cells and ctDNA to evaluate altered pathways that correlate with patient clinical response. Clinical trial information: NCT03829410. Research Sponsor: Trovagene.

TPS4117 **Poster Session (Board #109), Fri, 8:00 AM-11:00 AM**

A multicenter phase Ib/II study of DNA-PK inhibitor peposertib (M3814) in combination with capecitabine and radiotherapy in patients with locally advanced rectal cancer. *First Author: Paul Bernard Romesser, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Preoperative chemo-radiotherapy with or without sequential chemotherapy, followed by surgical intervention, is standard of care for patients with locally advanced rectal cancer (LARC). However, 1/3 of these patients still develop distant metastases, indicating the need for more effective therapies. DNA-dependent protein kinase (DNA-PK) regulates a key DNA damage repair pathway for double-strand break repair. Peposertib (M3814), a potent, selective, orally administered DNA-PK inhibitor, has been shown to potentiate the effect of ionizing radiation in a human colon cancer xenograft model and several colon cancer cell lines. Peposertib is being investigated in several different trials across multiple indications. This Phase Ib/II study (NCT03770689) aims to evaluate the safety, tolerability, pharmacokinetics (PK), and efficacy of the neoadjuvant treatment combination of peposertib, capecitabine, and radiotherapy (RT) in patients with LARC. **Methods:** Patients aged ≥18 years with histologically confirmed and resectable Stage II/III rectal adenocarcinoma are eligible. Induction chemotherapy is permitted, but residual disease must first be documented by MRI, digital rectal examination and endoscopy. Patients who received other anticancer therapies or those with prior pelvic RT are excluded. During open-label Phase Ib (open), 18–30 patients (n = 3 per cohort) are due to receive peposertib + capecitabine (orally, 825 mg/m^2 twice daily [BID]) + RT (45–50 Gy), 5 days/week. Peposertib 50 mg once daily (QD) is the starting dose. Additional dose levels will be between 100–800 mg QD. Dose escalation is determined by the safety monitoring committee and guided by a Bayesian 2-parameter logistic regression model. At Phase II (planned), 150 patients will be randomized (1:1) to receive oral capecitabine (825 mg/m^2 BID) + RT (45–50 Gy), with either oral peposertib (recommended phase II dose [RP2D]) or placebo, QD for 5 days/week. Primary objectives are to define a maximum tolerated dose and RP2D (Phase Ib), and to evaluate the efficacy of peposertib + capecitabine + RT in terms of pathological/clinical complete response (Phase II). Secondary objectives include assessment of antitumor activity (Phase Ib), quality of life outcomes (Phase II), and PK of peposertib, and the safety and tolerability of the combination therapy (both phases). One patient has received peposertib 50 mg QD and six patients have received peposertib 100 mg QD. Patients are currently receiving peposertib 150 mg QD. Clinical trial information: NCT03770689. Research Sponsor: Merck KGaA.

TPS4118 Poster Session (Board #110), Fri, 8:00 AM-11:00 AM

NIVACOR: Phase II study of nivolumab in combination with FOLFOXIRI/bevacizumab in first-line chemotherapy for advanced colorectal cancer RASm/BRAFm patients. *First Author: Angela Damato, Medical Oncology Unit. Clinical Cancer Center. AUSL-IRCCS Reggio Emilia, Reggio Emilia, Italy*

Background: FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) plus bevacizumab has been shown to be one of the therapeutic regimens in first line with the highest activity profile in patients (pts) with metastatic colorectal cancer (mCRC) unselected for biomolecular alterations. Tumors co-opt the PD-1/PD-L1 signaling pathway as one key mechanism to evade immune destruction. Anti-PD-1 monoclonal antibodies are FDA approved only for DNA mismatch repair deficient/microsatellite instability-high (MMRd/MSI-H), which are only about 5% among all mCRC. Nowadays, there are no data demonstrating anti-PD1 activity in stable and proficient (MMRp/MSS) disease. Another critical therapeutic target is the Vascular Endothelial Growth Factor A (VEGF-A), which acts on endothelial cells to stimulate angiogenesis; his inhibition with bevacizumab increase immune cell infiltration, giving a strong rationale for combining VEGF targeted agents with immune checkpoint inhibitors. Based on evidence, we explore the combination of triplet chemotherapy (FOLFOXIRI) with bevacizumab and nivolumab in pts with mCRC all-*RAS/BRAF* mutant regardless of microsatellite status. **Methods:** This is a prospective, open-label, multicentric phase II trial where pts with mCRC RAS/BRAF mutant in first line will receive nivolumab in combination with FOLFOXIRI/Bevacizumab every 2 weeks for 8 cycles followed by maintenance with bevacizumab plus nivolumab every 2 weeks. Bevacizumab will be administered intravenously at dose of 5 mg/kg every 2 weeks and nivolumab intravenously as a flat dose of 240 mg every 2 weeks. The primary endpoint is the overall response rate (ORR) and our hypothesis is that the treatment is able to improve the ORR from 66% to 80%. Secondary endpoints include overall survival, safety, time to progression, duration of response. Collateral translational studies evaluate the tumor mutational burden, and genetic alterations by circulating free DNA (cfDNA) obtained from plasma samples. The trial is open to enrollment, 4 of planned 70 pts have been enrolled. Clinical trial information: EudraCT Number: 2018-002893-38. Clinical trial information: NCT04072198. Research Sponsor: Bristol-Myers Squibb.

TPS4119 Poster Session (Board #111), Fri, 8:00 AM-11:00 AM

Multimodal fluorescence-guided surgery of colorectal peritoneal metastases, a phase I/II clinical trial. *First Author: Jan-Marie de Gooyer, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands*

Background: Successful treatment of patients with colorectal peritoneal carcinomatosis highly depends on complete surgical tumor resection of all tumor. Oncological outcomes can potentially be improved by intraoperative imaging using a tumor-targeting antibody conjugated to a fluorophore and a radiotracer. This enables preoperative radionuclide imaging, real-time intraoperative fluorescence imaging and gamma detection. In this study we investigate the feasibility, accuracy and safety of CEA-targeted preoperative SPECT/CT and intraoperative fluorescence imaging in patients with colorectal PC. **Methods:** In this phase I/II single arm protein dose escalation study patients with peritoneal metastases of colorectal origin who are scheduled for cytoreductive surgery and HIPEC will receive an intravenous injection of the CEA-targeting tracer ^{111}In-DOTA-labetuzumab-IRDye800CW. The first 15 patients will receive a single dose of 2,10 or 50 mg 6 to 7 days prior to surgery. Four to five days after injection SPECT/CT imaging of the thorax and abdomen is performed to determine intra-abdominal tumor load and detect extra-abdominal metatases. At day 6/7 after injection, standard cytoreductive surgical resection extended with real-time near-infrared fluorescence imaging and radio guidance is performed. After surgery, the peritoneal cavity will be re-examined for residual disease with fluorescence imaging. Resected specimens are analyzed microscopically, immunohistochemically (CEA and H&E) and by gamma counting. Blood samples are drawn for farmacokinetics and safety analysis at 180 minutes, 4 days, 6 days and 3 weeks after tracer injection. In the phase II dose expansion cohort, 14 more patients will receive the optimal dose as determined in the phase I trial. The primary objectives of the trial are to assess the safety, feasibility and accuracy of preoperative SPECT/CT and intraoperative fluorescence imaging after administration of 111In- labetuzumab-IRDye800CW in patients with peritoneal carcinomatosis of colorectal origin who will undergo cytoreductive surgery and HIPEC. The secondary objectives are to assess whether additional malignant lesions can be visualized by fluorescence imaging after cytoreductive surgery, to assess the intensity of fluorescence in malignant and non-malignant tissue, to assess the correlation between localization of the dual-labeled antibody and CEA expression in tumor and healthy tissue and to determine blood concentrations of the dual labelled antibody at several time points in patients. Clinical trial information: NCT03699332. Research Sponsor: Dutch Cancer Foundation.

TPS4120 Poster Session (Board #112), Fri, 8:00 AM-11:00 AM

TRACC: Tracking mutations in cell-free DNA to predict relapse in early colorectal cancer—A randomized study of circulating tumour DNA (ctDNA) guided adjuvant chemotherapy versus standard of care chemotherapy after curative surgery in patients with high risk stage II or stage III colorectal cancer (CRC). *First Author: Gayathri Anandappa, The Royal Marsden NHS Foundation Trust, London, United Kingdom*

Background: Adjuvant chemotherapy (ACT) is routinely offered to patients with high risk (HR) stage II or stage III CRC following potentially curative surgery. Over 50% of stage III and $>$ 80% of stage II patients are cured by surgery alone but are being exposed to unnecessary chemotherapy with short- and long-term side effects. Post-operative ctDNA identifies minimal residual disease (MRD) after surgery in CRC. Our national study, TRACC, compares ctDNA guided versus standard of care (SoC) decision making in patients undergoing ACT. **Methods:** This is a UK-wide, multi-centre, prospective, two-arm, randomised trial. Patients with HR risk stage II or stage III CRC who have undergone R0 resection and have detectable ctDNA in their pre-surgical sample are eligible. Patients who undergo neoadjuvant chemoradiotherapy (CRT) for locally advanced rectal cancer with detectable ctDNA pre-CRT are also eligible. Patients are randomised in a 1:1 ratio to receive either SoC ACT or ctDNA guided ACT. In the ctDNA guided arm, patients who are ctDNA negative post-operatively have chemotherapy de-escalated i.e., 3 months(m) of Capecitabine and Oxaliplatin (CAPOX) doublet ACT is reduced to 3 m single agent Capecitabine; 6 m single agent Capecitabine reduced to no chemotherapy. In this group, ctDNA is re-tested at 3 months and if detectable, patients receive 3 months of CAPOX. Primary end-point is 3-year disease free survival (DFS). Secondary end-points include overall survival, neurotoxicity, quality of life and health economics. Based on a standard 3-year DFS of 75% in SoC ACT arm, to demonstrate a non-inferiority margin of 1.25, 810 patients are required per arm (85% power, α = 0.1). Stratification is by tumour staging and site of primary tumour. Target accrual is over 4 years. The study opened to recruitment in January 2020 and is supported by the MRC-NIHR Efficacy and Mechanism Evaluation Grant (NIHR128529). Clinical trial information: NCT04050345. Research Sponsor: National Institute of Health Research-Biomedical Research Centre funding.

TPS4121 Poster Session (Board #113), Fri, 8:00 AM-11:00 AM

Phase II/III study of circulating tumor DNA as a predictive biomarker in adjuvant chemotherapy in patients with stage II colon cancer: NRG-GI005 (COBRA). *First Author: Van K. Morris, NRG Oncology, and UT-MD Anderson Cancer Center, Houston, TX*

Background: There are currently no validated predictive biomarkers for stage II resected colon cancer (CC) after adjuvant chemotherapy. However, circulating tumor DNA (ctDNA) that is shed into the bloodstream represents a highly specific and sensitive approach for identifying microscopic or residual tumor cells. For patients (pts) with CC, the detection of ctDNA is associated with persistent disease after resection and may outperform traditional clinical and pathological features as a prognostic factor to assess risk for recurrence. We hypothesize that for pts whose stage II colon cancer has been resected and who have no traditional high-risk features, a positive ctDNA status may identify those who will benefit from adjuvant chemotherapy. **Methods:** In this prospective phase II/III clinical trial, pts (N=1,408) with resected stage II CC without traditional high-risk features and whom the evaluating oncologist deems suitable for no adjuvant chemotherapy will be randomized 1:1 into 2 arms: standard-of-care/observation (Arm A), or prospective testing for ctDNA (Arm B). Postoperative blood will be analyzed for ctDNA with the GuardantHealth LUNAR panel, covering CC-relevant mutations and CC-specific methylation profiling. Pts in Arm B with ctDNA detected will be treated with 6 months of adjuvant (FOLFOX) chemotherapy. For all pts in Arm A, ctDNA status will be analyzed retrospectively at the time of endpoint analysis. The primary endpoints are clearance of ctDNA with adjuvant chemotherapy (phase II) and recurrence-free survival (RFS) for "ctDNA-detected" pts treated with or without adjuvant chemotherapy (phase III). Secondary endpoints will include time-to-event outcomes (OS, RFS, TTR) by ctDNA marker status and treatment, prevalence of detectable ctDNA in stage II CC, and rates of compliance with assigned intervention. Archived normal and matched tumor and blood samples will be collected for exploratory correlative research. The trial is actively accruing towards the phase II endpoint across all US and Canadian cooperative groups. Support: U10-CA-180868, -180822; UG1CA-189867; GuardantHealth. Clinical trial information: NCT04068103. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

TPS4122 Poster Session (Board #114), Fri, 8:00 AM-11:00 AM

Phase II study of durvalumab plus total neoadjuvant therapy (TNT) in locally advanced rectal cancer: The GEMCAD-1703 DUREC trial. *First Author: Jaume Capdevila, Medical Oncology Department, Vall d'Hebron University Hospital; Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain*

Background: In clinical stages II and III (cT3-4 and/or N+), preoperative chemoradiotherapy (CRT) or short-course radiation followed by total mesorectal escision (TME) have been the standard of care for the last 15 years. Induction chemotherapy (CT) before CRT (strategy known as TNT) results in fewer toxic effects and improved compliance. TNT may release tumor-neoantigens with platinum-based induction CT, and radiotherapy has the potential ability to induce an immunogenic cell death and counteract an immune-suppressive tumor microenvironment that provides the rationale for combining with immunotherapies. In addition, the presence of tumor infiltrating lymphocytes has been demonstrated in patients with rectal cancer treated with neoadjuvant CRT, reinforcing the rational for immune check-point inhibitors in this setting. We hypothesize that combining TNT with durvalumab (an optimized monoclonal antibody directed against programmed cell death-1 ligand 1) would improve outcome. **Methods:** DUREC is a multicenter, single-arm, open-label, phase Ib/II study for patients with magnetic resonance (mr) image middle or distal third, mrT3c-d/T4/N2 rectal adenocarcinoma. Treatment: Patients will receive 6 cycles of modified FOLFOX6 prior to CRT (capecitabine with 50.4 Gy in 28 fractions) and TME, combined with durvalumab 1500 mg every 4 weeks during induction CT, CRT and waiting period until surgery. To assess the tolerability and toxicity profile we plan to perform a run-in treatment phase including the first 6 patients in the study, holding recruitment until all of them will be operated and 30-days post-surgery period completed. If $\leq$ 2 durvalumab-related dose-limiting toxicities (DLTs) are observed, recruitment will continue. The primary objective is pathological complete response (pCR) rate. Secondary endpoints include toxicity, tumor regression grade, R0 resections, clear circumferential margins, surgical complications, NAR score, disease-free survival and a biomarker program on tumor tissue, blood samples and stool microbiota. Statistical design: 58 evaluable patients (assuming a P0 of 16% and a P1 of 30%, with 0.1 alpha and 0.1 beta); Study started recruitment on December 2019. Clinical trial information: 2018-004835-56. Research Sponsor: AstraZeneca, GEMCAD (Spanish multidisciplinary Group of Digestive Cancers).

TPS4123 Poster Session (Board #115), Fri, 8:00 AM-11:00 AM

A phase II study of induction PD-1 blockade in subjects with locally advanced mismatch repair-deficient rectal adenocarcinoma. *First Author: Andrea Cercek, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: The treatment of patients with locally advanced rectal cancer includes total neoadjuvant therapy with chemotherapy, chemoradiation followed by surgery. While most rectal cancers respond to combination induction chemotherapy, patients with mismatch repair deficient (dMMR) or MSI-H tumors have a significantly higher chance of progression with this treatment regimen. dMMR or MSI-H tumors have shown remarkable responses to PD-1 blockade, but the effect of neoadjuvant checkpoint inhibition has not been well studied. In this trial we will determine the pathologic complete response rate (pCR) of neoadjuvant anti-PD-1 blockade followed by standard chemoradiation in dMMR or MSI-H locally advanced rectal cancer. We hypothesize that treatment naïve dMMR or MSI-H rectal cancers will achieve a robust clinical response to PD-1 blockade and that the total neodjuvant therapy with PD-1 blockade followed by chemoradiation will improve pCR rates. **Methods:** Eligible patients $\geq$18 years of age with Stage II (T3-4, N-) or Stage III (any T, N+) histologically confirmed dMMR or MSI-H (by NGS) rectal adenocarcinoma will be enrolled. Patients will receive TSR-042 (500mg IV) every 3 weeks for a maximum of 8 cycles (6 months of treatment). Imaging, internal endoscopic exam and ctDNA blood draw will be performed at 6 weeks and every 3 months during induction anti-PD-1 treatment. Adverse events and surgical complications will be graded according to the NCI CTCAE v5 and the Clavien-Dindo classification, respectively. Following neoadjuvant checkpoint blockade, patients will undergo conventional chemoradiotherapy followed by surgical resection. The primary endpoint is pathologic complete response compared with historical control in pMMR patients. Patients will be followed up every 6 months for assessment of disease-free survival for up to five years. Clinical trial information: NCT04165772. Research Sponsor: Tesaro.

TPS4124 Poster Session (Board #116), Fri, 8:00 AM-11:00 AM

The PEGASUS trial: Post-surgical liquid biopsy-guided treatment of stage III and high-risk stage II colon cancer patients. *First Author: Sara Lonardi, Veneto Institute of Oncology (IOV)-IRCCS, Padua, Italy*

Background: Moving stage III Colon Cancer (CC) into the precision medicine space is a priority in view of the lack of molecular markers driving adjuvant treatment. Retrospective studies have demonstrated the tremendous prognostic impact of circulating tumor DNA (ctDNA) analysis after curative intent surgery, and suggested that lack of conversion of ctDNA from detectable to undetectable after adjuvant chemotherapy reflects treatment failure. With these premises, we have designed the PEGASUS trial (NCT04259944). **Methods:** PEGASUS is a prospective multicentric study designed to prove the feasibility of using liquid biopsy (LB) to guide the post-surgical and post-adjuvant clinical management in 140 microsatellite stable Stage-III and T4N0 Stage-II CC patients. The LUNAR1 test (Guardant Health, Redwood City, CA, USA) will be used for ctDNA determination. For the efficacy analysis, the PEGASUS cohort will be compared with a 3:1 matched cohort of 420 patients from the TOSCA trial (NCT00646607). A LB executed 2-4 weeks post-surgery will guide a "Molecular Adjuvant" treatment: i) ctDNA+ patients will receive CAPOX for 3 months and ii) ctDNA- patients will receive capecitabine (CAPE) for 6 months but will be retested after 1 cycle, and if found ctDNA+ will be switched to CAPOX treatment. At the end of the "Molecular Adjuvant" treatment a further LB will be performed and instruct subsequent treatment. Positive patients (ctDNA+/+ and ctDNA-/+) will receive an upscaled "Molecular Metastatic" systemic treatment for 6 months or until radiological progression or toxicity: i) ctDNA+/+ patients will be treated with FOLFIRI; ii) ctDNA-/+ patients with CAPOX. These patients will be subjected to a LB after 3 months and at the end of treatment: in case of positivity will be switched to FOLFIRI. ctDNA+/- patientswill receive a de-escalated treatment with CAPE for 3 months. 3 LB will be performed within 3 months and in case of positivity the patient will be switched to FOLFIRI. Patients with ctDNA-/- will be subjected to an interventional follow-up comprising 2 further LB and in case of positivity they will be switched to CAPOX treatment. PEGASUS is piggybacked to AlfaOmega (NCT04120935), a Master Observational Protocol that will follow patients from diagnosis to 5 years or recurrence/death (whichever comes first), collecting clinical data, radio-images and biological samples. AlfaOmega provides a clinical and logistic ecosystem for the seamless integration of PEGASUS clinical results with the biological underpinning of colon cancer. Clinical trial information: NCT04259944. Research Sponsor: Italian Association for Cancer Research.

4500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Trastuzumab with trimodality treatment for esophageal adenocarcinoma with HER2 overexpression: NRG Oncology/RTOG 1010. *First Author: Howard Safran, Brown University Oncology Research Group, Providence, RI*

Background: Trastuzumab is a monoclonal antibody against human epidermal growth factor receptor 2 (HER2). The primary objective of RTOG 1010 was to determine if trastuzumab increases disease-free survival (DFS) when combined with trimodality treatment for patients with HER2 overexpressing esophageal adenocarcinoma. **Methods:** This open label, randomized phase III trial included patients with newly diagnosed stage T1N1-2, T2-3N0-2 adenocarcinoma of the esophagus involving the mid, distal, or esophagogastric junction and up to 5cm of the stomach. All patients received chemotherapy (C) of paclitaxel, 50mg/m^2 and carboplatin AUC = 2, weekly for 6 weeks, with radiation (XRT: 3D-CRT or IMRT, 50.4 Gy in 28 fractions) followed by surgery. Patients were randomized 1:1 to receive weekly trastuzumab 4mg/kg week 1 then 2mg/kg/weekly x 5 during CXRT then 6 mg/kg for 1 dose prior to surgery and 6mg/kg every 3 weeks for 13 treatments after surgery. HER2 status was determined by IHC and gene amplification by FISH. With a 2-sided alpha of 0.05, 162 DFS events provide 90% power to detect a signal for an increase in median DFS from 15 to 25 months. DFS and overall survival (OS) were estimated by the Kaplan-Meier method. and arms were compared using the log rank test. The Cox proportional hazards model was used to analyze treatment effect. **Results:** 571 patients were entered for assessment of HER2 expression, 203 HER2+ patients randomized. The median follow-up for alive patients is 5.0 years. The estimated 2, 3, and 4-year DFS (95% CI) for the CXRT +trastuzumab arm were 41.8% (31.8%, 51.7%), 34.3% (24.7%, 43.9%), and 33.1% (23.6%, 42.7%), respectively, and for the CXRT arm were 40.0% (30.0%, 49.9%), 33.4% (23.8%, 43.0%), and 30.1% (20.7%, 39.4%), respectively; log-rank p = 0.85. The median DFS time is 19.6 months (13.5-26.2) for the CXRT +trastuzumab arm compared to 14.2 months (10.5-23.0) for the CXRT arm. The hazard ratio (95% CI) comparing the DFS of CXRT+trastuzumab arm to the CXRT arm was 0.97 (0.69, 1.36). The median OS time was 38.5 months (26.2-70.4) for the CXRT+trastuzumab arm compared to 38.9 months (29.0-64.5) for the CXRT arm, hazard ratio (95% CI): 1.01 (0.69, 1.47). There was no statistically significant increase in treatment-related toxicities with the addition of trastuzumab including no increase in cardiac events. **Conclusions:** The addition of trastuzumab to trimodality treatment did not improve DFS for patients with HER2 overexpressing esophageal adenocarcinoma. Supported by NCI grants U10CA180868, UG1CA189867, U10CA180822 and Genentech. Clinical trial information: NCT01196390. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

4501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Perioperative ramucirumab in combination with FLOT versus FLOT alone for resectable esophagogastric adenocarcinoma (RAMSES/FLOT7): Results of the phase II-portion—A multicenter, randomized phase II/III trial of the German AIO and Italian GOIM. *First Author: Salah-Eddin Al-Batran, University Cancer Center Frankfurt, Institut für Klinisch-Onkologische Forschung and IKF Klinische Krebsforschung GmbH am Krankenhaus Nordwest, Frankfurt, Germany*

Background: Periop. FLOT has become SOC for resectable, esophagogastric adenocarcinoma. However, patient's outcome is still poor. This trial evaluates the addition of the VEGF-R2 inhibitor ramucirumab (RAM) to FLOT for resectable patients (pts). **Methods:** This is a prospective, international, randomized, investigator-initiated phase II/III trial. Pts with resectable, Her2-negative, adenocarcinoma of the stomach and GEJ (≥ cT2 or cN+) were enrolled. Pts were randomized to 4 pre-and post-operative cycles of FLOT (docetaxel 50 mg/m^2; oxaliplatin 85 mg/m^2; leucovorin 200 mg/m^2; 5-FU 2600 mg/m^2, q2w) alone (Arm A) or the same regimen with RAM 8mg/kg q2w, followed by 16 cycles RAM (Arm B, FLOT-RAM). Important endpoints of phase II (exploratory) were major pathological (complete and nearly complete) response, centrally assessed acc. to Becker criteria, R0-resection rate, and safety. GEJ type I tumors and pts requiring transthoracic esophagectomy were excluded for safety reasons during the conduct of the study. **Results:** In total, 180 pts were randomized. Baseline characteristics were similar between arms (male, 73%; median age, 60y; cT3/T4, 83%; cN+, 78%; GEJ, 54%; signet-ring cells, 40%). However, the FLOT-RAM arm included more unfavorable pts with T4 (9% vs. 4%), Siewert type I tumors (18% vs. 13%), impaired ECOG PS of 1 (34% vs. 20%), and concomitant disease (87% vs. 79%). 91% of pts with FLOT and 92% with FLOT-RAM completed the 4 pre- cycles. R0-resection (in the full set) could be achieved in 83% of pts with FLOT and 97% of pts with FLOT-RAM (p = 0.0049). The rate of major path response was similar in both arms and was 30% for FLOT and 27% for FLOT-RAM. Surgical morbidity was observed in 37% of pts with FLOT and 44% of pts with FLOT-RAM. Mortality was 2.5% with FLOT and 5.9% with FLOT-RAM including GEJ type I tumors and dropped to 2.9% in both arms after excluding type I tumors per amendment. There was bit more G≥3 adverse events with FLOT-RAM (78% vs. 89%). **Conclusions:** In this phase II trial, the addition of ramucirumab to perioperative FLOT significantly improved R0-resection rates without an impact on path response, mainly because more patients could proceed to operation. The FLOT-RAM is safe, when type I tumors are excluded. Clinical trial information: NCT02661971. Research Sponsor: Lilly Deutschland GmbH.

4502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Perioperative trastuzumab and pertuzumab in combination with FLOT versus FLOT alone for HER2-positive resectable esophagogastric adenocarcinoma: Final results of the PETRARCA multicenter randomized phase II trial of the AIO. *First Author: Ralf Dieter Hofheinz, University Medical Center Mannheim, Tagestherapiezentrum am ITM, Mannheim, Germany*

Background: Perioperative FLOT is a standard of care for resectable, esophagogastric adenocarcinoma (EGA). This trial evaluates the addition of trastuzumab (tras) and pertuzumab (per) to FLOT for HER2-positive resectable patients (pts). **Methods:** PETRARCA is a prospective, multicenter, randomized, investigator initiated trial planned as a phase II/III investigation. We report the phase II part of this trial. Pts with HER2+ resectable EGA (≥ cT2 or cN+) were enrolled. Pts were randomized 1:1 to 4 pre- and post-operative cycles of FLOT (Docetaxel 50 mg/m^2; Oxaliplatin 85 mg/m^2; Leucovorin 200 mg/m^2; 5-FU 2600 mg/m^2, q2w) (Arm A) or the same regimen with tras 8/6 mg/kg and per 840 mg q3w, followed by 9 cycles tras/per (arm B). Primary endpoint for the phase II part was the rate of pathological complete remission (pCR). Main secondary endpoints were DFS, OS and safety. **Results:** The trial closed prematurely and did not proceed to phase III. In total, 81 pts were randomized (A, 41; B, 40). Baseline characteristics were balanced (overall, male 79%; median age 60; cT3/T4 86%; cN+ 85%; GEJ 75%). 93% in arm A and 90% in arm B completed pre-OP treatment as planned. More pts had at least one dose modification in arm B (A, 44%; B, 70%). The pCR rate was significantly improved with tras/per (A, 12%; B, 35%; p = 0.02). Likewise, the rate of pathological lymph node negativity was higher with tras/per (A, 39%; B, 68%). R0-resection rate (A, 90%; B, 93%) and surgical morbidity (A: 43%; B, 44%) were comparable. Moreover, in-house mortality was equal in both arms (overall 2.5%). Median DFS was 26 months in arm A and not yet reached in arm B (HR 0.58, p = 0.14). After a median follow-up of 22 months median OS was not yet reached. DFS and OS rates [with 95% CI] at 24 months were 54% [38-71%] and 77% [63-90%] in arm A and 70% [55-85%] and 84% [72-96%] in arm B, respectively. In terms of toxicity more ≥ grade 3 adverse events were reported with tras/per (75% vs. 85%), especially diarrhea (5% vs. 41%) and leukopenia (13% vs 23%). **Conclusions:** The addition of tras/per to perioperative FLOT significantly improved pCR and nodal negativity rates in pts with Her2+ resectable esophagogastric adenocarcinoma at the price of higher rates of diarrhea and leukopenia. Clinical trial information: NCT02581462. Research Sponsor: Roche.

4503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Pembrolizumab versus paclitaxel for previously treated patients with PD-L1–positive advanced gastric or gastroesophageal junction cancer (GC): Update from the phase III KEYNOTE-061 trial. *First Author: Charles S. Fuchs, Yale Cancer Center, Smilow Cancer Hospital, New Haven, CT*

Background: KEYNOTE-061 (NCT02370498) is a global phase 3 study of pembrolizumab vs paclitaxel as second-line therapy for GC. At the time of primary analysis (data cutoff: Oct 26, 2017), in patients with PD-L1–positive status (combined positive score [CPS] ≥1), pembrolizumab did not significantly prolong overall survival (OS) vs paclitaxel (9.1 months vs 8.3 months) but did elicit a longer duration of response (DOR) and a favorable safety profile vs paclitaxel. We present results of KEYNOTE-061 in patients with CPS ≥1, ≥5, and ≥10 after 2 additional years of follow-up (cutoff: Oct 7, 2019). **Methods:** Adult patients with GC that progressed after platinum + fluoropyrimidine chemotherapy were randomly assigned 1:1 to pembrolizumab 200 mg Q3W for up to 35 cycles (~2 y) or standard-dose paclitaxel. OS and progression-free survival (PFS) in the CPS ≥1 population were the primary end points. Comparisons were made using stratified log-rank tests. **Results:** At the time of this analysis, 366/395 patients with CPS ≥1 had died (92.6%). Pembrolizumab prolonged OS vs paclitaxel in PD-L1–positive patients (Table). No significant differences appeared between groups in PFS (Table). Objective response rate (ORR) was higher for pembrolizumab in the CPS ≥10 group, and DOR was longer with pembrolizumab using all CPS cutoffs (Table). There were fewer drug-related adverse events (AEs) with pembrolizumab than paclitaxel in the overall population (53% vs 84%). **Conclusions:** This long-term analysis found that second-line pembrolizumab prolonged OS among patients with PD-L1–positive GC and led to fewer drug-related AEs vs paclitaxel. Clinical trial information: NCT02370498. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Efficacy Outcomes.

	Pembrolizumab CPS ≥1 n = 196	Paclitaxel CPS ≥1 n = 199	Pembrolizumab CPS ≥5 n = 95	Paclitaxel CPS ≥5 n = 91	Pembrolizumab CPS ≥10 n = 53	Paclitaxel CPS ≥10 n = 55
OS, deaths, n (%)	176 (89.8)	190 (95.5)	84 (88.4)	86 (94.5)	44 (83.0)	51 (92.7)
OS, months, median (95% CI)	9.1 (6.2-10.7)	8.3 (7.6-9.0)	10.4 (6.7-15.5)	8.3 (6.8-9.4)	10.4 (5.9-18.3)	8.0 (5.1-9.9)
HR (95% CI)	0.81 (0.66-1.00)	—	0.72 (0.53-0.99)	—	0.69 (0.46-1.05)	—
P	0.03	—	0.02	—	0.04	—
PFS, months, median (95% CI)	1.5 (1.4-2.0)	4.1 (3.2-4.3)	1.6 (1.4-2.8)	4.0 (2.8-4.4)	2.7 (1.4-4.3)	4.0 (2.7-4.4)
HR (95% CI)	1.25 (1.02-1.54)	—	0.98 (0.71-1.34)	—	0.79 (0.51-1.21)	—
ORR, % (n)	16.3 (32)	13.6 (27)	20.0 (19)	14.3 (13)	24.5 (13)	9.1 (5)
DOR, months, (range)	19.1 (1.4+ to 47.1+)	5.2 (1.3+ to 16.8)	32.7 (4.1 to 47.1+)	4.8 (1.3+ to 15.3)	NR (4.1 to 47.1+)	6.9 (2.6 to 6.9)

4504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

SWOG S1505: Results of perioperative chemotherapy (peri-op CTx) with mfolfirinox versus gemcitabine/nab-paclitaxel (Gem/nabP) for resectable pancreatic ductal adenocarcinoma (PDA). *First Author: Davendra Sohal, University of Cincinnati, Cincinnati, OH*

Background: Clinical outcomes after curative treatment of resectable PDA remain suboptimal. To assess the potential of early control of systemic disease with multiagent peri-op CTx, we conducted a prospective trial in the National Clinical Trials Network. **Methods:** S1505 was a randomized phase II trial of peri-op CTx (12 weeks pre-, 12 weeks post-op) with either mFOLFIRINOX (Arm 1) or Gem/nabP (Arm 2). Eligibility required confirmed tissue diagnosis of PDA, ECOG PS 0 or 1, and resectable disease per Intergroup criteria. Primary outcome was 2-year overall survival (OS), using a "pick the winner" design; for 100 eligible patients (pts), accrual up to 150 pts was planned to account for cases deemed ineligible at central radiology review. We previously presented data on eligibility (ASCO 2019 abstr 4137). Here we present the final efficacy and toxicity results for the eligible pts. **Results:** From 2015 to 2018, 147 pts were enrolled; there were 102 eligible pts; 55 in Arm 1; 47 in Arm 2. For Arms 1 and 2 respectively: median age, 66 (44-76) and 64 (46-76) years; males, 36 (65%) and 24 (51%); and ECOG PS 0, 34 (62%) and 31 (66%) pts. Treatment details are shown in Table. For Arm 1 and Arm 2, respectively: Two-year OS was 41.6% and 48.8%; median OS was 22.4 months and 23.6 months. Neither arm's 2-year OS estimate was statistically significantly higher than the *a priori* threshold of 40% (p=0.42 in Arm 1 and p=0.12 in Arm 2). Median disease-free survival (DFS) after resection was 10.9 months in Arm 1 and 14.2 months in Arm 2 (p=0.87). **Conclusions:** We have demonstrated: 1) two-year OS of 41.6% (median 22.4 months) with mFOLFIRINOX and 48.8% (median 23.6 months) with Gem/nabP for all eligible pts starting treatment for resectable PDA; 2) post-resection DFS of 10.9 months and 14.2 months, respectively; 3) adequate safety and high resectability rates with peri-op CTx; 4) little evidence that either regimen improves OS compared with the historical standard. Clinical trial information: NCT02562716. Research Sponsor: U.S. National Institutes of Health.

Outcomes by Treatment Arm for Eligible Patients (N=102).

	Arm 1 (mFOLFIRINOX; N=55)	Arm 2 (Gem/nabP; N=47)
Started pre-op CTx	53 (96%)	45 (96%)
Completed pre-op CTx	46 (84%)	40 (85%)
Surgical resection	40 (73%)	33 (70%)
Complete or major pathologic response*	10 (25%)	14 (42%)
Started post-op CTx	33 (60%)	28 (60%)
Completed all treatment	27 (49%)	19 (40%)
Diarrhea^	15%	7%
Neutropenia^	19%	38%
Peripheral neuropathy^	9%	7%

*Denominator is those who underwent resection (40 and 33 for Arm 1 and 2, resepectively).
^Only grade 3 or higher

4505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

ESPAC-5F: Four-arm, prospective, multicenter, international randomized phase II trial of immediate surgery compared with neoadjuvant gemcitabine plus capecitabine (GEMCAP) or FOLFIRINOX or chemoradiotherapy (CRT) in patients with borderline resectable pancreatic cancer. *First Author: Paula Ghaneh, University of Liverpool, Liverpool, United Kingdom*

Background: Patients with borderline resectable pancreatic cancer have poor survival and low resection rates. Neoadjuvant therapy may improve the outcome for these patients. The aim of this trial was to determine the feasibility and efficacy of a comparison of immediate surgery versus neoadjuvant GEMCAP or FOLFIRINOX or CRT. **Methods:** Eligible patients with NCCN defined borderline resectable (following central review of the baseline CT scan) and biopsy proven pancreatic cancer were randomised (stratified by centre) to receive immediate surgery, or neoadjuvant therapy of either 2 cycles of GEMCAP, or 4 cycles of FOLFIRINOX or 50.4Gy capecitabine-based CRT in 28 daily fractions over 5 $^{1}/_{2}$ weeks. Patients were restaged at 4-6 weeks and underwent surgical exploration if still borderline resectable. Resected patients received adjuvant therapy. Follow up was 12 months. There was quality assurance of surgery and CRT. Primary endpoints were recruitment rate and resection rate (R1/R0). Secondary endpoints included overall survival and toxicity. A target of 90 patients was set to determine feasibility and resection rates. Rates will be presented as point estimates and survival compared across treatment arms using a log-rank test. Analyses will be on an ITT basis. **Results:** Between August 2014 and December 2018, 90 patients were randomised with 88 included in the full analysis set (32 immediate surgery, 20 GEMCAP, 20 FOLFIRINOX, 16 CRT). Median age was 63 years, 44% were men. WHO performance status was 0 and 1 in 45% and 55% respectively. Median CA19-9 was 603 kU/L at baseline. 44 (79%) patients completed neoadjuvant therapy. Recruitment rate was 21 patients per year. Resection rate was 62% for immediate surgery and 55% for neoadjuvant therapy (p=0.668). R0 resection rate on resected patients was 15% and 23% respectively (p=0.721). One year survival rate was 40% [95% CI, 26% – 62%] for immediate surgery and 77% [95%CI, 66% - 89%] for neoadjuvant therapy. Log-rank analysis showed an HR=0.27 [95% CI, 0.13 – 0.55]; $\chi 2$ (1) = 14.91, P<0.001. 9 out of the 51 neoadjuvant patients included in the safety set reported 12 serious adverse events of grade 3 or above. **Conclusions:** There was no difference in resection rate between arms, however neoadjuvant therapy had a significant survival benefit compared with immediate surgery. Clinical trial information: 89500674. Research Sponsor: Cancer Research UK.

4506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Donafenib versus sorafenib as first-line therapy in advanced hepatocellular carcinoma: An open-label, randomized, multicenter phase II/III trial. *First Author: Feng Bi, Department of Medical Oncology, West China Hospital, Sichuan University, Chengdu, China*

Background: Sorafenib is still the standard first-line therapy for advanced hepatocellular carcinoma (HCC). Donafenib, a novel multikinase inhibitor, showed potential benefits in a previous phase Ib study in HCC. **Methods:** In this open-label, randomized phase II/III trial (ZGDH3), patients with unresectable or metastatic HCC, a Child-Pugh liver function score ≤ 7, and no prior systemic therapy were enrolled from 37 sites across China and randomized (1:1) to receive oral donafenib (0.2 g) or sorafenib (0.4 g) twice daily until intolerable toxicity or disease progression. The primary endpoint was overall survival (OS). Efficacy analysis was primarily based on the full analysis set (FAS). **Results:** Between March 2016 and April 2018, 668 patients were randomized (donafenib, 334; sorafenib, 334) and included in the intention-to-treat (ITT) set, of whom 659 were analysed by FAS (328 *vs* 331). Donafenib was associated with a significantly longer median OS than sorafenib in both FAS (12.1 months *vs* 10.3 months, hazard ratio 0.831, 95% confidence interval 0.699–0.988, $p = 0.0363$) and ITT (12.0 months *vs* 10.1 months, 0.839, 0.706–0.996, $p = 0.0446$). There were no significant differences in median progression-free survival (3.7 months *vs* 3.6 months, $p = 0.2824$), objective response rate (4.6% *vs* 2.7%, $p = 0.2448$), and disease control rate (30.8% *vs* 28.7%, $p = 0.5532$). Grade 3 or worse adverse events (AEs) occurred in 191 (57.4%) and 224 (67.5%) patients ($p = 0.0082$), respectively, and AEs of special interest and those leading to treatment interruption occurred in 287 (86.2%) *vs* 309 (93.1%, $p = 0.0049$) and 101 (30.3%) *vs* 141 (42.5%, $p = 0.0013$). A numerically lower number of patients reported serious AEs (55 [16.5%] *vs* 67 [20.2%], $p = 0.2307$) with donafenib. Common AEs with donafenib included hand-foot skin reaction (50.5%), aspartate aminotransferase increased (40.5%), blood bilirubin increased (39.0%), platelet count decreased (37.8%), and diarrhea (36.6%). **Conclusions:** Donafenib significantly improves OS over sorafenib with favourable safety and tolerability. Donafenib is a promising superior first-line therapy for advanced HCC. Funding: Zelgen. Clinical trial information: NCT02645981. Research Sponsor: Zelgen.

4507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Apatinib as second-line therapy in Chinese patients with advanced hepatocellular carcinoma: A randomized, placebo-controlled, double-blind, phase III study. *First Author: Qiu Li, West China Hospital , Sichuan University, Chengdu, China*

Background: Chinese patients (pts) account for more than 50% of hepatocellular carcinoma (HCC) cases in the world and have special features in etiology, biological behavior, treatment strategy and prognosis. The aim of this study was to evaluate the efficacy and safety of apatinib, an inhibitor targeting vascular endothelial growth factor receptor-2, in Chinese pts with pretreated advanced HCC. **Methods:** In this randomized, placebo-controlled, double-blind, phase 3 trial done in 31 sites in China, pts with HCC who had received at least one line of systemic therapy (including sorafenib and oxaliplatin-based chemotherapy, which is another first-line standard-of-care in China) and had Child-Pugh liver function class A or B ≤7 points were enrolled. The pts were randomly assigned (2:1) to receive 750 mg apatinib orally once daily or placebo and stratified by ECOG performance status (0 or 1), previous sorafenib treatment (yes or no), and extrahepatic spread and/or macrovascular invasion (yes or no) in 28-day treatment cycles. The primary endpoint was overall survival (OS). **Results:** Between Apr 01, 2014 and May 03, 2017, 393 pts were randomized and received at least one dose of study treatment (261 in apatinib arm and 132 in placebo arm). The median OS was significantly longer with apatinib than that with placebo (8.7 months [95% CI 7.5-9.8] *vs* 6.8 months [95% CI 5.7-9.1]; hazard ratio 0.785 [95% CI 0.617-0.998]; p=0.0476). Pts in the apatinib arm also had prolonged median progression free survival (PFS) compared with those in the placebo arm (4.5 months [95% CI 3.9-4.7] *vs* 1.9 months [95% CI 1.9-2.0]; hazard ratio 0.471 [95% CI 0.369-0.601]; p<0.0001). The objective response rate was 10.7% (95% CI 7.2-15.1) with apatinib versus 1.5% (95% CI 0.2-5.4) with placebo. Treatment-related adverse events (TRAEs) were reported in 250 (97.3%) pts in the apatinib arm and 92 (70.8%) pts in the placebo arm. The most common TRAEs of grade 3 and 4 were hypertension (71 [27.6%] pts in the apatinib arm *vs* 3 [2.3%] pts in the placebo arm), hand-foot syndrome (46 [17.9%] *vs* 0), decreased platelet count (34 [13.2%] *vs* 1 [0.8%]), and decreased neutrophil count (27 [10.5%] *vs* 0). 24 (9.3%) pts with apatinib and 13 (10.0%) pts with placebo died due to adverse events, and none were deemed treatment-related by investigators. **Conclusions:** Apatinib significantly prolonged OS and PFS in Chinese pts with pretreated advanced HCC, and was well tolerated with a manageable safety profile. Clinical trial information: NCT02329860. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

4508 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Efficacy, tolerability, and biologic activity of a novel regimen of tremelimumab (T) in combination with durvalumab (D) for patients (pts) with advanced hepatocellular carcinoma (aHCC). *First Author: Robin Kate Kelley, University of California San Francisco, San Francisco, CA*

Background: The combination of dual immune checkpoint inhibitors (ICI) T (anti–CTLA-4) and D (anti–PD-L1) showed tolerability with a promising objective response rate (ORR) in the initial cohort of this study (NCT02519348). Subsequent evaluation of pts with solid tumors treated with increasing doses of T suggested priming with a higher dose of T may induce a stronger immune response and enhance anti-tumor activity. Thus, the randomized expansion cohorts comprised 4 arms evaluating T and D as monotherapies and 2 T+D regimens, including a novel T+D regimen featuring a single, priming dose of T. **Methods:** ICI-naïve pts with aHCC who progressed on, were intolerant to, or refused sorafenib were randomized to one of two T+D combinations: T300+D (T 300 mg + D 1500 mg 1 dose followed by D Q4 weekly [Q4W]) or T75+D (T 75 mg Q4W + D 1500 mg Q4W [4 doses] followed by D Q4W); or single agent D (1500 mg Q4W) or T (750 mg Q4W). Safety was the primary endpoint. ORR by blinded, independent central review using RECIST v1.1, duration of response (DoR), circulating lymphocytes, and overall survival (OS) were assessed. **Results:** At data cut-off (09/02/2019), 332 pts were enrolled. Median follow-ups were 11.7 months (mo) for T300+D, 14.6 (T75+D), 8.9 (D), and 15.8 (T). Treatment-related adverse event (trAE) incidences are shown (Table); no deaths were attributed to trAEs for T300+D or T. The T300+D arm had the highest confirmed ORR (DoR not reached [NR]) and longest OS (Table). A unique proliferative T cell profile was identified for pts in the T300+D arm, suggesting additive biologic activity for the combination, and showed pts with an OR exhibited high cytotoxic (CD8) counts. **Conclusions:** The encouraging clinical activity and tolerable safety profile suggest T300+D provides the best benefit-risk profile as opposed to T75+D or monotherapies. The unique pharmacodynamic activity of the T300+D regimen further supports its use in aHCC. T300+D and D are being evaluated in the ongoing phase III HIMALAYA study (NCT03298451) in first-line HCC vs sorafenib. Funding: AstraZeneca. Clinical trial information: NCT02519348. Research Sponsor: AstraZeneca.

	T300+D (n=75)	T75+D (n=84)	D (n=104)	T (n=69)
Grade 3/4 trAEs, %	35.1	24.4	17.8	42.0
Serious trAEs, %	13.5	11.0	10.9	21.7
Grade 5 trAEs, n	0	1[a]	3[b]	0
Discontinuation due to trAEs, %	10.8	6.1	7.9	11.6
Median OS (95% CI), mo	18.7 (10.8-NR)	11.3 (8.4-14.6)	11.7 (8.5-16.9)	17.1 (10.9-NR)
ORR (95% CI), %	22.7 (13.8-33.8)	9.5 (4.2-17.9)	9.6 (4.7-17.0)	7.2 (2.4-16.1)
Median DoR, mo	NR	13.2	14.8	24.0

[a]hepatic failure
[b]abnormal hepatic function, hepatic failure, pneumonitis

4509 Poster Discussion Session; Displayed in Poster Session (Board #117), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Intrathoracic versus cervical anastomosis after minimally invasive esophagectomy for esophageal cancer: A randomized controlled trial. *First Author: Moniek Verstegen, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands*

Background: Robust evidence is lacking whether Ivor Lewis minimally invasive esophagectomy (MIE) or McKeown MIE should be preferred for patients with mid to distal esophageal or gastro-esophageal junction Siewert I-II (GEJ) cancer. **Methods:** In this multicenter randomized controlled trial, patients with esophageal (below the level of the carina) or GEJ cancer planned for curative resection were recruited. Eligible patients were randomly assigned (1:1) to either Ivor Lewis MIE or McKeown MIE. The primary endpoint was anastomotic leakage (AL) requiring endoscopic, radiologic or surgical intervention. Secondary outcome parameters were overall AL rate, postoperative complications, length of stay and mortality. **Results:** A total of 262 patients were randomly assigned to Ivor Lewis MIE (n = 130) or McKeown MIE (n = 132). Seventeen patients were excluded from the trial due to not meeting inclusion criteria (n = 2), physical unfitness for surgery (n = 3), patients' choice (n = 3), interval metastases (n = 5) or peroperative metastases (n = 4). AL necessitating reintervention occurred in 15 (12.3%) of 122 patients after Ivor Lewis MIE and in 39 (31.7%) of 123 patients after McKeown MIE (relative risk 0.39, 95% CI 0.22-0.65; risk difference 19.4%, 95% CI 7.9%-31.8%). Overall AL rate was 12.3% after Ivor Lewis MIE and 34.1% after McKeown MIE. Severe complications (Clavien-Dindo $\geq$ 3b) were observed in 10.7% after Ivor Lewis MIE and in 22.0% after McKeown MIE. Pleural effusion requiring drainage occurred in 9.8% of patients after Ivor Lewis MIE and 21.1% of patients after McKeown MIE. RLN palsy rate was 0% after Ivor Lewis MIE and 7.3% after McKeown MIE. Median length of hospital stay was 10 days (IQR 8 – 15 days) after Ivor Lewis MIE and 12 days (IQR 9 – 18 days) after McKeown MIE. ICU length of stay and mortality rates were comparable between groups. **Conclusions:** These findings provide evidence for a lower rate of AL requiring reintervention after Ivor Lewis MIE compared to McKeown MIE for patients with mid to distal esophageal or GEJ cancer. Clinical trial information: NTR4333. Research Sponsor: ZonMw.

4510 Poster Discussion Session; Displayed in Poster Session (Board #118), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Laparoscopic sentinel node navigation surgery versus laparoscopic standard gastrectomy with lymph node dissection in early gastric cancer: Final three-year survival results of multicenter randomized controlled phase III trial (SENORITA trial). *First Author: Keun Won Ryu, National Cancer Center, Goyang, South Korea*

Background: The benefits and hazards of laparoscopic sentinel node navigation surgery (LSNNS), compared with laparoscopic standard gastrectomy (LSG) with lymph node dissection in early gastric cancer (EGC), are unknown. The SENORITA trial investigated the clinical impact of LSNNS in EGC in terms of short-term surgical outcomes, long-term survival and quality of life. **Methods:** This study is a prospective, multicenter, randomized controlled, non-inferiority trial. Patients with preoperatively diagnosed gastric adenocarcinoma with T1N0 of 3 cm or less in diameter, regardless of histology, except absolute indication for endoscopic resection were eligible. Patients were randomized to LSG or LSNNS using dual tracers. The primary endpoint is 3-year disease-free survival (3yDFS). Planned sample size per arm is 290 patients with the non-inferiority margin of 2.737 in hazard ratio (HR) assuming that LSG achieve 97% 3yDFS, 5% of type 1 error and 80% of power. Three-year recurrence-free survival (3yRFS), overall survival (3yOS) and disease specific death rate (3yDSDR) were evaluated as secondary endpoints. **Results:** From March 2013 to December 2016, 580 patients were randomized (LSG arm 292 vs. LSNNS arm 288). After 53 patients dropped out before surgery, operation was performed in 527 patients (269 vs. 258), representing the full analysis set. LSG was performed in 266 according to the protocol excluding 3 open conversion. After exclusion of 13 without LSNNS due to various reasons, LSNNS was performed in 245 patients according to the protocol. After median follow up of 47.5 months, 3yDFS were 95.5% and 91.8% (HR 1.901, CI 0.911 – 3.967), respectively. The 3yRFS was 98.9% and 95.2% (p=0.019), and 3yOS was 99.2% and 97.6% (p=0.166), and 3yDSDR was 99.5% and 99.1% (p=0.591), respectively. **Conclusion:** LSNNS in EGC did not show non-inferiority compared with LSG in terms of 3yDFS. However, 3yOS and 3yDSDR of LSNNS were comparable to LSG by the rescue surgery of recurrence. LSNNS might be an alternative surgical option instead of LSG in selected EGC patients. Clinical trial information: NCT01804998. Research Sponsor: Grant 2010150-1 from National Cancer Center, Korea.

4511 Poster Discussion Session; Displayed in Poster Session (Board #119), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Sintilimab in patients with advanced esophageal squamous cell carcinoma refractory to previous chemotherapy: A randomized, open-label phase II trial (ORIENT-2). *First Author: Jianming Xu, Department of Gastrointestinal Oncology, The Fifth Medical Center of the PLA General Hospital, Beijing, China*

Background: Patients (pts) with advanced esophageal squamous cell carcinoma (ESCC) refractory to first-line chemotherapy have limited treatment options. The study aims to evaluate the efficacy and safety of sintilimab, a PD-1 inhibitor, versus chemotherapy in these pts, and explore predictive value of PD-L1 and neutrophil-to-lymphocyte ratio (NLR) on efficacy of sintilimab. **Methods:** The open-label, multi-center phase 2 trial (NCT03116152) enrolled advanced ESCC pts refractory to first-line chemotherapy, and randomly assigned (1:1) them to receive sintilimab (200mg, Q3W) or chemotherapy (paclitaxel, 175mg/m^2, Q3W; or irinotecan, 180mg/m^2, Q2W), intravenously. The primary endpoint was overall survival (OS). Explorative endpoint were effects of PD-L1 and NLR on efficacy of sintilimab. **Results:** From May 16, 2017 to Aug 30, 2018, 190 pts were randomly assigned to sintilimab or chemotherapy (n = 95 per group). With the median follow-up of 7.2 months for sintilimab group and 6.2 months for chemotherapy group, the median OS in sintilimab was significantly higher than chemotherapy (7.2m vs. 6.2m, hazard ratio [HR] 0.70, P = 0.034). The objective response rate (ORR) was greater in sintilimab than chemotherapy with 12.6% vs. 6.3%, and the median duration of response was longer (8.3m vs. 6.2m). Incidences of treatment-related adverse events (TRAEs) of any grade (54.3% vs. 90.8%) and of grade 3-5 (20.2% vs. 39.1%) were both numerically less in sintilimab than in chemotherapy. The ORR in sintilimab versus chemotherapy in pts with tumor PD-L1 tumor proportion score (TPS) $\geq$1% and with TPS $\geq$10% were 20.2% vs. 0%, and 35.7% vs. 0%, respectively. In sintilimab group, pts with low NLR ($<$ 3) had a significant longer median OS (HR 0.54, P = 0.019) than with high NLR. **Conclusions:** Sintilimab was superior to chemotherapy with a significantly prolonged survival benefit and a favorable safety profile in pts with advanced ESCC refractory to first-line chemotherapy. High tumor PD-L1 expression (TPS $\geq$1% or $\geq$10%) might indicate more response benefit to sintilimab for these pts, and low NLR might be a positive predictive factor for sintilimab. Clinical trial information: NCT03116152. Research Sponsor: Innovent Biologics, Inc.

4512 Poster Discussion Session; Displayed in Poster Session (Board #120), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The association of molecular biomarkers with efficacy of pembrolizumab versus paclitaxel in patients with gastric cancer (GC) from KEYNOTE-061. *First Author: Charles S. Fuchs, Yale Cancer Center, Smilow Cancer Hospital, New Haven, CT*

Background: KEYNOTE-061 (NCT02370498) was a randomized, open-label, phase 3 study of pembrolizumab vs paclitaxel in patients with advanced gastric or gastroesophageal junction adenocarcinoma with tumor progression after first-line therapy (N =592). We explored the association of tissue tumor mutational burden (tTMB) status and clinical outcomes in patients with GC enrolled in KEYNOTE-061, including the relationship with PD-L1 combined positive score (CPS) and microsatellite instability-high (MSI-H) status. **Methods:** In patients from KEYNOTE-061 with evaluable tumor and matched normal whole exome sequencing (WES) data (N = 420; pembrolizumab, 218; paclitaxel, 202), the association of tTMB (continuous $\log_{10}$ scale) with confirmed ORR and PFS by blinded central radiology review per RECIST v1.1, and OS was evaluated within each treatment arm using logistic regression (ORR) and Cox proportional hazards regression (PFS; OS). The clinical utility of tTMB was assessed using the prespecified cutoff of 175 mut/exome. Clinical data cutoff: October 26, 2017. **Results:** tTMB was significantly associated (α=0.05) with ORR, PFS, and OS in patients treated with pembrolizumab (one-sided P<0.001) but not paclitaxel (two-sided P>0.600). The area under the receiver operating characteristics curve for tTMB and response (pembrolizumab vs paclitaxel) was 0.68 (95% CI, 0.56-0.81) vs 0.51 (95% CI, 0.39-0.63). Patient outcomes by tTMB cutoff are reported in Table. There was low correlation between tTMB and PD-L1 CPS in both treatment arms (r<0.18). tTMB remained significantly associated with all clinical end points with pembrolizumab after adjusting for PD-L1 CPS and with PFS and OS after excluding MSI-H patients. **Conclusions:** This exploratory analysis from KEYNOTE-061 is the first to demonstrate a strong association between tTMB and response to pembrolizumab in patients with GC. Data further suggest tTMB is a significant and independent predictor beyond PD-L1 status. Clinical trial information: NCT02370498. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	tTMB <175, pembrolizumab (n=178)	tTMB <175, paclitaxel (n=166)	tTMB ≥175, pembrolizumab (n=40)	tTMB ≥175, paclitaxel (n=36)
ORR, % (95% CI)	8.4 (4.8-13.5)	13.3 (8.5-19.4)	30.0 (16.6-46.5)	11.1 (3.1-26.1)
PFS, mo, median (95% CI)	1.5 (1.5-1.6)	4.1 (3.1-4.3)	4.1 (2.1-8.6)	4.1 (3.0-8.2)
HR (95% CI)	1.78 (1.43-2.22)	–	0.73 (0.44-1.22)	–
OS, mo, median (95% CI)	5.7 (4.7-8.7)	8.8 (8.3-9.9)	16.4 (10.8-NR)	8.1 (6.8-12.1)
HR (95% CI)	1.12 (0.89-1.41)	–	0.46 (0.27-0.81)	–

4513 Poster Discussion Session; Displayed in Poster Session (Board #121), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: A randomized, phase II, multicenter, open-label study (DESTINY-Gastric01). *First Author: Kohei Shitara, National Cancer Center Hospital East, Chiba, Japan*

Background: T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and topoisomerase I inhibitor. In a phase 1 trial of T-DXd (5.4 or 6.4 mg/kg), the objective response rate (ORR) was 43.2% (19/44) and median progression-free survival (mPFS) was 5.6 mo in patients with advanced HER2+ gastric cancer (GC). DESTINY-Gastric01 (DS8201-A-J202; NCT03329690) is an open-label, multicenter, randomized, phase 2 study of T-DXd in HER2-expressing advanced GC or GEJ adenocarcinoma; results are from the primary analyses for ORR and interim overall survival (OS) in HER2+ patients. **Methods:** Patients with centrally confirmed HER2+ (IHC 3+ or IHC 2+/ISH+ on archival tissue) GC that progressed on ≥ 2 prior lines were randomized 2:1 (T-DXd 6.4 mg/kg q3w or physician's choice [PC] irinotecan or paclitaxel). All patients received prior HER2 therapy. Stratification factors were region, ECOG PS (0;1), and HER2 status. The primary endpoint was unconfirmed ORR by independent central review. Secondary endpoints were OS (alpha controlled), PFS, disease control rate (DCR), duration of response (DOR), and safety. **Results:** 187 patients received T-DXd (n = 125) or PC (n = 62 [55 irinotecan; 7 paclitaxel]); 79.7% Japan, 20.3% Korea. Patients had a median of 2 prior lines of therapy, and 44.4% had ≥ 3. At data cutoff (8 Nov 2019), 22.4% of T-DXd and 4.8% of PC patients remained on treatment. ORR was 51.3% (61/119; 11 CR and 50 PR) with T-DXd vs 14.3% (8/56; all PR) with PC (P < .0001); confirmed ORR, 42.9% vs 12.5% (P < .0001); DCR, 85.7% vs 62.5% (P = .0005); mDOR, 11.3 vs 3.9 mo; mPFS, 5.6 vs 3.5 mo (HR, 0.47 [95% CI, 0.31-0.71]; P = .0003). OS was significantly prolonged with T-DXd (mOS, 12.5 vs 8.4 mo; HR, 0.59 [95% CI, 0.39-0.88]; P = .0097; prespecified O'Brien Fleming boundary, P = .0202); 12-month OS, 52.1% vs 28.9%. Grade ≥ 3 AEs occurred in 85.6% of patients with T-DXd vs 56.5% with PC; the most common were neutrophil count decreased (51.2%; 24.2%), anemia (37.6%; 22.6%), and white blood cell count decreased (20.8%; 11.3%). 12 patients (9.6%) had T-DXd–related interstitial lung disease (ILD; 2 grade 3, 1 grade 4, no grade 5) vs 0 with PC. 1 drug-related death (pneumonia [non-ILD] in the T-DXd arm) occurred. **Conclusions:** T-DXd demonstrated statistically significant and clinically meaningful improvements in ORR and OS compared with standard chemotherapy (paclitaxel or irinotecan) in patients with HER2+ advanced gastric or GEJ adenocarcinoma. Clinical trial information: NCT03329690. Research Sponsor: Daiichi Sankyo Co., Ltd.

4514 Poster Discussion Session; Displayed in Poster Session (Board #122), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab as second-line therapy for patients with advanced or metastatic gastroesophageal adenocarcinoma with or without prior docetaxel: Results from the phase II RAMIRIS Study of the AIO. *First Author: Sylvie Lorenzen, Klinikum rechts der Isar, Technische Universität München, III, Medizinische Klinik und Poliklinik, Munich, Germany*

Background: Ramucirumab (Ram) as monotherapy or plus paclitaxel is a proven second-line option for advanced gastroesophageal adenocarcinoma (GEA). More and more patients (pts) are pretreated with docetaxel in the perioperative or first-line setting. These pts may benefit more from another, non-cross resistant chemotherapy backbone regimen. This trial evaluates the addition of Ram to FOLFIRI as second line treatment. **Methods:** This is a multicenter, randomized, investigator initiated, phase II trial. Pts with GEA who have progressed after treatment with a fluoropyrimidine/platinum-containing regimen were randomized 2:1 to either FOLFIRI plus Ram every two weeks (Arm A) or paclitaxel (days 1, 8, 15 of a 28-day cycle) plus Ram every two weeks (Arm B). Major endpoints were overall survival (OS), objective response rate (ORR), disease control rate (DCR), progression free survival (PFS) and toxicity. **Results:** 111 pts (median age 61 years, 65% of pts had prior docetaxel therapy) were enrolled and 110 analyzed within intention to treat population (ITT, Arm A, 72; Arm B, 38). In the ITT, there was no significant difference in median OS (A, 6.8 vs. B, 7.6 months, HR 0.94, p = 0.77) and median PFS (A, 4.6 vs. B, 3.6 months, HR 0.72, p = 0.12). For pts with prior docetaxel use (71/110), median PFS was A, 4.3 vs. B, 2.0 months, HR 0.49, p = 0.008 and median OS was A, 7.5 vs. B, 6.4 months, HR 0.71, p = 0.25. In 101 pts with tumor assessment and included in the response analysis, ORR and DCR was 23% and 65% in Arm A and 11% and 60% in Arm B, respectively. 67 pts assessable for response were pre-treated with docetaxel. In these pts, ORR was 24% in Arm A and 9% in Arm B. Disease control rate (DCR) was 67% and 41% for Arm A and B respectively. Both therapies were similarly tolerable, final safety results will be shown. **Conclusions:** The RAMIRIS trial demonstrated feasibility of the combination of FOLFIRI and Ram. With a response rate of 24% and a median PFS of 4.3 months, docetaxel pre-treated pts seemed to derive pronounced benefit from FOLFIRI-Ram, providing a rationale for a phase III trial, which is currently ongoing. Clinical trial information: NCT03081143. Research Sponsor: Lilly.

4515 Poster Discussion Session; Displayed in Poster Session (Board #123), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase III APACT trial of adjuvant *nab*-paclitaxel plus gemcitabine (*nab*-P + Gem) versus gemcitabine (Gem) alone for patients with resected pancreatic cancer (PC): Outcomes by geographic region. *First Author: Michele Reni, IRCCS Ospedale, San Raffaele Scientific Institute, Milan, Italy*

Background: The APACT trial was one of the largest and most geographically diverse trials of adjuvant chemotherapy for resected PC, allowing for comparison of outcomes by geographic region. In this analysis, we report updated overall survival (OS) results for the intent-to-treat (ITT) population and examine outcomes by geographic region. **Methods:** Treatment-naive patients with histologically confirmed PC, macroscopic complete resection, Eastern Cooperative Oncology Group performance status 0 or 1, and carbohydrate antigen 19-9 < 100 U/mL were eligible. Stratification factors were resection status (R0/R1) and lymph node status (positive/negative). Treatment was initiated ≤ 12 weeks postsurgery. Patients received *nab*-P 125 mg/m^2 + Gem 1000 mg/m^2 or Gem 1000 mg/m^2 on days 1, 8, and 15 of six 28-day cycles. The primary endpoint was disease-free survival by independent review. Secondary endpoints were OS and safety. **Results:** The updated OS analysis (data cutoff date, January 2020) revealed a median OS of 41.8 months with *nab*-P + Gem compared with 37.7 months with Gem alone (hazard ratio [HR] 0.81; 95% CI, 0.68 - 0.97; nominal P = 0.047; Table). In each geographic region, the median OS with *nab*-P + Gem was numerically longer than with Gem alone. **Conclusions:** The updated OS analysis of the ITT population supports the previously reported trend favoring *nab*-P + Gem. The geographic regional analyses reveal numerically longer OS with *nab*-P + Gem vs Gem alone and variable outcomes by region; however, the differences do not support the trend observed in the ITT population, potentially due to limited sample sizes. Registration: EudraCT (2013-003398-91). Clinical trial information: NCT01964430. Research Sponsor: Bristol-Myers Squibb.

Survival Outcomes by Geographic Region.

	nab-P + Gem		Gem		HR	
Group	**n**	**Median (95% CI) OS, mo**	**n**	**Median (95% CI) OS, mo**	**(95% CI)**	***P* value**
ITT population	432	41.8 (35.55 - 46.75)	434	37.7 (31.11 - 40.51)	0.81 (0.68 - 0.97)	0.047
North America	144	38.5 (32.56 - 53.13)	156	35.0 (28.25 - 41.33)	0.73 (0.54 - 0.99)	0.11
Europe	203	41.8 (32.82 - 48.03)	205	38.1 (30.72 - 43.40)	0.88 (0.68 - 1.13)	0.40
Australia	30	31.5 (19.06 - NA)	20	28.1 (17.05 - 43.01)	0.65 (0.30 - 1.38)	0.39
Asia Pacific	55	45.5 (27.01 - NA)	53	40.6 (24.21 - NA)	0.83 (0.50 - 1.39)	0.43

NA, not applicable

4516 Poster Discussion Session; Displayed in Poster Session (Board #124), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine (GEM) and capecitabine (CAP) versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma: Five year follow-up. *First Author: John P. Neoptolemos, University of Heidelberg, Heidelberg, Germany*

Background: The ESPAC-4 trial demonstrated that adjuvant GEM/CAP for pancreatic cancer significantly improved survival compared to GEM monotherapy. The aim of this study is to evaluate the long-term outcomes in the ESPAC-4 trial. **Methods:** Patients with pancreatic ductal adenocarcinoma were randomized within 12 weeks of surgery (stratified for R0/R1 resection margin status and country) to have either six 4-week cycles of IV GEM alone or GEM with oral CAP. The primary endpoint was five-year survival; secondary endpoints were toxicity and relapse free survival. 722 patients (480 expected events), 361 in each arm, were needed to detect a 10% difference in 2-year survival rates with 90% power (log-rank test with 5% two-sided alpha). **Results:** Between Nov 10 2008 and Sep 11 2014, 732 patients were randomized with 730 included in the full analysis set (366 GEM, 364 GEM/CAP). Median age was 65 years, 57% were men. WHO performance status was 0, 1 or 2 in 42% 55% and 3% respectively. Postoperative median CA19-9 was 19 kU/L. Median maximum tumor size was 30 mm, 61% were R1 resections, 80% were node positive and 40% were poorly differentiated. The data freeze was on 24 February 2020; median follow up was 60 months with 531 overall deaths, 280 in GEM, and 251 in GEM/CAP. Median (95% CI) survival (months) for patients treated with GEM/CAP was 27.7 23.3 – 31.2) and 26.0 (22.7 – 28.4) for GEM. Five-year (95% CI) survival rates were 20 (16 – 25) % for GEM and 28 (23 – 33) % for GEM/CAP. Stratified log-rank analysis revealed an HR=0.84 [95% CI, 0.70 – 0.99]; χ^2 (1) = 3.87, P=0.049. 70 out of 366 GEM patients in the safety set reported 101 grade 3/4 serious adverse events, while 65 out of 359 GEM/CAP patients reported 97 grade 3/4 serious adverse events (P=0.724). **Conclusions:** Adjuvant GEM/CAP for pancreatic cancer had a statistically significant improvement in survival compared to GEM monotherapy. Clinical trial information: 96397434. Research Sponsor: Cancer Research UK.

4518 Poster Discussion Session; Displayed in Poster Session (Board #126), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A prospective randomized controlled trial of selective transarterial chemoembolization using drug-eluting beads loaded with epirubicin versus selective conventional transarterial chemoembolization using epirubicin-lipiodol for hepatocellular carcinoma: The JIVROSG-1302 PRESIDENT study. *First Author: Masafumi Ikeda, National Cancer Center Hospital East, Kashiwa, Japan*

Background: Transarterial chemoembolization (TACE) with selective catheterization into the segmental or subsegmental hepatic arteries supplying HCC is often performed to achieve the complete local control of HCC in the patients with a limited number of small sized nodules. To clarify which of TACE with drug-eluting beads loaded with epirubicin (DEB-TACE) or conventional TACE with epirubicin-lipiodol (cTACE) can achieve the complete response (CR) more frequently, we performed a randomized controlled trial of DEB-TACE vs. cTACE. **Methods:** Between March 2016 and May 2019, unresectable HCC patients with Child-Pugh class A or B who were scheduled to receive selective TACE were randomly assigned 1:1 to the DEB-TACE group and the cTACE group. The primary endpoint was the CR rate at 3 months, and the secondary endpoints were the CR rate at 1 month and rate of adverse events (AEs). The response and AEs were assessed according to the modified RECIST by an independent review committee and the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0., respectively. **Results:** A total of 200 patients (DEB-TACE, 99 patients; cTACE 101 patients) were enrolled from 22 Japanese institutions. The patient characteristics were well-balanced between the two groups. The median number of tumors was one in both groups and the median tumor size was 20.0 mm in the DEB-TACE group and 20.5 mm in the cTACE group. The table shows the CR rates and frequencies of AEs. The CR rates of cTACE at 3 and 1 months were significantly higher than those of DEB-TACE. The frequency of AEs (all grades), including pyrexia, malaise, increased serum total bilirubin (T-Bil) and increased serum alanine transaminase (ALT), was significantly higher in the cTACE group than in the DEB-TACE group. **Conclusions:** Selective cTACE appeared to have greater efficacy for local tumor control as compared to selective DEB-TACE, however, the frequencies of post-embolization syndromes were higher in the cTACE group than in the DEB-TACE group. Clinical trial information: UMIN000021250. Research Sponsor: National Cancer Center Research and Development Fund (26-A-27).

	DEB-TACE N = 99	cTACE N = 101	*p*-value
CR rate at 3 months	27.6%	75.2%	< 0.0001
CR rate at 1 month	35.7%	84.2%	< 0.0001
Any grade of AE: pyrexia	19%	46%	< 0.0001
Any grade of AE: malaise	11%	26%	0.0103
Any grade of AE: increased serum T-Bil	22%	49%	0.0001
Any grade of AE: increased serum ALT	35%	78%	< 0.0001

4519 Poster Discussion Session; Displayed in Poster Session (Board #127), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase Ib study of lenvatinib (LEN) plus pembrolizumab (PEMBRO) in unresectable hepatocellular carcinoma (uHCC). *First Author: Andrew X. Zhu, Massachusetts General Hospital Cancer Center and Jiahui International Cancer Center, Boston, MA*

Background: LEN is a multikinase inhibitor of VEGFR 1–3, FGFR 1–4, PDGFRα, RET, and KIT, approved for first line (1L) treatment of uHCC. PEMBRO, an anti-PD-1 monoclonal antibody, was granted accelerated approval for the treatment of patients (pts) with HCC after sorafenib therapy. We assessed the safety and efficacy of LEN + PEMBRO in uHCC. **Methods:** In this phase 1b trial (NCT03006926), pts received LEN 12 mg/day (bodyweight [BW] ≥60 kg) or 8 mg/day (BW <60 kg) orally + PEMBRO 200 mg IV on Day 1 of a 21-day cycle. Primary endpoints were safety and tolerability for Part 1 and objective response rate (ORR) and duration of response (DOR) by mRECIST and RECIST v1.1 per independent imaging review (IIR) in the 1L setting for Part 2. **Results:** 104 pts (part 1, n=6; part 2, n=98) were enrolled. No DLTs were reported in Part 1; 100 pts were included in the 1L analysis of LEN + PEMBRO–4 pts (part 1) excluded due to prior sorafenib. At data cutoff (October 31, 2019) and median follow-up of 10.6 months, 37 pts continued treatment (LEN only, n=3; both drugs, n=34); median duration of treatment was 7.9 months (LEN, 7.6 months; PEMBRO, 7.4 months). Median OS was 22.0 months (95% CI 20.4–not estimable [NE]), median PFS was 8.6 months (95% CI 7.1–9.7), and ORR was 36% (95% CI 26.6–46.2) (RECIST v1.1 per IIR). Additional efficacy outcomes are shown in the table. Treatment-emergent adverse events (TEAEs) occurred in 99% of pts (grade ≥3, 85%; grade ≥4, 23%). The most common grade ≥3 TEAE was hypertension (18% of pts). Treatment-related AEs (TRAEs) occurred in 95% of pts (grade ≥3, 67%; grade ≥4, 4%). The most common grade ≥3 TRAE was hypertension (17% of pts). 36% of pts had serious TRAEs and 3 pts died from a TRAE (acute respiratory failure/acute respiratory distress syndrome, n=1; intestinal perforation, n=1; abnormal hepatic function, n=1). **Conclusions:** LEN + PEMBRO has promising antitumor activity with a tolerable safety profile. An ongoing phase 3 trial (NCT03713593) is assessing LEN + PEMBRO vs LEN alone as 1L therapy for uHCC. Clinical trial information: NCT03006926. Research Sponsor: This study was sponsored by Eisai Inc., Woodcliff Lake, NJ, USA, and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., Kenilworth, NJ, USA.

	mRECIST per IIR*	RECIST v1.1 per IIR*	mRECIST per investigator review*
ORR, n (%)	46 (46)	36 (36)	41 (41)
95% CI	36.0–56.3	26.6–46.2	31.3–51.3
Complete response (CR)	11 (11)	1 (1)	5 (5)
Partial response (PR)	35 (35)	35 (35)	36 (36)
Median DOR, months (95% CI)	8.6 (6.9–NE)	12.6 (6.9–NE)	12.6 (6.2–18.7)
Median time to response, months (range)	1.9 (1.2–5.5)	2.8 (1.2–7.7)	2.7 (1.2–11.8)
Disease control rate†, n (%)	88 (88)	88 (88)	86 (86)
95% CI	80.0–93.6	80.0–93.6	77.6–92.1
Median PFS, months (95% CI)	9.3 (5.6–9.7)	8.6 (7.1–9.7)	8.2 (7.4–9.7)

*n=100 †CR + PR + stable disease (≥5 weeks)

4520 Poster Discussion Session; Displayed in Poster Session (Board #128), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II study assessing tolerability, efficacy, and biomarkers for durvalumab (D) ± tremelimumab (T) and gemcitabine/cisplatin (GemCis) in chemonaïve advanced biliary tract cancer (aBTC). *First Author: Do-Youn Oh, Seoul National University Hospital, Seoul, South Korea*

Background: In aBTC, GemCis is the standard of care as 1st-line treatment. Immunotherapies have shown early promising efficacy in some BTC patients (pts). We assessed D (anti-PD-L1) ± T (anti-CTLA-4) and GemCis in 1L BTC pts, including an extensive biomarker analysis (NCT03046862). **Methods:** Pts were first enrolled in the biomarker cohort (BMC) to receive 1 cycle of Gem 1000 mg/m^2 + Cis 25 mg/m^2 on D1 & D8, followed by GemCis + D 1120 mg and T 75 mg, Q3W until disease progression (PD). Subsequent pts were allocated to GemCis + D (3 combo cohort [3C]) or GemCis + D+T (4 combo cohort [4C]) until PD. In all cohorts, tumor biopsies were obtained pretreatment, after 1 cycle, and at PD. Blood samples for ctDNA were obtained every cycle. **Results:** 121 pts were enrolled. Median follow-up durations were 28.5 months (m; 95% CI, 26.5-30.5), 11.3 m (95% CI, 9.1-13.5), and 11.9m (95% CI, 8.4-15.4) in the BMC, 3C, and 4C arms, respectively. Efficacy data are shown (Table). The most common adverse events (AEs, any grade) were neutropenia (54.5%), nausea (59.5%), and pruritus (55.44%). The most common grade 3/4 AEs were neutropenia (50.4%), anemia (35.5%), and thrombocytopenia (16.5%). In the BMC cohort, frequent mutations were found in DNA damage repair, cell cycle regulation, and genome instability genes (eg, *ATM*, *BRCA2*, *POLE*, *MSH2*, *CDKN2A*). Distinct somatic variants were detected in responders vs non-responders. Baseline tissue TMB did not correlate with PFS or OS. Reductions in ctDNA variant allele frequency (VAF) were more prominent among responders during early D+T cycles. ctDNA VAF on C3, D1 was significantly correlated with ORR (P< 0.015). Pretreatment PD-L1 expression was not associated with efficacy, but PD-L1 expression after 1st GemCis cycle trended with improved PFS. **Conclusions:** These are the first clinical data of D±T plus chemotherapy in chemo-naïve aBTC pts. The addition of immunotherapy to chemotherapy was tolerable and showed very promising efficacy. Biomarker analyses show early signs of markers associated with response. The combination of GemCis + D is being investigated in the Phase 3 TOPAZ-1 trial (NCT03875235). Clinical trial information: NCT03046862. Research Sponsor: AstraZeneca.

	BMC (n = 30)	3C (n = 45)	4C (n = 46)
ORR (95% CI), %	50.0 (32.1-67.9)	73.4 (60.5-86.3)	73.3 (60.4-86.2)
DCR (95% CI), %	96.7 (90.3-100)	100 (100-100)	97.8 (93.5-100)
mDOR (95% CI), m	11.0 (3.9-11.8)	9.8 (8.1-11.4)	9.1 (4.5-15.0)
mPFS (95% CI), m	13.0 (10.1-15.9)	11.0 (7.0-15.0)	11.9 (10.1-13.7)
mOS (95% CI), m	15.0 (10.7-19.3)	18.1 (11.3-24.9)	20.7 (13.8-27.6)

4521 Poster Session (Board #129), Fri, 8:00 AM-11:00 AM

Neoadjuvant chemotherapy plus surgery for high-risk advanced gastric cancer: Long-term results of KDOG1001 trial. *First Author: Kei Hosoda, Department of Upper Gastrointestinal Surgery, Kitasato University School of Medicine, Sagamihara, Japan*

Background: In the phase 2, open-label, KDOG1001 (UMIN000003642) study, neoadjuvant chemotherapy (NAC) with docetaxel, cisplatin, and S-1 (DCS), followed by gastrectomy with D2 lymph node dissection for high-risk advanced gastric cancer showed feasibility of DCS therapy with an enough R0 resection rate of 90%. Here we present long-term results after a minimum follow-up of 3 years. **Methods:** Patients with bulky node metastasis (bulky N), linitis plastica (type 4), or large ulcero-invasive-type tumors (type 3) received up to four 28-day cycles of DCS neoadjuvant chemotherapy (docetaxel at 40 mg/m^2, cisplatin at 60 mg/m^2 on day 1, and S-1 at 40 mg/m^2 twice daily for 2 weeks) followed by gastrectomy with D2 lymphadenectomy. This analysis presents the final preplanned assessment of outcomes after 3 years. Primary endpoint was R0 resection rate. Secondary endpoints included overall survival (OS), progression free survival (PFS), completion rate of the protocol treatment, and pathological response rate (pRR) of DCS NAC. **Results:** Of 40 patients enrolled from May 2010 through January 2017, 7 (17.5%) had bulky N, 18 (45.0%) had type 4, and 16 (40%) had large type 3 with 1 (2.5%) having both large type 3 and bulky N2. All included patients underwent preoperative DCS chemotherapy followed by surgery with D2 lymphadenectomy with 32 (80%) completed postoperative S-1 therapy for 1 year. After a median follow-up for surviving patients of 67 mo (range, 36 mo to 110 mo) at the last follow-up in January 2020, 3-year OS was 78% [95% confidence interval (CI) 62–88%], while 3-year PFS was 63% (95% CI 47–76%). Completion rate of the protocol treatment was 62.5% (25/40) with pRR of 57.5% (23/40). In bulky N2, 3-y OS was 86% and 3-y PFS was 71% with pRR of 100%. In type 4, 3-y OS was 67% and 3-y PFS was 50% with pRR of 44%. In large type 3, 3-y OS was 88% and 3-y PFS was 75% with pRR of 56%. Patients with type 4 had significantly worse OS and PFS than those with the other types [HR 7.20 (95% CI 2.23–32.21) and HR 3.00 (95% CI 1.21–8.19)]. **Conclusions:** Preoperative chemotherapy with up to four cycles of DCS followed by gastrectomy plus adjuvant S-1 therapy is a promising treatment strategy for patients with bulky node metastasis, type 4 and large type 3 gastric cancers. For type 4 cancer, further improvement of treatment strategy is needed. Clinical trial information: 000003642. Research Sponsor: None.

4522 Poster Session (Board #130), Fri, 8:00 AM-11:00 AM

A phase II study of rh-endostatin combined with paclitaxel and nedaplatin in treating patients with recurrent or metastatic esophageal squamous cell carcinoma (ESCC). *First Author: Zhiqiang Wang, Department of Medical Oncology, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Sun Yat-sen University, Guangzhou, China*

Background: For patients (pts) with metastatic ESCC, the prognosis is poor. Rh-endostatin (endostar), a potent inhibitor of angiogenesis, has shown clinical activity when combined with chemoradiotherapy in treating locally advanced ESCC. This single-arm phase 2 study was designed to assess the efficacy and safety of endostar combined with paclitaxel and nedaplatin in treating pts with recurrent or metastatic ESCC. **Methods:** Eligible pts had recurrent or metastatic ESCC and Karnofsky score ≥70. Endostar (30 mg/day, continuous infusion, day 1-14) plus paclitaxel (150 mg/m^2, day 4) and nedaplatin (80 mg/m^2, day 4) were administered every 3 weeks for 6 cycles followed by maintenance therapy with endostar. Primary endpoint was progression-free survival (PFS). Secondary endpoints included objective response rate (ORR), disease control rate (DCR), overall survival (OS) and adverse events (AEs). **Results:** From January 2015 to August 2019, 53 pts were enrolled. 44 (83%) pts were male. The median age was 59 years. 43 (81%) pts had pathology of poor or moderate differentiated ESCC. The middle and lower thirds of the esophagus (81%) were the most common primary tumor sites. 11 (21%) patients had undergone esophagectomy. At the time of treatment, 49 (93%) pts were diagnosed with clinical stage IVB. The most common metastatic sites were lymph node (91%), lung (32%) and liver (26%). 50 pts were assessable for response. No complete response was observed. 21 pts achieved a best response of partial response and 14 pts had stable disease. ORR was 42% and DCR was 70%. The median PFS and OS was 5.1 months (95% CI 3.7-6.6 months) and 13.2 months (95% CI 8.0-18.4 months) respectively. The most common AEs observed during this study were anemia (49.1%), neutropenia (34%), fatigue (28.3%) and anorexia (26.4%). The most common Grade 3/4 AE observed was neutropenia (17%). **Conclusions:** The combination of endostar plus paclitaxel and nedaplatin is a well tolerated treatment modality with promising activity in previously untreated recurrent or metastatic ESCC. Its efficacy and safety could be further studied in randomized trials. Clinical trial information: NCT02350517. Research Sponsor: Simcere.

4523 Poster Session (Board #131), Fri, 8:00 AM-11:00 AM

Pembrolizumab (pembro) versus standard of care chemotherapy (chemo) in patients with advanced gastric or gastroesophageal junction adenocarcinoma: Asian subgroup analysis of KEYNOTE-062. *First Author: Hironaga Satake, Kobe City Medical Center General Hospital, Kobe City, Japan*

Background: First-line treatment with pembro or pembro + chemo vs chemo alone was evaluated in patients with PD-L1 combined positive score (CPS) ≥1, HER2-negative advanced gastric cancer in the randomized, active-controlled, phase 3 KEYNOTE-062 study (NCT02494583). We present results from the Asian subpopulation receiving pembro monotherapy or chemo. **Methods:** Eligible patients were randomly assigned 1:1:1 to pembro 200 mg, pembro + chemo (cisplatin + 5-FU or capecitabine), or placebo + chemo every 3 weeks for ≤35 cycles (~2 years). Randomization was stratified by region, disease status, and fluoropyrimidine treatment. Primary end points for this analysis were overall survival (OS) in patients with CPS ≥1 and patients with CPS ≥10; progression-free survival (PFS) and objective response rate (ORR) were exploratory end points. Data cutoff was March 26, 2019. **Results:** Globally, 256 patients received pembro monotherapy and 250 received chemo. Pembro was noninferior to chemo for OS in CPS ≥1 per prespecified margins (median OS, 10.6 vs 11.1 months, respectively; HR [99.2% CI], 0.91 [0.69-1.18]). In the Asian population 62 patients received pembro and 61 received chemo; 26 and 22 had CPS ≥10 (Table). Compared with the global population, Asian patients had a higher proportion of ECOG performance status 0, more diagnoses of stomach cancer, and a greater proportion with 0-2 metastatic sites. Median OS was longer with pembro than chemo using both CPS cutoffs (HR [95% CI]: CPS ≥1, 0.54 [0.35-0.82]; CPS ≥10, 0.43 [0.21-0.89]); 12- and 24-month OS rates were higher for pembro using both CPS cutoffs (12-month OS: CPS ≥1, 69% vs 54%; CPS ≥10, 81% vs 68%; 24-month OS: CPS ≥1, 45% vs 23%; CPS ≥10, 54% vs 27%). The HR (95% CI) for PFS was 1.11 (0.76-1.64) for CPS ≥1 and 0.71 (0.36-1.39) for CPS ≥10. **Conclusions:** In Asian patients with advanced gastric cancer, OS favored pembro in patients with CPS ≥1 and CPS ≥10. Clinical trial information: NCT02494583. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	CPS ≥1		CPS ≥10	
	Pembrolizumab n = 62	Chemotherapy n = 61	Pembrolizumab n = 26	Chemotherapy n = 22
Median OS, months	22.7	13.8	28.5	14.8
HR (95% CI)	0.54 (0.35-0.82)	—	0.43 (0.21-0.89)	—
12-month OS, %	69.4	54.1	80.8	68.2
24-month OS, %	44.8	23.0	53.6	27.3
Median PFS, months	4.1	6.5	7.2	6.9
HR (95% CI)	1.11 (0.76-1.64)	—	0.71 (0.36-1.39)	—
12-month PFS, %	26.9	21.3	25.1	18.3
ORR, %	22.6	37.7	26.9	31.8

4524 Poster Session (Board #132), Fri, 8:00 AM-11:00 AM

HX008, an anti-PD1 antibody, plus irinotecan as second-line treatment for advanced gastric adenocarcinoma: A phase II clinical trial. *First Author: Yan Song, Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: Patients with advanced gastric or gastro-oesophageal junction cancer that progresses on chemotherapy have poor outcomes. We investigated HX008, an Anti-PD1 Antibody, with irinotecan in patients with advanced gastric or gastro-oesophageal junction cancer that progressed on first-line chemotherapy with a platinum and/or fluoropyrimidine. **Methods:** This study is a multicenter, open, phase II clinical study of recombinant humanized anti-pd-1 monoclonal antibody HX008 injection plus Irinotecan that was conducted at 11 hospitals in China. Eligible patients are adults with histologically confirmed advanced gastric or gastro-oesophageal junction cancer. Subjects participating in this study are required to submit a archived tumor tissue specimen or newly obtained biopsy of tumor lesions at the site of no previous radiotherapy and peripheral blood (2mL) for detection of PD-L1 and MSI/MMR expression. The samples will be tested for expression of PD-L1 and MMR by immunohistochemistry (IHC) in the central laboratory, and MSI levels will be determined by polymerase chain reaction (PCR) and gel electrophoresis. Subjects received PD-1 monoclonal antibody HX008 at 200mg (d1, intravenous drip, once every 3 weeks) plus irinotecan at 160mg/m2 (d1, intravenous drip, 60 ~ 120min, once every 2 weeks). Response was assessed every 6 weeks in accordance with Response Evaluation Criteria in Solid Tumors version 1.1. Primary endpoints was objective remission rate (ORR). **Results:** Between October 2018 and September 2019, a total of 58 patients with advanced gastric or gastro-oesophageal junction cancer were enrolled in this study. Median (range) age was 61 (27-71) years, and most patients were male (72.4%). Among 53 patients who were evaluated, 15 (28.3%) experienced objective response and 22 (41.5%) experienced stable disease (SD). The median progression free survival (PFS) was 5.4 months, the one-year survival rate was 71.3%. The most common treatment-related adverse events of grade 3 or 4 included neutropenia(31.0%), anemia(15.5%), loss of appetite (6.9%), vomiting(5.2%), nausea(3.4%), diarrhea (1.7%) and fatigue (1.7%). There were no treatment-related deaths. **Conclusions:** HX008 injection plus Irinotecan demonstrated promising activity and manageable safety in patients with advanced gastric or gastro-oesophageal junction cancer that progressed on first-line chemotherapy with a platinum and fluoropyrimidine. Clinical trial information: NCT03704246. Research Sponsor: None.

4525 Poster Session (Board #133), Fri, 8:00 AM-11:00 AM

A phase Ib study of nivolumab plus trastuzumab with S-1/capecitabine plus oxaliplatin for HER2-positive advanced gastric cancer (Ni-HIGH study): Safety evaluation. *First Author: Daisuke Takahari, Department of Gastroenterology, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan*

Background: Addition of an anti-PD-1 antibody to trastuzumab (Tmab) reportedly enhances ADCC activity of Tmab, leading to an additive antitumor effect. We investigated the safety and tolerability of nivolumab (Nivo) plus Tmab combined with S-1 or capecitabine (Cape) and oxaliplatin (Ox) for pts with HER2-positive (+) advanced gastric cancer (AGC). Here, we report the safety evaluation results. **Methods:** This open-label, phase 1b study was conducted at four centers in Japan. The study consisted of safety (n = 12) and expansion (n = 24–30) parts. Chemotherapy-naïve pts aged ≥ 20 years with histopathologically confirmed HER2+ AGC and measurable lesions were eligible. In the safety evaluation, pts were assigned to cohort 1 or 2 in sequence. Pts received Nivo (360 mg, day 1), Tmab (course 1: 8 mg/kg; course 2–: 6 mg/kg, day 1), Ox (130 mg/m^2, day 1) and either S-1 (40 mg/m^2 bid, days 1–14; cohort 1) or Cape (1000 mg/m^2 bid, days 1–14; cohort 2) every 3 weeks until disease progression or unacceptable toxicity. The primary purpose of the safety evaluation was to determine the toxicity and tolerability of this combination therapy. An independent data and safety monitoring committee assessed the tolerability of the study treatments before starting the second treatment course. A preliminary evaluation of tumor response on the cut-off date (December 16, 2019) was also performed. **Results:** From November 2018 to August 2019, 12 pts with HER2+ AGC were enrolled in the safety part (six pts each in cohorts 1 and 2). During the 1st course, all 12 pts experienced at least one adverse event (AE). The most common AEs were peripheral sensory neuropathy (PSN) (n = 4) and leukocytopenia (n = 3) in cohort 1 and PSN (n = 5) and anorexia (n = 4) in cohort 2. AEs of grade ≥ 3 were observed in only one pt in cohort 1 (grade 3 neutropenia). No pt suspended or discontinued study treatments due to AEs. One pt in cohort 1 reduced dose of S-1 due to grade 2 erythema and continued the subsequent courses with the dose. After a median follow-up of 6.1 (range, 3.1–13.3) months, one pt from cohort 1 achieved a complete response, eight pts (four in each cohort) achieved a partial response, and three pts (one in cohort 1 and two in cohort 2) showed stable disease. No progressive disease was observed. **Conclusions:** Both Nivo plus Tmab and either S-1 or Cape plus Ox are tolerable in pts with HER2+ AGC. Both cohorts 1 and 2 have progressed to the expansion part of the study. Clinical trial information: 000034222. Research Sponsor: ONO pharmaceutical co.

4526 Poster Session (Board #134), Fri, 8:00 AM-11:00 AM

Assessment of FcgRIIIA single nucleotide polymorphisms (SNPs) on the efficacy of IgG1 monoclonal antibodies (mAbs) in PANGEA study patients (pts) with advanced gastroesophageal adenocarcinoma (aGEA). *First Author: Anthony Serritella, University of Chicago Medical Center, Chicago, IL*

Background: Targeted therapies (Ttx) have had limited efficacy in aGEA. The phase IIa PANGEA trial assessed the outcomes of pts treated with IgG1 mAbs targeting receptor tyrosine kinases (RTKs) or PD-1 based on predefined molecular groups. The fragment C (Fc) portion of mAbs binds to IgG receptors (FcgR) of immunologic effector cells such as natural killer (NK) cells, leading to antibody-dependent cell-mediated cytotoxicity (ADCC). The FcgR subclass, FcgRIIIA, has genetic variants with different Fc binding affinities. A single nucleotide polymorphism (SNP) in FcgRIIIA substitutes phenylalanine (F) with valine (V) at amino acid position 158, enhancing FcgR's affinity for the IgG1 Fc domain. Pts with V/V or V/F FcgRIIIA allotypes have enhanced NK cell binding affinity compared to the homozygous F/F allotype. We evaluated the association of FcgRIIIA SNPs on Ttx outcomes amongst PANGEA pts and another cohort of aGEA pts treated with IgG1 mAbs. **Methods:** Whole-blood samples were identified from aGEA pts (N = 104), including 70/80 available PANGEA pts, who were treated with an IgG1 mAb (trastuzumab 24, anti-EGFR 21, anti-PD1 30, ramucirumab 48) in at least 1 Ttx line. After lymphocyte DNA extraction, FcgRIIIA genotyping was performed. The Cox proportional hazard model and log-rank tests, adjusted for pt age, were used to assess for an association of genotype with overall survival (OS). **Results:** Of 104 genotyped pts, the F/F, F/V & V/V genotypes were observed at a frequency of 32%, 51% and 17% respectively. There was no significant difference in median OS (mOS) between the F/F, F/V or V/V or comparing F/F vs V/F+V/V overall, nor in the PANGEA-only cohort. A trend of increased mOS was seen in 20 non-PANGEA pts harboring F/V or V/V compared to 14 F/F pts (mOS 43.4 vs 23.1 months, HR 0.41 [0.15-1.14] p = 0.09). However, 3-year OS rates trended higher in V/F+V/V pts (22%, 16/71) compared to F/F pts (7%, 2/33) (p = 0.09). At 3 years, 50% of V/V+V/F non-PANGEA pts were alive versus 13% of F/F pts (p = 0.04), while 13% of V/V+V/F PANGEA pts were alive versus 0% of F/F pts (p = 0.32). **Conclusions:** Amongst pts receiving IgG1 mAbs, the high affinity V FcgRIIIA SNP enriched for a subgroup of 'extreme responders' alive 3 years from diagnosis. Multivariate analyses accounting for baseline characteristics in a larger number of pts are ongoing to further elucidate the role of FcgRIIIA SNPs as predictive biomarkers. These findings may have implications on IgG1 mAb ADCC optimization. Research Sponsor: K23 award CA178203-01A1 from the National Cancer Institute, the University of Chicago Comprehensive Cancer Center Award in Precision Oncology-Cancer Center Support Grant P30CA014599, the Castle Foundation, Live Like Katie Foundation Award, Other Foundation.

4527 Poster Session (Board #135), Fri, 8:00 AM-11:00 AM

Tumor response and growth rate of nivolumab treatment in advanced gastric cancer: Real-world data from a large observational/translational study, JACCRO GC-08 (deliver trial). *First Author: Ryohei Kawabata, Department of Surgery, Osaka Prefectual General Medical Center, Osaka, Japan*

Background: Nivolumab (Nivo) demonstrated survival benefit in previously treated gastric cancer (GC) patients (pts), with a response rate (RR) of 11% and a disease control rate (DCR) of 40% (Kang YK, et al. *Lancet* 2017). There are few real-world data of Nivo and its predictive markers are needed in GC. It has been demonstrated that some tumors grow rapidly after Nivo treatment, but the proportion is uncertain. **Methods:** DELIVER trial was a prospective, multicenter, observational/translational study which assessed pts with advanced GC treated with Nivo alone and ECOG Performance Status (PS) 0-2 (UMIN000030850). The aims were to evaluate the efficacy and safety of Nivo in real world, and to discover novel host-related immune-biomarkers (gut microbiome, genetic polymorphism, gene expression, and metabolome) using fecal and blood samples which were collected before and after Nivo treatment. The RR, DCR, progression-free survival, overall survival, and tumor growth rate (TGR) were estimated as the efficacy. The response was evaluated by first imaging based on RECIST version 1.1. The TGR was calculated as a percentage increase in tumor volume during 1 month (Champiat et al. *Clin Cancer Res* 2017). **Results:** A total of 501 pts was enrolled in this study from Mar 2018 to Aug 2019, and 487 pts were evaluable for analysis (median age 70-y, 71% male, ECOG PS0/1/2 42%/44%/14%, tub/por/sig 45%/41%/5%, 21% HER2-pos, 42% pts with ascites). The DCR was 39.2% (95%CI 34.9-43.7) in evaluable pts. In 282 pts with measurable lesions, the RR was 6.7% (95%CI 4.1-10.3) and DCR was 36.5%. Sub-analysis by patient background indicated that DCR was 41% for PS0, 42% for PS1, and 24% for PS2. In addition, the DCR was lower in pts with ascites compared to those without ascites (28.6% vs. 47.0%, p= 0.005). The TGR decreased after introduction of Nivo in 124 (56.6%) of 219 evaluable pts for TGR; however, 20.5% pts were identified as experiencing hyper-progressive disease (HPD) which was defined as a ≥2-fold increase of the TGR before and after Nivo. When defining HPD as a ≥2-fold increase of tumor growth kinetics ratio and 50% increase of tumor burden, 9.6% pts experienced it. **Conclusions:** The real-word data of the large observational trial showed a comparable DCR to that of clinical trial in advanced GC treated with Nivo. This trial revealed the tumor behavior and some pts who experienced rapid tumor growth after Nivo treatment in clinical practice; biomarkers for HPD and the definition should be established. Clinical trial information: UMIN000030850. Research Sponsor: Ono Pharmaceutical and Bristol-Myers Squibb.

4528 Poster Session (Board #136), Fri, 8:00 AM-11:00 AM

Evaluation of spatiotemporal heterogeneity of PDL1 expression in gastroesophageal adenocarcinoma (GEA) at baseline diagnosis and after chemotherapy. *First Author: Katherine I. Zhou, University of Chicago, Chicago, IL*

Background: PDL1 expression is a predictive marker for response to anti-PD1/PDL1 agents (IO) for GEA. As a prognostic biomarker, data are conflicting. Molecular heterogeneity of various biomarkers for GEA has been established. To characterize heterogeneity of PDL1 expression and its clinical relevance, we compared PDL1 expression in primary (1^O) and metastatic (met) tumors of newly diagnosed stage IV advanced GEA (aGEA), and before and after chemotherapy treatment (tx) for stage II–IV GEA. We assessed the prognostic relevance of PDL1 expression in aGEA. **Methods:** We retrospectively reviewed a cohort of 130 patients (pts) diagnosed with GEA in 2013–2019, with a total of 328 tumor samples with PDL1 expression data. PDL1 was defined as positive if combined positive score (CPS) was ≥1 using the 22C3 pharmDx assay. Analysis was performed by McNemar's test for paired PDL1 and univariate Cox proportional-hazards model for overall survival (OS). **Results:** Of 328 tumors, 45% were PDL1+ and 55% PDL1-. CPS ranged 0–100 (median 1, IQR 0–5), and CPS was ≥10 for 19% of tumors. Concordance between PDL1 status of paired baseline 1^O and baseline met tumors was 63% (32/51) (Table). Of 31 PDL1+ baseline 1^O tumors, 52% (16/31) had PDL1- paired baseline met tumors, while of 20 PDL1- baseline 1^O tumors, only 15% (3/20) had PDL1+ paired baseline met tumors. Only 35% (18/51) of met tumors were PDL1+, compared to 61% (31/51) PDL1+ 1^O tumors ($p<$ 0.003). Post-tx tumors exhibited 62% (46/74) concordance of PDL1 status compared to pre-tx 1^O tumors. Of 43 PDL1+ baseline tumors, 35% (15/43) were PDL1- post-tx; of 31 PDL1- baseline tumors, 42% (13/31) were PDL1+ post-tx (p= 0.71). In pts with aGEA at diagnosis, OS did not significantly differ depending on baseline 1^O tumor PDL1 status (median OS of 17.9 [95% CI 14.6–26.5] months for PDL1- and 16.7 [12.0–26.3] months for PDL1+; p= 0.6), nor depending on baseline met PDL1 status. **Conclusions:** PDL1 expression demonstrated notable baseline discordance between 1^O and met tumors, particularly directional from PDL1+ 1^O tumor to PDL1- met. Discordance before and after chemotherapy was also observed, but with similar proportions of PDL1+ pre-tx and post-tx tumors. These findings may have predictive IO therapeutic implications if confirmed in larger independent analyses. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

	Baseline met PDL1-	Baseline met PDL1+	Post-tx PDL1-	Post-tx PDL1+
Baseline 1^O PDL1-	17	3	18	13
Baseline 1^O PDL1+	16	15	15	28

4529 Poster Session (Board #137), Fri, 8:00 AM-11:00 AM

Phase II study of intraperitoneal paclitaxel combined with S-1 plus cisplatin for gastric cancer with peritoneal metastasis: SP + IP PTX trial. *First Author: Daisuke Kobayashi, Department of Gastroenterological Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan*

Background: Intraperitoneal (IP) chemotherapy is a promising treatment option for gastric cancer with peritoneal metastasis. Although a phase III study failed to show a statistically significant superiority of IP paclitaxel (PTX) combined with S-1 and intravenous PTX over S-1/cisplatin (SP), the standard of care as a first-line treatment in Japan, the sensitivity analysis suggested clinical efficacy of the IP PTX. Thus, attempts to combine IP PTX with other systemic therapies with higher efficacy have been warranted. After a dose-finding study, we sought to explore efficacy of a new regimen that combined IP PTX with SP. **Methods:** Gastric cancer patients with peritoneal metastasis confirmed by diagnostic imaging, laparoscopy or laparotomy were enrolled in the phase II multi-institutional prospective trial. In addition to the established SP regimen (S-1 administered orally at a dose of 80 mg/m^2 bid for 21 days followed by a 14-day rest and cisplatin administered intravenously at a dose of 60 mg/m^2 on day 8), IP PTX was administered on days 1, 8 and 22 at a dose of 20 mg/m^2. The primary endpoint is overall survival (OS) rate at one year after treatment initiation. Secondary endpoints are progression free survival (PFS), response rate and toxicity. **Results:** Fifty-three patients were enrolled and fully evaluated for OS and toxicity. The median number of courses was 7 (range 1-20). The 1-year OS rate was 74% (95% CI, 60-83%). The median survival time was 19.4 months (95% CI, 16.7 months-). The 1-year PFS rate was 57% (95% CI, 42-69%). The overall response rate was 20% (95% CI, 1-72%) in 5 patients with target lesions. Cancer cells ceased to be detected by peritoneal cytology in 23 (64%) of 36 patients. Fourteen (26%) patients underwent gastrectomy after response to chemotherapy. The incidences of grade 3/4 hematological and non-hematological toxicities were 43% and 47%, respectively. The frequent grade 3/4 toxicities included neutropenia (23%), anemia (29%), diarrhea (13%) and anorexia (17%). Intraperitoneal catheter and implanted port-related complications were observed in 4 patients. There was 1 treatment-related death. **Conclusions:** IP PTX combined with SP is well tolerated and active in gastric cancer patients with peritoneal metastasis. Clinical trial information: UMIN000023000. Research Sponsor: Japan Society of Clinical Oncology.

4530 Poster Session (Board #138), Fri, 8:00 AM-11:00 AM

Gastric inflammatory prognostic index (GIPI) to predict efficacy of PD-1/PD-L1 immune checkpoint inhibitors in metastatic gastroesophageal junction (GOJ)/gastric cancer (GC) patients. *First Author: Cristina Morelli, Tor Vergata University Hospital, Rome, Italy*

Background: ICIs demonstrated improved overall survival (OS) in heavily pretreated mGOJ/GC pts. Pts selection exclusively based on PD-L1 tissue expression appears to be suboptimal, despite data from subgroup analyses of KEYNOTE trials. Strong rationale suggests a potential predictive role of inflammatory biomarkers in ICIs treated mGOJ/GC pts. **Methods:** Ten systemic inflammatory markers [platelets, monocytes, neutrophil/lymphocyte ratio (NLR), platelets-lymphocyte ratio, lymphocytes, sum of mononuclear cells, albumin, lactate dehydrogenase, c-reactive protein (CRP) and serum globulin] were retrospectively analyzed at baseline in 57 mGOJ/GC pts with unknown PD-L1 status treated in second-line with ICIs, and correlated with OS. Least Absolute Shrinkage and Selection Operator (LASSO) method was used to select variables (preliminarily subject to optimal coding using HR smoothed curves for OS) with the highest prognostic value. Selected variables were then analyzed in a multivariate Cox Regression Model and used to build a GIPI nomogram. **Results:** NLR and CRP taken as continuous variables and albumin categorized as $<$ vs $>$ 30 g/dL were found as the most meaningful independent predictors of OS and used to build the GIPI nomogram. Nomogram-based lowest (l), mid-low, mid-high and highest (h) risk quartiles were associated with median(m)OS of 14.9, 7.1, 5.6 and 2.1 months (mos), respectively [HR of l vs h 4.94, p 0.0002]. By optimally dichotomizing CRP and NLR, pts with one or more of the following risk factors: NLR $>$6, CRP $>$15 mg/L, albumin $<$30 g/dL (n: 29) had a mOS of 3.9 mos vs 14.2 mos of pts with no risk factor (n: 28) (HR 2.48, p 0.001). **Conclusions:** GIPI, combining NLR, CRP and Albumin, is the first inflammatory index with a significant prognostic value in mOGJ/GC pts receiving second-line ICIs. Its implementation in correlation with PD-L1 expression in the present cohort is ongoing. GIPI merits validation in independent cohorts and prospective clinical trials. Research Sponsor: None.

4531 Poster Session (Board #139), Fri, 8:00 AM-11:00 AM

X versus XELOX versus PF in definitive concurrent chemoradiotherapy (DCRT) for local advanced squamous esophageal cancer (ESCC): Update from a multicenter, open-label, randomized III trial, CRTCOESC trial. *First Author: Ruinuo Jia, Henan Key Laboratory of Cancer Epigenetics, Cancer Hospital, The First Affiliated Hospital, College of Clinical Medicine, Medical College of Henan University of Science and Technology, Luoyang, China*

Background: PF (5-fluorouracil plus cisplatin) is the standard regimen for local advanced ESCC with DCRT. CRTCOESC aims to evaluate the effect and safety of X (capecitabine) regimen versus XELOX (capecitabine plus oxaliplatin) and PF in Chinese local advanced ESCC with DCRT by randomized, open-label, multicenter designed. **Methods:** Patients with ESCC (T2-4N0-2M0) were randomized to 3 groups as X (capecitabine 625mg/m^2, bid d1-5, 6 weeks), XELOX (oxaliplatin : 65mg/m^2 , d1 , 8 , 22, 29; capecitabine: 625mg/m^2, bid d1-5; 6 weeks), or PF (cisplatin: 75mg/m^2 d1 , 29, 5-Fu : 750mg/m^2 CIV24h d1-4 , d29-32), Intensity Modulated Radiation Therapy (IMRT) was delivered by 50Gy/2Gy currently. In addition, quadratic randomize were done within all groups to decide whether 2 cycles chemotherapy adding or not after DCRT. 2-year OS and Grade 3-5 AEs were the primary endpoints, 2-year PFS and short-term efficacy (STE) as rates of CR and ORR (CR+PR+SD) (confirmed by gastroscopy biopsy at 16 weeks) were the secondary endpoints. **Results:** 244 pts successfully were accrued from 13 centers during 2014.10-2020.1. 209 pts were finished DCRT and 193 were evaluated STE at 16 weeks. 192 and 147 pts were followed up for 1- and 2- years respectively. There were no differences between 3 groups on patients' baseline characters including age, gender, ECGO score, clinical stage, pathology grade and smoking. In X, XELOX and PF groups, the 2-year OS were 63.8% (30/46), 61.5% (32/52) and 62.5% (30/49) (P = 0.973), the median OS were 39.7 (6.567), 40 (5.195) and 34 (5.736) (months, P = 0.703); the incidences of AEs (grade 3-5) were 26.5% (18/68), 33.8% (25/74) and 49.3% (33/67) (P = 0.0193); the 2-year PFS were 54.3% (25/46), 53.8% (28/52) and 51% (25/49) (P = 0.939), the median PFS were 29.06 (6.124), 17.4 (8.745) and 24.833 (6.777) (months, P = 0.811); the CR rate were 43.8% (28/64), 41.4% (29/70), and 42.4% (25/59) (P = 0.964), and the ORR were 85.6%, 88.6%, and 96.6% (P = 0.119), respectively. There were no differences on OS, PFS and rates of CR and ORR between 3 groups but the incidence of AEs in X group was the lowest significantly. Subgroup analysis results shown adding 2 cycles chemotherapy after CRT had both OS and PFS advantages but lacked statistically significance. **Conclusions:** Compared with PF, DCRT with X or XELOX shown lower incidence of AEs and similar OS, PFS and STE. X regimen carried out the lowest AEs incidence. Adding 2 cycles chemotherapy after DCRT seemly had advantages on OS and PFS. Clinical trial information: NCT02025036. Research Sponsor: National Natural Science Foundation of China.

4532 Poster Session (Board #140), Fri, 8:00 AM-11:00 AM

Final results of a phase II trial of first-line FOLFIRINOX for advanced gastroesophageal cancers. *First Author: Ramon Jin, Washington University School of Medicine, St. Louis, MO*

Background: Standard first-line regimens for patients with metastatic gastroesophageal adenocarcinomas have moderate clinical benefit with objective response rates (ORR) of approximately 40-50%. FOLFIRINOX has been shown to be an effective and well-tolerated first line therapy in other GI cancers. In this open-label, single-arm phase II study of patients with advanced gastroesophageal adenocarcinomas, we sought to evaluate the safety and clinical activity of FOLFIRINOX. **Methods:** The primary endpoint was ORR, and secondary endpoints included safety profile, progression free survival (PFS), overall survival (OS), time to progression (TTP), clinical benefit rate (CBR), and duration of response. Estimated sample size included 41 patients with HER2 negative disease with 90% power to detect an ORR$\geq$60% with alpha of 0.10. No enrollment goal was planned for HER2 positive patients, but they were allowed participation to receive study treatment in combination with trastuzumab. Treatment consisted of 400mg/m2 5-FU bolus, 400 mg/m2 leucovorin, 2400 mg/m2 5-FU infusion over 46 hours, 180 mg/m2 irinotecan, and 85 mg/m2 oxaliplatin. Trastuzumab was administered intravenously as a 6 mg/kg loading dose then given 4 mg/kg every 14 days for HER2 positive patients. This trial is registered with ClinicalTrials.gov, NCT01928290. **Results:** From November 2013 to May 2019, 67 patients were enrolled, of which 26 (39%) had HER2 positive disease. Median follow-up was 16.1 months. ORR was 61% (25/41) for HER2 negative and 85% (22/26) for HER2 positive groups. Overall, one patient (2%) had a complete response, 36 patients (69%) had partial responses, and 13 patients (19%) had stable disease for $>$6 months; therefore, CBR was 96%. Median PFS was 11.9 months, median OS was 17.4 months. 41 patients (83.7%) had dose modification or treatment delay with the most common toxicities being neutropenia, diarrhea, peripheral sensory neuropathy, and nausea with no unexpected toxicities. **Conclusions:** FOLFIRINOX is a highly effective three-drug regimen for first-line treatment of advanced gastroesophageal cancer with expected, tolerable toxicities. Clinical trial information: NCT01928290. Research Sponsor: Washington University School of Medicine Internal Funding.

4533 Poster Session (Board #141), Fri, 8:00 AM-11:00 AM

Disease-free survival as a surrogate for overall survival in neoadjuvant trials of gastroesophageal adenocarcinoma: Pooled analysis of individual patient data from randomized controlled trials. *First Author: Ulrich Ronellenfitsch, University Hospital Halle (Saale), Department of Visceral, Vascular and Endocrine Surgery, Halle (Saale), Germany*

Background: Disease-free survival (DFS) is an appealing surrogate endpoint for overall survival (OS) in trials on neoadjuvant or adjuvant cancer therapy, because it is available faster and with less follow-up effort. The aim of this study was to assess if DFS can be a valid surrogate endpoint for OS when comparing neoadjuvant treatment followed by surgery to surgery alone for gastroesophageal adenocarcinoma. **Methods:** Individual patient data (IPD) from eight randomized controlled trials (n = 1,126 patients) which compared neoadjuvant therapy followed by surgery with surgery alone for gastroesophageal adenocarcinoma were used for the analysis. Correlation between OS-time and DFS-time was calculated. Kaplan-Meier survival curves and corresponding hazard ratios (HRs) for treatment effects were separately determined for each trial. Subsequently, HRs were pooled in a meta-analysis using a random-effects model. An error-in-variables linear regression model was used to compare observed and predicted values. The minimum treatment effect on DFS necessary to predict a non-zero treatment effect on OS was estimated by calculating the surrogate threshold effect. **Results:** OS-time correlated strongly with DFS-time. HRs for OS and DFS were highly similar for all single trials. The meta-analysis yielded almost identical overall HRs for treatment effects on OS and DFS. The determination coefficient for the association between HRs for OS and DFS was 0.912 (95% confidence interval 0.75-1.0), indicating a strong trial-level surrogacy between OS and DFS. The surrogate threshold effect was calculated at 0.79, indicating that a future trial yielding a hazard ratio for the treatment effect on DFS < 0.79 could be expected with a 95% probability to yield a hazard ratio for the treatment effect on OS < 1. **Conclusions:** DFS and OS strongly correlate both after neoadjuvant therapy followed by surgery and after surgery alone for gastroesophageal adenocarcinoma. Likewise, the treatment effects on the two endpoints are very similar. Consequently, DFS can be regarded an appropriate surrogate endpoint for OS in trials on neoadjuvant therapy for gastroesophageal adenocarcinoma. Research Sponsor: None.

4534 Poster Session (Board #142), Fri, 8:00 AM-11:00 AM

First-in-human phase I study of BVAC-B cell therapy in HER2-positive advanced gastric cancer. *First Author: Jii Bum Lee, Yonsei Cancer Center, Seoul City, South Korea*

Background: BVAC-B is an autologous B cell- and monocyte-based immunotherapeutic vaccine transfected with recombinant HER2/neu gene and loaded with alpha-galactosyl ceramide, a natural killer T cell ligand. It may have activity against HER2/neu positive cancer. Preclinical data in mouse models have shown promising anti-tumor activity by eliciting broad spectrum of immune responses against HER2/neu positive tumor cells. We report here the results of phase 1 study of BVAC-B in HER2 positive advanced gastric cancer. **Methods:** Metastatic gastric cancer with IHC $> 1+$ of HER2/neu were eligible for enrollment. Two weeks before treatment, subjects were admitted to hospital for collection of PBMC and plasma by lymphapheresis. The PBMC were sent to Cellid for vaccine manufacturing which took a day. BVAC-B was given intravenously at 0, 4, 8, and 12 weeks. Subjects received low (2.5X 10^7 cells/dose), medium (5.0X 10^7 cells/dose) or high dose (1.0X 10^8 cells/dose). Endpoints included safety, tolerability and MTD for phase 2 trial. Exploratory outcomes included immune responses after BVAC-B administration. **Results:** As of January 29, 2020, 8 subjects were treated with BVAC-B at doses of 2.5X 10^7 cells/dose (n=1), 5.0X 10^7 cells/dose (n=1) and 1.0X 10^8 cells/dose (n=6). Median line of therapy at which BVAC-B was administered was 4 (range, 2-9). Mean duration treatment was 1.8 (range 1-4) cycles. The most common treatment related adverse events were fever (n=4, 50%). One subject enrolled in medium dose experienced cytokine release syndrome (G2) with high fever (39.3℃) and hypotension 8 hours after first administration, but was manageable with hydration and supportive management. Other adverse events included increase of AST and ALT (G1, n=1 and G2, n=2), and hypotension (G1, n=1). There were no adverse events which led to treatment discontinuation. Immunologic response analysis showed that BVAC-B induced activation of natural killer T cells, natural killer cells, HER2/neu specific T cells, and release of HER2/neu specific antibody upon vaccinations in few patients who were evaluated. **Conclusions:** BVAC B is feasible and has acceptable toxicity profile. We considered all dose evaluated in this study available for phase 2 study, given that the maximum tolerated dose is expected to exceed the maximum dose administered in this study. For clinically relevant effect, further studies are warranted, including earlier line of exposure to BVAC-B as well as combination treatments. Clinical trial information: NCT03425773. Research Sponsor: Ministry of Trade, Industry & Energy (MOTIE), Korea Institute for Advancement of Technology (KIAT) through the Research and Business Development Program (No. N056300021).

4535 Poster Session (Board #143), Fri, 8:00 AM-11:00 AM

Personalized neoantigen/cancer testis antigen nanovaccine (PVAC) mobilize specific therapeutic immunity for high-risk resected gastric cancer. *First Author: Qin Liu, The Comprehensive Cancer Center of Drum Tower Hospital, Medical School of Nanjing University & Clinical Cancer Institute of Nanjing University, Nanjing, China*

Background: 35% of stage IIIB/C Gastric cancer patients will recurrent after D2 gastrectomy within one year. Mutation-derived epitopes (neoantigens) has been demonstrated to induce tumor cell specific immune responses controlling the tumor growth. Nanovaccine can increase antigen presentation efficiency and elicit potent antitumor T cell responses with robust therapeutic efficacy. We hypothesized that vaccination with neoantigens/cancer testis (CT) antigens could expand pre-existing and induce antigen-specific T-cells populations, favouring of tumor control enhancement. Here, we report the first-in-human application of this concept in gastric cancer. **Methods:** Patient-specific mutation-containing neoantigens were selected on the basis of tumour-specific mutations whole-exome sequencing (WES) and RNA sequencing. Cancer testis antigens were obtained according to immunohistochemical staining and HLA-binding affinity prediction. PVAC is an amphiphiles nanovaccine loaded with multiple personalized neoantigens/cancer testis antigens designed to induce antigen specific T cells and associated antitumor responses. PVAC will be administrated to stage IIIB/IIIC gastric carcinoma after six cycles of adjuvant chemotherapy (S-1/Oxaliplatin or S-1/docetaxel). Each patient received PVAC by subcutaneous injection on Days 1, 4, 8, 15, 22, 43, 64, 85, 169, administrated with the adjuvant montanide ISA 51 VG. Safety, immunogenicity and clinical efficacy will be evaluated. **Results:** 25 stage IIIB or IIIC gastric cancer patients were enrolled in this study. Mean age was 54.3 years old (range: 34-70), and ECOG performance scores were 0 or 1. Repeated dosing has been well tolerated with mild local discomfort and no DLTs. Three patients were observed grade 2 local skin reactions in the injection sites. No SAEs related to PVAC have been observed. Among median follow up time of 12.6 months (range: 8.5-25.0 months), only two patients had local recurrence at 24.0 months and 10.5 months after surgery, respectivelt. The rest 23 patients remain disease free on study. Neoantigen specific T cell responses have been detected by IFN-γ Elispot from PBMCs. **Conclusions:** PVAC is a multiple neoantigen/CT antigens nanovaccine that personalizes tumor specific antigens and the individual patient's capacity to respond. Addition of PVAC may prolong progression-free survival (PFS) after the standard of care chemotherapy. Clinical trial information: ChiCTR1800017319. Research Sponsor: the National Natural Science Foundation of China.

4536 Poster Session (Board #144), Fri, 8:00 AM-11:00 AM

Camrelizumab combined with FOLFOX as neoadjuvant therapy for resectable locally advanced gastric and gastroesophageal junction adenocarcinoma. *First Author: Ying Liu, Department of Medical Oncology, Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China*

Background: Neoadjuvant chemotherapy has been demonstrated to improve the pathological complete response(pCR) and 5-year survival rate of patients with locally advanced gastric and gastroesophageal junction adenocarcinoma (GC/GEJC). Immunotherapy has become a new promising treatment for advanced GC/GEJC. Therefore, we intended to evaluate the safety and efficacy of Camrelizumab (anti-PD-1 antibody) combined with FOLFOX as the neoadjuvant therapy for patients with locally advanced GC/GEJC. **Methods:** Eligiblepatients were locally advanced GC/GEJC with clinical stage≥T2 and/or positive lymphoglandula confirmed by endoscopic ultrasonography (EUS) and imaging. They received 4 cycles neoadjuvant therapy which including Camrelizumab(200mg ivgtt D1), FOLFOX(Oxaliplatin 85mg/m^2 ivgtt D1, 5-Fu 400mg/m^2 iv D1, LV 200mg/m^2 ivgtt D1, 5-Fu 2.4mg/m^2 CIV 46 hours) every 14 days. Imaging evaluation was performed in 2-4 weeks after neoadjuvant therapy. Patients without progression disease (PD) received D2 radical gastrectomy. The primary endpoint was pCR, the secondary endpoints were R0 resection rate and safety. **Results:** From July 24 2019 to January 31 2020, 16 patients were eligible. The median age was 57 years (29-72 years). A total of 11(69%) males and 5(31%) females, ECOG PS 0 (n=9, 56%) , ECOG PS 1 (n=7, 44%). All the patients completed 4 cycles treatment and none of them was confirmed PD by image. One of the patients refused gastrectomy and withdraw from the study. The other 15 patients underwent operation. Unfortunately, intraperitoneal metastases were confirmed in 2 patients during operation. 13 patients received D2 radical gastrectomy and all of them experienced R0 resection. Among the 13 evaluable patients, 1 patient (8%) was observed pCR, 3 patients (23%) experienced TRG1, 10 patients (77%) achieved stage reduction. Notably, 8 patients (62%) had lymphonodus pCR. The grade 3-4 treatment-related AEs were neutropenia (n=3, 19%), leukopenia (n=2, 13%) and anorexia (n=1, 6%). No serious AEs resulted in termination of treatment. Either severe immune-related AEs or treatment-related death was not observed. **Conclusions:** Camrelizumab combined with FOLFOX as neoadjuvant regimen in patients with locally advanced GC/GEJC showed promising pCR with good tolerance. Clinical trial information: NCT03939962. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

Patient characteristics.

Characteristics	N	%
Clinical stage (T≥3)	16	100
Clinical stage (N≥1)	16	100
HER-2 postive	0	0
MMR deficient	0	0
EBV postive	2	13
PD-L1 CPS < 1	7	44
PD-L1 5<CPS≥1	4	25
PD-L1 CPS≥5	5	31

4537 Poster Session (Board #145), Fri, 8:00 AM-11:00 AM

The association of tissue tumor mutational burden (tTMB) using the Foundation Medicine genomic platform with efficacy of pembrolizumab versus paclitaxel in patients (pts) with gastric cancer (GC) from KEYNOTE-061. *First Author: Kohei Shitara, National Cancer Center Hospital East, Kashiwa, Japan*

Background: KEYNOTE-061 (NCT02370498) was a randomized, open-label, phase 3 study of pembrolizumab vs paclitaxel in pts with advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma with tumor progression after first-line therapy (N = 592). In this analysis, we evaluated tTMB using FoundationOne CDx (F1CDx; Foundation Medicine) in pts with gastric or GEJ cancer in KEYNOTE-061. **Methods:** In pts with evaluable F1CDx tTMB data (n = 204), we analyzed the association of tTMB with confirmed objective response rate (ORR), progression-free survival (PFS), and overall survival (OS) within each treatment arm using one-sided (pembrolizumab) and two-sided (paclitaxel) Wald test nominal *P* for logistic regression (ORR) and Cox proportional hazards regression (PFS; OS) adjusted for ECOG performance status; significance was prespecified at 0.05. The clinical utility of tTMB was assessed using the prespecified cutoff of 10 mut/Mb for F1CDx. Clinical data cutoff: Oct 26, 2017. **Results:** tTMB was positively associated with ORR ($P < 0.001$; AUROC, 0.68), PFS ($P < 0.001$), and OS ($P = 0.003$) with pembrolizumab but not paclitaxel (ORR, $P = 0.047$; AUROC, 0.30; PFS, $P = 0.605$; OS, $P = 0.084$). Pt outcomes by tTMB cutoff are reported in the Table; prevalence of TMB ≥10 mut/Mb was 17%. In pts with microsatellite stable disease-only, HRs (95% CI) by treatment arm for OS by F1CDx cutoff were 0.40 (0.14-1.17) for tTMB ≥10 mut/Mb (n = 21) vs 0.97 (0.70-1.34) for tTMB <10 mut/Mb (n = 168). **Conclusions:** In this exploratory analysis from KEYNOTE-061, tTMB as determined by F1CDx demonstrated a positive association with clinical outcomes with pembrolizumab, but not paclitaxel, in pts with GC; these findings are consistent with those reported with whole exome sequencing. Pembrolizumab demonstrated an OS benefit vs paclitaxel in the subgroup with tTMB ≥10 mut/Mb, which remained when pts with microsatellite instability-high disease were excluded. Clinical trial information: NCT02370498. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	tTMB <10 mut/Mb, pembrolizumab (n = 88)	tTMB <10 mut/Mb, paclitaxel (n = 81)	tTMB ≥10 mut/Mb, pembrolizumab (n = 20)	tTMB ≥10 mut/Mb, paclitaxel (n = 15)
ORR, % (95% CI)	10.2 (4.8-18.5)	14.8 (7.9-24.4)	40.0 (19.1-63.9)	13.3 (1.7-40.5)
PFS, mo, median (95% CI)	1.5 (1.5-2.1)	3.4 (2.8-4.2)	5.7 (1.5-NR)	6.5 (4.1-NR)
Pembrolizumab vs paclitaxel, HR (95% CI)	1.45 (1.06-1.98)	—	0.69 (0.31-1.52)	—
OS, mo, median (95% CI)	5.1 (3.6-8.6)	7.8 (5.8-9.4)	NR (9.1-NR)	8.1 (6.5-14.4)
Pembrolizumab vs paclitaxel, HR (95% CI)	0.97 (0.70-1.34)	—	0.34 (0.14-0.83)	—

4538 Poster Session (Board #146), Fri, 8:00 AM-11:00 AM

PILGRIM: Phase III clinical trial in evaluating the role of hyperthermic intraperitoneal chemotherapy for locally advanced gastric cancer patients after radical gastrectomy with D2 lymphadenectomy(HIPEC-01). *First Author: Shu-zhong Cui, Affiliated Cancer Hospital & Institute of Guangzhou Medical University, Guangzhou, China*

Background: Gastric cancer remains the 3rd leading cancer related death worldwide due to early disease recurrence. We hypothesize that hyperthermic intraperitoneal chemotherapy (HIPEC) may effectively prevent local regional recurrence for locally advanced gastric cancer patients who received curative intent surgery. **Methods:** Pathology proven gastric cancer patients with clinical T3/T4NxM0 disease are eligible for the study and will be randomized to either control group, who will receive standard radical gastrectomy and D2 lymph node dissection or HIPEC group, who will receive the same surgery and HIPEC with paclitaxel x 2 within the first week after surgery. All patients will receive either XELOX or SOX adjuvant chemotherapy. The primary end point is overall survival. **Results:** 648 patients from 16 high volume gastric medical centers were enrolled between May, 2015 and March, 2019. 331 and 317 patients were randomized to control and HIPEC groups respectively. The median follow-up time is 12.1 months. The common grade 3/4 toxicities (> 5%) in control and HIPEC groups are anemia 6% vs. 4.1%, intraabdominal infection 5.4% vs. 3.8%, pneumonia 9.7% vs. 9.8%, fever 10.6% vs. 11.4% and hypoalbunemia 15.1% vs. 16.7% respectively. All three perioperative death (within 30 days after surgery) occurred in control group. One patient died from duodenum stump leak which led to multiple organ failure. One patient died from anastomotic led to intraabdominal infection and shock. The 3rd death was suicide caused by severe depression. At the time of this report, the number of event has not reached for final efficacy analysis. **Conclusions:** It is safe to administer HIPEC to patients received radical gastrectomy with D2 lymph node dissection within one week of surgery. The primary analysis will be expected in one year. Clinical trial information: NCT02356276. Research Sponsor: The Clinical Research Promotion Project of Guangzhou Medical University for Building High Level University; The Guangzhou High-Level Clinical Key Specialty Construction.

4539 Poster Session (Board #147), Fri, 8:00 AM-11:00 AM

Translational analysis of esophageal adenocarcinoma (EAC) patients treated with oxaliplatin and capecitabine (Xelox) +/- the dual ErbB inhibitor AZD8931 in the DEBIOC study. *First Author: Anita Lavery, The Patrick G Johnston Centre for Cancer Research, Queen's University Belfast, Belfast, United Kingdom*

Background: The Dual Erb B Inhibition in Oesophago-gastric Cancer (DEBIOC) trial reported an acceptable safety profile for neoadjuvant Xelox +/- AZD8931 but limited efficacy. We utilized EAC patient samples from DEBIOC to evaluate the impact of neoadjuvant Xelox +/-AZD8931 on biological pathways using a unique software driven solution. **Methods:** 24 pre-treatment FFPE EAC biopsies and 17 matched surgical resection specimens were transcriptionally profiled using the Almac Diagnostics Xcel Array. Gene expression data was analyzed using the Almac clara^T total mRNA report V3.0.0, reporting on 92 gene expression signatures and 7337 single genes associated with 10 key biologies. Paired Wilcoxon tests (5% significance level) were used to evaluate changes in clara^T scores pre- and post-treatment. EGFR and Her2 expression were assessed by IHC and FISH. **Results:** 15 patients received Xelox+AZD8931 and 9 Xelox alone. Hierarchical clustering of biopsies identified 4 major clusters: Inflammation active, Genomic Instability active, EGFR & MAPK active, and EMT & Angiogenesis active. Comparison of signature scores pre- and post- neoadjuvant treatment demonstrated a significant reduction in scores relating to DNA damage repair (DDR) deficiency (Almac DNA Damage assay, $p < 0.0001$; BRCAness Profile, $p = 0.0025$; HRD Gene Signature, $p < 0.0001$; BRCA1ness Signature, $p = 0.0004$) and a significant increase in angiogenesis signatures (Almac Angiogenesis Assay, $p = 0.0002$; Angio Predictive G model, $p = 0.0228$; Angiogenesis Signature A, $p = 0.0034$) and EMT signatures (EMT Signature, $p = 0.0031$, EMT Enrichment Score, $p = 0.0013$, PanCan EMT Signature B, $p = 0.0001$). Comparing pre- and post-treatment signature scores in patients treated with Xelox +/-AZD8931 revealed a significant reduction in EGFR Sensitivity Signature ($p = 0.0088$), ERBB2-specific Gene Expression Signature ($p = 0.0127$) and Hallmark PI3K-AKT-MTOR Signaling ($p = 0.0195$) in those treated with Xelox + AZD8931 in keeping with the mechanism of action of AZD8931. Downregulation of AKT signaling was confirmed in AZD8931 treated and resistant cell lines. **Conclusions:** We report the use of a novel software tool to apply 92 gene expression signatures to EAC biopsy and resection specimens from the DEBIOC trial to provide insight into mechanisms of action. Neoadjuvant treatment was associated with a reduction in DDR deficiency and an increase in angiogenesis and EMT signatures whilst a reduction in EGFR, Her2 and AKT pathways was noted with AZD8931 treatment. Research Sponsor: AstraZeneca, Other Government Agency, Cancer Research UK, OGcancerNI, Wellcome Trust.

4540 Poster Session (Board #148), Fri, 8:00 AM-11:00 AM

Phase Ib/II open-label, randomized evaluation of 2L atezolizumab (atezo) + PEGPH20 versus control in MORPHEUS-pancreatic ductal adenocarcinoma (M-PDAC) and MORPHEUS-gastric cancer (M-GC). *First Author: Andrew H. Ko, University of California San Francisco, San Francisco, CA*

Background: The MORPHEUS platform consists of multiple, global, open-label, randomized Phase Ib/II trials designed to identify early efficacy signals and safety of treatment (tx) combinations across cancers. Within MORPHEUS, atezo (anti–PD-L1) was tested with PEGylated recombinant human hyaluronidase (PEGPH20), an anti–stromal and extracellular matrix modulator, in patients (pts) with metastatic (m) PDAC or advanced/mGC. **Methods:** In 2 separate randomized trials, eligible pts with 2L mPDAC or mGC received atezo (1200 mg IV q3w) + PEGPH20 (3 μg/kg IV on D1, 8, 15). Control tx for M-PDAC (NCT03193190) was mFOLFOX6 or gemcitabine + *nab*-paclitaxel. In M-GC (NCT03281369), control tx was ramucirumab + paclitaxel. Primary endpoints were ORR (investigator-assessed RECIST 1.1) and safety. **Results:** Pts were followed up for ≥ 18 wk in M-PDAC (data cutoff: Aug 5, 2019) and ≥ 24 wk in M-GC (data cutoff, Jul 11, 2019). In M-PDAC, 66 pts received atezo + PEGPH20 and 42 received control in both preliminary and expansion phases. Confirmed ORRs were 6.1% (95% CI: 1.7, 14.8) and 2.4% (95% CI: 0.06, 12.6), respectively. Duration of response ranged from 5.3 to 11.3 mo in tx arm and was 3.9 mo in control. Median PFS was 1.5 mo (95% CI: 1.4, 2.6) and 2.3 mo (95% CI: 1.6, 4.0), respectively. Median OS was 7.1 mo (95% CI: 4.6, 9.5) and 6.8 mo (95% CI: 5.6, 8.3). Updated survival data will be presented. Respectively, 62.2% and 59.5% of pts had Gr 3-4 AEs; Gr 5 AEs were seen in 4.5% and 2.4% of pts; serious AEs (SAEs) occurred in 45.5% and 45.2% of pts; 16.7% and 4.8% of pts had tx-related AEs leading to tx withdrawal. The most common tx-related AEs were myalgia (65.2%) and peripheral edema (28.8%) in the combination arm. In M-GC, 13 pts received atezo + PEGPH20 and 12 received control. Confirmed ORRs were 0% (95% CI: 0, 24.7) and 16.7% (95% CI: 2.1, 48.4), respectively. Gr 3-4 AEs were seen in 30.8% and 75.0% of pts, respectively. No Gr 5 AEs occurred in either arm. SAEs occurred in 7.7% and 50.0% of pts, respectively. Only 1 pt in the control arm had a tx-related AE leading to tx withdrawal. While tumor hyaluronan (HA) appears to be associated with poor prognosis in the M-PDAC control, there was no clear association between HA levels and response to atezo + PEGPH20. PK data will also be presented. **Conclusions:** Limited efficacy was seen with the chemotherapy-free combination of atezo + PEGPH20 in PDAC. No efficacy was seen in GC. The safety of atezo + PEGPH20 was consistent with each agent's known safety profile; no new safety signals were identified. Clinical trial information: NCT03193190. Research Sponsor: F. Hoffmann La-Roche Ltd.

4541 Poster Session (Board #149), Fri, 8:00 AM-11:00 AM

Enhanced efficacy of anti-VEGFR2/taxane therapy after progression on immune checkpoint inhibition (ICI) in patients (pts) with metastatic gastroesophageal adenocarcinoma (mGEA). *First Author: Lionel Aurelien Kankeu Fonkoua, Mayo Clinic, Rochester, MN*

Background: Anti-VEGFR2 therapy (ramucirumab/paclitaxel [RAM/TAX]) and ICI are approved as 2nd- and 3rd-line therapy (Tx), respectively, for pts with mGEA. We unexpectedly saw durable responses in 2 pts on RAM/TAX after progression on an ICI trial (KN-059; PMID 29674442). We performed a pilot to examine the clinical activity of ICI followed by RAM/TAX. Then we retrospectively compared the outcomes of pts who received this serial Tx to pts who received RAM/TAX without prior ICI. **Methods:** All pts with mGEA at Mayo Clinic who received RAM/TAX (2014-19) were included (N = 87). Outcomes were best objective response rate (ORR: complete [CR] or partial response) per RECIST1.1, progression-free survival (PFS), duration of response (DOR), and overall survival (OS). Chi square and multivariate (MV) logistic and Cox regression were used. **Results:** 15 consecutive pts with measurable mGEA received ICI immediately followed by RAM/TAX after irRECIST progression. Most pts (95%) did not respond to ICI. Yet on RAM/TAX, 100% (15/15) had tumor reduction (range -8% to -100%) with an ORR of 73% (11/15), including 3 CRs. In these pts (who received ICI followed by RAMTAX), PFS on RAMTAX was longer than on last chemotherapy before ICI (12.3 vs 3.0 m, $P < .001$). Outcomes on RAM/TAX in these pts were significantly better than in pts who received RAM/TAX alone (see Table). Associations were strengthened after adjusting for total lines of Tx, line of Tx of RAM/TAX, age, and ECOG PS. Exploratory analysis of paired tumor biopsies collected pre-ICI and on RAM/TAX in a small subset revealed that the frequency of intratumoral immunosuppressive $FOXP3^+$ Tregs decreased on RAM/TAX, whereas the frequency of antitumor $CD8^+$ T cells was preserved. **Conclusions:** RAM/TAX immediately preceded by ICI was associated with significantly higher OS, ORR, and DOR than RAM/TAX alone, suggesting ICI may enhance efficacy of subsequent anti-VEGFR/taxane therapy. This novel sequence of therapy will be tested prospectively in a new randomized phase 2 trial (NCT04069273). Research Sponsor: None.

	RAM/TAX ...		
	With preceding ICI *n = 19* [a]	Without preceding ICI *n = 68*	p
ORR	58%	18%	< .001
DOR	10.5 m	4.3 m	.021
OS	15.0 m	7.6 m	.003

[a]Includes 4 pts with non-measurable disease

4543 Poster Session (Board #151), Fri, 8:00 AM-11:00 AM

Impact of frontline doublet versus triplet therapy on clinical outcomes: Exploratory analysis from the RAINBOW study. *First Author: Samuel J Klempner, The Angeles Clinic and Research Institute, Los Angeles, CA*

Background: Treatment (tx) of advanced gastric cancer (GC/GEJ) is highly heterogeneous, with substantial variability in tx patterns. Frontline tx choice may affect outcomes of subsequent tx, thereby influencing choice/efficacy of second-line (2L) tx. In RAINBOW, 2L ramucirumab(R) plus paclitaxel(P) significantly improved overall survival (OS) of patients (pts) with GC/GEJ. Here we explore efficacy, safety and quality of life (QoL) based on prior tx. **Methods:** Pts were grouped into doublet (DB) or triplet (TP) regimens based on prior cytotoxic tx received. OS and PFS were estimated using Kaplan-Meier method and tx effects on OS and PFS were evaluated by Cox PH model; safety and QoL were assessed descriptively for DB vs TP. **Results:** Use of DB and TP was similar between arms, with 23% in R+P and 26% in placebo (PB)+P arm receiving TP. Baseline characteristics were generally balanced between tx arms within DB and TP subgroups, with majority of TP administered in western regions (91%). Pts ≥65 years of age was 40% for DB and 28% for TP. DB pts (n = 498; 75%) received S1+cis (n = 97, 15%) and cape+ox (n = 71; 11%) as most common prior tx, while TP pts (n = 163; 25%) received epi+cape+ox (n = 74, 11%) and epi+cis+5FU (n = 53, 8%). Similar to ITT population, R+P improved OS and PFS in both DB and TP subgroups (Table). Patterns of overall and Grade ≥3 TEAEs between arms were similar regardless of prior tx. Higher rates of serious TEAEs were reported in TP pts (57%, 49%) than DB pts (44%, 40%) in R+P and PBO+P arms, respectively. Similar trend was observed for TEAEs leading to discontinuation for TP (40%, 30%) vs DB (29%, 22%) in respective tx arms. Baseline QoL scores were similar between tx arms within subgroups, but mean scores were > 5 points worse (range 0-100) for prior TP for role functioning, fatigue, pain, and appetite loss. Changes in mean scores were generally similar between arms and within subgroups. **Conclusions:** This exploratory analysis of RAINBOW suggests that although safety-related outcomes were less favorable in pts with prior TP, regardless of tx arm, similar improvements in efficacy were noted for R+P irrespective of prior DB or TP. Clinical trial information: NCT01170663. Research Sponsor: Eli Lilly and Company.

	Received prior DB		Received prior TP		ITT	
	R+P (N = 253)	PB+P (N = 246)	R+P (N = 76)	PB+P (N = 87)	R+P (N = 330)	PB+P (N = 335)
mOS, mo (95%CI)	9.8 (9.0, 11.2)	7.8 (6.9, 9.0)	8.1 (6.0, 11.0)	5.5 (4.2, 7.5)	9.6 (8.5, 10.8)	7.4 (6.3, 8.4)
HR (95%CI)	0.86 (0.70, 1.05)		0.69 (0.49, 0.98)		0.81 (0.68, 0.96)	
mPFS, mo (95%CI)	4.4 (4.2, 5.4)	2.9 (2.8, 3.6)	4.6 (3.8, 5.6)	2.9 (2.3, 3.5)	4.4 (4.2, 5.3)	2.9 (2.8, 3.0)
HR (95%CI)	0.65 (0.54, 0.79)		0.59 (0.41, 0.85)		0.64 (0.54, 0.75)	

4544 Poster Session (Board #152), Fri, 8:00 AM-11:00 AM

Impact of body measurements (BM) on overall survival (OS) and quality of life (QoL) in real-world patients (pts) with metastatic esophageal cancer. *First Author: Joelle Soriano, Princess Margaret Cancer Center, Toronto, ON, Canada*

Background: Body fat and muscle influence prognosis in many cancer types. However, this association is unclear for real-world MEC pts, who are often in worse performance status than their previous baseline. In addition, the relationship of BM at presentation and QoL is unknown. We used real-world MEC pts to assess the importance of BM in OS and QoL. **Methods:** BM were done at baseline computed tomography in MEC pts, treated from 2006-2014 at the Princess Margaret Cancer Centre. Two radiologists (correlation 0.9-1.0) assessed L3 level using SliceOMatic to determine Skeletal Muscle Index (SMI - muscle area at L3 normalized by height), Visceral Adiposity Tissue (VAT), and Subcutaneous Adiposity Tissue (SAT). We used previously published cut-offs for sarcopenia based on sex and BMI, and the highest tertile as the cut-off for adiposity. We used prospectively collected QoL surveys including EuroQol 5D-5L (EQ5D) and the Functional Assessment of Cancer Therapy – Esophageal (FACT-E). **Results:** Of 200 pts, 164 (82%) were male, 180 (92%) were non-Asian; mean age was 62 y; ECOG: 0-1 = 142 (71%), 2 = 58 (29%); 69% had adenocarcinoma; 5% were underweight, 44% normal weight, 30% overweight, and 21% obese. 40 (20%) pts completed QoL measures. We found that 104 (52%) were sarcopenic at baseline, 66 (33%) had high VAT, and 67 (34%) had high SAT. A multivariable Cox model showed that sarcopenia and VAT were independent prognostic variables for three-year OS: sarcopenia increased the risk of death by 50% (adjusted hazard ratio, aHR 1.50, p 0.02), whereas every 100-cm^2 increase in VAT improved OS by 24% (aHR 0.76, p 0.03). Finally, sarcopenic pts had significantly worse physical well-being (p 0.01) on FACT-E after adjusting for sex and age. Numerically, the EQ5D also showed lower scores in sarcopenic pts but this was not statistically significant (p 0.18). **Conclusions:** In MEC pts, sarcopenia and low visceral adiposity result in worse OS; sarcopenia is also significantly associated with poor QoL. Future work will need to focus on potential rehabilitation strategies such as nutritional support and exercise training to offset the poor prognosis associated with sarcopenia and reduced adiposity. Research Sponsor: None.

	aHR (95% CI)	P-value
Sarcopenic (ref: non-sarcopenic)	1.50 (1.0-2.1)	0.02
VAT (per 100cm2)	0.97 (0.9-0.9)	0.03
SAT (per 100cm2)	1.01 (0.9-1.0)	0.39
BMI < 18.5 (ref: 18.5-24.9)	1.36 (0.6-2.8)	0.41
BMI 25-29.9 (ref: 18.5-24.9)	0.81 (0.5-1.2)	0.35
BMI 30+ (ref: 18.5-24.9)	1.28 (0.7-2.2)	0.39

Cox model, OS adjusted for age, sex, ECOG, number of metastatic sites.

4545 Poster Session (Board #153), Fri, 8:00 AM-11:00 AM

Final analysis of single-arm confirmatory study of definitive chemoradiotherapy including salvage treatment in patients with clinical stage II/III esophageal carcinoma: JCOG0909. *First Author: Yoshinori Ito, Department of Radiation Oncology, Showa University School of Medicine, Tokyo, Japan*

Background: Definitive chemoradiotherapy (dCRT) consisting of 5-fluorouracil (5-FU) and cisplatin (CDDP) with 60 Gy radiotherapy (RT) for clinical (c) Stage II/III esophageal carcinoma (EC) is a standard treatment for patients (pts) refusing surgery (S) in Japan based on the previous trial (JCOG9906). However, poor survival, high incidence of late toxicities, and severe complications of salvage S are problems. We conducted a single-arm confirmatory study of CRT modifications including salvage treatment (ST) to reduce CRT toxicities and facilitate ST to improve survival. We reported the 3-year survival at 2018 ASCO Annual Meeting. We report the final data after 5-year follow-up. **Methods:** EC pts with cStage II/III (UICC 6th, non-T4), PS 0-1, and age 20-75 years were eligible. Chemotherapy (CT) was CDDP (75 mg/m^2 on days 1, 29) and 5-FU (1000 mg/m^2/d on days 1-4, 29-32). RT was administered to a total dose of 50.4 Gy with elective nodal irradiation of 41.4 Gy. Good responders after dCRT received additional 1-2 cycles of CT. For residual or recurrent disease, salvage endoscopic resection (ER) or S was performed based on the prespecified criteria. Planned sample size was 95, with one-sided alpha of 5% and power of 80%, expected and threshold 3-year overall survival (OS) as 55% and 42%. Key secondary endpoint was ST related toxicity. Final analysis was planned after 5-year follow-up for all pts. **Results:** From 4/2010 to 8/2014, 96 pts were enrolled, two were ineligible and 94 were included in efficacy analysis (cStage IIA/IIB/III, 22/38/34). Complete response was achieved in 55 pts (59%). Salvage ER and S were performed in 5 (5%) and 27 pts (29%). R0 resection of salvage S was achieved in 23 (85%). With a median follow-up of 5.95 years, 3- and 5-year OS was 74.2% (90% CI 65.9-80.8%) and 64.5% (95% CI 53.9-73.3%). 5-year progression-free survival and esophagectomy-free survival were 48.3% (95% CI 37.9-58.0%) and 54.9% (95% CI 44.3-64.4%). 5-year OS after salvage S was 31.0% and hazard ratio of R1-2 to R0 was 5.635 (95% CI: 1.818-17.467). No complications occurred after salvage ER. Five pts (19%) showed ≥ grade 3 operative complications and 1 treatment related death due to bronchus-pulmonary artery fistula occurred after salvage S. Only 9 pts (9.6%) showed grade 3 late toxicities. And no late operative complications more than grade 3 were observed. **Conclusions:** This combined modality treatment of dCRT with ST showed acceptable toxicities, favorable 5-year survival, and promising esophageal preservation. Clinical trial information: jRCTs031180110. Research Sponsor: National Cancer Center Research and Development Funds.

4546 Poster Session (Board #154), Fri, 8:00 AM-11:00 AM

Evaluation of spatiotemporal heterogeneity of tumor mutational burden (TMB) in gastroesophageal adenocarcinoma (GEA) at baseline diagnosis and after chemotherapy. *First Author: Katherine I. Zhou, University of Chicago, Chicago, IL*

Background: Tumor mutational burden (TMB) may be a predictive marker for response to anti-PD1/PDL1 agents (IO). Molecular heterogeneity of various biomarkers for GEA has been established. To characterize heterogeneity of TMB and its clinical relevance, we compared TMB in primary (1^O) & metastatic (met) tumors at baseline newly diagnosed stage IV advanced GEA (aGEA), and before & after chemotherapy treatment (tx) for stage II–IV GEA. We assessed the prognostic relevance of TMB in aGEA. **Methods:** We retrospectively reviewed a cohort of 127 patients (pts) diagnosed with GEA in 2012–2019, for a total of 280 tumor samples with TMB data. TMB level was defined as low (≤5/Mb), intermediate (int) (> 5/Mb, ≤15/Mb), or high (hi) (≥15/Mb), determined by Foundation One. Analysis was performed by Fisher's exact test for PDL1/TMB, McNemar's test for paired TMB, and univariate Cox proportional-hazards model for overall survival (OS). **Results:** Of 280 tumors, 50% (140/280) had low TMB, 45% (125/280) int TMB, & 5% (15/280) hi TMB. TMB ranged 0–58.6/Mb (median 5.3/Mb). Of tumors with hi TMB, 53% (8/15) were MSI-Hi, while of MSI-Hi tumors, 100% (8/8) were TMB hi. TMB level did not correlate with PDL1 status (p= 0.83). Concordance between TMB levels of paired baseline 1^O and baseline met tumors was 66% (29/44) (Table). TMB level was lower in the met than in the 1^O in 23% (10/44) of cases, and higher in the met in 11% (5/44). Of 4 TMB hi baseline 1^O tumors, 2 were not TMB hi in the met; of 40 TMB low/int baseline 1^O tumors, 0 were TMB hi in the met (p= 0.16). Post-tx tumors exhibited 71% (42/59) concordance of TMB levels compared to pre-tx 1^O tumors. Of 2 TMB hi baseline tumors, 1 was not TMB hi in the post-tx tumor; of 57 TMB low/int baseline tumors, 0 were TMB hi in the post-tx tumor (p= 0.32). In pts with aGEA at diagnosis, OS did not significantly differ depending on baseline 1^O tumor TMB level (median OS of 21.4 [95% CI 15.4–27.9] months for TMB low, 14.6 [10.9–23.5] months for TMB int, and 9.6 [3.9–NA] for TMB hi; p= 0.3), nor depending on baseline met TMB level. **Conclusions:** Notable baseline spatial discordance of TMB was observed, particularly TMB hi 1^O to low/int met. Discordance was also observed before & after tx, without significant increase towards TMB hi temporally. Spatiotemporal heterogeneity may impact the role of TMB as a predictive biomarker & warrants further study. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

	Baseline met TMB low	Baseline met TMB int	Baseline met TMB hi	Post-tx TMB low	Post-tx TMB int	Post-tx TMB hi
Baseline 1^O TMB low	16	5	0	21	7	0
Baseline 1^O TMB int	8	11	0	9	20	0
Baseline 1^O TMB hi	1	1	2	0	1	1

4547 Poster Session (Board #155), Fri, 8:00 AM-11:00 AM

Morphologic and molecular analysis of early-onset gastroesophageal adenocarcinomas. *First Author: Namrata Setia, University of Chicago, Chicago, IL*

Background: The incidence of early-onset gastroesophageal adenocarcinomas (EO-GEA) is increasing, and these tumors now constitute > 30% of all gastroesophageal cancers. Besides hereditary gastric cancer syndromes, which form ~3% of EO-GEA, the morphologic and molecular spectrum of these tumors is not well-studied. **Methods:** Next-generation sequencing (NGS) data obtained from routine clinical care from patients with EO-GEA, defined as age ≤50 years, from 3 tertiary care centers was evaluated and compared with tumor profiles of 2,081 patients with GEA from cBioPortal for Cancer Genomics. Available histologic slides were reviewed, and the tumors were classified into Lauren and WHO subtypes. Tumor-detected pathogenic variants of potential germline origin were identified from the NGS data. **Results:** The study cohort was formed by 79 patients with gastroesophageal (42%) and gastric (58%) adenocarcinoma. The most commonly mutated genes included *TP53* (28.5%), *CDH1* (10%), *ARID1A* (5%), *KRAS* (3.9%) and *PIK3CA* (3.9%). EO-GEA were less likely to harbor *TP53* (28.5% vs. 57.5%, p 0.003) and *ARID1A* (5% vs. 20.6%, p 0.002) mutations when compared with cBioPortal data. Based on the Lauren scheme, the tumors were classified into intestinal (40%), diffuse (24%), mixed (12%), and indeterminate (15%) subtypes. Driver mutations in *CDH1*,*TP53*, *FBXW7*, *BAP1* genes were seen in diffuse/mixed subtype, and *TP53*, *ARID1A*, *KRAS*, *PIK3CA*, *APC*, *ATM*, *NBN*, *MUTYH* genes in intestinal subtype. The indeterminate subtype showed *TP53* mutations and additional alterations, including *SMARCB1*/*SMARCA4* loss leading to rhabdoid/undifferentiated morphology. *ERBB2* amplification was more likely to be present in intestinal and indeterminate subtypes (p = 0.003).*CD274* amplification/PD-L1 expression was more likely to be present in indeterminate subtype (p < 0.0001). Potential germline variants included mutations in gastric cancer susceptibility genes such as *CDH1* (2.5%) and *APC* (1%), and other cancer susceptibility genes such as *ATM* (4%), *NBN* (1%), *MUTYH* (1%) and *POLD1* (1%). **Conclusions:** The molecular profile of EO-GEA is distinct from traditional gastric cancers. Histologic subtypes of EO-GEA correlate with distinct genomic alterations. Our findings also support multigene germline panel testing in parallel for patients with EO-GEA. Research Sponsor: None.

4548 Poster Session (Board #156), Fri, 8:00 AM-11:00 AM

Perioperative FLOT in elderly patients with resectable gastric cancer: Subgroup analysis from the observational RealFLOT study. *First Author: Elisa Giommoni, Medical Oncology, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy*

Background: The treatment strategy for patients with resectable gastric cancer changed in the last few years with perioperative treatments. FLOT regimen (fluorouracil, oxaliplatin, docetaxel) turned out to be feasible and effective, offering significant improvement in survival outcomes. However, the safety profile of triplet therapies for elderly patients deserves a special attention and, consequently, the best treatment strategy for these patients is still debated. **Methods:** Focusing on the elderly patient population (age ≥65 years), real-world data from patients with resectable gastric or gastro-oesophageal junction (GEJ) adenocarcinoma (T≥2 and/or N+) enrolled in the observational RealFLOT study were collected. **Results:** A total of 206 patients with resectable gastric or GEJ adenocarcinoma received perioperative FLOT at 15 Italian centers in routine clinical practice, between September 2016 and September 2019. The median age was 63 years (range 36-77) and 43% of patients enrolled (n = 89) were ≥65 years. Among elderly patients, 46 (52%) received FLOT for at least 4 full-dose cycles in the preoperative phase, 82 (92%) underwent surgery, and 56 (62%) started the postoperative phase. The primary end point of the study, pathological complete response (pCR) rate, was similar among patients aged ≥65 and < 65 (6.7% vs 7.7%, respectively). The distribution of pathological stages did not differ according to age (p = 0.473), and disease-free survival (DFS) is unrelated to the age of patients (log-rank 0.57; p = 0.89). The incidence of grade (G) 3-4 adverse events (AEs) was similar in the two age groups (Table) and the 30-day mortality rates after surgery did not differ according to age. **Conclusions:** FLOT regimen demonstrated to be feasible and safe in elderly patients since no differences were observed in terms of pCR, DFS and safety profile according to age. Research Sponsor: None.

Preoperative and postoperative G3-4 AEs registered.

Preoperative	**Patients ≥65 (n = 89)**	**Patients < 65 (n = 117)**
- Hematological	17%	22%
- Gastrointestinal	10%	4%
Postoperative	**Patients ≥65 (n = 56)**	**Patients < 65 (n = 86)**
- Hematological	14%	19%
- Gastrointestinal	9%	10%

4549 Poster Session (Board #157), Fri, 8:00 AM-11:00 AM

Interim safety analysis of the DANTE trial: Perioperative atezolizumab in combination with FLOT versus FLOT alone in patients with resectable esophagogastric adenocarcinoma—A randomized, open-label phase II trial of the German Gastric Group at the AIO and SAKK. *First Author: Nils Homann, Klinikum Wolfsburg, Med. Klinik II, Wolfsburg, Germany*

Background: The DANTE study evaluates atezolizumab in the perioperative treatment of locally advanced, potentially resectable gastric or GEJ adenocarcinoma in combination with perioperative FLOT. Here, we report the protocol-defined interim safety analysis. **Methods:** DANTE is a multinational, prospective, multicenter, randomized, investigator-initiated, open label phase II trial. Patients (pts) with locally advanced, potentially resectable adenocarcinoma of the stomach and GEJ (≥cT2 and/or N-positive) without distant metastases are enrolled. Pts are randomized 1:1 to 4 preoperative 2-week cycles of FLOT followed by surgery and 4 additional cycles of FLOT plus atezolizumab at 840 mg every 2 weeks, followed by a total of 8 additional cycles of atezolizumab at 1200 mg every 3 weeks as monotherapy (arm A) or FLOT alone (arm B). Primary endpoint is time to disease progression or relapse after surgery (PFS/DFS). **Results:** Recruitment started in Sep 2018; by Feb 2020, a total of 175 pts have been randomized. This analysis is based on the first 40 pts (20 pts in each arm). The pts had a median age of 62 y and 75% of pts had an ECOG PS of 0 in both arms. The cohort was well balanced in terms of tumor location and clinical stage. 5% of the 40 patients (overall 7.4% of 175 pts enrolled) showed microsatellite instability. 90% of pts enrolled completed all pre-operative cycles in each arm. Total number of adverse events with relation to study treatment was 154 in arm A and 148 in arm B. Total number of serious adverse events (SAE; related or not) was 16 in Arm A and 14 in arm B. 20% of pts in each arm had an SAE due to perioperative morbidity. No surgical mortality was observed. 18 and 19 pts proceeded to operation in arms A and B, respectively. Premature treatment discontinuation occurred in 2 pts in each arm: disease progression (1) and deterioration of general health condition (1) in arm A; and pts' wish (1) and death (1) in arm B. Median hospitalization time was 15 days in arm A and 16 days in arm B. **Conclusions:** Perioperative atezolizumab plus FLOT is feasible and safe. The study continues recruitment. Clinical trial information: NCT03421288. Research Sponsor: Roche.

4550 Poster Session (Board #158), Fri, 8:00 AM-11:00 AM

A population-based study on gender differences in tumor and treatment characteristics and survival of curable gastroesophageal cancer. *First Author: Marianne C. Kalff, Department of Surgery, Amsterdam UMC, Amsterdam, Netherlands*

Background: Although curative treatment options for gastroesophageal cancer are identical for men and women, outcomes may vary. This study examined differences in tumor and treatment characteristics and survival between men and women with potentially curable gastroesophageal cancer. **Methods:** Nationwide data was acquired from the Netherlands Cancer Registry. Patients with a potentially curable gastroesophageal carcinoma (cT1-T4a or cTx, any cN, cM0 or cMx) diagnosed between 2006 and 2017 were selected. Patient stratification was performed for tumor location and histology. The primary endpoint, relative survival, was compared between men and women with esophageal adenocarcinoma (EAC), esophageal squamous cell carcinoma (ESCC) and gastric adenocarcinoma (GAC), adjusted for the normal life expectancy for men and women separately. **Results:** In total, 13,391 patients with an EAC (79.1% men), 5,103 patients with an ESCC (54.7% men), and 8,149 patients with a GAC (60.1% men) were included. Women with gastroesophageal cancer were older than men. Lower cT-stages were observed in women with EAC and ESCC (both $p < 0.001$) and lower cN-stages were observed in women in all groups, although clinical T- and N-stage were more frequently graded as cTx and cNx in women. In women, EAC tumors were less frequently located in the distal esophagus (70.4% vs. 58.6%, $p < 0.001$), ESCC tumors had a more proximal tumor location ($p < 0.001$), and GAC tumors were more frequently located at the antrum (32.3% vs. 37.2%, $p < 0.001$). For EAC and GAC, but not for ESCC, men were more frequently allocated to a potentially curative treatment; endoscopic resection, surgical resection or definitive chemoradiotherapy (EAC: 74.6% vs. 60.1%, $p < 0.001$; GAC: 69.0% vs. 65.4%, p 0.001; ESCC: p 0.117). An inferior 5-year relative survival was observed in women with EAC (34.3% vs. 30.1%, $p < 0.001$) and GAC (36.1% vs. 33.2%, p 0.016). In women with ESCC a superior 5-year relative survival was observed (24.4% vs 28.5%, p 0.001). **Conclusions:** Remarkable differences in 5-year relative survival were observed between men and women with gastroesophageal cancer, in addition to important differences in tumor stage, tumor location and treatment. Strikingly, men with esophageal and gastric adenocarcinoma were more frequently allocated to a potentially curative treatment compared to women. These findings illustrate the need for further exploration and consideration of gender differences in gastroesophageal cancer treatment. Research Sponsor: None.

4551 Poster Session (Board #159), Fri, 8:00 AM-11:00 AM

Diagnostic accuracy of CT-staging of advanced gastric cancer following neoadjuvant chemotherapy. *First Author: Jong Keon Jang, Asan Medical Center, Seoul, South Korea*

Background: Neoadjuvant or perioperative chemotherapy has been accepted as a standard treatment globally in patients (pts) with locally advanced gastric cancer (LAGC). In PRODIGY phase III study (n = 530), we have demonstrated that neoadjuvant chemotherapy with DOS regimen (docetaxel, oxaliplatin, S-1) led to significant tumor downstaging and improved PFS in Korean LAGC pts (Kang, et al. ESMO 2019). Although CT has been performed to re-stage the tumor after neoadjuvant chemotherapy, there has been a relative paucity of diagnostic accuracy data. This study is to evaluate the diagnostic performance of restaging of LAGC after neoadjuvant chemotherapy using CT in PRODIGY study population. **Methods:** Of 266 pts, who had been diagnosed LAGC of T2-4 or N+ stage as assessed with CT and randomized to neoadjuvant chemotherapy arm (CSC) in PRODIGY study, 214 pts underwent gastrectomy were included in this analysis. The post-chemotherapy T- and N- stage was determined based on CT scan taken just prior to surgery and compared with the pathologic stage (AJCC 7th edition). Two experienced radiologists independently evaluated depth of primary tumor and reached consensus if any discrepancy between two readers. Diameter of short axis of the largest regional lymph node was measured to predict metastatic lymph node. Result of histopathologic T- and N-staging using surgical specimen was used as reference standard. **Results:** The study cohort consisted of pathologic T0 (n = 22), T1(n = 39), T2(n = 31), T3(n = 79), and T4(n = 43). The overall diagnostic accuracy of CT was 45%. For each T-stage, accuracy of T0,T1,T2,T3, and T4 was 0%, 26%, 29%, 55% and 79%, respectively. Rate of over- and under- staging was 47% and 8%, respectively. Accuracy for prediction of downstaging to early gastric cancer (T0-T1) was 83%. Interobserver agreement of T-staging was moderate (k = 0.41). There were 98 patients of N+ and 116 patients of N- at histopathology. Area under the curve of receiver operating characteristics to differentiate lymph node metastasis was 0.63. Sensitivity and specificity of size criteria of the largest lymph node (cut off value: $>$ 6mm, $>$ 7mm, and $>$ 8mm) to predict pathologic N+ were 90% and 17%, 78% and 34%, and 68% and 51%, respectively. **Conclusions:** Re-staging using CT after neoadjuvant chemotherapy showed suboptimal accuracy and over-staged residual tumor. However, it predicted downstaging of gastric cancer with high accuracy. Research Sponsor: None.

4553 Poster Session (Board #161), Fri, 8:00 AM-11:00 AM

Prediction of esophageal fistula from esophageal cancer CT images using multi-view multi-scale attentional convolutional neural network (MM-Atten-CNN). *First Author: Yiyue Xu, Department of Radiation Oncology, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, China*

Background: We aimed to propose a risk model based on MM-Atten-CNN for predicting esophageal fistula in patients with esophageal cancer (EC) from computerized tomography (CT) -based radiomics. **Methods:** EC patients who didn't received esophageal surgery between July 2014 and August 2019 were collected. Of these, 186 patients (cases) who developed esophageal fistula were enrolled and compared with 372 controls (1:2 matched with the diagnosis time of EC, sex, marriage, and race). All 558 patients were divided into training set (n = 390) and validation set (n = 168) randomly. The MM-Atten-CNN risk model was trained over 2D slices from nine views of planes, where there were three patches of contextual CT, segmented tumor and neighbouring information in each view. In the training set (130 cases and 260 controls), data augmentation was performed including pixel shifting [-10, -5, +5, +10] and rotation [-10, +10]. In total, there were (130+260) *16*2 = 12480 subjects used for training. Finally, the risk model was validated in the validation set (56 cases and 112 controls) and measured by accuracy (acc), sensitivity (sen), and specificity (spe). **Results:** The developed risk model achieved (acc, sen, spe) of (0.839, 0.807, 0.926), which were more predictive for the occurrence of esophageal fistula when compared to CNN models using single coronal view (acc 0.763, sen 0.581, spe 0.837), multi-view 2D contextual CT slices (acc 0.779, sen 0.656, spe 0.896), and 3D CNN using contextual CT volumes (acc 0.781, sen 0.689, spe 0.852). **Conclusions:** MM-Atten-CNN CT-based model improved the performance of esophageal fistula risk prediction, which has the potential to assist individualized stratification and treatment planning in EC patients. Research Sponsor: None.

4554 Poster Session (Board #162), Fri, 8:00 AM-11:00 AM

PET-directed chemoradiation (CRT) with induction FOLFOX compared to induction carboplatin/paclitaxel (CP) in patients with locally advanced esophageal adenocarcinoma (EA). *First Author: Rebecca Carr, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Induction chemotherapy with PET-directed CRT and surgery is the standard treatment for locally advanced EA at our institution. Following results of the CALGB 80803 trial, FOLFOX has recently replaced CP as the preferred induction regimen. **Methods:** We retrospectively evaluated patients with locally advanced EA treated with induction CP vs FOLFOX, followed by trimodality therapy between January 2010 and June 2019. Patients treated with CP with RT followed by surgery without induction chemo were also included. We compared pathological complete response (pCR) and near pCR (ypN0 with ≥90% response) rates in the induction FOLFOX group to the induction CP and no-induction groups. Univariable and multivariable analyses were used to adjust for confounding factors. Disease-free survival (DFS) was estimated by the Kaplan-Meier method and compared between groups using max-combo weighted log rank test. **Results:** 445 patients were included. Patients in the induction FOLFOX group had significantly higher pCR and near pCR rates vs induction CP patients. Notably, pCR rate was 38% among FOLFOX PET responders vs 19% in non-responders. In multivariable analysis, compared to induction CP, induction FOLFOX administration was an independent predictor of near pCR (OR: 2.22, 95%CI: 1.20-4.20, p = 0.012). Compared to 24% pCR rate among no-induction patients, induction FOLFOX pCR rate was slightly higher at 32%. DFS by 2-years was higher in induction FOLFOX compared to no-induction-treated patients (62% vs. 42%, p = 0.05). Postoperative complication rates were similar among the three groups. **Conclusions:** PET-directed CRT with FOLFOX instead of CP improves pCR and near pCR rates. Improved DFS was observed in the FOLFOX vs no-induction patients. Longer follow-up is needed to confirm any survival benefits. Research Sponsor: None.

Treatment Group	Induction FOLFOX	Induction CP	p-value (Induction FOLFOX vs Induction CP)	No-induction	p-value (Induction FOLFOX vs no-induction)
Total Number	71	237		137	
Number of PET Responders	50	140		N/A	
pCR: n (%)	23 (32.4%)	38 (16.0%)	0.004	33 (24%)	0.2
pCR in PET Responders	19/50 (38%)	29/140 (21%)	0.022		
pCR in PET Non-Responders	4/21 (19%)	9/97 (9.3%)	0.2		
Near pCR: n (%)	40 (56.3%)	81 (34.2%)	0.001	60 (44%)	0.11
Near pCR in PET Responders	29/50 (58%)	56/140 (40%)	0.032		
Near pCR in PET Non-Responders	11/21 (52%)	25/97 (26%)	0.034		
Median Follow-Up among survivors in Months (range)	12.3 (5.3-78.6)	41.1 (0.7-108.5)		18.7 (0.7-82.7)	
2-year DFS (95% CI)	62% (48-78%)	51% (45-58%)	0.23	42% (34-53%)	0.05

4556 Poster Session (Board #164), Fri, 8:00 AM-11:00 AM

Intestinal and tumor microbiome analysis combined with metabolomics of the anti-PD-L1 phase II PERFECT trial for resectable esophageal adenocarcinoma. *First Author: Nicolien C. de Clercq, Amsterdam UMC, University of Amsterdam, Department of Internal and Vascular Medicine, Amsterdam, Netherlands*

Background: Both human and rodent studies provide evidence for a role of the microbiome in patients who respond to checkpoint inhibition (CI). So far, no study has unraveled the physiological link between intestinal and tumor microbiome composition in relation to response to CI. The PERFECT trial was a single-arm phase II feasibility study investigating the addition of atezolizumab (PD-L1 inhibitor) to neoadjuvant chemoradiotherapy (nCRT) for resectable esophageal adenocarcinoma (NCT03087864). An exploratory objective of this trial was to evaluate intestinal and tumor microbiome composition including plasma metabolomics as potential biomarkers for immunological and pathological response. **Methods:** Using 16S rRNA gene sequencing, we analyzed fecal, duodenal and tumor samples at baseline (V0), 3 weeks after start of atezolizumab (V1), and 1 week before surgery (V2). We compared microbiome composition and metabolomics from patients with pathological complete response (pCR; ypT0N0) to patients with a pathological incomplete response. Differences in alpha diversity metrics were tested using mixed linear models. Beta-diversity associations were assessed using permutational MANOVA (adonis) and multilevel PCA (mixOmics). Biomarkers were identified using a machine learning model (XGboost) feature selection. Plasma metabolomics (Metabolon) were determined with liquid chromatography mass spectrometry (LC-MS). **Results:** Microbiome profiles were significantly altered after start of treatment in all sample types. None of the sample types showed a relation between alpha or beta diversity and pCR. On taxonomical level, we found that the tumor and duodenal baseline samples were weak predictors for response (AUC 0.60 and 0.62, respectively), but better compared to fecal microbiome composition (AUC = 0.49). We identified the top 20 microbes that predicted pCR best in tumor and fecal samples and found significant correlations with metabolites involved in bile acid metabolism. **Conclusions:** Both tumor and duodenal baseline biopsies were better predictors of pathological response compared to fecal microbiome. Microbes predictive of pCR showed significant correlations with metabolites involved in bile acid metabolism, which is known to indirectly influence immunosurveillance in cancer. Data on immune response in relation to the microbiome and metabolomics are expected Spring 2020. Clinical trial information: NCT03087864. Research Sponsor: Roche.

4557 Poster Session (Board #165), Fri, 8:00 AM-11:00 AM

Prognostic significance of nutritional markers in metastatic gastric and esophageal adenocarcinoma. *First Author: Lucy Xiaolu Ma, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada*

Background: Malnutrition and sarcopenia (defined as low skeletal muscle mass) are recognized as poor prognostic factors in many cancers. Studies to date in gastroesophageal cancer have largely focused on patients (pts) undergoing curative intent surgery. This study aims to evaluate the prognostic utility of nutritional markers and sarcopenia in pts with de novo metastatic gastric and esophageal adenocarcinoma (GEA). **Methods:** Pts with de novo metastatic GEA seen at the Princess Margaret Cancer Centre from 2010-2016 with available pre-treatment abdominal computed tomography imaging were identified from an institutional database. Nutritional index (NRI) was calculated using weight and albumin, with moderate/severe malnutrition defined as NRI < 97.5. Skeletal muscle index (SMI) normalized by height was calculated at the L3 level using Slice-O-Matic software. Sarcopenia was defined as SMI $< 34.4 cm^2/m^2$ in women and $< 45.4 cm^2/m^2$ in men based on previously established consensus. **Results:** Of 175 consecutive pts, median age was 61, 69% were male, 79% had ECOG performance status 0-1, and 71% received chemotherapy. Median BMI was 24.2 (range 15.7-39.8), 70% of pts had $> 5\%$ weight loss in the preceding 3 months, and 29% had moderate/severe malnutrition. 68 pts (39%) were sarcopenic, of whom 46% were malnourished. Median overall survival (OS) was 9.3 months (95% CI 7.3-11.4) for all pts. OS was significantly worse in malnourished pts (5.5 vs 10.9 months, $p = 0.000475$) and displayed a non-significant trend in sarcopenic pts (7.8 vs 10.6 months, $p = 0.186$). On univariable Cox proportional hazards (PH) analysis, ECOG ($p < 0.001$), number of metastatic sites ($p = 0.029$) and NRI ($p < 0.001$) were significant prognostic factors, while BMI ($p = 0.57$) and sarcopenia ($p = 0.19$) were not. On multivariable Cox PH analysis, ECOG ($p < 0.001$) and NRI ($p = 0.025$) remained significant as poor prognostic factors for OS. **Conclusions:** This study demonstrates in a large cohort of de novo metastatic GEA pts that ECOG and NRI were significantly associated with poor OS. NRI was superior to BMI alone. Early identification of malnourished pts using NRI may allow for supportive interventions to optimize nutritional status. Further study is needed to determine whether these factors can be modified to improve prognosis in these pts. Research Sponsor: None.

4558 Poster Session (Board #166), Fri, 8:00 AM-11:00 AM

Molecular correlates of PD-L1 expression in patients (pts) with gastroesophageal (GE) cancers. *First Author: Jingyuan Wang, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA*

Background: The increased PD-L1 expression evaluated by combined positive score (CPS) is associated with improved efficacy of immunotherapy in GE cancers. The impact of tumor molecular alterations on PD-L1 expression is still not well-studied. We aimed to characterize specific molecular features of tumors with different CPS levels in GE cancers. **Methods:** 2,707 GE tumors [1,662 gastric/GE junction adenocarcinoma (GA), 856 esophageal adenocarcinoma (EA), 75 esophageal squamous (ES) and 114 GE unspecified] collected between 2000.8 and 2019.7 were analyzed using NextGen DNA sequencing (NGS), immunohistochemistry (IHC) and fragment analysis (FA) (Caris Life Sciences, Phoenix, AZ). Tumor mutation burden (TMB) was calculated based on somatic nonsynonymous missense mutations. dMMR/MSI status was evaluated by a combination of IHC, FA and NGS. PD-L1 expression measured by IHC (22c3) was evaluated by CPS scores. Molecular alterations were compared in three groups (CPS $\geq$ 10, H; CPS = 1~9, M; CPS = 0, L) using Fisher-Exact or Chi-square and adjusted for multiple comparison by Benjamini-Hochberg. Significance was determined by adjusted (adj) $p < .05$. **Results:** Overall, CPS-H, M, and L were seen in 18% (n = 494), 28% (n = 765) and 53% (n = 1,448) of GE tumors respectively. CPS-H was the most prevalent in ES (43%) followed by GA (19%) and lowest in EA (14%). Overall, TMB was similar between CPS-L and M, but was significantly increased in H (average TMB = 8.4 vs. 8.6 vs. 11 mt/MB, adj $p < .0001$); the effect was seen in EA and GA, but not in ES. An overall significant association between MSI/dMMR status and PD-L1 expression levels was seen (2%, 3.2% and 12% in CPS-L, M and H, adj $p < .05$) in GE tumors; the significance was seen in GA, but not in EA or ES. Amplifications of *PD-L1* (H: 1.5%, M: 0.1% and L: 0) and *PD-L2* (H: 1.1%, M: 0.1%, L: 0) were the highest in CPS-H, while *ASPSCR1* (H: 0, M: 0, L: 1%) and *TNFRSF14* (H: 0, M: 0.4, L: 2%) were the lowest (adj $p < .01$). Genes involved in epigenetic modification (top 5: *ARID1A*, *ASXL1*, *BCL9*, *BCOR*, *CREBBP*), MAPK (*KRAS*, *MAP2K1*) and mismatch repair (*MLH1*, *MSH6*) had the highest mutation rates in CPS-H, compared to M and L ($p < .0001$). In contrast, *CDH1* had higher mutation rates in CPS-L (12%), compared to M and H (5% and 5%) ($p < .0001$). **Conclusions:** This is the largest study to investigate the distinct molecular landscape of pts with different PD-L1 expression levels in GE cancers. Our data may provide novel insights for pt selection (e.g. pts with gene mutations involved in epigenetic modification) and the development of rational combination immunotherapy (e.g. drugs targeting MAPK pathway). Research Sponsor: National Cancer Institute (grant number P30CA014089), The Gloria Borges WunderGlo Foundation-The Wunder Project, Dhont Family Foundation, San Pedro Peninsula Cancer Guild, Daniel Butler Research Fund and Call to Cure Fund.

4559 Poster Session (Board #167), Fri, 8:00 AM-11:00 AM

Pembrolizumab with trastuzumab and chemotherapy (PTC) in HER2-positive metastatic esophagogastric cancer (mEG): Plasma and tumor-based biomarker analysis. *First Author: Steven Brad Maron, Memorial Sloan Kettering, New York, NY*

Background: Pembrolizumab can be safely combined with trastuzumab and chemotherapy and has promising activity with median OS 27 months and 91% objective response rate in HER2-positive mEG cancer irrespective of PD-L1 status (NCT02954536; Janjigian ESMO 2019). Tumor biopsies and blood samples were collected in this phase II trial to identify molecular and immune predictors of response and resistance to PTC. **Methods:** Pre-treatment and post-progression biopsies were analyzed using WES and IHC (HER2, PD-L1). Peripheral blood was collected pre-treatment, every 9 weeks on-treatment and at progression for plasma ctDNA (Guardant 360, Guardant Health, Redwood, CA). Tumor-matched DNA alterations were identified by correlating ctDNA and solid tumor WES results. Landmark PFS analysis was used to compare ctDNA clearance status at 9 weeks post-treatment. **Results:** Baseline ctDNA was analysed from 31 of 37 patients of whom 84% (26/31) had tumor-matched ctDNA detected at baseline. Patients who cleared ctDNA at 9 weeks (n = 17/23) achieved a longer median PFS than those who did not - mPFS 12.3 months (95% CI 7.44-NA vs 3.9 months (95% CI 2.01-NA) (log-rank $p = 0.02$). On serial blood monitoring of 16 patients with eventual radiographic progression, ctDNA re-appearance preceded CT detection in 8 (50%) patients. WES was completed in 31 patients with pre-treatment, and 12 patients post-progression, including matched samples from 10 patients. Loss of HER2 over-expression/amplification was noted in 44% (7/16) of post-progression samples by IHC/FISH (2 IHC 0/1, 5 FISH-). In paired post-progression samples on WES, we observed loss of *ERBB2* in 2 patients, and new amplifications of *CCND1/3, FGF3/4/19, CDK6/12, KRAS, MYC*, and *MET*, as well as mutations in *KRAS, PIK3CD and PIK3RA*. Plasma analysis at progression demonstrated copy number increases and/or new amplifications in *MET*, *CKD6*, *PIK3CA*, *KRAS*, *FGFR2*, *EGFR* and *CCDN1* as well as *KRAS*, *RB1*, *PTEN*, *NF1, NOTCH1*, *BRAF*, and *FGFR1* mutations. **Conclusions:** The majority of patients with previously untreated HER2 positive mEG have detectable plasma ctDNA at baseline. The re-appearance of ctDNA during therapy may serve as an early predictor of progression and help identify genetic drivers of acquired resistance. Loss of *ERBB2* over-expression/amplification and activating MAPK alterations occur at PTC progression. Evaluation of tumor immune environment by multiplex IHC and additional ctDNA analysis is underway. Research Sponsor: U.S. National Institutes of Health, Conquer Cancer Foundation of the American Society of Clinical Oncology, Other Foundation, Other Government Agency.

4560 Poster Session (Board #168), Fri, 8:00 AM-11:00 AM

A phase II study of efficacy and safety of RC48-ADC in patients with locally advanced or metastatic HER2-overexpressing gastric or gastroesophageal junction cancers. *First Author: Zhi Peng, Department of Gastrointestinal Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital and Institute, Beijing, China*

Background: RC48-ADC is an antibody-drug conjugate (ADC) drug comprised of a novel humanized anti-HER2 IgG1, a linker, and a microtubule inhibitor, MMAE. The MoA included inhibition of HER2 signal pathway and cytotoxicity of MMAE. RC48-ADC has demonstrated promising anti-tumor activity in preclinical and early clinical studies. The current study is designed to evaluate the efficacy and safety of RC48-ADC in heavily treated patients with HER2-overexpressing (IHC 2+ or 3+) gastric or gastro-esophageal junction cancers. **Methods:** This is an open-label, multicenter, single-arm, phase II study. Eligibility criteria include: histologically confirmed gastric or gastro-esophageal junction cancers, HER2-overexpression (IHC 2+ or 3+), ECOG PS 0-1, post-to ≥2 prior systemic treatment. The patients received RC48-ADC, 2.5 mg/kg, q2w until disease progression, unacceptable toxicity, withdrawal, or study termination. The primary endpoint was ORR. PFS, OS, and safety were also evaluated. **Results:** Patient enrollment started in July 2017, and completed in November 2019. By the data cut-off date on 17-Dec-2019, 127 patients were enrolled. The median age was 58 years. At baseline, 59 patients (46.5%) had received ≥ 3 lines prior treatment. For the overall 127 patients, the investigator-assessed confirmed ORR was 18.1% (95% CI: 11.8%, 25.9%). Sub-group ORR was 19.4% and 16.9% for the patients post to 2 lines and ≥ 3 lines, respectively. For the 111 patients who were monitored for ≥ 2 cycles of efficacy assessments (i.e. 12 weeks), the ORR was 20.7% (95% CI: 13.6%, 29.5%). For the 127 patients, the mPFS was 3.8 months (95% CI: 2.7, 4.0, 89 events [70.1%]) and the mOS was 7.6 months (95% CI: 6.6, 9.2, 52 events [40.9%]). The most commonly reported treatment-related AEs were leukopenia (52.0%), alopecia (51.2%), neutropenia (48.0%), and fatigue (42.5%). **Conclusions:** RC48-ADC demonstrated a clinically meaningful response and survival benefit in the heavily treated patients with HER2-overexpressing gastric or gastro-esophageal junction cancers. The safety profile was in line with the previously reported data of RC48-ADC. RC48-ADC showed positive benefit/risk ratio for the target population. Clinical trial information: NCT03556345. Research Sponsor: RemGen, Ltd.

4561 Poster Session (Board #169), Fri, 8:00 AM-11:00 AM

Personalized antibodies for gastroesophageal adenocarcinoma (PANGEA): Secondary and final primary efficacy analyses. *First Author: Daniel V.T. Catenacci, University of Chicago Medical Center and Biological Sciences, Chicago, IL*

Background: Targeted therapies (tx) have had limited benefit in advanced (aGEA) due to baseline spatial (primary vs metastatic tumor PT/MT) & temporal molecular heterogeneity (BMH/TMH). We previously reported PANGEA methods & results: 35% BMH rate & 1^{O} OS results achieving 1yr OS of 66% & mOS of 16.4 months (m) using the personalized tx strategy (Catenacci *et al.* GI ASCO 2020 Abstr356). Here we will report the TMH rates at progressive disease points (PD1 & PD2), ORR/PFS/DCR in each of 3 tx lines, time to strategy failure (TTF), & updated OS/safety. **Methods:** PANGEA enrolled newly diagnosed aGEA pts who then received up to 3 cytotoxic (cx) tx lines (L). Baseline tissue biomarker profiling (BP) was mandated on PT/MT & PD1/PD2, & ctDNA analysis throughout. After initiating 1L cx & upon learning MT BP results, antibody (AN) was added by a predefined prioritized tx algorithm incorporating tissue & blood BP (Table). At PD1, pts went to 2L cx + initial AN. Upon results of PD1 BP, pts changed AN only if BP evolved per tx algorithm. The same was done at PD2. The 1^{O} endpoint was 1yr OS; enrolling 68 pts provided 80% power to detect a 63% 1yr OS compared to historical 50% 1yr OS (HR 0.67), using a 1-sided test (0.10 alpha). **Results:** 80 pts were enrolled, & 68 tx'd per protocol. At data cut-off 2/1/20, 15 pts were still on trial with only 2 of these pts on tx <12m (8 pts in 1L, 5 in 2L, 2 in 3L). All 68 pts had at least 1 dose of 1L tx, 87% 2L tx, & 36% 3L tx. AN assigned by the tx algorithm at 1L, OS, TTF, & $ORR_1/PFS_1/DCR_1$ of 1L tx are shown in Table; 2L & 3L ORR/DCR outcomes will be shown. The 3yr & 4yr OS rates were 12% & 8%. TMH leading to molecular subgroup change by tx algorithm was 51% after 1L & 36% after 2L; details & results by subgroup will be provided. Any grade >3 non-heme tox thru all 3 tx lines was seen in 25% of pts. **Conclusions:** PANGEA showed superior 1^{O} & 2^{O} endpoint efficacy, even when excluding HER2- pts, compared to historical outcomes. Clinical trial information: NCT02213289. Research Sponsor: U.S. National Institutes of Health, Other Foundation, U.S. National Institutes of Health.

PTA[1]	1L AN	Total N=80 N (%)	1Yr OS[5]	ORR_1 %	DCR_1	mOS	$mPFS_1$ m	mTTF
IO[2]	nivolumab	5 (6)	67	100	100	21.2	7.9	19.9
MSI-H		1 (1)	100					
PDL1>10		4 (5)	50					
TMB-H >15		0						
EBV+		0						
HER2 amp[3]	trastuzumab	16 (20)	73	93	100	26.1	15.1	24.6
EGFR amp[3]	ABT-806	8 (10)	75	67	100	14.9	6.4	12.9
FGFR2 amp[3]	none[4]	4 (5)	33	33	67	5.5	4.4	4.4
	FPA-144	3 (4)	100					
		1 (1)						
MET amp[3]	none[4]	9 (11)	33	43	78	10.7	7.3	9.4
RAS-like	ramucirumab	20 (25)	62	63	95	15.1	9.4	13.7
EGFR expressed	ABT-806	9 (11)	44	43	100	6.7	4.9	5.6
All-negative	ramucirumab	9 (11)	70	75	100	14	8.1	12.8
Per Protocol (ITT)	**ALL**	**68 (85)**	**66**	**72**	**99**	**15.7**	**8.2**	**13.8**
IIT excluding HER2	ALL but Tras	42 (53)	64	64	98	14.9	7.8	12.9

1 MT priority over PT 2 priority over HER2 only 2L+ 3 priority to highest gene copy 4 not in ITT

4562 Poster Session (Board #170), Fri, 8:00 AM-11:00 AM

Health-related quality-of-life assessment in accordance with reconstruction procedures for distal gastrectomy for stage I gastric cancer using data from JCOG0912. *First Author: Keiichi Fujiya, Division of Gastric Surgery, Shizuoka Cancer Center, Shizuoka, Japan*

Background: There are three major reconstruction methods after gastrectomy for distal gastric cancer; Billroth-I (B-I), Roux-en-Y (RY) and pylorus-preserving gastrectomy (PPG). These procedures can affect postoperative health-related quality-of-life (HRQoL), but the method is often selected due to physician's preference or each institutional policy without solid evidence. We aimed to explore differences in HRQoL after each reconstruction procedure selected in JCOG0912, a phase III noninferiority trial comparing open and laparoscopic distal gastrectomies for stage I gastric cancer. **Methods:** Among 33 institutions participated in JCOG0912, 4 major cancer centers were selected for HRQoL assessment. HRQoL was assessed using the EORTC QLQ-C30 and STO22 before (baseline) and at 1, 3, 12, and 36 months after surgery as preplanned exploratory analysis. **Results:** Excluding 2 patients who didn't answer the questionnaire, 590 patients were analyzed in this study. For reconstruction, B-I was performed for 222 patients (37.7%), RY for 178 (30.2%) and PPG for 189 (32.1%). Proportion of the opted reconstruction procedures was not different in open and laparoscopic gastrectomies. Global health status (GHS) scores of QLQ-C30 were not different among 3 groups at any time point. In comparison of B-I and RY, B-I was better than RY in constipation, while RY was better than B-I in diarrhea and reflux symptoms. In comparison of B-I and PPG, B-I was better than PPG in constipation and reflux symptoms, while PPG was better than B-I in diarrhea. When comparing RY and PPG, RY was better than PPG in constipation and reflux symptoms, while PPG was better than RY in taste (table). **Conclusions:** GHS scores were similar regardless of the reconstruction procedure, however postoperative symptoms including reflux, constipation, and diarrhea were various according to reconstruction methods. Research Sponsor: Japan National Cancer Center, Ministry of Health, Labour and Welfare of Japan, Japan Agency for Medical Research and Development.

		Months after surgery	HRQoL score	*p*
B-I (reference: RY)	Constipation	1	-7.3	0.016
	Diarrhea	1/3/12/36	7.2/7.2/8.1/8.0	0.003/0.003/0.001/ < 0.001
	Reflux	36	3.5	0.043
B-I (reference: PPG)	Constipation	1/3/12/36	-10.1/-11.2/-8.2/-7.6	0.002/ < 0.001/0.005/0.008
	Diarrhea	1/3/12	5.5/11.3/9.7	0.031/ < 0.001/ < 0.001
	Reflux	1/3/12	-6.7/-4.7/-6.0	0.001/ < 0.001/ < 0.001/ < 0.001
RY (reference: PPG)	Constipation	3/12/36	-7.9/-6.5/-6.5	0.005/0.022/0.021
	Reflux	1/3/12/36	-6.6/-5.7/-8. 9/-6.9	0.001/ < 0.001/ < 0.001/ < 0.001
	Taste	3/12/36	5.3/3.9/3.1	0.014/0.044/0.040

4563 Poster Session (Board #171), Fri, 8:00 AM-11:00 AM

Cabozantinib (cabo) combined with durvalumab (durva) in gastroesophageal (GE) cancer and other gastrointestinal (GI) malignancies: Preliminary phase Ib CAMILLA study results. *First Author: Anwaar Saeed, University of Kansas Medical Center, Kansas City, KS*

Background: Cabo targets multiple tyrosine kinases, including VEGFR, MET, and AXL, and has been reported to show immunomodulatory properties that may counteract tumor-induced immunosuppression, providing a rationale for combining it with PD-L1 inhibitors like durva. We conducted a phase Ib GI basket trial to evaluate the safety & efficacy of this regimen in advanced GE adenocarcinoma (GEA), colorectal cancer (CRC), & hepatocellular carcinoma (HCC). **Methods:** Patients received cabo and durva in 3+3 dose escalation then expansion to determine the dose limiting toxicity (DLT), Recommended Phase 2 Dose (RP2D), ORR, PFS & OS. Cabo was dosed at 20mg QD, 40mg QD, and 60mg QD in the first, second, and third cohorts respectively. Durva was dosed at 1500mg IV Q4W in all cohorts. DLT window was 28 days. Scans were obtained every 8 wks. Treatment beyond progression was allowed. **Results:** 23 Pts (16 M, 7 F), median age 60 yrs (range 33-79) were currently enrolled. 12 in the dose escalation cohort with cabo 20mg (6 pts), or 40mg (3 pts), or 60mg (3 pts). 11 pts enrolled in the dose expansion cohort with cabo 60mg. 8 pts had GEA, 13 pts had CRC, and 2 pts had HCC. Median number of prior chemotherapies was 3 (range 1-3). 3 pts were not evaluable for DLT due to missing ≥30% of DLT window doses, not related to DLT. No DLTs were observed. Drug-related Grade (G) 1&2 AEs included fatigue (83%), abnormal LFTs (39%), anorexia (26%), diarrhea (26%), nausea (13%), & hand foot syndrome (13%). One pt each developed drug related G3 hypertension, hyperthyroidism, thrombocytopenia, & thromboembolic event, all occurring outside the DLT window. 19 pts were evaluable for response: 4 PR (2 GEA & 2 CRC), 12 SD, 3 PD; ORR 21%; clinical benefit rate 84%; median time to PD 16 wks (range 8-40+). **Conclusions:** RP2D was determined to be Cabo 60mg QD and Durva 1500mg Q4W. Enrollment to phase I dose expansion is ongoing. RP2D may be adjusted based on additional experience & long-term tolerability. Early efficacy data was encouraging. This is an investigator-initiated trial funded by Exelixis & Astrazeneca. Clinical trial information: NCT03539822. Research Sponsor: AstraZeneca and Exelixis.

4564 Poster Session (Board #172), Fri, 8:00 AM-11:00 AM

Final results of a phase III randomized trial of comparison of three paclitaxel-based regimens concurrent with radiotherapy for patients with local advanced esophageal squamous cell carcinoma. *First Author: Dashan Ai, Fudan University Shanghai Cancer Center, Shanghai, China*

Background: Paclitaxel (PTX) is effective in concurrent chemoradiation (CCR) against esophageal squamous cell carcinoma (ESCC). Which regimen, among cisplatin (DDP) (TP), carboplatin (CBP) (TC) or 5-Fu (TF) in combination with PTX concurrent with radiotherapy, provides best prognosis with minimum adverse events (AEs) is still unknown. **Methods:** The study compared two pairs of regimens: TF vs. TP and TF vs. TC concurrent with radiotherapy. Patients with histologically confirmed ESCC (clinical stage II, III or IVa) 20 were randomized into the three groups. Patients in TP group were treated with 2 cycles of CCR followed by 2 cycles of consolidation chemotherapy with TP (DDP 25 mg/m2/d, d1-3, PTX 175 mg/m2, d1, q28d). Patients in TF group were treated with 6 cycles of TF (5-Fu 300 mg/m2, civ 96h, PTX 50 mg/m2, d1, qw) in CCR followed by 2 cycles of TF (5-FU 1800 mg/m2, civ 72h, PTX 175 mg/m2, d1, q28d) in consolidation chemotherapy. Patients in TC group were treated with 6 cycles of TC (CBP AUC = 2, d1, PTX 50 mg/m2, d1, qw) in CCR followed by 2 cycles of TC (CBP AUC = 5, d1, PTX 175 mg/m2 d1, q28d) in consolidation chemotherapy. The radiotherapy dose in all groups was 61.2 Gy delivered in 34 fractions. The primary endpoint was overall survival (OS) and the secondary endpoints were progression-free survival (PFS) and adverse events. **Results:** Between July 2015 and January 2018, 321 ESCC patients in 11 centers were enrolled. Median follow-up of patients who survived was 36.3 months (IQR 27.9–45.2). The 3-yr OS was 58.2% in TF group and 59.5% in both TP and TC group. (TF vs. TP, HR 0.935, 95% CI 0.627-1.417; TF vs. TC, HR 0.881, 95% CI 0.578-1.342; $P = 0.839$). No significant differences were found in 3-yr PFS between TF, TP and TC groups [48.3% vs. 45.5%(TP) or 48.3% (TC). $P = 0.820$]. TP group had a significant higher incidence of acute Grade 3/4 neutropenia [60.7% vs. 16.8%(TF) or 32.7%(TC)], thrombocytopenia [13.1% vs. 2.8%(TF) or 4.7%(TC)], anemia [5.6% vs. 1.9%(TF) or 3.7% (TC)], fatigue [10.3% vs. 1.9%(TF) or 0.9%(TC)] and vomiting [5.6% vs. 0%(TF) or 0.9%(TC))]than other two groups ($P< 0.05$). TF group had a significant higher incidence of Grade 3/4/5 esophagitis [11.2% vs. 0.9%(TP) or 4.7%(TC))]and pneumonitis [4.6% vs. 0%(TP) or 1.9% (TC)]than other two groups ($P< 0.05$). **Conclusions:** No statistical differences were found in OS and PFS among TF, TP and TC groups. TC might be an option used in CCR in ESCC patients with mild of side effects compared with other two groups, although it did not significantly prolong OS. Clinical trial information: NCT02459457. Research Sponsor: 2015 Prospective Clinical Research Fund of Fudan University Shanghai Cancer Center.

4565 Poster Session (Board #173), Fri, 8:00 AM-11:00 AM

Second primary malignancies in patients with clinical T1bN0 esophageal squamous cell carcinoma after definitive therapies: Supplementary analysis of the JCOG trial, JCOG0502. *First Author: Seiichiro Mitani, Aichi Cancer Center Hospital, Nagoya, Japan*

Background: Esophageal squamous cell carcinoma (ESCC) is associated with synchronous or metachronous cancer at other primary sites. Previous studies have suggested that patients (pts) with ESCC are still at a high risk of second primary malignancies after definitive therapies. In particular, early-stage ESCCs result in good prognosis, which is associated with a higher risk of second primary malignancies. **Methods:** The JCOG0502 was a phase III trial, which included a randomized and a non-randomized part and compared esophagectomy with definitive chemoradiotherapy in clinical T1bN0 ESCC. We additionally reviewed data of all pts enrolled in the JCOG0502 for second primary malignancies. Lugol-voiding lesions (LVLs) were assessed in the noncancerous esophageal mucosa before the treatments. **Results:** Among 379 enrolled pts, 213 pts received esophagectomy and the remaining received chemoradiotherapy. Patient characteristics of overall cohort were as follows: male, 85%; median age, 63 (range, 41–75) years; upper- /middle- /lower thoracic esophagus, 11/63/27%; alcohol consumption history, 79%; smoking history, 66%; prevalence of no LVLs/several LVLs/many LVLs/unknown, 45/36/8/11%. With a median follow-up of 7.1 years, a total of 118 second malignancies were observed in 99 pts (26%). Cumulative incidences of second malignancies after 3, 5, 10 years were 9, 15, 36%, respectively. Most common primary tumor sites were head and neck (35%), followed by stomach (20%) and lung (14%). In multivariable analyses, several LVLs [hazard ratio (HR): 2.24, 95% confidential interval (CI): 1.32–3.81, vs. no LVLs] and many LVLs (HR: 2.88, 95% CI: 1.27–6.52, vs. no LVLs) were significantly associated with the development of second malignancies. Regarding the three most common types of cancers, 62 out of the 77 cancers (81%) were diagnosed in clinical stage 0–I. Seventeen pts died due to second primary malignancies. There were 4 and 3 deaths from head and neck and lung cancer, respectively. Whereas, mortality caused by stomach cancer was not observed. **Conclusions:** In the JCOG0502, the incidence of second malignancies was high, indicating that careful follow-up is required for ESCC pts even after treatment completion. The presence of LVLs in esophagus was identified as an independent predictive factor for second primary malignancies, which may be useful for surveillance strategies. Clinical trial information: UMIN000000551. Research Sponsor: Japanese Ministry of Health, Labour and Welfare.

4566 Poster Session (Board #174), Fri, 8:00 AM-11:00 AM

Prognostic role of mismatch repair deficiency (MMR-D) in patients receiving first-line fluoropyrimidine and platinum (FP) doublet chemotherapy for metastatic and locally advanced unresectable gastric cancers (GCs). *First Author: Eo Jin Kim, Asan Medical Center, Seoul, South Korea*

Background: Although chemotherapy has been suggested to have the potential to cause a detrimental effect on treatment outcomes of localized GC with MMR-D, it remains unclear whether chemotherapy for metastatic/recurrent/unresectable GC with MMR-D would also adversely affect the survival outcomes. Anti PD-1 antibody (Ab) showed remarkable efficacy in patients with MMR-D and is being actively investigated in combination with cytotoxic chemotherapy. Hence, we aim to evaluate the impact of MMR status on treatment outcomes of advanced GC. **Methods:** We reviewed our database to identify all patients with HER2 negative, metastatic, recurrent, and locally advanced unresectable GC who received FP doublet chemotherapy from January 2015 to August 2018. For those who had an available tumor tissue, MMR protein expression was assessed by immunohistochemistry (IHC) and correlated with clinical characteristics and treatment outcomes. **Results:** Out of 895 patients identified from the database, 543 underwent IHC testing for MMR. The median age was 58 years (range, 24 – 86) with male comprising 64.0%. Most patients had initially metastatic disease (n = 382, 70.3%) followed by recurrent (n = 127, 23.3%) and locally advanced unresectable disease (n = 34, 6.3%). MMR-D was found in 4.4% (n = 24) and associated with age ≥ 65 years (50% vs. 29.9%; P = 0.04) and signet ring cell histology (0% vs. 17.7%, P = 0.01). According to our prognostic model (Koo DH et al, 2011), only 4.2% of patients with MMR-D were classified as Poor-risk group (vs. 16.8% of patients with MMR-P, $p= 0.10$). In the Good-risk group, patients with MMR-D (n = 10) had significantly shorter median progression-free survival (PFS, 6.0 vs. 9.0 months, P = 0.05) and overall survival (OS, 10.1 vs 20.9 months, P = 0.047) compared to those with MMR-P (n = 188), while there was no significant difference in survival outcomes depending on MMR status in the Moderate and Poor-risk groups. In multivariate analysis for OS, MMR status was a significant prognostic factor for OS in Good-risk group GC patients. **Conclusions:** GC patients with MMR-D had poorer median PFS and OS than those with MMR-P on standard cytotoxic chemotherapy in the Good-risk group. Thus, for Good-risk GC patients with MMR-D, anti PD-1 Ab alone might be considered rather than combining cytotoxic chemotherapy. Further investigation with next-generation sequencing is in process to determine underlying molecular mechanisms and will be presented in ASCO 2020. Research Sponsor: None.

4567 Poster Session (Board #175), Fri, 8:00 AM-11:00 AM

HER2 heterogeneity in adenocarcinoma of the distal esophagus and stomach. *First Author: Rogier Butter, Amsterdam UMC - University of Amsterdam, Amsterdam, Netherlands*

Background: Patients with HER2 positive adenocarcinoma of the esophagus or stomach are eligible for HER2 targeted therapy, which can improve survival in selected patients. Previous research shows that HER2 gene amplification and HER2 overexpression is frequently heterogeneous within these tumors. Biopsies taken from heterogeneous tumors for predictive testing may therefore result in false-negative outcomes. The objective of this study was to assess HER2 amplification and expression in biopsies and paired resection specimens with adenocarcinoma of the esophagus or stomach, from patients who did not receive neoadjuvant systemic therapy. **Methods:** Paired biopsies and resection specimens of patients with adenocarcinomas of the esophagus or stomach were retrospectively selected. Immunostaining was performed on all samples using antibody 4B5 (Ventana Medical Systems) and *Silver-In-Situ-Hybridization* was performed in selected cases. Scoring for HER2 was performed according to the method described by Hofmann et al. (2008). **Results:** We included 378 cases for analysis. In both biopsies and resection specimens 14% of the cases were HER2 positive. Intratumor heterogeneity in HER2 positive tumors was present in 45% (n= 24/53) in biopsies and 75% (n= 39/52) in resection specimens. In HER2 positive resection specimens, 65% (n= 34/52) of paired biopsies were also positive. In the 18 remaining discordant tumors (resection HER2 positive, biopsy negative), intratumor heterogeneity was present in 16/18 cases. For HER2 negative resection specimens all paired biopsies were also HER2 negative. SISH was performed in 110 tumors. Agreement of HER2 gene amplification between biopsy and resection specimens was observed in 86% (n = 95/110). Five HER2 negative biopsies were positive in the resection specimen. **Conclusions:** The results of this study indicate that predictive HER2 assessment in adenocarcinoma of the esophagus or stomach can lead to false negative results based on biopsies. As a result, patients with HER2 positive tumors can unintentionally be denied neoadjuvant HER2 targeted therapy. The set of patients investigated in this present study is unique because of the absence of any systemic and/or radiation therapy between the biopsy and the resection of the tumor. Hopefully these results can help in developing methods for improved patient selection for HER2 targeted therapy. Research Sponsor: F. Hoffmann-La Roche AG.

4568 Poster Session (Board #176), Fri, 8:00 AM-11:00 AM

PD-L1 positive esophagogastric (EG) cancer is associated with distinct bacteria. *First Author: Steven Brad Maron, Memorial Sloan Kettering, New York, NY*

Background: Pembrolizumab is approved for chemotherapy-refractory PD-L1 CPS >1 mEG cancer. In clinical trials, pts with MSI-H, EBV+ and PD-L1 CPS >10 EG cancers derive the greatest benefit with immune checkpoint blockade (ICB). Pre-clinical data suggest that the gut microbiome modulates response to ICB; however, the EG cancer microbiome has not been characterized in EG cancer with respect to PD-L1 and MSI-H status. Therefore, we evaluated the EG tumor microbiome in the context of PD-L1 expression in order to define biologically unique EG tumor phenotypes for future therapeutic development. **Methods:** Clinical and pathologic characteristics, including age, stage at diagnosis, tumor PD-L1 CPS, HER2 IHC, EBV ISH, genomic analysis, treatment history and survival status were reviewed. CPS was stratified *a priori* using cutoffs of >1/>10/>20 due to biologic differences. MSK-IMPACT, a capture-based next-generation sequencing platform that detects mutations, copy-number alterations, and select fusions was used to detect non-human bacterial reads identified in the NCBI NT database. Bacterial species found in >2 pts were analyzed and stratified by highest PD-L1 CPS score for each individual patient (Vanderbilt, AMP 2018) and Bonferroni correction was used for odds ratio (OR) confidence intervals where each unique species was considered an independent hypothesis. **Results:** Molecular data from 311 pts was clinically annotated. PD-L1 results (Table) correlated with bacterial species identified on tumor sequencing. PD-L1 CPS >1 was associated with *Selenomonas sputigena* (OR: 8.2, 95% CI:1.2-53.6), and PD-L1 CPS >20 was associated with presence of *Bifidobacterium dentium* (OR: 7.4, 95% CI:1.1-48.5) and *Prevotella denticola* (OR: 4.2, 95% CI: 1.1-16.6) after multiple comparison correction for the 166 bacterial species identified in the cohort. No differences were seen between PD-L1 < 10 vs >10. Four patients were also found to have EBV+ tumors using this approach, including the 1/54 patients identified by EBER ISH. **Conclusions:** PD-L1 > 20 EG cancer represents a biologically unique subset, enriched for *Bifidobacterium dentium* and *Prevotella denticola*. Correlation between PD-L1 expression, microbial and immune environment, and survival on ICB is underway. Research Sponsor: U.S. National Institutes of Health, Conquer Cancer Foundation of the American Society of Clinical Oncology.

PD-L1	All Pts (%) n = 313	MSI-H (%) n = 16	EBV+ (%) n = 4
CPS < 1	152 (49)	2 (12.5)	0
CPS 1-9	92 (29)	2 (12.5)	1 (25)
CPS 10-19	28 (9)	4 (25)	1 (25)
CPS >20	41 (13)	8 (50)	2 (50)

4569 Poster Session (Board #177), Fri, 8:00 AM-11:00 AM

Radiotherapy after esophageal cancer stenting (ROCS): A pragmatic randomized controlled trial evaluating the role of palliative radiotherapy in maintaining swallow. *First Author: Anthony Thomas Byrne, Velindre Cancer Centre, Cardiff, United Kingdom*

Background: Most patients with oesophageal cancer (OC) present with incurable disease; 80% of new cases, and deaths, occur in low and middle income nations. Median survival for advanced disease is 3-5 months, a majority requiring intervention for dysphagia. Insertion of self expanding metal stents is the commonest way of palliating, but dysphagia may recur within three months owing to tumour progression. Evidence reviews have called for trials of combination treatment for OC dysphagia. The ROCS study (funding - UK NIHR programme) examined effectiveness of palliative radiotherapy, following stent, in maintaining swallow. It also examined impact on quality of life, bleeding events, and survival. **Methods:** A multicentre RCT with follow up monthly for a year. Patients referred for stent insertion as primary management of dysphagia related to incurable OC were recruited in secondary care, with all planned follow up at home. Patients were randomised 1:1 to stent insertion alone or stent insertion plus palliative radiotherapy at a dose of 20Gy in five fractions or 30Gy in ten fractions. Primary outcome was difference in proportions of participants with recurrent dysphagia at 12 weeks, defined as deterioration of 11 points or more in the dysphagia scale of the EORTC QLQ-OG25 questionnaire. Secondary outcomes included quality of life, bleeding risk, survival. **Results:** 220 patients were randomised Dec 2013-Aug 2018 at 23 UK sites. Addition of radiotherapy did not reduce the proportion of primary events at 12 weeks: 49% in control arm vs 45% in the intervention, adjusted OR 0.82 (95%CI 0.40-1.68; p = 0.587) and it was less cost effective. Sensitivity analyses did not alter the results. Dysphagia deterioration-free survival was similar in both arms: adjusted HR 0.92 (95%CI 0.68-1.26; p = 0.618). Median survival was 19.7 weeks in control arm and 18.9 weeks in the intervention. Those in the radiotherapy arm had significantly fewer bleeding events (18.6% compared to 10.3%), giving a number needed to treat of 12. **Conclusions:** Palliative external beam radiotherapy is widely accessible to patients with advanced cancer. ROCS is the largest trial assessing its role in combination with stenting for OC dysphagia, and is the first to prospectively assess impact on bleeding risk. It demonstrates no reduction in risk of dysphagia recurrence at 12 weeks, nor impact on survival. Reductions in bleeding events should be considered in the context of patient described trade offs of fatigue and burdens of attending hospital. Clinical trial information: NCT01915693. Research Sponsor: UK National Institute for Health Research Health Technology Assessment (HTA) Programme.

4570 Poster Session (Board #178), Fri, 8:00 AM-11:00 AM

Identification of SLX4 as the most frequently mutated gene in homologous recombination deficiency in Asian gastric cancer. *First Author: Shi Zhang, Department of Gastrointestinal Surgery, Second Affiliated Hospital, Guangzhou Medical University, Guangzhou, China*

Background: Gastric cancer is the third most common malignancy worldwide. Homologous recombination (HR) is a type of genetic recombination, and homologous recombination deficiency (HRD) is highly involved in multiple types of cancers and can predict response to anticancer therapies. However, homologous recombination deficiency is not well characterized in patients with Asian gastric cancer. **Methods:** 196 Asian patients with gastric cancer were analyzed in this study. A list of 102 genes related to HRD was compiled based on previous literature. Haplox 605-gene panel was used to capture the sequencing library. Mutations related to HRD were analyzed following next-generation sequencing. In addition, tumor mutational burden (TMB) was calculated by dividing the total number of mutations by the size of the coding region. The correlation analysis between HRD and TMB was also conducted. **Results:** In total, 43 (21.94%) of 196 Asian patients with gastric cancer harbored at least one HRD gene. The top 10 mutant HRD genes included *SLX4* (3.57%), *ATR* (2.04%), *RECQL* (1.53%), *NBN* (1.53%), *ERCC4* (1.53%), *BAP1* (1.53%), *ATM* (1.53%), *RAD54L* (1.02%), *BRCA1* (1.02%) and *PARP1* (1.02%). In addition, the occurrence of HRD mutations was significantly correlated with a higher TMB. The median TMB of HRD group (8.28 muts/Mb) was significantly higher than that of the Non-HRD group (3.07 muts/Mb) ($p < 0.01$). The overall upper quantile value (4.80 muts/Mb) was used to screen patients with high TMB (TMB-H). The TMB-H in HRD group was significantly higher than the Non-HRD group (44.19% VS 17.92%, $p < 0.01$). **Conclusions:** Our study described that *SLX4* was the most frequently mutated HR-related gene in Asian gastric cancer. Moreover, the positive correlation with homologous recombination deficiency (HRD) and tumor mutational burden (TMB) was observed in these patients. Research Sponsor: None.

4571 Poster Session (Board #179), Fri, 8:00 AM-11:00 AM

A novel gene signature for predicting response to chemoradiotherapy in locally advanced esophageal adenocarcinoma. *First Author: Divya Sahu, Department of Molecular Diagnostics and Experimental Therapeutics, Beckman Research Institute of City of Hope, Monrovia, CA*

Background: While neoadjuvant chemoradiotherapy (CRT) has emerged as an important treatment modality in patients with locally advanced esophageal adenocarcinoma (EAC), ~60%-70% of patients do not respond to such treatments; but are exposed to their toxicity nonetheless. This highlights the clinical need for the development of biomarkers that can robustly predict response to CRT and spare others from the toxicity and expense associated with these treatments. Herein, we systematically and comprehensively identified a biomarker signature that predicts response to neoadjuvant therapy in EAC patients. **Methods:** A cohort of 31 EAC patients treated with chemotherapy or chemoradiotherapy was assembled, with a majority of patients receiving carboplatin, paclitaxel and concurrent radiotherapy. Specifically, we performed a capture based targeted sequencing in *paired* biopsy specimens obtained at baseline and 3-6 weeks post-treatment. In addition, we also analyzed the predictive potential of a panel of immune-related genes (TIM3, LAG3, IDO1 and CXCL9) in these matched pre- and post-treatment tissues. **Results:** In our cohort, based upon pathologic response to neoadjuvant CRT, 8 EAC patients were categorized as non-responders, while 23 were deemed as responders to CRT. Among responders, the most frequently mutated genes were MKI67, SYNE1, PCLO, RECQL4, MSH3, NOTCH2, ILR7, CIITA, LRRK2 and EML4, and the overall tumor mutation burden (TMB) was significantly reduced for these genes in post-treatment samples (*P*=5.73E-03). Similarly, in non-responders NLRP1, MAP3K1, ASMTL, and ALK harbored frequent mutations, and the TMB was significantly reduced for these genes in post-treatment samples (*P*=5.57E-03). We compared responders and non-responders from the pre-treatment samples and identified differentially mutated genes including EPHA5, ZNF217, RELN, PALB2 and MYO18A. Similarly, responders had all four immune-related genes significantly up-regulated in post-treatment samples than pre-treatment samples. We constructed a risk-stratification model that comprised of mutational score from 5 differentially mutated genes, together with 4 immune-related genes, which achieved an AUC of 0.96 in predicting response to CRT in EAC patients (*P*=1.03E-04). **Conclusions:** Using a systematic biomarker discovery approach, we have developed a novel biomarker signature that robustly predicts response to CRT in EAC patients and has a significant potential for personalized management of locally advanced EAC patients. Research Sponsor: None.

4572 Poster Session (Board #180), Fri, 8:00 AM-11:00 AM

Durvalumab following multimodality therapy for locally advanced esophageal and GEJ adenocarcinoma: Updated survival and early translational results from Big Ten Cancer Research Consortium Study. *First Author: Hirva Mamdani, Barbara Ann Karmanos Cancer Institute, Detroit, MI*

Background: Concurrent chemoradiation(CRT) followed by esophagectomy is a standard of care for locally advanced esophageal(LA-EAC) and GEJ adenocarcinoma. Approximately 50% of patients(pts) experience disease relapse within the 1st yr after treatment(tx) completion. Immune checkpoint inhibitors have activity in metastatic PD-L1 positive EAC. Preclinical studies have shown radiation +/- chemotherapy upregulates PD-1/PD-L1 pathway. **Methods:** We conducted a phase II trial evaluating safety and efficacy of PD-L1 inhibitor durvalumab(durva) in pts with LA-EAC and GEJ adenocarcinoma who had residual disease in surgical specimen after neoadjuvant CRT and R0 resection. Pts received durva 1500mg IV every 4 weeks for up to 1yr. **Results:** Initially 24 pts were enrolled, study was expanded to enroll additional 13 pts. Median age: 61yrs (range, 43-73). 31 received carbo/paclitaxel and 6 received cis/5-FU concurrently with RT. 24(64.9%) pts had positive lymph nodes(LN) at the time of surgery following CRT: N3(n = 3,8.1%), N2(n = 10, 27%), N1(n = 11,29.7%).17 pts relapsed: 11 on tx, 6 had late relapses. 3/5 late relapses were locoregional and were re-treated with chemo-RT. Remaining relapses were systemic with lung and LN being the most common sites. 2 of 3 pts who developed grade 3 irAEs are alive and disease free at 17 and 23 mo. RFS/OS:1 yr- 79.2%/95.5%, 2yr-55.5%/67.4%. 20/37 pts have HER-2 status available: 5/6 HER2 positive pts had disease relapse, 1 is undergoing tx. Molecular profiling is available on 8 relapsed pts: all were microsatellite stable with low TMB and PD-L1 $<$ 10% CPS. Mutations in DNA repair genes (*ARID1A, ATM, ATR, CHEK2*), and *PIK3CA* E542K were more prevalent among late relapsing pts. Circulating tumor cells (CTCs) analysis is available for 10/37 pts. 4/5 pts where CTCs increased from C1 to C4 had disease relapse. Molecular profiling of the remaining pts and correlation of PD-L1 expression, TMB, specific genes mutations, CTCs, and Immunoscore with outcomes with durva is being evaluated will be presented at the meeting. **Conclusions:** Adjuvant durva following trimodality therapy for LA-EAC and GEJ adenocarcinoma improved 1-yr RFS to 79.2% compared to historical rate of 50%.2-yr RFS and OS data are encouraging in this high risk pt population. HER-2 positivity may be associated with lack of benefit from durva. Mutations in DNA repair genes are prevalent in pts with delayed relapse. Rise in CTCs during durva tx may be an early marker of disease relapse. Clinical trial information: NCT02639065. Research Sponsor: AstraZeneca/MedImmune.

4574 Poster Session (Board #182), Fri, 8:00 AM-11:00 AM

Hepatic arterial infusion of oxaliplatin plus raltitrexed in patients with unresectable hepatocellular carcinoma (HAIROX): A phase II, single-arm, prospective study. *First Author: Shiguang Chen, Fujian Cancer Hospital, Fuzhou, China*

Background: Chemoembolisation and oral sorafenib are the recommended treatment for unresectable hepatocellular carcinoma (HCC); however, some patients respond poorly to these. Hepatic arterial infusion (HAI) chemotherapy may have potential benefit in these patients. We aimed to investigate the efficacy and safety of HAI of oxaliplatin plus raltitrexed in patients with unresectable HCC. **Methods:** In this phase II, single-arm clinical trial, we enrolled patients aged 18–70 years with unresectable HCC at the Fujian Cancer Hospital (China). We performed HAI with oxaliplatin (100 mg/m^2 for 4 hours) and raltitrexed (3 mg/m^2 for 1 hour). Treatment was repeated every 3 weeks and was discontinued either because of disease progression, unacceptable toxicity levels, or refusal of further treatment. We used Simon's two-stage design. The primary endpoint was the objective response rate according to the Response Evaluation Criteria in Solid Tumors version 1.1. **Results:** Fifty-one patients were screened between January 5, 2018 and August 7, 2019. Of these, 39 patients (34 men and 5 women; median age, 53 years) were enrolled and included in the intention-to-treat population. Objective response was achieved in 18 (51.4%) of 35 patients in the per-protocol population and in 18 (46.2%) of 39 patients in the intention-to-treat population. Treatment-related grade 4 adverse events or deaths were not reported, and the observed grade 3 adverse events were elevated aspartate aminotransferase levels (5[12.8%]), elevated alanine aminotransferase levels (1 [2.6%]), leukopenia (1 [2.6%]), thrombocytopenia (1 [2.6%]), and abdominal infection (1 [2.6%]). **Conclusions:** HAI of oxaliplatin plus raltitrexed showed promising efficacy and acceptable toxicity levels in patients unresectable HCC, and further evaluation is warranted. Clinical trial information: ChiCTR-OOC-17014182. Research Sponsor: None.

Treatment responses of HAI of oxaliplatin plus raltitrexed in unresectable HCC.

	Intention-to-treat population (n=39)	Per-protocol population (n=35)
Complete response	1(2.6%)	1(2.9%)
Partial response	17(43.6%)	17(48.6%)
Stable disease	13(33.3%)	13(37.1)
Overall response	18(46.2%)	18(51.4%)
Disease control	31(79.5%)	31(88.6%)

4575 Poster Session (Board #183), Fri, 8:00 AM-11:00 AM

Peripheral blood immune correlates associated with TGF-β inhibition (galunisertib) and stereotactic body radiotherapy (SBRT) in patients with advanced hepatocellular carcinoma (HCC). *First Author: Max Miller Wattenberg, University of Pennsylvania Abramson Cancer Center, Philadelphia, PA*

Background: TGF-β is a pleiotropic cytokine with immunosuppressive activity. In mouse models, blockade of TGF-β signaling enhances the activity of radiation and invokes T cell dependent anti-tumor immunity. We previously reported preliminary safety and efficacy results from a pilot study combining galunisertib (LY2157299), an oral TGF-β inhibitor, with SBRT for the treatment of patients with advanced HCC. Here, we investigate immunological mechanisms and potential biomarkers associated with therapeutic activity. **Methods:** Patients with advanced HCC who had progressed on or refused sorafenib were treated with galunisertib (150 mg PO BID) on days 1-14 of each 28-day cycle. SBRT (18 Gy) was delivered in a single dose between days 15-28 of cycle 1. Blood was collected at baseline, following two weeks of galunisertib and following SBRT for high-dimensional analysis using a 37-marker CyTOF panel. Patients were dichotomized based on best response as either progressor (PD) or non-progressor (PR+SD). The frequency of immune subsets was compared between groups. **Results:** Fifteen patients were enrolled and treated. One patient was not evaluable. The most common adverse event was grade 1 or 2 fatigue in 53% of patients. The only possibly-related grade 3 event was achalasia in one patient which coincided with disease progression. Two patients achieved a PR and six patients had SD (DCR 57%) with a median progression-free survival of 3.7 months and a median overall survival of 9.0 months. For most patients, regardless of outcome, galunisertib treatment was associated with a decrease in activated Ki67+ Treg cells. However, pre-treatment immune composition within the blood of progressors and non-progressors was distinct. At baseline, progressors had an increased frequency of naive-like CD8+ T cells, whereas non-progressors had an increased frequency of non-classical monocytes. After combination therapy, only non-progressors showed a significant increase in CD8+PD1+TIGIT+ T cells. **Conclusions:** Galunisertib combined with SBRT was well-tolerated with modest efficacy. Immune profiling of the blood revealed distinct pre- and post-treatment signatures that differentiated patients with progression versus non-progression. These findings show that the combination of anti-TGF-β therapy with radiation can mediate disease control and identify potential correlates of efficacy. Clinical trial information: NCT02906397. Research Sponsor: Lilly Oncology, Conquer Cancer Foundation of the American Society of Clinical Oncology, U.S. National Institutes of Health.

4576 Poster Session (Board #184), Fri, 8:00 AM-11:00 AM

IDH1 mutation detection in plasma circulating tumor DNA (ctDNA) and association with clinical response in patients with advanced intrahepatic cholangiocarcinoma (IHC) from the phase III ClarIDHy study. *First Author: Elia Aguado, Agios Pharmaceuticals, Inc., Cambridge, MA*

Background: Mutations in isocitrate dehydrogenase 1 (*IDH1*) are detected in ~13% of IHCs. Ivosidenib (IVO) is a first-in-class, oral inhibitor of the mutant IDH1 (mIDH1) protein. In ClarIDHy, a global, phase 3, double-blind study in previously treated patients with advanced m*IDH1* IHC (N = 186), IVO demonstrated an improvement in progression-free survival (PFS) vs placebo (hazard ratio 0.37, p $<$ 0.001) (Abou-Alfa et al., Ann Oncol 2019; NCT02989857). Feasibility of m*IDH1* detection in plasma ctDNA from patients with IHC was demonstrated and was highly concordant with mutation status in tumor tissue (Aguado-Fraile et al., Cancer Res 2019). This analysis was extended to the larger patient cohort from ClarIDHy, and longitudinal m*IDH1* detection from ctDNA was assessed and correlated with clinical response. **Methods:** Baseline plasma and tumor tissue samples were obtained before randomization; longitudinal plasma samples were collected on day 1 of each treatment cycle. m*IDH1* status in tissue was prospectively and centrally confirmed using Oncomine Focus Assay. A BEAMing digital PCR test was used for quantification of m*IDH1* in plasma. *IDH1* mutation clearance (*IDH1*-MC) was achieved when plasma m*IDH1* variant allele frequency was below the assay's sensitivity (0.02% for R132C/L/S/G; 0.04% for R132H). **Results:** m*IDH1* detection in plasma ctDNA and tissue was concordant in 92% (193/210) of samples screened. As of 31 Jan 2019, median PFS was 2.7 months for IVO vs 1.4 months for placebo. Longitudinal analysis with biomarker data available as of Jan 2020 demonstrated *IDH1*-MC in plasma from 10 IVO-treated patients with PFS $\geq$2.7 months (n = 36) vs 0 patients with PFS $<$ 2.7 months (n = 40). No *IDH1*-MC was observed in patients treated with placebo, irrespective of response (n = 49). **Conclusions:** These results reinforce the feasibility of *IDH1*-R132 detection in plasma from patients with IHC, with a 92% concordance with detection in tumor tissue, supporting m*IDH1* detection in liquid biopsy as a viable patient selection strategy where tissue exhaustion can limit conventional methods. Plasma *IDH1*-MC was also observed in a subset of IVO-treated patients who achieved disease control. Clinical trial information: NCT02989857. Research Sponsor: Agios Pharmaceuticals, Inc.

4577 Poster Session (Board #185), Fri, 8:00 AM-11:00 AM

Algorithm for blood-based panel of methylated DNA and protein markers to detect early-stage hepatocellular carcinoma with high specificity. *First Author: Naga P. Chalasani, Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, IN*

Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related deaths worldwide. Though biannual ultrasound surveillance with or without alpha-fetoprotein (AFP) testing is recommended for at-risk patients, its sensitivity for early-stage HCC detection is suboptimal. We therefore evaluated performance of a biomarker panel incorporating methylated DNA markers (MDMs) and proteins for early HCC detection in at-risk patients with chronic liver disease. **Methods:** In an international, multicenter, case-control study, blood specimens were collected from patients with HCC per AASLD criteria and controls matched for age and liver disease etiology. All patients had underlying cirrhosis or chronic HBV infection. Whole blood was collected in cell-free DNA stabilizing and serum-separation tubes and shipped to a central laboratory for processing. The levels of 5 MDMs, AFP, and AFP-L3 were assessed along with age and sex. We used 537 samples in a 5-fold validation for developing a LASSO regression algorithm to classify samples as HCC positive or negative. Model robustness was tested by perturbing the data *in silico* and analyzing results with the predictive algorithm. Algorithm performance was compared to AFP alone and the GALAD score (Gender, Age, AFP-L3, AFP, and DCP). **Results:** The study included 136 HCC cases (81 early-stage—BCLC stage 0/A) and 401 controls. With specificity set at 89%, we developed a model using sex, AFP, and 3 MDMs (HOXA1, TSPYL5, B3GALT6) with higher sensitivity (70%) for early-stage HCC compared to GALAD (54%) or AFP (31% at 20 ng/mL or 52% at ≥7.7 ng/mL) (Table). The AUC for the HCC marker panel was 0.91 (95% CI 0.89 – 0.94) compared to GALAD (0.88; 95% CI 0.85 – 0.91) or AFP (0.84; 95% CI 0.81 – 0.87). The panel performed similarly in viral (AUC = 0.94) and non-viral (AUC = 0.89) etiologies. **Conclusions:** The robust algorithm based on novel blood-based biomarkers presented here provides higher sensitivity for early-stage HCC compared to other available blood-based biomarkers and, therefore, could significantly impact HCC clinical management and patient outcomes. Further clinical studies to validate the algorithm are ongoing. Clinical trial information: NCT03628651. Research Sponsor: Exact Sciences.

Performance of HCC marker panel.

	Sensitivity % (95% CI)		Specificity % (95% CI)	All-Stage AUC (95% CI)
	Early-Stage	All-Stage		
Current HCC marker panel	70 (60 – 80)	81 (74 – 87)	89 (86 – 92)	0.91 (0.89 – 0.94)
GALAD	54 (43 – 65)	68 (59 – 75)	89 (86 – 92)	0.88 (0.85 – 0.91)
AFP (≥7.7 ng/mL)	52 (41 – 63)	64 (56 – 72)	89 (86 – 92)	0.84 (0.81 – 0.87)
AFP (20 ng/mL)	31 (21 – 42)	46 (38 – 55)	98 (96 – 99)	

4578 Poster Session (Board #186), Fri, 8:00 AM-11:00 AM

Associating liver partition and portal vein ligation for staged hepatectomy versus portal vein embolization in staged hepatectomy for hepatocellular carcinoma: A randomized comparative study. *First Author: Gang Huang, Eastern Hepatobiliary Surgery Hospital, National Innovation Alliance for Hepatitis and Liver Cancer, Shanghai, China*

Background: Both Portal Vein Embolization (PVE) and Associating Liver Partition and Portal vein ligation for Staged hepatectomy (ALPPS) have been used in patients with unresectable hepatocellular carcinoma (HCC) due to insufficient volumes in future liver remnant (FLR). But it remains unclear for which thetapy has better long-term overall survival. **Methods:** This study was a single-center, prospective randomized comparative study. Patients were randomly assigned in a 1:1 ratio to the 2 groups. The primary endpoints was three-year overall survival rates. **Results:** Between November 2014 to June 2016, 76 patients with unresectable HCC due to inadequate volume of FLR were randomly assigned to ALPPS groups (n = 38) and PVE groups (n = 38). Thirty-seven patients (97.4%) in the ALPPS Group compared with 25 patients (65.8%) in the PVE Group were able to undergo staged hepatectomy (risk ratio 1.48, 95% CI 1.17-1.87, $p < 0.001$). The three-year overall survival (OS) rate of the ALPPS group (65.8%) (95% CI 50.7-80.9) was significantly better than the PVE Group (42.1%) (95% CI 26.4-57.8), (HR 0.50, 95% CI 0.26-0.98, two-sided p = 0.036). Major postoperative complications rates after the stage-2 hepatectomy were 54.1% in the ALPPS group and 20.0% in the PVE group ((risk ratio 2.70, 95% CI 1.17-6.25, p = 0.007). **Conclusions:** ALPPS resulted in significantly better long-term overall survival outcomes, at the expenses of a significantly higher perioperative morbidity rate compared with PVE in patients who had initially unresectable HCC. Clinical trial information: ChiCTR-IOC-14005646. Research Sponsor: Science Fund for Creative Research Groups, NSFC, China, (81521091).

4579 Poster Session (Board #187), Fri, 8:00 AM-11:00 AM

Primary tumor (p-bx) versus metastatic tumor (m-bx) tissue versus liquid biopsy (lb) in intrahepatic cholangiocarcinoma (IHCC): A comparative comprehensive genomic profiling (CGP) study. *First Author: Jeffrey S. Ross, Foundation Medicine, Cambridge, MA*

Background: Genomic alterations (GA) characteristic of IHCC are well known. We queried whether GA from Pbx would differ from Mbx and Lbx in IHCC. **Methods:** Hybrid-capture based CGP was performed on 1,268 tissue samples of advanced stage IHCC using Pbx in 1,048 cases and Mbx from 220 cases and 364 Lbx cases (solid tissue: 318-327 genes, Lbx: 72 genes). Tumor mutational burden (TMB) was determined on 0.8-1.1 Mbp of sequenced DNA. PD-L1 expression in tumor cells (Dako 22C3) was measured by IHC. **Results:** Mbx sites included: lymph nodes (63), soft tissues (47), peritoneum (34), lung/pleura (27), omentum (15), bone (10), abdomen (7), GYN tract (5), liver (4), brain (2), Upper GI (2), colon (2), bladder (1), and adrenal (1). The GA/sample and biomarkers of immuno-oncology (IO) drug response were similarThe *KRAS* mutation frequency including G12C alterations was doubled in Mbx compared to Pbx and Lbx ($p < 0.001$). Frequencies of untargetable GA were similar overall. *IDH1* ($p < 0.001$) and *FGFR2* GA known to be enriched in IHCC were less frequent in Mbx than Pbx. Both *IDH1* and *FGFR2* were identified in Lbx. GA in *STK11* ($p < 0.001$) and *SMAD4* (p = 0.0016) were more frequently identified in Mbx. **Conclusions:** GA found in Pbx vs Mbx and Lbx in IHCC are significantly different; the Mbx cohort features greater *KRAS* and lower *IDH1* and *FGFR2* GA. Lbx detected more IDH1 GA than Mbx. This suggests that the Mbx group may contain non-IHCC cases whose metastatic lesions were actually derived from other primary sites and incorrectly assigned the diagnosis of IHCC. Research Sponsor: Foundation Medicine Inc.

	Pbx	Mbx	Lbx
Cases	1,048	220	364
Males/Females	49%/51%	56%/44%	52%/48%
Median age (range)	65 (23-89+)	64 (29-89+)	66 (29-88)
GA/tumor	4.2	4.3	-
Top Currently Untargetable GA	*TP53* 32% *CDKN2A* 31% *CDKN2B* 23% *ARID1A* 19% *KRAS* 16% *MTAP* 16% *BAP1* 15% *TERT* 8% *SMAD4* 5% *MYC* 5%	*TP53* 35% *CDKN2A* 32% *CDKN2B* 24% *ARID1A* 16% *KRAS* 34% *MTAP* 16% *BAP1* 11% *TERT* 4% *SMAD4* 11% *MYC* 5%	*TP53* 40% *CDKN2A* (SV only) 4% *CDKN2B* (SV only) 1% *ARID1A* - *KRAS* 13% *MTAP* - *BAP1* - *TERT* 6% *SMAD4* - *MYC* 1%
Top Potentially Targetable GA	*IDH1* 16% *FGFR2* 11% *ERBB2* 8% *PIK3CA* 7% *BRAF* 6% *IDH2* 4% *KRAS* G12C < 1%	*IDH1* 6% *FGFR2* 8% *ERBB2* 6% *PIK3CA* 8% *BRAF* 4% *IDH2* 5% *KRAS* G12C 2%	*IDH1* 9% *FGFR2* 4% *ERBB2* 4% *PIK3CA* 7% *BRAF* 4% *IDH2* 3% *IDH2* 3% *KRAS G12C* 1%
IO Resistance GA	*PBRM1* 12% *STK11* 2% *MDM2* 4% *KEAP1* 1%	*PBRM1* 14% *STK11* 8% *MDM2* 7% *KEAP1* < 1%	*PBRM1* - *STK11* 3% *MDM2* 2% *KEAP1* -
MSI-High	< 1%	1%	0% (n = 224)
Median TMB	2.5	2.5	-
TMB > 10 mut/Mb	4%	4%	-
TMB > 20 mut/Mb	1%	1%	-
PD-L1 IHC Low Positive	15% (n = 345)	18% (n = 66)	-
PD-L1 IHC High Positive	5% (n = 345)	4% (n = 66)	-

4580 Poster Session (Board #188), Fri, 8:00 AM-11:00 AM

Adjuvant lenvatinib in combination with TACE for hepatocellular carcinoma patients with high risk of postoperative relapse (LANCE): Interim results from a muticenter prospective cohort study. *First Author: Jin-hong Chen, Department of General Surgery, Huashan Hospital, Cancer Metastasis Institute, Fudan University, Shanghai, China*

Background: Surgical resection was the main treatment for hepatocellular carcinoma (HCC) in China. Multiple clinical studies had demonstrated that the overall survival (OS) of the surgical resection group was significantly better than the transcatheter arterial chemoembolization (TACE) or radiotherapy group even for HCC patients with BCLC stage B or C. There was no standard adjuvant therapy for HCC patients to decrease the post-operative tumor relapse. For HCC patients with high recurrence risk, TACE significantly reduced tumor recurrence, prolonged the disease free survival (DFS) and OS, and was recommended as the adjuvant therapy. However, its effect is not very satisfactory. The purpose of this study was to assess the efficacy and safety of lenvatinib in combination with TACE versus TACE alone as adjuvant therapy in HCC patients with high recurrence risk after resection. **Methods:** This is a muti-center prospective cohort study. The criteria of HCC patients with high postoperative recurrence risk included: accompanied with gross vascular or bile duct invasion (tumor thrombi in portal vein, hepatic vein or bile duct); or tumor rupture or invasion of adjacent organs; or grade 2 of microvascular invasion (MVI) (M2) along with the tumor number more than 3 or the maximum diameter of tumor larger than 8cm or tumor showed invasive growth with unclear boundaries and imcomplete capsules. The patients were divided into two groups, the lenvatinb (8mg qd for weights < 60kg and 12mg qd for weights≥60kg) in combination with TACE (Len+TACE) group and the TACE group. **Results:** A total of 90 patients were enrolled into the study, while 45 patients in the Len+TACE group and 45 in TACE group. The media age was 52 years (range from 23 to 73 years). Most patients were males (82.2%) and 66 patients had HBV background (73.3%). There were no significant differences between the two groups in the baseline clinicopathological characteristics including gender, age, HBV background, liver cirrhosis, liver function, tumor characteristic and AFP level. The media DFS was 12.0 months (95% CI 8.0-NA) in the Len+ TACE group, which was longer than that of TACE group (8.0 months, 95% CI 6.0-12.0, P = 0.0359; HR 0.5, 95% CI 0.3-1.0). The most common grade 3 or 4 adverse events were hypertension (11.1%) and diarrhea (7.7%) in the Len+TACE group. **Conclusions:** Lenvatinib in combination with TACE was effective and safe as adjuvant therapy, which can prolong the DFS of HCC patients with high recurrence risk after resection. Clinical trial information: NCT03838796. Research Sponsor: China National Key Projects for Infectious Disease (No.2017ZX10203207).

4581 Poster Session (Board #189), Fri, 8:00 AM-11:00 AM

A multicenter nonrandomized controlled trial to evaluate the efficacy of surgery versus radiofrequency ablation for small hepatocellular carcinoma (SURF cohort trial). *First Author: Ryosuke Tateishi, Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan*

Background: In parallel with a multicenter randomized controlled trial that reported an equal recurrence-free survival (RFS) of early-stage hepatocellular carcinoma (HCC) patients who underwent either surgery (SUR) or radiofrequency ablation (RFA), we also enrolled HCC patients who fulfilled the enrollment criteria but did not give consent to participate in the RCT. **Methods:** All patients gave informed consent to participate in this study. Inclusion criteria were as follows: primary HCC with less than or equal to 3 tumors, each measuring 3 cm or smaller; without vascular invasion or extrahepatic metastasis; Child-Pugh score of 7 or less; and ages between 20 and 79 years. The feasibility for both treatments was confirmed by a joint chart review by surgeons and hepatologists. The primary endpoint was RFS and overall survival. A pre-specified interim analysis was performed to compare RFS. **Results:** Between April 2009 and August 2015, 740 patients (371 in SUR, 369 in RFA) were enrolled from 49 participating hospitals in Japan. The SUR group had significantly fewer patients with chronic hepatitis C (56.6% vs. 69.4%), higher median value of platelet count (145 vs. 120 $\times$ 10^9/L), and more patients with $>$ 2 cm tumors (49.9% vs. 27.9%); most patients had a single tumor (91.1% vs. 88.3%). During the median follow-up period of 5 years, tumor recurrence was observed in 192 of SUR and 218 of RFA with 3-year RFS being 66.0% and 61.7%, respectively (P = 0.091). In subgroup analysis, RFS was significantly better in SUR in patients with $\leq$ 2 cm tumors (62.9% vs. 51.7% in 3 years; hazard ratio [HR] 0.72, 95% confidence interval [CI] 0.56-0.93; P = 0.014), whereas the difference was not significant in those with $>$ 2 cm tumors (52.7% vs. 46.4%; HR 0.85, 95% CI 0.63-1.18; P = 0.34). The adjusted HR for RFS using inversed probability of treatment weighting was 0.89 (95% CI, 0.72-1.10; P = 0.287). **Conclusions:** The imbalance in patient characteristics reflected a real-world practice. Factors related to background liver disease rather than tumor characteristics might have a larger impact on the recurrence in early HCC. Clinical trial information: C000001796. Research Sponsor: Health Labour Sciences Research Grant from The Ministry of Health Labour and Welfare of Japan.

4582 Poster Session (Board #190), Fri, 8:00 AM-11:00 AM

A multicenter randomized phase II study of nivolumab in combination with gemcitabine/cisplatin or ipilimumab as first-line therapy for patients with advanced unresectable biliary tract cancer (BilT-01). *First Author: Vaibhav Sahai, University of Michigan, Ann Arbor, MI*

Background: Patients (pts) with advanced biliary tract cancers (BTC) have poor prognosis with a median overall survival (OS) less than 12 months (mos). This randomized phase 2, multi-institutional, study was designed to investigate the role of combinational immunotherapy, using nivolumab (nivo) with gemcitabine (gem)/cisplatin (cis), or nivo with ipilimumab (ipi) in pts with untreated advanced BTC. **Methods:** Key eligibility criteria include histologically confirmed unresectable or metastatic BTC without prior systemic therapy, measurable disease per RECISTv1.1, ECOG PS 0-1, and absence of autoimmune disease or chronic steroid use. Arm A included gem 1000 mg/m^2 and cis 25 mg/m^2 d1, 8 Q3w + nivo 360 mg d1 Q3w for 6 mos followed by nivo 240 mg Q2w monotherapy for a total duration of 2 yrs; Arm B included nivo 240 mg Q2w and ipi 1 mg/kg Q6w for 2 yrs, in absence of disease progression. Primary endpoint is progression-free survival (PFS) rate at 6 mos with an alternative hypothesis of 80% (null hypothesis of 59%, one-sided alpha 0.05, power 80%) for each non-comparative arm. Secondary endpoints include overall response rate (ORR) per immune related (ir) RECIST, median PFS and OS and safety. Exploratory objectives include biomarker analysis using include sequential whole exome/transcriptome and immune cell subsets in tissue and blood. **Results:** 71 eligible pts (49% male, 83% Caucasian) with 35 in Arm and 36 in Arm B with a median age of 62 (range 20-80) yrs, and majority with metastatic disease (90%) were enrolled across 6 US sites. PFS rate at 6 mos was 70% in Arm A and 18.6% in Arm B. The median PFS was 8.8 mos (95% CI, 6.1 to 11.3) in Arm A and 4.1 mos (95% CI, 2.4-5.2) in Arm B. Ten patients on Arm A and 2 on Arm B remain on active treatment; additional 7 are in follow-up for OS. ORR, safety data and median OS evaluation are underway and will be presented at the meeting. Exploratory analyses are pending. **Conclusions:** The observed PFS rates at 6 mos in either arm are insufficient to reject the null hypothesis of 59% PFS at 6 months. While Arm B is inferior, Arm A appears to be as effective as standard of care although OS estimates are pending maturity. Clinical trial information: NCT03101566. Research Sponsor: Bristol-Myer's Squibb, University of Michigan Rogel Cancer Center.

4583 Poster Session (Board #191), Fri, 8:00 AM-11:00 AM

Adjuvant concurrent chemoradiotherapy in extrahepatic cholangiocarcinoma. *First Author: Walid Labib Shaib, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: Resected cholangiocarcinomas are rare and have high relapse rates. Adjuvant chemotherapy is the standard of care (BiLCAP Trial). Adjuvant radiation therapy benefit is not well defined. This study aims to evaluate survival outcomes of the effect of adjuvant chemoradiotherapy compared to chemotherapy in extrahepatic cholangiocarcinoma (EHC) using the National Cancer Database (NCDB). **Methods:** Patients with resected EHC between 2004 and 2013 were identified from the NCDB using ICD-O-3 histology and topography codes: 8140, 8160, 8161, 8162 and C24.0. Patients with neoadjuvant therapy were excluded from this analysis. Univariate and multivariable analyses were conducted, and Kaplan-Meier Curves were used to compare overall survival (OS) based on treatment received. **Results:** A total of 236 EHC patients were identified. Males comprised 60.6% and 88.1% were Caucasian. Median age was 64 (range, 31-84) years. The majority were distal (72.0%, N = 157) followed by perihilar (20.6%, N = 45), hilar (6.4%, N = 14) and cystic (0.9%, N = 2). Distribution across stages I-III was 28.8% (N = 68), 56.8% (N = 134), and 14.4% (N = 34), consecutively. Adjuvant chemotherapy was given in 37.7% (N = 89) and adjuvant chemoradiotherapy in 62.3% (N = 147). The median dose of radiation was 50.4 Gy. Adjuvant chemoradiotherapy was mostly given in regional node positive disease (p = 0.016) and negative surgical margin (p = 0.002) compared to regional node negative disease and positive surgical margin, respectively. The use of adjuvant chemoradiotherapy was associated with improved OS compared to chemotherapy alone in univariate (HR 0.64; 95% CI 0.44-0.93; p = 0.019) and multivariable analysis (HR 0.65; 95% CI 0.44-0.96; p = 0.030). Median survival and 1 year-OS for patients that received chemoradiotherapy was 33.8 months (95% CI 28, NA) and 87.7% (80.9%, 92.1%) compared to chemotherapy alone which was 23.8 months (95% CI 18.9, 35.4) and 75.5% (64.9%, 83.3%). **Conclusions:** Adjuvant chemoradiotherapy was associated with improved survival in patients with resected EHC compared to chemotherapy alone. This conclusion warrants further prospective studies to confirm these results. Research Sponsor: None.

4584 Poster Session (Board #192), Fri, 8:00 AM-11:00 AM

Different organ-specific response to nivolumab to determine the survival outcome of patients with advanced hepatocellular carcinoma (aHCC). *First Author: Han Sang Kim, Yonsei Cancer Center, Seoul, South Korea*

Background: Previously, two phase III clinical trials of immune checkpoint inhibitors (ICI) failed to meet their primary endpoints, leading to doubts regarding the clinical activity of ICI monotherapy in patients with aHCC. Here, we comprehensively examined clinicopathological factors and estimated their association with survival outcomes in aHCC patients treated with nivolumab. **Methods:** A total of 261 eligible patients from 5 high-volume centers who were treated with nivolumab between June 9, 2012 and March 14, 2018 and had measurable diseases were reviewed. We reviewed more than 80 clinicopathological factors and categorized them into 6 areas: 1) demographics (n = 16); 2) baseline laboratory values (n = 19); 3) tumor burden (n = 12); 4) previous treatment (n = 12); 5) treatment response (n = 5); 6) toxicity profiles (n = 18). Their association with survival outcomes were evaluated, and organ-specific response evaluation, adapted from RECIST 1.1, was conducted. **Results:** Of the 261 patients, 218 (84%) had extrahepatic spread. The median follow-up time was 4.5 months. The median progression-free survival (PFS) and overall survival (OS) were 2.3 months (95% CI, 1.8-2.8) and 6.3 months (95% CI, 5.0-8.2). Objective response rate was 15%. Subgroup analyses revealed that compensated liver function (Child-Pugh score A5/6), surrogate markers for low tumor burden (low AFP, low PIVKA, and low LDH level), inflammatory markers (low C-reactive protein [CRP], low erythrocyte sedimentation rate [ESR], low neutrophil-to-lymphocyte ratio [NLR], high lymphocyte-to-monocyte ratio [LMR]), and low intrahepatic tumor burden were significantly associated with longer OS. A total of 456 individual lesions (liver, n = 249; lung, n = 124; lymph node, n = 35; others such as boner soft tissues, n = 48) were examined. Organ-specific response rates (hepatic tumor, 9%; lung, 25%; lymph node, 37%; others metastasis, 15%) were different, of which intrahepatic tumor was the least responsive organ to ICI treatment in aHCC. **Conclusions:** Underlying liver function, the tumor extent and burden, and the degree of plasma lymphocytes are crucial for determining tumor response to ICI in aHCC. Antitumor immune response to ICI differs in an organ-specific manner. The hepatic tumors of HCC may be less responsive to nivolumab than extrahepatic lesions. Research Sponsor: None.

4585 Poster Session (Board #193), Fri, 8:00 AM-11:00 AM

Clinical value of atezolizumab + bevacizumab for first-line unresectable hepatocellular carcinoma (HCC): A network meta-analysis. *First Author: Arndt Vogel, Hannover Medical School, Hannover, Germany*

Background: The IMbrave150 pivotal study in unresectable HCC showed superiority of atezolizumab + bevacizumab (atezo + bev) vs sorafenib for OS and PFS. Based on these data supporting first-line atezo + bev for HCC, we conducted a network meta-analysis (NMA) to compare the efficacy of atezo + bev with other systemic and local therapies approved for HCC. **Methods:** A systematic literature review identified randomized controlled trials in adults with locally advanced or metastatic HCC and no prior systemic therapy for HCC. Studies of therapies now approved for any line of HCC treatment with data reported for first-line treatment since sorafenib approval in 2007 were eligible. Screening of 8783 records yielded 55 trials for inclusion; 9 studies were eligible for the evidence network. Reported hazard ratios (HRs) for OS and PFS were extracted from published studies. The IMbrave150, REFLECT and CheckMate-459 study populations were considered sufficiently similar to compare. A generalized linear model with random effects was used to estimate indirect treatment effects. Informative priors for the heterogeneity of treatment effects across trials were adopted given the limited number of trials to inform each pairwise comparison. HRs with 95% credible intervals (CrIs) and Bayesian posterior probability of atezo + bev being superior to other treatments were calculated for each treatment comparison. The base case NMA compared the relative efficacy of atezo + bev vs sorafenib observed in the IMbrave150 study with the relative effect of other therapies. Sensitivity analyses were performed to compare subgroup results as appropriate based on disease etiology, extrahepatic spread and geography. **Results:** NMA results suggested improved OS with atezo + bev vs lenvatinib (HR, 0.63; 95% CrI: 0.32, 1.25; probability of atezo + bev being superior to lenvatinib: 93.7%) or nivolumab (HR, 0.68; 95% CrI: 0.35, 1.38; probability of atezo + bev being superior to nivolumab: 90.3%) and improved PFS with atezo + bev vs lenvatinib (HR, 0.91; 95% CrI: 0.23, 3.65; probability of atezo + bev being superior to lenvatinib: 61.5%) or nivolumab (HR, 0.63; 95% CrI: 0.16, 2.59; probability of atezo + bev being superior to nivolumab: 85.5%). **Conclusions:** This NMA suggested greater OS and PFS benefits with first-line atezo + bev treatment vs other therapies approved for treatment of unresectable HCC. Research Sponsor: F. Hoffmann-La Roche, Ltd.

4586 Poster Session (Board #194), Fri, 8:00 AM-11:00 AM

A randomized phase II feasibility study of individualized stereotactic body radiation therapy (SBRT) versus transarterial chemoembolization (TACE) with DEBDOX beads as a bridge to transplant in hepatocellular carcinoma (HCC). *First Author: Francis W. Nugent, Beth Isreal/Lahey Health, Burlington, MA*

Background: For HCC pts undergoing LT, loco-regional treatment as a "bridge" is standard. The best bridging modality is unclear. SBRT is safe and effective when used in pts with advanced HCC. We prospectively compared SBRT to TACE as a bridge for HCC pts undergoing LT. **Methods:** From 9/2014-10/2019, 60 pts within Milan Criteria with CTP Class A/B8 cirrhosis were consented. 54 pts were randomized to TACE vs. SBRT. TACE pts (n =30) were scheduled to receive 2 treatments one month apart utilizing DEBDOX beads. TACE pts were hospitalized after each TACE. Pts receiving SBRT (n =24) received a median total dose of 45Gy delivered over 5 fractions using fiducials. Mean liver dose, Veff, and NTCP determined prescription dose. Pts were assessed by using mRECIST criteria at 2 months and every 3 months thereafter until LT or death. Toxicity and QOL were assessed before treatment, during treatment, two weeks post-treatment, and then every three months using the PIQ-6 Pain Impact Questionnaire and the SF-36v2 Health Survey. The 1° endpoint was time to recurrent or residual dz. Secondary endpoints were toxicity, pathologic response, radiologic response, number of subsequent treatments, cost, and QOL. 50 pts are evaluable for review. **Results:** See table. **Conclusions:** For early stage HCC patients with CTP Class A/B liver cirrhosis, SBRT appears as effective as TACE at controlling HCC prior to LT, may engender less toxicity, and eliminates the need for hospitalization. A larger multi-center trial is ongoing. Clinical trial information: NCT02182687. Research Sponsor: Wise Grant, Pharmaceutical/Biotech Company.

Demographics	SBRT (n=21)	TACE (n=29)
Med. CTP score	6.0	6.0
Stage I HCC	81.0%	86.2%
Med. Time to 1° endpoint (mos)	10.4 (95%CI: 4.2 to 12.0)	9.2 (95%CI: 5.3 to 11.0)
QOL	SBRT (n=14)	TACE (n=26)
ΔPain sum score	0.7+/-4.5	3.9+/-7.4
ΔWML score	0.4+/-5.8	4.1+/-8.2
SF36v2:		
ΔPCS	-3.7+/-5.2	-2.0=/-4.8
ΔMCS	3.3+/-5.7	-1.5+/-4.9

4587 Poster Session (Board #195), Fri, 8:00 AM-11:00 AM

Effect of pembrolizumab (pembro) on hepatitis B viral (HBV) load and aminotransferase (ALT) levels in patients (pts) with advanced hepatocellular carcinoma (aHCC) in KEYNOTE-224 and KEYNOTE-240. *First Author: Stephen Lam Chan, The Chinese University of Hong Kong, Hong Kong, China*

Background: The effect of PD-1 inhibition on HBV infection is unclear, and pts with HBV are often excluded from trials. This analysis evaluated HBV viral load and liver function (ALT levels) in pts with HBV infection in 2 trials of pembro: KEYNOTE-224 and KEYNOTE-240. **Methods:** Eligible pts with aHCC post first-line sorafenib and controlled HBV received pembro 200 mg IV Q3W until progression. Pts with active HBV (HBsAg positive and/or HBV DNA detectable) and inactive HBV (anti-HBc positive, HBsAg negative, and HBV DNA not detectable) at baseline (BL) were included. **Results:** Of 104 pts in KEYNOTE-224 and 413 pts in KEYNOTE-240, 8 (7.7%) and 101 (24.5%) had active HBV and 13 (12.5%) and 102 (24.7%) had inactive HBV, respectively. All pts with HBV received nucleos(t)ide analogs. In KEYNOTE-240, 2 (2.8%) pts with active HBV in the pembro arm and 1 (3.4%) in placebo (pbo) had a > 1 log increase (incr) of HBV DNA and 1000 IU/mL over BL; none in the pembro arm were associated with ALT elevation. No pts with inactive HBV in KEYNOTE-240 and no pts in KEYNOTE-224 had a > 1 log incr and 1000 IU/mL over BL. No pts in KEYNOTE-224 and 28 (38.9%) with active HBV and 1 (1.4%) with inactive HBV in the pembro arm, and 8 (27.6%) with active HBV and 0 with inactive HBV in the pbo arm in KEYNOTE-240 had a > 1 log decrease (decr) in HBV DNA. **Conclusions:** Few pts with aHCC and HBV had viral load incr with pembro. In KEYNOTE-240 no clinically meaningful differences between pembro and pbo were observed. ALT elevation was not associated with viral load incr with pembro. These data suggest that pembro is unlikely to significantly affect underlying HBV infection in pts with aHCC receiving HBV antiviral therapy. Clinical trial information: KEYNOTE-224, NCT02702414; KEYNOTE-240, NCT02702401. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Pts with HBV, n (%)	Active HBV KEYNOTE-224 Cohort 1 Pembro (n = 8)	Active HBV KEYNOTE-240 Pembro (n = 72)	Active HBV KEYNOTE-240 Pbo (n = 29)	Inactive HBV KEYNOTE-224 Cohort 1 Pembro (n = 13)	Inactive HBV KEYNOTE-240 Pembro (n = 73)	Inactive HBV KEYNOTE-240 Pbo (n = 29)
> 1 log decr	0	28 (38.9)	8 (27.6)	0	1 (1.4)	0
> 1 log incr + 1000 IU/mL	0	2 (2.8)	1 (3.4)	0	0	0
> 2 log incr	0	3 (4.2)	1 (3.4)	0	1 (1.4)	0
> 3 log incr	0	0	1 (3.4)	0	0	0
ALT ≥3×BL + > 100 U/L post-BL	1 (12.5)	6 (8.3)	3 (10.3)	1 (7.7)	15 (20.6)	2 (6.9)
ALT and AST to > 5×ULN and/or > 3×BL	1 (12.5)	6 (8.3)	3 (10.3)	0	12 (16.4)	5 (17.2)
> 1 log incr + 1000 IU/mL + ALT elevation[a]	0	0	1 (3.4)	0	0	0
2 log incr + ALT ≥3×BL + > 100 U/L post-BL	0	0	1 (3.4)	0	0	0

[a]ALT elevation: met 1 of 3 criteria ± 7 days of time of viral flare:
1) BL ALT < 2×ULN and post-BL ALT ≥5×ULN
2) BL ALT ≥2×ULN and post-BL ALT > 3×BL level
3) ALT > 500 U/L regardless of BL level

4588 Poster Session (Board #196), Fri, 8:00 AM-11:00 AM

Combination immunotherapy with ipilimumab and nivolumab in patients with advanced biliary tract cancers. *First Author: Oliver Klein, Medical Oncology Unit, Austin Health, Heidelberg, Australia*

Background: Patients (pts) with advanced biliary tract cancers (BTC) have a poor prognosis with first and second line chemotherapy resulting in modest survival benefits. Immunotherapy using single agent anti-PD-1 therapy has also shown low activity with an objective response rate (ORR) of less than 10%. Combined CTLA-4/PD-1 blockade using ipilimumab (ipi) and nivolumab (nivo) has demonstrated superior efficacy compared to single agent anti-PD-1 therapy in pts with advanced melanoma and renal cell carcinoma. To date, no trials in BTC pts with ipi/nivo therapy have been reported. **Methods:** 39 pts with metastatic BTCs were enrolled into the CA 209-538 clinical trial for rare cancers. Patients received nivo 3mg/kg and ipi 1mg/kg q 3 weekly for 4 doses, followed by nivo 3mg/kg q 2 weekly. Treatment continued for up to 96 weeks, or until disease progression or the development of unacceptable toxicity. Response (RECIST 1.1) was assessed every 12 weeks. The primary endpoint was clinical benefit rate (CBR = CR +PR + SD). Exploratory endpoints include correlation of efficacy with biomarkers including PD-L1 expression and tumour mutation burden. **Results:** 39 pts with BTC were enrolled and 33 pts (85%) had received at least one prior line of systemic treatment (0-2 lines). The ORR was 24% and the CBR 45% with the median duration of response not been reached (range 2-26+months). Responses were observed in 3/14 intrahepatic, 1/10 extrahepatic, 0/2 unspecified cholangiocarcinoma and 5/13 gallbladder ca pts. None of the responding pts had a microsatellite instable tumour. 2 pts with durable partial responses were subsequently rendered surgically free of disease. Median OS and PFS were 6.1 and 3.1 months respectively. 22 (56%) pts experienced an immune –related adverse event (irAE) with grade3/4 irAEs being observed in 8 (20%) pts. **Conclusions:** Combination immunotherapy with ipi/nivo demonstrates significant clinical activity in a subset of patients with advanced microsatellite stable BTC. The response rate compares favourably to clinical trials investigating single agent anti-PD-1 therapy. Clinical trial information: NCT02923934. Research Sponsor: Australian Federal Department of Health.

4589 Poster Session (Board #197), Fri, 8:00 AM-11:00 AM

Genomics and translational precision oncology for 803 patients with biliary tract cancer. *First Author: Jianzhen Lin, Peking Union Medical College Hospital and Chinese Academy of Medical Sciences, Beijing, China*

Background: Both incidence and mortality of biliary tract cancer (BTC) are increasing, and BTCs are characterized by poor prognosis and limited antitumoral treatments. There is no well-received regimen as the non-first-line treatment in patients with advanced BTCs, leading to the urgency of umbrella-setting personalized therapies according to genomic alterations. **Methods:** We performed genomic sequencing in a total of 803 BTCs, including 160 patients with whole-exome sequencing and 643 patients with hybrid capture–based comprehensive genomic profiling. Our molecular tumor board developed precise targeted therapies for patients with actionable targets. **Results:** Overall, the median tumor mutation burden was 3.0 (IQR: 0.8-6.1) Mut/Mb, with 10.5% patients of hypermutated BTCs. The most frequently mutated genes included *TP53* (51%), *KRAS* (23%), *ARID1A* (16%) and *SMAD4* (11%). The most common genes with significantly amplified oncogenes were *CCND1* (6.97%), *MET* (6.72%) and *MDM2* (6.6%), while the frequently deleted tumor-suppressor genes are *CDKN2A* (5.73%) and *CDKN2B* (5.35%). The mutational map of BTCs highlighted pathways of receptor-tyrosine kinase (RTK)/RAS and *p53* signaling were frequently altered. Somatic truncating mutations of mismatch repair genes were identified in 6.1% (49/803) of patients, and germline pathogenic mutations in DNA damage response genes occurred in 8% (64/803) of BTCs. In addition, we demonstrate the amplified chromosomal focal at 7q31.2 was an oncogenic factor and it independently predicts both disease-free survival and overall survival of BTC patients. When molecular screening was linked to targeted therapies, 25.4% (204/803) of patients could match biomarker-assigned drug treatment (BADT). The frequent actionable biomarkers included amplifications of *ERBB2* and *MET*, *FGFR2/3* fusions and *IDH1* mutations. For 46 patients with refractory BTCs received BADT, the objective response rate was 26.1%, with a median progression-free survival (mPFS) of 5.0 (95%CI: 3.5-6.5) months, and 56.8% patients achieved a $\geq$1.3 ratio of PFS2/PFS1. 4 of 6 (67%) patients with high microsatellite instability (MSI-H) BTCs had a responsive status after immunotherapy of PD1 inhibitor, confirming that MSI-H status was a robust biomarker of anti-PD1 treatments. **Conclusions:** Our study established the largest cohort in Chinese BTC patients to investigate the tumor mutational profiling and its translational clinical applications. Clinical trial information: NCT02715089. Research Sponsor: International Science and Technology Cooperation Projects.

4590 Poster Session (Board #198), Fri, 8:00 AM-11:00 AM

A phase II open-label, single-center, nonrandomized trial of Y90-radioembolization in combination with nivolumab in Asian patients with advanced hepatocellular carcinoma: CA 209-678. *First Author: Wai Meng David Tai, National Cancer Center Singapore, Singapore, Singapore*

Background: Nivolumab (N) and Y90-radioembolization (RE) are both therapeutic options in advanced hepatocellular carcinoma (aHCC). Increasing evidence suggests that radiotherapy synergizes with immune checkpoint inhibitors to augment anti-tumour effects. **Methods:** Eligible Child-Pugh A aHCC patients (pts) were treated with Y90-RE followed by N 240mg, 21 days after Y90-RE and every 2 weeks thereafter. Pre- and on-treatment tumor biopsies together with circulating biomarkers were obtained. Primary end-point was overall response rate (ORR) (per RECIST v 1.1). Overall response was defined as the composite overall response observed for the lesions within Y90-RE field and outside Y90-RE field. Key secondary end points included disease control rate (DCR), progression free survival (PFS), overall survival (OS), and safety. 36 evaluable pts were needed to assess whether the addition of N improved the ORR of Y90-RE from 21% to 41% as determined by Simon two-stage optimal design with 80% power and one sided significance level of 0.05. **Results:** Forty pts were enrolled of which 36 were evaluable. At baseline: 63.9% were HepB in aetiology; 63.9% BCLC stage C; 47.2% had AFP $>$ 400ng/mL; number of liver lesions – median 5 (range 1- 20); size of largest liver lesion – median 80mm (range 14-177mm); 27.8% had prior TACE; and 13.9% had prior systemic therapy. ORR was 31% (95% CI 16.4 - 48.1%). Eight out of 11 responders had not progressed at study cut-off. DCR was 58.3%. 81% of target lesions within Y90-RE field regressed. With a median follow up of 16.4 months, median PFS and OS were 4.6 months (95% CI 2.3m - 8.4m) and 15.1 months (95% CI 7.8m - NE) respectively. Six- and 12-month PFS rates were 44.2% (95% CI 27.3% - 59.9%) and 26.1% (95% CI 11.2% - 43.8%) respectively. Overall, N+ Y90-RE was well tolerated and safe; only 11% had grade 3/4 treatment related adverse events (AEs). Responders demonstrated significant alterations of LIF, MIG and Eotaxin3 levels in the pre-treatment cytokine analyses. **Conclusions:** Combination N+Y90-RE resulted in an encouraging ORR of 31% (95% CI 16.4 - 48.1%) in aHCC. 81% of target lesions within Y90-RE field regressed suggesting synergy in combining Y90-RE with nivolumab. This combination is safe and tolerable with low G3/4 treatment related AEs of 11%. Further biomarker analyses will be presented at the meeting. Clinical trial information: NCT03033446. Research Sponsor: National Medical Research Council Singapore, BMS, SIRTEX.

4591 Poster Session (Board #199), Fri, 8:00 AM-11:00 AM

A retrospective analysis of post second-line chemotherapy treatment outcomes for patients with advanced or metastatic cholangiocarcinoma and FGFR2 fusions. *First Author: Milind M. Javle, MD Anderson Cancer Center, Houston, TX*

Background: Cholangiocarcinoma (CCA) is the most common biliary tract malignancy with an estimated incidence of 8,000–10,000 patients/year in the US. Chemotherapy is the most common second-line treatment with reported outcomes in patients with CCA. Response rates of $<$ 10% and median progression-free survival (PFS) times of ~3–4 months have been reported with second-line chemotherapy regimens, including FOLFOX in the ABC-06 trial. Fibroblast growth factor receptor 2 (*FGFR2*) fusions occur in 13–17% of CCA and multiple targeted agents are in development for patients with *FGFR2* fusions. To date, the outcome of patients with CCA and *FGFR2* fusions receiving standard second-line chemotherapy is unknown. **Methods:** Patients with advanced CCA and *FGFR2* fusions after prior treatment with gemcitabine-based chemotherapy were enrolled in a single-arm phase 2 study (NCT02150967) and received the FGFR1–3 selective TKI infigratinib (previously BGJ398) 125 mg orally qd on d1–21, cycles repeated q28 days until unacceptable toxicity, disease progression, investigator discretion, or withdrawal of consent. A retrospective analysis of a subset of patients who received infigratinib as third- or later-line treatment was performed. Investigator-assessed PFS and best overall response (BOR, per RECIST 1.1) following second-line chemotherapy (pre-infigratinib) and third-line or later-line infigratinib were calculated. **Results:** Of the 71 patients (44 women; median age 53 years) with *FGFR2* fusions enrolled at the time of analysis (datacut 8 August 2018), 37 (52%) were included in this retrospective analysis. Median PFS with standard second-line chemotherapy was 4.63 months (95% CI 2.69–7.16) compared with 6.77 months (95% CI 3.94–7.79) for third- and later-line infigratinib. BOR for second-line chemotherapy was 5.4% (95% CI 0.7–18.2) compared with 21.6% for third- and later-line infigratinib (95% CI 9.8–38.2). **Conclusions:** Outcomes from second-line chemotherapy in patients with CCA and *FGFR2* fusions were similar to those reported in the literature for all patients with CCA regardless of genomic status and remain dismal. Infigratinib administered as third- and later-line treatment resulted in a meaningful PFS and ORR benefit in patients with CCA and *FGFR2* fusions. Clinical trial information: NCT02150967. Research Sponsor: QED Therapeutics.

4592 Poster Session (Board #200), Fri, 8:00 AM-11:00 AM

Clinical activity and safety of penpulimab (Anti-PD-1) with anlotinib as first-line therapy for advanced hepatocellular carcinoma (HCC). *First Author: Shun Chang Jiao, Department of Oncology, The First Medical Center of Chinese PLA General Hospital, Beijing, China*

Background: Advanced HCC is a deadly disease with few systemic therapeutic options. VEGF blockade potentiates the effect of PD-1 inhibition by opposing the immunosuppressive effects of VEGF-A (increased DC maturation, enhanced T-cell infiltration, reduced MDSCs and Tregs in tumors). A sBLA has been submitted for an anti-PD-L1 + anti-VEGF combination as 1L treatment for advanced HCC. Penpulimab is a novel humanized anti-PD-1 IgG1 antibody with complete removal of Fc receptor mediated effect, and featuring slow antigen binding off-rate and high receptor occupancy. Anlotinib is a multi-targeted tyrosine kinase inhibitor selective for VEGF receptors 1/2/3, FGF receptors 1-4, PDGF receptors α and β, and c-kit. **Methods:** In this open-label, multicenter phase Ib/II study, treatment-naive pts with advanced HCC received penpulimab 200mg Q3W in combination with anlotinib 8mg QD (2 weeks on 1 week off) until loss of clinical benefit or unacceptable toxicity. The primary objectives were to assess antitumor activity by ORR (RECIST v1.1). The secondary objectives were to assess antitumor activity by DCR, DoR, TTP, and to assess the safety and tolerability of the combination. **Results:** As of Jan 14, 2020, 31 pts (median age 56 years [23-74], male 81%, ECOG 0/1 [64%/36%], BCLC B/C [23%/77%], HBV/HCV [61%/7%]) received combined therapy (a median of 6 [1-15] doses). Treatment-related adverse events (TRAEs) occurred in 93.5% of pts (G3 in 9.7% [3/31], no G4, and leading to treatment discontinuation in 6.5% [2/31]). Most frequent TRAEs were increased AST (35.5%), increased ALT (29%), asthenia (22.6%), decreased platelet count (19.4%), increased blood bilirubin (19.4%), increased bilirubin conjugated (19.4%), and rash (16.1%). Of 25 evaluable pts (with the opportunity to be followed-up for $\geq$2 scans, 12 weeks), confirmed ORR was 24% (6/25) and DCR was 84% (21/25). Five responders remained in response with DoR ranging 1.4+ to 6.9+ months. Median TTP was not reached and 6m-TTP rate was 63% (95% CI: 38%, 81%). **Conclusions:** Penpulimab in combination with anlotinib had a manageable safety profile and encouraging antitumor activities in patients with advanced HCC. No unexpected AEs were identified beyond the established safety profile for each agent. Evaluation of penpulimab + anlotinib (10 mg QD) in a phase 3 study for 1L HCC is currently underway. Clinical trial information: NCT04172571. Research Sponsor: Akeso Biopharma, Inc., Zhongshan, China.

4593 Poster Session (Board #201), Fri, 8:00 AM-11:00 AM

Perioperative circulating tumor DNA analysis to predict patient prognosis in liver cancer. *First Author: Ledu Zhou, Department of General Surgery, Xiangya Hospital, Central South University, Changsha 410008, China., Changsha, China*

Background: Resection is a major method for early-stage liver cancer patients. Unfortunately, there still a few patients with post-operation recurrences. Circulating tumor DNA (ctDNA) had been reported as a biomarker in reflecting tumor load and treatment efficacy in some cancer species. Here, we report an application of ctDNA in the perioperative period of liver cancer using targeted sequencing with a 1021-gene panel. **Methods:** 97 patients diagnosed with liver cancer were enrolled in this study. Postoperative peripheral blood samples were collected within 7 days after surgery and analyzed using hybridization capture based NGS ERSeq method from all patients. Whether a mutant gene was detected in the peripheral blood was defined as ctDNA(+) and ctDNA(-), respectively. **Results:** Multivariate Cox analysis showed that the post-operation ctDNA was an independent poor prognostic predictor (AFP, RR: 1.0002, 95% CI: 1.0001-1.0002; ctDNA, RR: 3.738, CI: 1.872-7.691). 21 patients were ctDNA(+), and all of them had recurrenced (21/21, 100%), while 76 patients were ctDNA(-), and only 12 (12/76, 15.8%) patients had recurrenced. The median disease-free survival time was 5.0 months in ctDNA(+) group and the ctDNA(-) group had not reach the median time (Log-rank test, $P < 0.0001$). ctDNA combined with AFP would effectively predict the prognosis of patients after surgery. AFP(H) (> = 400 ng/mL) and ctDNA(+) patients have the worst prognosis and all of the patients had relapsed, while AFP(L) (< 400 ng/mL) and ctDNA(-) patients had the best prognosis, with less than 20% of patients had relapsed (Log-rank test, $P < 0.0001$). The median disease-free survival time was 2.0, 6.0 and 7.0 months in ctDNA(+)-AFP(H) (n = 8), ctDNA(-)-AFP(H) (n = 30) and ctDNA(+)-AFP(L) (n = 13) groups, respectively, while ctDNA(-)-AFP(L) group (n = 46) had not reach the median time statistically (Log-rank test, $P = 0.0364$). **Conclusions:** In summary, Perioperative ctDNA detection has great potential value clinically, and it also suggests that patients with positive ctDNA after surgery should receive some adjuvant treatments as soon as possible to improve the survival time. Research Sponsor: National Nature Science Foundation of China.

4594 Poster Session (Board #202), Fri, 8:00 AM-11:00 AM

Predictive value of changes in plasma vascular endothelial growth factor at eight weeks after lenvatinib administration in patients with unresectable hepatocellular carcinoma. *First Author: Kaoru Tsuchiya, Department of Gastroenterology and Hepatology, Musashino Red Cross Hospital, Tokyo, Japan*

Background: Lenvatinib (LEN) has been used in patients with unresectable hepatocellular carcinoma (u-HCC) and there is no established predictive biomarker. Previously it was reported that a plasma vascular endothelial growth factor (VEGF) concentration decrease at 8 weeks after starting sorafenib might predict favorable overall survival (OS) in patients with u-HCC (Tsuchiya, et al. Cancer, 2013). We aimed to investigate the value of changes in plasma VEGF at 8 weeks after LEN administration in patients with u-HCC. **Methods:** Forty-six patients with u-HCC who received LEN between April 2018 and August 2019 at our institution were enrolled. Plasma concentrations of VEGF and serum α-fetoprotein (AFP) levels were measured at baseline, 4 and 8 weeks after administration of LEN. A VEGF decrease was defined as > 5% decrease during 8 weeks after the beginning of LEN therapy. AFP response was defined as > 20% decrease during 8 weeks according to the previous reports. **Results:** Median overall survival (OS) was not reached and progression-free survival (PFS) was 5.9 months. Median observation period and treatment duration were 10.1 and 6.3 months. The objective response rate and disease control rate by mRECIST criteria were 43.5% and 82.6%. Median PFS in patients who had a VEGF decrease at week 8 (n = 29) was significantly longer than those who did not have a VEGF decrease (n = 17; 7.1 months vs 5.0 months; p = 0.014). AFP response was not associated with PFS. There were no significant differences in baseline VEGF, AFP, ALBI score, and extrahepatic metastasis between the patients with and without a VEGF decrease. A VEGF decrease was significantly associated with radiological objective response (p = 0.001) and 18 of 20 patients who achieved CR (n = 3) or PR (n = 17) had a VEGF response in LEN therapy. **Conclusions:** A decrease of plasma VEGF level at 8 weeks in patients with u-HCC on LEN was significantly associated with PFS. Changes in plasma VEGF could become a new biomarker for molecular targeted therapies including VEGF inhibitors in patients with unresectable HCC. Research Sponsor: Japan Agency for Medical Research and Development.

4595 Poster Session (Board #203), Fri, 8:00 AM-11:00 AM

Comparison of response using mRECIST versus RECIST 1.1 Criteria in advanced hepatocellular carcinoma: A retrospective analysis of multicenter clinical trials. *First Author: Jayant Narang, Parexel Informatics Inc, Rochester, NY*

Background: mRECIST 2010 criteria for Hepatocellular Carcinoma (HCC) response assessment were focused on a concept of measuring viable tumor tissue showing enhancement in arterial phase of contrast enhanced CT/MRI, whereas RECIST 1.1 focuses mainly on the morphological measurements quantifying the tumor size irrespective of viability of the tumor and associated response to therapy. RECIST 1.1 does not address measures of antitumor activity other than tumor shrinkage, underestimating responses in HCC. **Methods:** We retrospectively analyzed multiple, phase III, multi-center clinical trials using both mRECIST and RECIST 1.1 criteria, read separately. The intent was to compare the overall responses at post-baseline assessments read independently by the two criteria. A total of 1682 subjects with 6159 post-baseline imaging timepoints were included in the analysis. The Overall response rate (ORR) as measured by sum of complete response (CR) and partial response(PR) and the Complete response rate (CRR) were evaluated. In addition, we also assessed the number of not evaluable (NE) time points by each criteria separately. We tested the following hypotheses 1. mRECIST may have better ORR and CRR compared to RECIST 1.1. 2. RECIST 1.1 may have more timepoints with Stable disease (SD) compared to mRECIST. 3. mRECIST may have more Not evaluable (NE) timepoints due to stringent imaging specifications. **Results:** The results are tabulated in the table below: **Conclusions:** The results above suggest that mRECIST shows more than double the CRR than RECIST 1.1, and the ORR is 62% higher using mRECIST than RECIST 1.1. Stable disease as expected was more commonly observed in RECIST 1.1 analysis. A NE response was 60% more common in mRECIST criteria evaluation. Our analysis confirms that reduction in viable tumor/enhancing area using contrast-enhanced radiologic imaging is the more optimal method to assess treatment response in HCC, and using RECIST 1.1 tumor measurement of a longest diameter as the sole measure of response, may not be adequate in response assessment for HCC. Our analysis validates and supports more widespread adoption of mRECIST in HCC tumor response assessment. Our results also indicate the need for uniform image acquisition and rigorous image quality control for a valid response in mRECIST criteria. Research Sponsor: None.

mRECIST versus RECIST 1.1 Overall Response.

	mRECIST	RECIST 1.1
CR	111	46
PR	1497	966
SD/NN (Stable Disease/Non-CR Non-PD)	1994	2661
PD (Progressive Disease)	2509	2457
NE	48	29
ORR	26.10%	16.41%
CRR	1.8%	0.7%

4596 Poster Session (Board #204), Fri, 8:00 AM-11:00 AM

Complete responses (CR) in patients receiving atezolizumab (atezo) + bevacizumab (bev) versus sorafenib (sor) in IMbrave150: A phase III clinical trial for unresectable hepatocellular carcinoma (HCC). *First Author: Richard S. Finn, Jonsson Comprehensive Cancer Center, Geffen School of Medicine at UCLA, Los Angeles, CA*

Background: In the Phase III IMbrave150 trial, statistically significant and clinically meaningful improvements in OS and PFS were seen with atezo + bev vs sor in pts with unresectable HCC who had not received prior systemic therapy (Cheng, ESMO Asia, 2019). Historically, CR rates have been low in HCC clinical trials. Here we report the baseline characteristics for IMbrave150 pts with a CR. **Methods:** IMbrave150 enrolled systemic treatment-naive pts with unresectable HCC. Pts were randomized 2:1 to receive either atezo 1200 mg IV q3w + bev 15 mg/kg IV q3w or sor 400 mg BID until unacceptable toxicity or loss of clinical benefit per investigator. Co-primary endpoints were OS and PFS by independent review facility (IRF)–assessed RECIST 1.1. The key secondary endpoints IRF ORR per RECIST 1.1 and IRF ORR per HCC mRECIST were also part of the study statistical testing hierarchy. **Results:** The ITT population included 336 pts randomized to atezo + bev and 165 pts randomized to sor. With a median follow-up of 8.6 mo (data cutoff, Aug 29, 2019), OS HR was 0.58 (95% CI: 0.42, 0.79; $P = 0.0006$) and PFS HR was 0.59 (95% CI: 0.47, 0.76; $P < 0.0001$) with atezo + bev vs sor. ORR was 27% vs 12% ($P < 0.0001$) per IRF RECIST 1.1 and 33% vs 13% ($P < 0.0001$) per IRF HCC mRECIST with atezo + bev vs sor, respectively. For responders (per IRF RECIST 1.1), median time to response was 2.8 mo (range, 1.2-11.3) with atezo + bev and 3.3 mo (range, 1.2-7.2) with sor. CR per IRF-assessed RECIST 1.1 was achieved by 18 pts in the atezo + bev arm and 0 pts in the sor arm. The baseline characteristics for atezo + bev CR pts are shown in the table. Additional characteristics will be shown. **Conclusions:** IMbrave150 demonstrated statistically significant and clinically meaningful improvement in both OS and PFS with atezo + bev vs sor in pts with unresectable HCC who have not received prior systemic therapy. Pts achieved CRs regardless of poor prognostic factors or etiology. Atezo + bev may be a practice-changing treatment for pts with unresectable HCC. Clinical trial information: NCT03434379. Research Sponsor: F. Hoffmann-La Roche, Ltd.

n (%)	CR pts; atezo + bev (n = 18)	All pts; atezo + bev (n = 336)
≥ 65 y	7 (39)	161 (48)
Asia excluding Japan | Rest of world	8 (44) | 10 (56)	133 (40) | 203 (60)
ECOG PS 1	5 (28)	127 (38)
Etiology, HBV | HCV | non-viral	9 (50) | 5 (28) | 4 (22)	164 (49) | 72 (21) | 100 (30)
Child-Pugh class, A5 | A6	12 (67) | 6 (33)	239 (72) | 94 (28) (n = 334)
BCLC stage, A | B | C	1 (6) | 4 (22) | 13 (72)	8 (2) | 52 (16) | 276 (82)
MVI | EHS | MVI and/or EHS	6 (33) | 10 (56) | 12 (67)	129 (38) | 212 (63) | 258 (77)
AFP ≥ 400 ng/mL	3 (17)	126 (38)
Prior local therapy	12 (67)	161 (48)

4597 Poster Session (Board #205), Fri, 8:00 AM-11:00 AM

Results from TreeTopp: A randomized phase II study of the efficacy and safety of varlitinib plus capecitabine versus placebo in second-line (2L) advanced or metastatic biliary tract cancer (BTC). *First Author: Milind M. Javle, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Patients with advanced or metastatic BTC who progress on first-line (1L) gemcitabine-based doublet chemotherapy have few 2L treatment options. Varlitinib is a reversible small molecule pan human epidermal growth factor receptor (HER) inhibitor with low nanomolar potency against HER1 (EGFR), HER2 and HER4 with promising early results in advanced BTC. **Methods:** TreeTopp (NCT03093870) was a global, multicenter, double blind phase 2 study in which patients with advanced BTC who progressed after 1L therapy that included ≥6 doses of gemcitabine, with radiographically measurable disease based on RECIST v1.1, ECOG PS 0 or 1 and albumin ≥3 g/dL were randomized (1:1) to varlitinib (300 mg BID) plus capecitabine (1000 mg/m^2 BID 14 days on/ 7 off)(V+C) or placebo plus capecitabine (P+C). The dual primary endpoints were Objective Response Rate (ORR) and Progression Free Survival (PFS) defined as the time from randomization to radiological progression assessed by Independent Central Review. Secondary end points included Overall Survival (OS). **Results:** Overall, 127 patients were randomized (V+C, n = 64; P+C, n = 63) from May−Dec 2018 and demographics/baseline characteristics were generally well balanced, although the V+C arm had a lower proportion of females vs. P+C (31% vs. 48%). The odds ratio for ORR was numerically higher with V+C vs. P+C was 2.278 (9.4% vs. 4.8%, p = 0.42), the HR for PFS for V+C vs. P+C was 0.90 (median PFS, 2.8 vs. 2.8 months; p = 0.63), and the HR for OS for P+C vs. V+C was 1.11 (median OS, 7.8 vs. 7.5 months; p = 0.66). Although not powered to evaluate sub-group interactions, in sub-group analysis, V+C showed PFS benefit versus P+C in two sub-groups; gallbladder cancer (GBC, HR = 0.55, 95% CI: 0.25, 1.22; median PFS, 2.9 vs. 1.6 months) and females (HR = 0.59, 95% CI: 0.28, 1.23; median PFS, 4.1 vs. 2.8 months). There was no PFS benefit for V+C vs. P+C among males and non-GBC. Toxicities were generally balanced between arms apart from a slightly higher incidence of hyperbilirubinemia, diarrhea and fatigue in the V+C vs. P+C arm. Grade 3/4 toxicities were reported in 66% and 59% of patients in the V+C and P+C arms, respectively. **Conclusions:** V+C is well tolerated but did not improve ORR, PFS or OS vs. P+C in 2L advanced BTC. Exploratory analyses suggested that patients with GBC and female patients achieved comparatively higher median PFS with V+C vs. P+C. Clinical trial information: NCT03093870. Research Sponsor: ASLAN Pharmaceuticals.

4598 Poster Session (Board #206), Fri, 8:00 AM-11:00 AM

Comprehensive gene expression analysis of IDH1/2 mutant biliary cancers (BC). *First Author: Francesca Battaglin, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA*

Background: Isocitrate dehydrogenases (IDH) mutations (mut) identify a distinct subtype of BC that has yet to be fully characterized. We recently showed that *IDH1/2* mutant (mIDH) BC harbor specific gene alterations involving chromatin remodeling and DNA repair, and a differential immune markers profile compared to other mIDH GI tumors. Here we aim to further dissect the molecular profile of mIDH BC through a comprehensive gene expression profiling analysis. **Methods:** 524 BC samples (303 intrahepatic cholangiocarcinoma, IHCC, 67 extrahepatic cholangiocarcinoma, EHCC, 141 gallbladder, 13 unspecified) collected between February to December of 2019 were included. Samples were analyzed using NextGen DNA sequencing (NextSeq, 592 gene panel), whole transcriptome RNA sequencing (NovaSeq) and immunohistochemistry (Caris Life Sciences, Phoenix, AZ). EBseq was used to identify differentially expressed genes in mIDH vs wild type (WT) tumors with control for FDR ($Q < 0.2$). Pathway and functional enrichment analysis was performed using g:Profiler and Enrichr. **Results:** mIDH frequency in our cohort was 11.4% (60/524), with higher prevalence of *IDH1* mut (8.8%). IHCC showed the highest mut prevalence: *IDH1* 13.5%, *IDH2* 4.6%. mIDH was more common in females ($P = 0.0036$). A total of 774 genes were significantly differentially expressed between mIDH and WT: 582 underexpressed (Fold change, FC: 0.025~0.699); 192 overexpressed (FC: 1.43~3.3). Pathway enrichment showed a significant decrease of gene expression in cytokine-cytokine receptor interaction ($Q = 0.002$) and inflammatory response genes ($Q = 0.005$) in mIDH. Interferon-γ- and PD1 signaling-related genes expression was significantly lower in mIDH vs WT ($Q = 0.02$) including *IFNG* (FC 0.32), *NKG7* (FC 0.36), *CD8B* (FC 0.37), *BATF* (FC 0.40), *PD1* (FC 0.53), *SLAMF6* (FC 0.55) and *PD-L2* (FC 0.60). Wnt and cadherin signaling were also enriched for altered expression in several genes in mIDH BC (Q = 3.86e-7 and < 0.00001, respectively). **Conclusions:** To our knowledge, this is the largest and most extensive gene expression profiling study focused on mIDH BC. Our data show for the first time a distinct gene expression profile characterizing mIDH tumors which display significant downregulation of inflammatory response pathways and immune-related genes. These findings contribute to further the understanding of mIDH BC and may inform the future development of rational combination therapies. Research Sponsor: NCI P30CA014089, the Gloria Borges WunderGlo Foundation-The Wunder Project, the Dhont Family Foundation, the San Pedro Peninsula Cancer Guild, the Daniel Butler Research Fund, the Call to Cure Research Fund and the Fong Research Project.

4599 Poster Session (Board #207), Fri, 8:00 AM-11:00 AM

Final results of a randomized, open label, perioperative phase II study evaluating nivolumab alone or nivolumab plus ipilimumab in patients with resectable HCC. *First Author: Ahmed Omar Kaseb, GI Medical Oncology Department, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: In resectable hepatocellular carcinoma (HCC) surgical resection is associated with high recurrence rates. However, there is no approved neo-adjuvant or adjuvant therapies yet. Neoadjuvant immunotherapy effect has never been reported in this setting in HCC. **Methods:** This is a randomized phase II trial of nivolumab (Arm A) or nivolumab + ipilimumab (Arm B) as peri-operative treatment for patients (pts) with HCC who are eligible for surgical resection. Pts in Arm A are given nivolumab 240 mg iv, every 2 weeks (wks) for a total of 3 doses followed by surgery on week 6. Pts in Arm B are treated with nivolumab per same schedule as arm A plus concurrent ipilimumab 1 mg/kg on day 1. Adjuvant part of study starts 4 weeks after surgery, with Nivolumab at 480 mg iv every 4 weeks for 2 years in arm A. Pts in Arm B are treated with nivolumab per same schedule as arm A plus concurrent ipilimumab 1 mg/kg every 6 weeks times 4 doses after resection. The primary objective was the safety/tolerability of nivolumab +/- ipilimumab. Secondary objectives include overall response rate, pathologic complete response (pCR) rate and time to progression. Exploratory objectives include evaluating the pre- and post-treatment immunological changes in tumor tissues and peripheral blood. **Results:** 30 patients were enrolled, 2 patients withdrew consent, one patient was not eligible at time of therapy, and 27 randomized (13 to Arm A and 14 to Arm B). 21 patients proceeded with resection as planned and surgery was aborted for 6 patients; 1 for frozen abdomen due to old surgery, 2 for small residual volume, and 3 for progressive disease. Pts age ranged between 32-83 yo, 75 % were males, 7 pts had HCV, 7 had HBV and 7 had no hepatitis. Pathologic complete response (pCR) was observed in 5/21 pts (24% pCR rate) – 2 in Arm A and 3 Arm B, and 3/21 pts (16%) – 1 in Arm A, 2 in Arm B, achieved major pathologic response (necrosis effect of 50-99%). 5 patients in Arm B and 1 in Arm A experienced grade 3 or higher toxicity prior to surgery. No grade 4 or higher toxicity were observed and surgery was not delayed or cancelled due to oxicity. **Conclusions:** Our study reached its primary endpoint of safety. Importantly, we report a 40% pathologic response rate = pCR rate of 24%, and major necrosis rate of 16% for resectable HCC after preoperative immunotherapy in a randomized phase II pilot trial. After future validation, these promising results may contribute to a paradigm shift in the perioperative treatment of resectable HCC. Clinical trial information: NCT03222076. Research Sponsor: M.D. Anderson Cancer Center.

4600 Poster Session (Board #208), Fri, 8:00 AM-11:00 AM

Genome-wide plasma cell-free DNA methylation profiling to identify high-performing biomarkers for early detection of hepatocellular carcinoma. *First Author: Xin-Rong Yang, Zhongshan Hospital Liver Cancer Institute, Shanghai, China*

Background: Hepatocellular carcinoma (HCC) represents the second most common cause of cancer deaths worldwide. □-fetoprotein (AFP) is the most common serological test used for screening and diagnosis of HCC. However, it is widely recognized that AFP has lower sensitivity with sub-optimal specificity. Tumor-originated circulating cell-free DNA (cfDNA) provides new opportunity for non-invasive detection of liver cancer. **Methods:** HCC-specific differentially methylated regions (DMRs) were identified by whole genome bisulfite sequencing (WGBS) in 44 pairs of HCC tissues and adjacent tissues. We then performed methylome profiling on cfDNA from HCC patients and healthy individuals by targeted bisulfite sequencing covering genome-wide CpG islands, shelves, and shores. We employed machine learning approaches to build diagnostic models based on cfDNA regional methylation level to classify the plasma of HCC (n = 140) from that of healthy individuals (n = 84). Further analyses were performed in the validation cohort, including 155 HCC patients, and a control group with 96 healthy individuals, 21 chronic hepatitis B infection (CHB)/liver cirrhosis (LC) patients and 34 patients with benign hepatic lesions (BHL). Area under the receiver operating characteristic curve (AUC-ROC) was used to evaluate diagnostic performance. **Results:** A random forest classifier achieved an AUC of 0.97 (sensitivity: 92.9%; specificity: 89.4%) with 10-fold cross-validation using a panel of 39 DMR markers. The AUC of the diagnostic panel was 0.93 (sensitivity: 81.3%; specificity: 90.7%) in validation cohort, and it performed equally well in detecting BCLC stage 0+A (AUC = 0.90; sensitivity: 74.7%) and AFP negative (AUC = 0.92; sensitivity: 79.4%) HCC, as well as differentiating HCC from CHB/LC and BHL. Based on these results, we have further developed a small targeted bisulfite sequencing panel covering 127 CpG sites for non-invasive diagnosis of HCC. The panel had similar performance in training and validation cohorts, an AUC of 0.96 (sensitivity: 90.7%, specificity: 88.2%) in the training set, and 0.91 (sensitivity: 80.0%, specificity: 88.7%) in the validation set. **Conclusions:** Our diagnostic panel with 39 DMR markers showed high sensitivity and specificity in HCC diagnosis as well as surveillance in high-risk populations for developing HCC. More importantly, simple diagnostic model show similar diagnostic performance for early HCC diagnosis, which was easily to transfer to clinical application in the future. Research Sponsor: BGI Genomics.

4601 Poster Session (Board #209), Fri, 8:00 AM-11:00 AM

Phase Ib dose escalation and cohort expansion study of the novel myeloid differentiating agent MTL-CEBPA in combination with sorafenib in patients with advanced hepatocellular carcinoma (HCC). *First Author: Debashis Sarker, Guy's Hospital, King's College London, London, United Kingdom*

Background: MTL-CEBPA is the first small activating RNA to enter clinical trials and upregulates C/EBPα, a master regulator of myeloid cell differentiation. We previously reported a favourable safety profile of MTL-CEBPA as a single agent in HCC (Sarker D et al, ASCO 2018). After discontinuation of MTL-CEBPA, 3 out of 5 patients (pts) treated with sorafenib off study had a complete response (CR) of 7-18 months duration; 2 pts of which demonstrated resolution of lung metastases for > 1 year. Here we provide new data on pts prospectively treated with MTL-CEBPA + sorafenib. **Methods:** Primary objective was to assess safety and tolerability of MTL-CEBPA 90-130mg/m^2 QW or BIW in combination with sorafenib 400mg BD administered to HCC patients either concomitantly or sequentially, in cohorts either tyrosine kinase inhibitor (TKI) naive or resistant. Secondary objectives included preliminary assessment of activity by response rate (RECIST v1.1) and immune landscape analysis. **Results:** As at the cut off date of 1 Feb 2020, 12 pts have been treated with MTL-CEBPA co-administered with sorafenib and 14 pts with MTL-CEBPA followed by sorafenib (23M/3F, median age 65.5years, range 44-83, ECOG PS 0/1: 18/8). The most common treatment-related AEs (all grades/grade 3-4) in these groups include facial flushing (4/0), raised AST (4/2) raised ALT (2/1), fatigue (5/0), raised ALP (2/0), and anaemia (2/2), diarrhoea (3/0), rash (2/0) and anorexia (1/0). Of 14 evaluable pts in the TKI naive cohorts, 2 pts had CR, 3 pts had partial response and 7 had stable disease. 9/10 pts in the TKI resistant cohorts evaluable for efficacy had stable disease. Flow cytometry demonstrated statistically significant decreases in frequency of immature CD66$^+$CD10$^-$ neutrophils and myeloid derived suppressor cells. IHC demonstrated significant reduction in M2 macrophages in tumour biopsies. **Conclusions:** MTL-CEBPA + sorafenib is well tolerated with an acceptable safety profile. This study has confirmed signals of objective response to the combination treatment in TKI naïve HCC patients with viral aetiology, warranting expanded development in these patients. Updated efficacy and safety data will be presented. Clinical trial information: NCT02716012. Research Sponsor: MiNA Therapeutics.

	TKI naïve		TKI resistant	
Best objective response (n)	**Viral**	**Non-viral**	**Viral**	**Non-viral**
Complete Response	2	0	0	0
Partial Response	2	1	0	0
Stable Disease	3	4	5	4
Progressive Disease	1	1	0	1
Total Evaluable	8	6	5	5
Non-Evaluable (withdrawn)	3	5	0	0
Non-Evaluable (ongoing)	1	1	1	0

4602 Poster Session (Board #210), Fri, 8:00 AM-11:00 AM

Immediate post-thermal ablation biopsy of colorectal liver metastases to predict oncologic outcomes. *First Author: Nikiforos Vasiniotis Kamarinos, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Thermal ablation (TA) is used as a local cure for selected colorectal liver metastases (CLM) with minimal risk. A critical limitation of TA has been early local tumor progression (LTP). The goal of this study is to establish the role of ablation zone (AZ) biopsy in predicting LTP. **Methods:** This institutional review board-approved prospective study included patients with CLM of 5cm or less in maximum diameter, with confined liver disease or stable, limited extrahepatic disease. Both radiofrequency(RF) and microwave(MW) ablation modalities were used. A biopsy of the center and margin of the AZ was performed immediately after ablation. The applicators were also examined for the presence of viable tumor cells. All samples containing morphologically identified tumor cells were further interrogated with immunohistochemistry to determine the proliferative and viability potential of the detected tumor cells. Ablation margin size was evaluated on the first CT scan performed 4–8 weeks after ablation and was confirmed by 3D assessment with Ablation Confirmation Software (Neuwave™). Variables were evaluated as predictors of time to LTP with the competing-risks model (uni- and multivariate analyses). **Results:** Between November 2009 and February 2019, 102 patients with 182 CLMs were enrolled. Mean tumor size was 2.0 cm (range, 0.6–4.8 cm). MW was used in 95/182 (52%) tumors and RF in 87/182 (48%). Median follow-up was 19 months. Technical effectiveness was evident in 178/182 (97%) ablated tumors on the first contrast material–enhanced CT at 4–8-weeks post-ablation. The cumulative incidence of LTP at 12 months was 19% (95% confidence interval [CI]: 14, 27). Samples from 64 (35%) of the 178 technically successful cases contained viable tumor. At univariate analysis, tumor size, minimal margin size, and biopsy results were significant in predicting LTP. In a multivariate model, margin size of less than 5 mm ($P < .001$; hazard ratio [HR], 4.3), and positive biopsy results ($P = .02$; HR, 1.8) remained significant. LTP within 12 months after TA was noted in 3% (95% CI: 1, 6) of tumor-negative biopsy CLMs with margins of at least 5 mm. **Conclusions:** Biopsy and pathologic examination of the AZ predicts LTP regardless of TA modality used. This can optimize ablation as a potential local cure for patients with limited CLM. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

4603 Poster Session (Board #211), Fri, 8:00 AM-11:00 AM

A randomized phase II study of oxaliplatin/5-FU (mFOLFOX) versus irinotecan/5-FU (mFOLFIRI) chemotherapy in locally advanced or metastatic biliary tract cancer refractory to first-line gemcitabine/cisplatin chemotherapy. *First Author: Jin Won Kim, Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seognnam, South Korea*

Background: In locally advanced or metastatic biliary tract cancer (BTC), second-line chemotherapy is challenging after progression from first-line gemcitabine/cisplatin, although mFOLFOX has been proven to be superior to active symptom control in ABC-06 trial. Irinotecan is an active drug in other gastrointestinal cancers. This study evaluated whether mFOLFIRI was superior to mFOLFOX in second-line treatment of BTC. **Methods:** Patients diagnosed with BTC with disease progression after prior gemcitabine/cisplatin were randomized (1:1) to either mFOLFOX (oxaliplatin 100mg/m2 over 2 hours, leucovorin 100mg/m2 over 2 hours, 5-fluorouracil 2400mg/m2 over 46 hours, every 2 weeks) or mFOLFIRI (irinotecan 150mg/m2 over 2 hours, leucovorin 100mg/m2 over 2 hours, 5-fluorouracil 2400mg/m2 over 46 hours). Randomization was stratified by tumor location (intrahepatic vs extrahepatic vs gallbladder vs ampulla of vater) and ECOG performance status (0, 1 vs 2). Primary end-point was overall survival (OS) rate at 6 months. **Results:** In total, 120 patients were enrolled and 114 patients were treated (mFOLFOX:57, mFOLFIRI:57). Median age was 63 years old. Most patients had ECOG 0/1 (89.5%). Tumor location was intrahepatic in 47 patients (41.2%), extrahepatic in 27 (23.7%), gallbladder in 35 (30.7%) and ampulla of vater in 5 (4.4%). At the median follow-up duration of 10.7 months (95% CI, 8.2-13.2), 6-month OS rate was 58.1% in mFOLFOX and 46.0% in mFOLFIRI. Of 102 evaluable patients (mFOLFOX:51, mFOFIRI:51), objective response rate and disease control rate were 5.9% (95% CI, 0-12.4) and 64.7% (95% CI, 51.6-77.8) in mFOLFOX and 3.9% (95% CI, 0-9.2) and 58.8% (95% CI, 45.3-72.3) in mFOLFIRI. Median progression-free survival was 2.8 months (95% CI, 2.3-3.3) in mFOLFOX and 2.1 months (95% CI, 1.3-2.9) in mFOLFIRI ($p = 0.682$). Median OS was 6.6 months (95% CI, 5.6-7.6) in mFOLFOX and 5.9 months (95% CI, 4.3-7.5) in mFOLFIRI ($p = 0.887$). The most common grade 3/4 adverse events were neutropenia (26.3%) and AST/ALT elevation (15.8%) in mFOLFOX and neutropenia (24.6%) and anemia (17.5%) in mFOLFIRI. Peripheral neuropathy (36.8%) and thrombocytopenia (35.1%) in mFOLFOX and vomiting (19.3%) and cholangitis (10.5%) in mFOLFIRI occurred more frequently. No chemotherapy-related deaths were reported. **Conclusions:** In second-line treatment of BTC, mFOLFIRI was tolerable But, mFOLFIRI was not superior to mFOLFOX. Adverse events were different between two groups. Clinical trial information: NCT03464968. Research Sponsor: CJ health care, Jeil pharmaceutical company.

4604 Poster Session (Board #212), Fri, 8:00 AM-11:00 AM

Safety of ^{177}Lu-DOTATATE in patients with advanced neuroendocrine tumors: Data from a U.S. expanded access program. *First Author: Martin S. Auerbach, Department of Molecular and Medical Pharmacology, University of California, Los Angeles, CA*

Background: The NETTER-1 clinical trial showed that peptide receptor radionuclide therapy (PRRT) with ^{177}Lu-DOTATATE increased progression-free survival in patients with somatostatin-receptor-positive advanced midgut neuroendocrine tumors (NETs) compared with high-dose octreotide long-acting repeatable, and was associated with few serious adverse events (AEs). To assess the safety profile of ^{177}Lu-DOTATATE in a real-world population, we analyzed safety data from a US expanded access program (NCT02705313). **Methods:** Patients had inoperable, histologically proven, somatostatin-receptor-positive, locally advanced or metastatic midgut NETs (Ki-67 index ≤ 20%) that progressed after somatostatin analog therapy. Exclusion criteria were: surgery, radiotherapy or chemotherapy in the last 12 weeks; treatment with an interferon, mTOR inhibitor, or other systemic therapy in the last 4 weeks; or ongoing octreotide therapy that could not be interrupted for PRRT. Patients with impaired renal function (serum creatinine > 1.7 mg/dL or creatinine clearance < 50 mL/min) or serious coexisting conditions were excluded. The analysis included patients who received ≥ 1 cycle of ^{177}Lu-DOTATATE between July 5, 2016 and December 21, 2018. Data were collected from the first cycle to the latest data collection point (up to October 7, 2019). **Results:** 299 patients received a mean ^{177}Lu-DOTATATE cumulative dose of 552 mCi (20.4 GBq) (standard deviation [SD]: 220 mCi [8.1 GBq]) over a mean of 2.8 cycles (SD: 1.1). Mean age was 60.8 years (SD: 11.7); 38.5% of patients were men. Over a mean follow-up of 131 days (SD: 87), 48.8% of patients reported treatment-related AEs (TRAEs), with a maximum severity of grade 1, 2 and 3 for 26.8% (n = 80), 18.1% (n = 54) and 4.0% (n = 12) of patients, respectively; there were no grade 4–5 TRAEs. The most common TRAEs of any grade (≥ 5.0% of patients) were nausea (31.1%), vomiting (13.7%), fatigue (9.4%) and thrombocytopenia (6.0%). The most prevalent grade 3 TRAEs were lymphocyte count decrease (1.0%) and thrombocytopenia (0.7%). Serious TRAEs occurred in 1.0% of patients (carcinoid crisis, dehydration, syncope and vomiting). AEs led to dose modification in 1.7% of patients, dose delay in 6.4% (most commonly due to nausea [2.0%] or thrombocytopenia [2.0%]) and discontinuation in 1.3% (due to thrombocytopenia [1.0%] and extravasation [0.3%]). **Conclusions:** In a real-world population of US patients with advanced midgut NETs, ^{177}Lu-DOTATATE treatment was well tolerated with few TRAEs, consistent with the safety profile in the NETTER-1 trial. Clinical trial information: NCT02705313. Research Sponsor: Advanced Accelerator Applications, a Novartis company.

4605 Poster Session (Board #213), Fri, 8:00 AM-11:00 AM

Risk of cancer-specific death for patients diagnosed with neuroendocrine tumors: A population-based analysis. *First Author: Julie Hallet, Odette Cancer Centre, Toronto, ON, Canada*

Background: While patients with neuroendocrine tumours (NETs) are known to experience prolonged overall survival, the contribution of cancer-specific and non-cancer deaths is undefined. We examined cancer-specific and non-cancer death after NET diagnosis. **Methods:** We conducted a population-based retrospective cohort study of adult patients with NETs from 2001-2015 by linking administrative healthcare datasets. Using competing-risks methods, we estimated the cumulative incidence of cancer-specific and non-cancer death and stratified by primary NET site and metastatic status. Sub-distribution hazard models examined prognostic factors. **Results:** Among 8,607 included patients, median follow-up was 42 months (interquartile range: 17-82). The risk of cancer-specific was higher than that of non-cancer death, with 27.3% (95%CI: 26.3-28.4%) and 5.6% (95%CI: 5.1-6.1%) at 5 years. Cancer-specific deaths largely exceeded non-cancer deaths in synchronous and metachronous metastatic NETs. Patterns varied by primary tumour site, with highest risks of cancer-specific death in broncho-pulmonary and pancreatic NETs. For non-metastatic gastric, small intestine, colonic, and rectal NETs, the risk of non-cancer death exceeded that of cancer-specific deaths. Advancing age, higher material deprivation, and metastases were independently associated with higher hazards, and female sex and high comorbidity burden with lower hazards of cancer-specific death. **Conclusions:** Among all NETs, the risk of dying from cancer is higher than that of dying from other causes. Heterogeneity exists by primary NET site. Some patients with non-metastatic NETs are more likely to die from non-cancer than from cancer causes. This information is important for counselling, decision-making, and design of future trials. Cancer-specific mortality should be included in outcomes when assessing treatment strategies. Research Sponsor: CIHR.

4606 Poster Session (Board #214), Fri, 8:00 AM-11:00 AM

Outcome analyses in patients with metastatic gastroenteropancreatic neuroendocrine tumors receiving peptide receptor radionuclide therapy with ^{177}Lu-DOTATATE – Impact of treatment order and combination on mortality. *First Author: Alexander Rheinhard Siebenhuener, Klinik für Medizinische Onkologie und Hämatologie, UniversitätsSpital Zürich, Zürich, Switzerland*

Background: Neuroendocrine tumors of the gastroenteropancreatic tract present heterogeneous with several systemic treatment options in the advanced setting. PRRT with ^{177}Lu-DOTATATE targeting the SSTR-2 receptor of these tumors showed effective responses in the NETTER-1 trial in the short as well as long term follow-up of patients. The aim of our study was to determine the HRQoL and outcome of GEP-NET patients. **Methods:** 41 GEP-NET patients who received ^{177}Lu-DOTATATE (mean: 3 cycles) between 2012 and 2017 at University Hospital Zurich (USZ) were included in this retrospective analysis. HRQoL parameters (fatigue, insomnia, loss of appetite, abdominal pain, nausea, emesis, diarrhea, weight loss) were assessed before and after treatment. At least 3 weeks after the last PRRT cycle, data on blood parameters, HRQoL, and overall survival data were extracted from patient records. To determine factors influencing the success of PRRT therapy and survival, we recorded pre- and post-PRRT treatments (e.g. selective internal radiation therapy/SIRT, somatostatin analogue therapy/SSA, TKI or chemotherapy) and the time-point of PRRT in the therapeutic sequence was analyzed. **Results:** Baseline rates of HRQoL and ECOG performance status were assessed (baseline mean: ECOG 0). PRRT was well tolerated, with most patients reporting no significant deterioration in HRQoL after treatment. Blood parameters (hemoglobin, leucocyte and platelet counts, creatinine) and glomerular filtration rate were not significantly affected by PRRT therapy. The number of previous treatments did not influence survival after PRRT; neither did the length of the time period between first diagnosis and PRRT. Patients with a SIRT treatment prior to PRRT had an elevated mortality odds ratio of 4.083. If SIRT was applied to patients with a pancreatic tumor, the mortality odds ratio was 1.33 compared to patients without a pancreatic tumor. Post-PRRT SSA increased the odds for survival, with a mortality odds ratio of 2.33 for patients without SSA after PRRT. **Conclusions:** Patients with advanced GEP-NETs may benefit from PRRT with ^{177}Lu-DOTATATE, as this treatment appears to be well tolerated and does not significantly impair the HRQoL or symptom load. SIRT before PRRT seems to lower the chances of response and reduces survival instead using this sequence vice versa. This trend was also seen if SSA was not used after PRRT. But these trends have to be proven in prospective trials. Research Sponsor: None.

4607 Poster Session (Board #215), Fri, 8:00 AM-11:00 AM

Multicenter analysis of treatment outcomes for well differentiated grade 3 neuroendocrine tumors (NET G3). *First Author: Leonidas Apostolidis, Department of Medical Oncology, National Center for Tumor Diseases, Heidelberg University Hospital, Heidelberg, Germany*

Background: Well differentiated grade 3 neuroendocrine tumors (NET G3) have been distinguished from poorly differentiated neuroendocrine carcinomas (NEC) in the most current WHO classifications from 2017 and 2019. Retrospective data suggest that commonly applied first-line chemotherapy protocols with cisplatin or carboplatin in combination with etoposide (PE) are less effective in NET G3 than NEC. Therefore, current treatment guidelines suggest alternative first-line treatment protocols like temozolomide-based (TEM), streptozotocin-based (STZ) and FOLFOX which have only been studied in second-line so far. The aim of this multicenter analysis was to evaluate treatment outcomes for NET G3 with a focus on the efficacy of different first-line regimens. **Methods:** We performed retrospective analysis of all patients with NET G3 in the NEN databases of 3 German cancer centers. All histopathological findings were reviewed by the investigators in order to comply with the most current WHO classification. **Results:** A total of 131 patients could be identified. Median Ki67 was 30 %, primary tumors were located in the pancreas in 71 % of cases, 20 patients had a history of prior NET G1/G2 diagnosis. Median overall survival (OS) was 138.1 months with a median follow-up of 20.4 months. 125 patients received palliative first-line therapy: PE n = 34, FOLFOX n = 36, TEM (mostly temozolomide+capecitabine) n = 21, STZ n = 19, other (including targeted agents, somatostatin analogues, PRRT and multimodal combination approaches) n = 15. Overall response (ORR) and disease control rate was 35.3 % and 67.6 % for PE, 52.8 % and 80.6 % for FOLFOX, 28.6 % and 66.7 % for TEM, 47.4 % and 68.4 % for STZ, 20.0 % and 73.3 % for other respectively. Median progression-free survival for PE was 5.2 months. Compared to PE, PFS in the other treatment groups was 6.0 months for FOLFOX (p = 0.164), 12.0 months for TEM (p = 0.059), 5.7 months for STZ (p = 0.519), 14.1 months for other (p = 0.003). All non-PE patients combined showed a significantly prolonged PFS vs. PE (9.0 vs. 5.2 months; p = 0.011). 89 patients received second-line systemic therapy with a median PFS of 5.3 months. **Conclusions:** In this first multicenter analysis of different treatment strategies for NET G3, patients receiving upfront treatment with non-PE regimens had a significantly prolonged PFS. Of the single defined protocols, FOLFOX showed the highest ORR, and TEM the longest PFS. Further prospective evaluation of the optimal therapeutic strategy for this newly defined tumor entity is needed. Research Sponsor: None.

4608 Poster Session (Board #216), Fri, 8:00 AM-11:00 AM

Australasian Gastrointestinal Trials Group (AGITG) CONTROL NET Study: Phase II study evaluating the activity of ^{177}Lu-Octreotate peptide receptor radionuclide therapy (LuTate PRRT) and capecitabine, temozolomide CAPTEM)—First results for pancreas and updated midgut neuroendocrine tumors (pNETS, mNETS). *First Author: Nick Pavlakis, Northern Cancer Institute, St Leonards, Sydney, Australia*

Background: CAPTEM is an accepted regimen for patients (pts) with advanced pNETs. Single agent ^{177}Lu-Octreotate PRRT is now a standard of care for progressive WHO Grade (G) 1/2 mNETs. High activity was seen with LuTate/CAPTEM in a single arm Phase I/II trial. This study was undertaken to determine the relative activity of adding CAPTEM to LuTate PRRT in pts with mNETs and pNETs. **Methods:** Non-comparative randomised open label parallel group phase II trial with 2:1 randomisation to PRRT/CAPTEM (experimental arm) vs. PRRT (mNETs control) and CAPTEM (pNETS control). PRRT/CAPTEM: 7.8GBq LuTate day(D) 10, 8 weekly (wkly) x 4, with b.i.d. oral CAP 750mg/m^2 D1-14 & TEM 75mg/m^{2}D10-14, 8 wkly x 4; PRRT: 8 wkly x 4; CAPTEM 8 wkly x 4. Primary endpoint: Progression free survival (PFS). mNETS- at 15 months (mo) assuming 15mo PFS 66.4% in control arm, aiming for PFS ³ 80%; pNETS- at 12mo assuming 12mo PFS 60% in control arm, aiming for PFS ³ 75%. Secondary endpoints: Objective tumour response rate (complete or partial) (OTRR), clinical benefit rate (OTRR, stable disease) (CBR), toxicity, quality of life. **Results:** 75 pts enrolled (Dec 2015 – Nov 2018): mNETs 33 PRRT/CAPTEM and 14 PRRT; pNETS 19 PRRT/CAPTEM and 9 CAPTEM. mNETS: Median follow-up 35mo; 15mo PFS was 90% (95% CI: 73-97%) v 92% (95% CI: 57-99%); OTRR 31% vs 15%; and CBR 97% vs 92% for PRRT/CAPTEM v PRRT respectively. Treatment related adverse events (AEs): 24/32 PRRT/CAPTEM pts had at least one G3 event (75%) vs 5/13 (38%, PRRT); and 4/32 pts at least one G4 event (13%) v 1/13 (8%) respectively, mostly haematologic (haem). Only one patient failed to complete therapy (PRRT/CAPTEM). pNETS: Median follow-up 34mo; 12mo PFS was 76% (95% CI: 48-90%) v 67% (95% CI: 28-88%); OTRR 68% vs 33%; and CBR 100% vs 100% for PRRT/CAPTEM v CAPTEM respectively. Treatment related AEs: 5/18 PRRT/CAPTEM pts had at least one G3 event (28%) vs 3/9 (33%) CAPTEM; 3/18 pts at least one G4 event (17%) v 1/9 (11%) respectively. **Conclusions:** CAPTEM/PRRT is active, meeting its target landmark PFS for CAPTEM/PRRT (12mo pNETs; 15mo mNETs) with numerically greater OTRR in both pNETs and mNETs, but with more haem toxicity in mNETs. As activity was high in both control arms longer follow up is required to determine if the relative activity of PRRT/CAPTEM is sufficient to warrant Phase III evaluation. Clinical trial information: ACTRN12615000909527. Research Sponsor: Unicorn Foundation, Tour de Cure Australia.

4609 Poster Session (Board #217), Fri, 8:00 AM-11:00 AM

Pretherapeutic ^{68}Ga-DOTATATE PET SUV predictors of survival of radionuclide therapy for metastatic neuroendocrine tumors. *First Author: Rahul Ladwa, Princess Alexandra Hospital & University of Queensland, Brisbane, Australia*

Background: Peptide receptor radionuclide therapy (PRRT) is an effective treatment option in patients with advanced neuroendocrine tumours (NETs). Patients are pre-selected based on ^{68}Gallium-DOTA-(0-Tyr3)-octreotate Positron Emission Tomography (^{68}Ga-DOTATATE PET) uptake. The level of uptake in tumour on the baseline ^{68}Ga-DOTATATE PET scan has been explored as a predictor of response in NETs with inconclusive evidence. The aim of this study is to determine the correlation between ^{68}Ga-DOTATATE PET SUV parameters to survival outcomes. **Methods:** We retrospectively analysed 142 lesions (up to five lesions per patient) in 73 patients with NET undergoing PRRT with ^{177}Lutetium octreotate (8.0-8.3GBq) and pretherapeutic ^{68}Ga-DOTATATE PET/CT in a single institution. Standardised uptake values (SUVs) max and mean were correlated with progression-free survival (PFS) and overall survival (OS). **Results:** A total of 73 patients were included in the analysis. The median age was 63 (28-89) years. NET origin was gastroenteric (49%), pancreatic [pNET] (38%), bronchial (10%) and other (3%). Ki-67 proliferation index ($<$ 3%: 36%, 3-20%: 36%, $>$ 20%-$<$ 50%: 8%, unknown: 21%) was seen. Pretherapeutic SUV max but not SUV mean was higher in pNETs (P = 0.04). No difference was seen with Ki-67 index. The median PFS was 32 (95%CI: 26-38) months. Median PFS was reduced with increasing ECOG performance status [PS] (P= 0.029), increasing tumour grade (P = 0.003), increasing Ki-67 proliferation index (P = 0.013), reduced SUV max (P= 0.003), reduced SUV mean (P= 0.001). Multivariate analysis confirmed SUV mean (HR =-1.71 [95%CI: -2.66- -0.80]; P$<$0.01) and Ki-67 index (HR = 1.11 [1.06-1.17]; P $<$ 0.01) as maintaining significance when incorporating ECOG PS (HR = 1.96 [0.68-5.47]; P = 0.22). The mean OS was 40 [37-44] months. A higher SUV max (SUV max $<$ 30: 34 [30-40] months vs SUV max $>$ 30: 48 [44-51]; P$<$0.01) and higher SUV mean (SUV mean $<$ 20: 33 [28-39] months vs SUV mean $>$ 20: 47 [43-51]; P$<$0.01) were associated with improved mean OS. Mean OS was not affected by ECOG performance status (P = 0.896), primary site of origin (P = 0.567) and Ki-67 index (P = 0.110). **Conclusions:** ^{68}Ga-DOTATATE PET SUV measures correlated with an improved PFS on multivariate analysis as well as improved OS in this select group of patients suitable for PRRT. Those patients with lower SUV mean may benefit from escalation of therapy such as increasing administered therapeutic activity. Research Sponsor: None.

4610 Poster Session (Board #218), Fri, 8:00 AM-11:00 AM

Efficacy and safety of surufatinib in United States (US) patients (pts) with neuroendocrine tumors (NETs). *First Author: Arvind Dasari, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Surufatinib (S) is a targeted inhibitor of tyrosine kinases VEGFR1, 2, & 3, FGFR1, and CSF-1R. Safety and efficacy of S has previously been studied in China in early phase development, and in 2 randomized phase 3 placebo controlled trials (NCT02588170 & NCT02589821). These trials enrolled pts with NETs of extrapancreatic (epNET) and pancreatic (panNET) origin, respectively. Both trials are completed, stopping at their pre-planned interim analysis after meeting the primary endpoint of improved PFS. S demonstrated significant efficacy in pts with advanced epNETs, achieving a median Progression Free Survival [mPFS] of 9.2 v 3.8 months when compared to placebo. The mPFS achieved in pts with advanced panNETs is currently pending future disclosure at an upcoming scientific conference. **Methods:** A dose escalation (ESC)/expansion (EXP) study was conducted to evaluate and confirm the effects of S in US pts. Dose ESC was completed and the maximum tolerated dose and recommend phase 2 dose was determined to be 300mg QD; the same as previous trials. The primary objective of EXP was to evaluate anticancer activity in pts with select indications including panNETs and epNETs. **Results:** As of 21-Jan-20, 32 pts with heavily pre-treated progressive NETs (median prior lines of treatment [Tx]: 3; range 1-8) were enrolled. The 32 pts included 16 pts with panNET and 16 with epNET. All previously received everolimus and/or sunitinib. The median duration of Tx at the time of the data cut-off was 19 wks for all pts; 30.9 wks for panNET and 11 for epNET. 19 pts remain on active Tx (13 epNET and 6 panNET pts), 9 pts discontinued due to progression of disease, 2 withdrew consent and 2 discontinued due to adverse event (AE) (grade 3 tricuspid valve insufficiency, and grade 3 GI bleed). An objective response rate of 9.4% was observed. 3 panNET pts achieved a confirmed partial response (PR) and 1 had an unconfirmed PR per RECIST 1.1; no epNET pts achieved a PR. The safety profile of S remains consistent with previously completed trials. 27 pts (84.4%) had reported at least one adverse event (AE), and 16 pts (50%) reported $\geq$ grade 3 AE's. The most common AE's reported were: hypertension, fatigue, diarrhea, proteinuria and nausea. Pharmacokinetics (PK) analyses has shown similar exposure in panNET and epNET pts as was observed in ESC, and pts from the collective pool of pts. **Conclusions:** S has demonstrated promising antitumor activity in US pts with progressive NETs with a manageable safety profile. Additionally, PK and dose exposure data is consistent with trial results from large randomized phase 3 trials. Clinical trial information: NCT02549937. Research Sponsor: Hutchison MediPharma International Inc.

4611 Poster Session (Board #219), Fri, 8:00 AM-11:00 AM

Correlation of DLL3 expression in gastroenteropancreatic neuroendocrine neoplasms with loss of RB1 and prognostic significance. *First Author: Chiara Liverani, Osteoncology and Rare Tumors Center, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy*

Background: Neuroendocrine neoplasms (NENs) are a rare subgroup of tumors with challenging management due to their unpredictable and heterogeneous behaviour. The identification of clinically useful biomarkers is a top priority need in this disease. The negative notch regulator DLL3 has gained increasing attention in small cell lung carcinoma, large cell neuroendocrine carcinoma and neuroendocrine prostate cancer, confirming the tumor suppressor function of Notch-1 signaling in neuroendocrine cells. **Methods:** A retrospective immunohistochemical analysis of DLL3, PD-L1 and RB1 was performed on FFPE samples from 43 patients with gastroenteropancreatic (GEP)-NENs and correlated with clinical characteristics. **Results:** DLL3 was expressed in high-grade (G3) GEP-NENs. The presence of DLL3 was significantly associated with poorly differentiated NEC (77.8% positive tumors), while none of the patients with well-differentiated NET expressed this marker. Expression of DLL3 was correlated with loss of RB1 and negative ^{68}Ga-PET/CT scan. The 85.7% of DLL3- positive tumors showed loss of RB1 expression, while only 1 out of 35 DLL3- negative tumors had RB1 loss. DLL3 was expressed in 75% of patients with negative ^{68}Ga-PET/CT, while only in 25% of patients with positive ^{68}Ga-PET/CT scan. The presence of DLL3 was negatively associated with PFS and OS. Median PFS was 41.9 months in DLL3-negative patients versus 7.9 months in DLL3-positive patients; median OS was 72.9 months in DLL3-negative patients versus 11.7 months in DLL3-positive patients. No correlation was found with DLL3 and PD-L1 expression. The presence of PD-L1 was not associated with any clinical characteristics. **Conclusions:** DLL3 is expressed in high grade GEP-NENs and is associated with loss of RB1, negative ^{68}Ga-PET/CT scan and unfavourable clinical outcome. The presence of DLL3 discriminates poorly differentiated NEC from well-differentiated NET. DLL3 could represent the ideal prognostic factor to stratify patients with GEP-NENs and a candidate therapeutic target in NEC patients. Research Sponsor: None.

4612 Poster Session (Board #220), Fri, 8:00 AM-11:00 AM

Inefficacy of chromogranin a assays as neuroendocrine tumor diagnostic tools compared to the NETest. *First Author: Anna Malczewska, Medical University of Silesia, Katowice, Poland*

Background: Chromogranin A (CgA) remains a commonly used diagnostic and monitoring tool for neuroendocrine tumor disease despite NCCN guidelines identifying it as a category 3 (major concerns about utility) biomarker. Several commercial assays have been developed to measure this protein (or its fragments) and are available both at CLIA-certified laboratories (USA) as well as in NET Centres of Excellence (CoEs - Europe). CgA is typically reimbursed by insurance companies and appears in several guidelines (e.g., ENETS). We sought to directly evaluate the accuracy of detecting NET disease using two different CgA assays, one in the USA (NEOLISA, EuroDiagnostica, IBL-America, CLIA-certified laboratory) and one in an ENETS CoE (CgA ELISA, Demeditec Diagnostics, Germany). We compared the results to the NETest, a circulating mRNA assay, recently validated as an *IVD* for NETs. **Methods:** Patients: NETs (n=258) including lung: n=43; duodenum n=9; gastric: n=44; pancreas: n=67; small bowel: n=40; appendix: n=10; rectum: n=45. No image-evidence of disease (n=122) (IND) and image-positive disease (IPD) (n=136). CgA assays (plasma): NEOLISA, ULN $>$108ng/ml, DD: ULN$>$99ng/ml. Data mean$\pm$SEM. NETest (whole blood): qRT-PCR - multianalyte algorithmic analyses, CLIA-laboratory. All samples de-identified and assessed blinded. Statistics: Mann-Whitney U-test, Pearson correlation & McNemar-test. **Results:** In the entire group (n=258), NEOLISA assay CgA levels were significantly ($p$$<$0.0001) higher (216$\pm$91ng/ml) vs. the DD-assay (76$\pm$8ng/ml). The assays exhibited a high concordance in output (Pearson r=0.81, $p$$<$0.0001), but there were 10.9% (n=31) discordant results. This reflected the NEOLISA assay detecting more CgA-positive samples. IPD group: CgA-positives were detected in 48/136 (35%, NEOLISA) vs. 28 (21%, DD-assay). McNemar's Chi^2=15.04, $p$$<$0.001 OR: 11.0, indicating the NEOLISA was significantly better than the DD-assay. The NETest, in contrast, was positive in 135/136 (99%; OR: 87-106, $p$$<$0.0001). IND group: CgA-positives were detected in 12/122 (10%, NEOLISA) vs. 9 (7%, DD-assay; p=NS). The majority (75%) of positives were associated with gastric NETs. The NETest was positive in 7 (6%); 4 were gastric NETs and 3 exhibited elevated CgA. **Conclusions:** Two standard CgA assays used for NET management (one accepted by Medicare in the USA, the second used at a CoE in Europe) only detect NET disease in 21-35% of cases. In contrast, a circulating mRNA fingerprint, the NETest, is ~99% accurate for detecting NET disease. Research Sponsor: None.

4613 Poster Session (Board #221), Fri, 8:00 AM-11:00 AM

Health-related quality-of-life results from SANET-ep: A phase III study of surufatinib versus placebo for advanced extrapancreatic neuroendocrine tumors. *First Author: Chunmei Bai, Peking Union Medical College Hospital, Beijing, China*

Background: In the phase 3 study (SANET-ep, NCT02588170), surufatinib significantly prolonged progression free survival compared with placebo in patients with progressive, well-differentiated advanced extrapancreatic neuroendocrine tumors (epNETs) (ESMO 2019 Abs. LBA76). Here, we report the results of health-related quality-of-life (HRQoL) from this study. **Methods:** Eligible patients were randomized in a 2:1 ratio to receive surufatinib or placebo, 300 mg, orally, once daily, until disease progression or intolerable adverse events. Patient-reported outcome questionnaires, including the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and the QLQ-G.I.NET-21, were collected at baseline, Day 15 of the first cycle (28 Days/cycle), and Day 1 of every cycle thereafter and at discontinuation. Time until definitive deterioration (TUDD) was defined as time from randomization to deterioration of 10 points in domain score compared with baseline score (without subsequent observations of deterioration of less than 10 point or any improvement as compared to baseline score), or death due to any cause. TUDD and mean change from baseline based on a longitudinal repeated measures analysis of each domain were analyzed retrospectively. Significance testing was at two-sided 0.05 without adjustment for multiplicity. **Results:** Of 198 pts randomized (surufatinib n = 129; placebo n = 69), 197 (99.5%) patients completed HRQoL questionnaires at baseline. The questionnaire compliance rate was > 90% for most on-treatment assessments. The TUDD was significantly longer in the surufatinib arm versus the placebo arm in the dyspnea domain (hazard ratio [HR] 0.52, p = 0.0103) and social function scale (HR 0.58, p = 0.0222), while the TUDD of diarrhea was significantly shorter in the surufatinib arm compared to placebo (HR 2.68, p = 0.0074). There was no significant difference of TUDD in the remaining domains of QLQ-C30 and G.I.NET-21. There was also no significant difference of the mean change of scores from baseline by repeated measures in the domains between the two arms except diarrhea (increase of 14.0 points [95% CI 9.6, 18.4] in the surufatinib arm versus 2.1 points [95% CI -4.1, 8.4] in the placebo arm, p = 0.0007). **Conclusions:** Treatment with surufatinib resulted in superior efficacy, acceptable toxicity, while generally maintaining HRQoL, which support surufatinib as a treatment option in this patient population that was previously treated with available therapies for epNETs. Clinical trial information: NCT02588170. Research Sponsor: Hutchison MediPharma Limited.

4614 Poster Session (Board #222), Fri, 8:00 AM-11:00 AM

Toxicity analysis of capecitabine/temozolomide in NETs. *First Author: Taymeyah E. Al-Toubah, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: The capecitabine/temozolomide regimen has significant activity in advanced NETs. Concerns exist regarding risk of opportunistic infections and long-term myelotoxicity. Analysis of large patient cohorts is needed for evaluation of rare toxicities and for assessment of risk factors. **Methods:** Retrospective study of all patients with advanced neuroendocrine neoplasms seen at the Moffitt Cancer Center between 1/2008 and 6/2019 who received treatment with CAPTEM. Patients who initiated treatment at outside institutions were included if they were prescribed treatment at appropriate doses and if complete records were available. **Results:** 462 patients met eligibility criteria for evaluation: 210 (45%) females and 252 (55%) males with a median age of 59. Median starting doses of CAP and TEM were 658mg/m^2 and 180mg/m^2 respectively. Median duration on treatment was 8 months. 25% of patients required a dose reduction and 16% discontinued due to toxicity of any grade. Incidence of grade 4 thrombocytopenia was 7%: 10% in females and 5% in males (p = 0.02). 4 cases were complicated by bleeding (0.8%). Incidence of grade 4 neutropenia was 3%: 5% in females and 1% in males (p = 0.004). Incidence of grade 4 lymphopenia was 2%. Only one case (0.2%) of suspected PCP was observed in a patient taking corticosteroids. There were 5 cases of herpes zoster and no other opportunistic infections. 3 patients developed myelodysplastic or myeloproliferative disease, all of whom had also received prior PRRT with Lutetium-Dotatate. There were no acute treatment related deaths, although one patient died 2 months after a thrombocytopenic bleed. **Conclusions:** Severe myelotoxicity is rare, but risks of grade 4 thrombocytopenia and neutropenia are significantly increased in females compared to males. Gender-based dosing should be considered. While alkylating agents are often associated with MDS, there were no cases except among patients who also had received PRRT, a known risk factor. PCP is not a significant risk with this regimen in patients not concurrently on corticosteroids. Research Sponsor: None.

4615 Poster Session (Board #223), Fri, 8:00 AM-11:00 AM

Phase II clinical trial of nab-paclitaxel plus gemcitabine in elderly patients with previously untreated locally advanced or metastatic pancreatic adenocarcinoma: BIBABRAX study. *First Author: Jaime Feliu Batlle, Medical Oncology Department, La Paz University Hospital, Madrid, Spain*

Background: FOLFIRINOX and nab-paclitaxel plus gemcitabine (nab-P+G) are the standard of care in the first-line treatment of mPC patients (pt) with good performance status. However, no standards of care exist for elderly (> 70 years) pt as they are usually excluded in clinical trials. This study aimed to evaluate whether the clinical benefit of nab-P+G could be extended to elderly pt with mPC. **Methods:** This was an open-label, single-arm, multicenter, phase II trial, to assess the efficacy and safety of Nab-P+G in elderly pt (≥ 70 years) with ECOG PS 0–1 and untreated unresectable locally advanced or metastatic PC. Pt received four-week cycles of intravenous (i.v.) nab-paclitaxel 125 mg/m2, followed by i.v. gemcitabine 1,000 mg/m2, on days 1, 8 and 15, until disease progression. Efficacy was evaluated according RECIST v 1.1 criteria and safety according NCI-CTCAE v 4.0 criteria. **Results:** Eighty pt were enrolled in the study. Median age was 74.6 years (range 70-87.9), 57.5% were men, 71% had ECOG PS 1 and 86% metastatic disease. 16.3% of patients had a history of prior tumor surgical resection, 12.5% received chemotherapy and 3.8% radiotherapy. Primary tumor was located in head (32.5%), tail (25.0%) and body (22.5%). Nab-P and G was reduced in 49% and 41% of pt respectively. 15 pt definitely interrupt study treatment due to toxicity: neurotoxicity (7), asthenia (5), neutropenia (1), leukocytosis (1) and hepatotoxicity (1). Time until definite deterioration (reduction ≥10 points as compared to baseline in EORTC-QLQ C30) was 1.6 months and deterioration-free rate at 3 months was 54.3%. Overall response rate was 13.8%, clinical benefit rate 67.5%, median PFS 7.2 months and median OS 9.2 months. The most common treatment-related adverse events were asthenia (60.0%), diarrhea (40.0%), neutropenia (33.8%), hair loss (28.8%), thrombocytopenia (26.3%), and nausea (23.8%). Only asthenia and neutropenia presented a relatively high incidence of grade 3 and 4 toxicities (21.3%). At least 1 SAE was reported in 55% of pt. **Conclusions:** BIBABRAX study confirms the clinical benefit of nab-P+G in an elderly population with mPC, in terms of survival, clinical response and tolerance, therefore it could be considered a treatment option for elderly patients. However, it was unable to demonstrate the preplanned benefit on the quality of life. Further research is needed on treatment strategies that could reduce deterioration of the quality of life in these pt. Clinical trial information: NCT02391662. Research Sponsor: Celgene.

4617 Poster Session (Board #225), Fri, 8:00 AM-11:00 AM

Circulating tumor DNA is prognostic and potentially predictive of eryaspase efficacy in patients with advanced pancreatic adenocarcinoma. *First Author: Jean-Baptiste Bachet, Pitié-Salpêtrière Hospital, Paris, France*

Background: Eryaspase is composed of L-asparaginase encapsulated in erythrocytes. It has demonstrated significant efficacy in combination with chemotherapy in a randomized phase 2 trial in second-line in patients with advanced pancreatic adenocarcinoma. We assessed, in this study, the prognostic and predictive value of circulating tumor DNA (ctDNA) in plasma samples of patients included in the eryaspase phase 2 trial. **Methods:** Samples prospectively collected pre-treatment at each 28-day cycle were centrally analyzed by next-generation sequencing (BPER method). Prognostic values of baseline ctDNA and ctDNA early changes between day 0 and 28 were assessed in both arms combined on objective response rate (ORR), progression free survival (PFS) and overall survival (OS). We conducted interaction test between ctDNA positivity and treatment arm, and the predictive value of ctDNA for eryaspase efficacy was investigated. **Results:** Patients with at least one available plasma sample have been included (n = 122/141). The presence of ctDNA at baseline was identified in 68% (77/113) of patients and was an independent negative prognostic factor for OS (4.6 vs 8.8 months; p = 0.0025) and PFS (1.6 vs 3.3 months; p = 0.00043). Early change in ctDNA levels was assessed by separating patients into three categories (one without detectable ctDNA, and two according to radio median value between day 0 and day 28) that were significantly correlated with ORR, PFS and OS. A significant interaction was observed between the presence of ctDNA and eryaspase efficacy. In patients with ctDNA detectable at baseline, eryaspase was associated with better PFS (HR = 0.53; 95% CI: 0.3-0.94) and OS (HR = 0.52; 95% CI: 0.29-0.91). **Conclusions:** We confirm from a prospective randomized trial that 1/ the presence of ctDNA at baseline is a major prognostic factor, 2/ the early change of ctDNA correlates with treatment outcome and 3/ the ctDNA could be a predictive biomarker of eryaspase efficacy. Clinical trial information: NCT02195180. Research Sponsor: Erytech.

4618 Poster Session (Board #226), Fri, 8:00 AM-11:00 AM

Concordance between independent and investigator assessment of disease-free survival (DFS) in the APACT trial. *First Author: Michele Reni, IRCCS Ospedale, San Raffaele Scientific Institute, Milan, Italy*

Background: APACT was a phase III trial of adjuvant *nab*-paclitaxel + gemcitabine (*nab*-P + Gem) vs Gem alone in patients with resected pancreatic cancer (PC) and the first adjuvant PC trial to use independently assessed DFS as the primary endpoint (DFS by investigator review was a prespecified sensitivity analysis). We examined concordance between independent and investigator DFS review. **Methods:** For the independent assessment, reviewers determined recurrence by computed tomography or magnetic resonance imaging but were blinded to treatment and clinical data. Investigator-assessed DFS was based on all available data. Concordance was summarized by κ statistics. Patients who did not have recurrence or were alive were censored at the last tumor assessment date with disease-free status or the randomization date if the last tumor assessment with disease-free status was missing. Patients who received new anticancer therapy or cancer-related surgery prior to recurrence or death were censored at the date of last tumor assessment with disease-free status prior to the start of new anticancer therapy or cancer-related surgery or the randomization date if the last tumor assessment date with disease-free status prior to the start of subsequent new anticancer therapy or cancer-related surgery was missing. All censoring rules were the same for analysis of DFS by independent and investigator review. **Results:** Median DFS by independent review was 19.4 (*nab*-P + Gem) vs 18.8 (Gem) months (hazard ratio [HR] 0.88; 95% CI, 0.73 - 1.06; $P = 0.18$); median investigator-assessed DFS was 16.6 (*nab*-P + Gem) vs 13.7 (Gem) months (HR 0.82; 95% CI, 0.69 - 0.97; nominal $P = 0.017$). Moderate concordance was found between independent- and investigator-assessed DFS (Table); similar results were observed in the *nab*-P + Gem (concordance, 78%; κ coefficient, 0.56) and Gem alone (concordance, 76%; κ coefficient, 0.53) arms. **Conclusions:** The results reflect the complexities of defining the recurrence timepoint accurately and suggest that radiological review in the absence of clinical context is suboptimal for recurrence detection in resected PC. These findings may inform future clinical trial design. Registration: EudraCT (2013-003398-91); ClinicalTrials.gov (NCT01964430). Clinical trial information: NCT01964430. Research Sponsor: Bristol-Myers Squibb.

Concordance of DFS (Total; N = 814).

		Investigator	
	Independent	**No (n = 293)**	**Yes (n = 521)**
Concordance, n (%)	No (n = 427)	266 (33)	161 (20)
	Yes (n = 387)	27 (3)	360 (44)
κ coefficient (95% CI)		0.54 (0.49 - 0.60)	

4619 Poster Session (Board #227), Fri, 8:00 AM-11:00 AM

PANasta Trial: Cattell Warren versus Blumgart techniques of pancreatico-jejunostomy following pancreato-duodenectomy—A double-blinded multi-centered trial, trial results. *First Author: Christopher Halloran, University of Liverpool, Liverpool, United Kingdom*

Background: Pancreatic anastomosis failure following pancreatic head excision, for suspected pancreatic cancer, leads to longer recovery and failure to start or complete adjuvant chemotherapy. The aim of this study is to evaluate whether a Blumgart anastomosis (BA) reduces the post operative pancreatic fistula (POPF) rate compared to a more traditional Cattell-Warren anastomosis (CWA). **Methods:** Patients with suspected pancreatic cancer, undergoing elective pancreato-duodenectomy were randomized intra-operatively to either a BA or a CWA. Anastomoses were constructed according to prior agreed techniques and an operative manual describing key surgical steps. Quality control of these key steps and adherence to the arm of randomization was ensured by operative photographs. Surgical drain amylase was measured post-operatively to establish the primary end point of POPF. These were graded A (biochemical) or B and C (clinically relevant, CR-POPF). Secondary endpoints included: Entry in adjuvant therapy, hospital stay, mortality and survival. Overall survival was estimated using the method of Kaplan Meier and defined as the time from randomisation until death by any cause with alive patients censored at the end of study date. **Results:** Between May 5 2015 and August 7 2017, 238 patients were randomized, 2 patients withdrew, leaving 236 patients for analysis (112 BA, 124 CWA). Median age was 70 years, 63% were men. Median time from diagnosis to randomization (surgery) was 33 days for both arms. In the BA arm there were 28 POPF's (15-A, 10-B and 3-C) and 32 in the CWA arm (18-A, 12-B and 2-C), p = 0.887. In total 27 patients (11.4%) developed a CR-POPF, BA 13 (5.5%), CWA 14 (5.9%), p = 0.857. 75% of eligible patients entered chemotherapy, with a median (IQR) time to the start treatment of 2.55 (2.27, 3.15) months for the BA group and 2.87 (2.56, 3.75) for the CWA group. Median hospital stay (IQR) in days was 13 (10-24) for BA and 14.5 (10-22) for CWA, p = 0.232. The overall surgical related mortally at 90 days was 1.7%. 44 study deaths were observed, 35 were due to disease progression (BA 19, CWA 16). A hazard ratio (95% CI) of 0.72 (0.4, 1.311) shows better, but not statistically significant survival for the CWA group. **Conclusions:** This is the largest surgical trial ever conducted comparing these techniques and there was no significant difference in the POPF rate between the BA and CWA anastomoses. In a UK population the clinically relevant POPF rate is 11% and 75% of eligible patients enter chemotherapy. Clinical trial information: ISRCTN52263879. Research Sponsor: Cancer Research UK.

4620 Poster Session (Board #228), Fri, 8:00 AM-11:00 AM

Landscape of DNA-damage-repair/homologous recombination deficiency (DDR/HRD) in hepatopancreaticobiliary (HPB) cancers. *First Author: Wungki Park, Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY*

Background: Biallelic HR-gene mutations (HRm) confer HRD and sensitivity to DDR-targeted therapies including platinum and PARPi in pancreatic cancer (PDAC). The landscape of DDR/HRD phenotypes in HPB cancers and their clinical implication is yet to be evaluated, the subject of this effort. **Methods:** Hybrid capture-based comprehensive genomic profiling was performed in a CLIA-certified, CAP-accredited lab (Foundation Medicine, Inc.) on up to 395 genes, including the HR-genes (*BRCA1/2, PALB2, RAD50/51B/C/D, MRE11, ATRX, ATR, ATM, BAP1, BRIP1, CHEK2, NBN,* and *FANCA*). Putative DDR/HRD phenotype was assessed using percent genome under LOH (gLOH) (PMID: 28916367). Variant zygosity was assessed as previously described (PMID: 29415044). From an independent PDAC subgroup among HPB cancers, we evaluated their outcomes on first-line platinum. **Results:** From a total of 11,174 tumors, pathogenic DDR/HRm were identified in 18% (1980/11174) of HPB cancers, 15% (863/5941) of PDAC, 25% (744/2998) of cholangiocarcinoma, 15% (141/958) of hepatocellular carcinoma, and 17% (152/873) of gallbladder carcinoma. We observed a majority (63%) of DDR/HRm with LOH. Rigorous filtering for tumor purity and copy number quality metrics yielded 34% (4051/11774) cases evaluable. The median gLOH of any biallelic DDR/HRm was 12.9% compared to 8.8% in no DDR/HRm (p=5.7E-33). Strength of the association varied by gene, with the strongest association in *BRCA1* (22.3, p=1.5E-10), *BRCA2* (20.1, p=1.7E-35), *RAD51C* (16.7, p=7.8E-4), *PALB2* (16.4, p=1.4E-5), *BRIP1* (14.3, p=0.02), *RAD51B* (13.7, p=0.02), and *ATM* (13.6, p=7.7E-12) (Table). Most other DDR/HR-genes and monoallelic DDR/HRm had weak gLOH. PDAC accounted for 60% of this HPB dataset. In an independent dataset of PDAC at MSK (n=262), biallelic DDR/HRm patients (n=29, 11%) had mostly germline mutations and had significantly improved median PFS on first-line platinum vs. non-platinum (13.3 [95%CI: 9.57-NR] vs 3.8 [95%CI: 2.79-NR] months, $p<0.0001$). **Conclusions:** Biallelic DDR/HRm is a distinct population of HPB cancers beyond PDAC and may confer better phenotype in DDR-targeted treatment. Further independent validation is underway. Research Sponsor: U.S. National Institutes of Health, Parker Institute for Cancer Immunotherapy MSKCC Pilot Award.

gLOH in biallelic HRm. (Total n=4051).

Gene	**Biallelic Total (n=438, 10.8%)**	**Median gLOH biallelic**	**gLOH >16% biallelic (n, %)**	**p-value (biallelic vs. no_HRD)**
no_HRD (Reference)	(3241, 80)	8.76	(469, 14.5)	
BRCA1	(23, 0.57)	22.3	(16, 69.6)	1.45E-10
BRCA2	(83, 2.0)	20.1	(66, 79.5)	1.66E-35
RAD51C	(8, 0.20)	16.7	(5, 62.5)	0.00078
RAD51B	(7, 0.17)	13.7	(3, 42.9)	0.016

4621 Poster Session (Board #229), Fri, 8:00 AM-11:00 AM

Olaparib sensitivity observed in metastatic pancreatic cancer (mPaC) with a wide spectrum of germline *BRCA1* and *BRCA2* mutations (gBRCAm). *First Author: Talia Golan, The Oncology Institute Sheba Medical Center, Tel-Hashomer, Israel*

Background: The POLO study (NCT02184195) showed that mPaC patients (pts) with a deleterious or suspected deleterious gBRCAm, and whose disease had not progressed during ≥16 weeks of first-line platinum-based chemotherapy, had significantly longer progression-free survival (PFS, primary endpoint) with maintenance olaparib vs placebo: median 7.4 vs 3.8 months, hazard ratio (HR) 0.53; $P=0.004$. PFS benefit was observed in pts with g*BRCA1*m (HR 0.40) and g*BRCA2*m (HR 0.63). The POLO study represents the largest BRCAm prevalence study in pancreatic cancer. We report additional exploratory analysis to further characterize patient gBRCAm profiles, including the relationship with efficacy. **Methods:** Pts were enrolled based on either a previously identified gBRCAm status from a local test result and subsequently confirmed by central testing, or a prospectively identified gBRCAm. Pts received maintenance olaparib 300 mg twice daily (tablet) or placebo. PFS was assessed by blinded independent central review (modified RECIST v1.1). **Results:** Of 3194 prospectively screened pts, a valid BRCA test result was obtained for 3175 (99%) from 12 countries; gBRCAm prevalence was 6.2% in pts not previously known to harbor a gBRCAm (196/3175; 1.6% g*BRCA1*m, 4.5% g*BRCA2*m). In countries (n=8) with >100 pts prospectively tested, highest gBRCAm prevalence was 9.2% (USA) and lowest 4.0% (Spain). Prevalence by race (>100 pts); 6.4% Caucasian, 4.6% Asian. In total, 154 pts with a gBRCAm satisfied all eligibility criteria and were randomized (106 prospectively tested and 48 by local test [44/48 subsequently confirmed by Myriad testing]). 37/154 (24%) randomized pts carried a common Ashkenazi Jewish founder mutation, the majority being from Israel (21 pts). From a total of 151 variants, frameshift mutations were most frequent (g*BRCA1*m 69.6%, g*BRCA2*m 71.4%) followed by nonsense mutations (g*BRCA1*m 6.5%, g*BRCA2*m 17.1%). The efficacy (PFS) of olaparib vs placebo in the different subgroups are shown in the table. **Conclusions:** In pts with mPaC enrolled in POLO, g*BRCA2*m were more prevalent than g*BRCA1*m and mutation type was predominantly frameshift. PFS benefit was consistent across a heterogenous spectrum of gBRCAm and with the previously reported full analysis set. Clinical trial information: NCT02184195. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

gBRCAm profile	**n**	**HR**	**95% CI**
Deleterious	151	0.55	0.36–0.84
Frameshift	106	0.67	0.43–1.06
Non-founder	93	0.51	0.30–0.88
Founder*	61	0.65	0.36–1.18

*common Ashkenazi Jewish and other founder mutations

4622 Poster Session (Board #230), Fri, 8:00 AM-11:00 AM

A phase I trial targeting advanced or metastatic pancreatic cancer using a combination of standard chemotherapy and adoptively transferred nonengineered, multiantigen specific T cells in the first-line setting (TACTOPS). *First Author: Brandon George Smaglo, Baylor College of Medicine, Houston, TX*

Background: Immunotherapy is emerging as a potent therapy for a range of hematologic malignancies and solid tumors. To target pancreatic carcinoma we have developed an autologous, non-engineered T cell therapy using T cell lines that simultaneously target the tumor-associated antigens (TAAs) PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin. These multiTAA-specific T-cell lines could be consistently prepared by culturing PBMCs in the presence of a Th1-polarizing/pro-proliferative cytokine cocktail, and adding autologous pepmix-loaded DCs as APCs. **Methods:** Patients with locally advanced or metastatic pancreatic adenocarcinoma who achieved cancer control with three months of standard chemotherapy were eligible to receive up to 6 infusions of multiTAA T-cells (fixed dose - $1x10^7$ cells/m^2). While also continuing the same chemotherapy, T-cells were given at monthly intervals from month four, onwards. The primary study endpoints were safety and feasibility of completing all 6 planned infusions, with secondary and tertiary endpoints including anti-tumor effects, patient survival, in vivo expansion and T cell persistence of the infused cells as well as recruitment of the endogenous immune system. **Results:** Between June 2018 and December 2019, we treated 13 patients with multiTAA T-cells. For 12/13 patients, we generated sufficient cells for all 6 planned doses; 2 doses were available for the remaining patient. Of the 13 patients, 8 maintained cancer control for a longer than expected duration, compared to historical controls. With administration of T-cells, 3 of these 8 patients had partial responses and 1 patient had a radiographic complete response (per RECIST). These responses were seen in patients with metastatic cancer. Notably, no patient had infusion-related systemic- or neuro-toxicity. Thus, infusion of autologous multiTAA-targeted T cells directed to PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin has been safe and provided durable clinical benefit to patients with pancreatic adenocarcinoma. **Conclusions:** Autologous, TAA cytotoxic T-cells can reliably be generated and safely administered to patients in conjunction with standard of care chemotherapy. In some patients, addition of T-cells may extend duration of first line therapy cancer control and induce additional tumor responses, and activation of the endogenous immune system has been documented in all patients. Exploration in a higher phase study is warranted. Clinical trial information: NCT03192462. Research Sponsor: V-Foundation and PanCan.

4623 Poster Session (Board #231), Fri, 8:00 AM-11:00 AM

Survival outcomes of patients with resectable pancreatic cancer treated with upfront surgery versus neoadjuvant chemotherapy: A retrospective tertiary care center experience. *First Author: Fang Liu, University Hospital, Cleveland, OH*

Background: The role of neoadjuvant chemotherapy (NAC) for resectable pancreatic cancer (RPC) remains controversial. We sought to compare the outcomes of NAC with upfront surgery (UFS). **Methods:** The study retrospectively enrolled patients with RPC who had UFS or received neoadjuvant FOLFIRINOX (FFX) or gemcitabine plus albumin-bound paclitaxel (GA). Between-group differences were assessed with T-test for continuous variables, and Chi-square / Fisher's exact test for categorical variables. The overall survival (OS) and recurrence-free survival (RFS) were determined by the Kaplan-Meier method with Wilcoxon test for the difference between groups. The effects of NAC vs. UFS on OS and RFS were further estimated using Cox regression controlling the effects of age and CA 19-9. **Results:** Between 2011 and 2019, 131 patients with RPC underwent UFS followed by adjuvant chemotherapy (gemcitabine, n = 65; gemcitabine/capecitabine, n = 18; FFX, n = 9). Up to 32 patients (24.4%) could not receive adjuvant chemotherapy due to surgical complications or poor recovery. Total 50 patients with RPC received NAC (FFX, n = 32; GA, n = 18). Median of 5.5 cycles of FFX or 3 cycles of GA were given prior to surgery. Resection rate was 72% (FFX 62.5%; GA 88.9%). The rest (28%) were no longer surgical candidates due to disease progression rather than toxicities from NAC. On surgical pathological review, complete resection (R0) was achieved in 83.3% of resected cases after NAC (FFX 90%; GA 75%) and 79.4% with UFS. The tumor size distribution was: pT1 11.1%, pT2 41.7%, pT3 44.4% with NAC; pT1 5.4%, pT2 18.3%, pT3 76.3% with UFS. The nodal status distribution was: pN0 27.8%, pN1 55.5%, pN2 16.7% with NAC; pN0 23.7%, pN1 71.0%, pN2 5.3% with UFS. Median pre-treatment CA 19-9 was 321.95 unit/mL in the NAC group and 79.99 unit/mL in the UFS group ($p = 0.009$). Median age was 70.5 in the NAC group and 72 in the UFS group ($p = 0.374$). There was no significant difference in the performance status between the two groups. In Kaplan-Meier analysis, there was a significant difference of OS between UFS and NAC with median OS of 648 days under UFS versus 884 days under NAC ($p = 0.029$); the median of RFS was 390 days under UFS versus 392 days under NAC ($p = 0.953$). The hazard ratio (NAC vs UFS) adjusted for CA19-9 and age was 0.7 ($p = 0.176$) for OS and 0.98 ($p = 0.918$) for RFS. **Conclusions:** We observed a signal of tumor downstaging, higher R0 rate, and improved OS with NAC compared with UFS. Further prospective trials are needed to validate these results. Research Sponsor: None.

4624 Poster Session (Board #232), Fri, 8:00 AM-11:00 AM

Liposomal irinotecan plus fluorouracil/leucovorin versus FOLFIRINOX as the second-line chemotherapy for patients with metastatic pancreatic cancer: Multicenter study of the Korean Cancer Study Group (KCSG). *First Author: Hongjae Chon, CHA Hospital, Seongnam, South Korea*

Background: There is no clear consensus on the second-line treatment for patients with metastatic pancreatic cancer (mPC). The aim of this study was to compare the efficacy and tolerability between liposomal irinotecan (nal-IRI) plus fluorouralcil/leucovorin (FL) and FOLFIRINOX (oxaliplatin/irinotecan/leucovorin/fluorouracil) in patients who failed to first-line gemcitabine-based therapy. **Methods:** In this retrospective study, 378 mPC patients who received nal-IRI/FL (n = 104) or FOLFIRINOX (n = 274) as the second-line treatment across 11 institutions from January 2015 to August 2019 were analyzed. The primary end point was progression free survival (PFS), and secondary end points were overall survival (OS), overall response rate, and tolerability. **Results:** There were no significant differences between the two groups in terms of baseline characteristics, except first-line regimen (previous gemcitabine/nab-paclitaxel, nal-IRI/FL, 85.6% vs. FOLFIRINOX, 51.5%; previous gemcitabine monotherapy, 5.8% vs. 24.5%). The median follow-up time was 6.0 months. The median PFS (nal-IRI/FL, 3.7 months vs. FOLFIRINOX, 5.0 months) and OS (nal-IRI/FL, 7.7 months vs. FOLFRINOX, 9.7 months) were comparable between two groups ($P = 0.40$ and 0.13, respectively). The overall response rate was not significantly different between two groups (nal-IRI/FL, 14% vs. FOLFRINOX, 16%; $P = 0.644$). In multivariate analysis, poor ECOG status, presence of liver metastasis, high NLR, and high CA19-9 were independent prognostic factors for PFS and OS, but chemotherapy regimen (nal-IRI/FL vs. FOLFRINOX) was not. In a subgroup analysis of patients with liver metastasis, FOLFIRINOX exerted significant PFS (median: 2.1 months vs. 4.1 months for nal-IRI/FL vs. FOLFIRINOX, respectively; $P = 0.02$) and OS (median: 6.7 months vs. 8.4 months for nal-IRI/FL vs. FOLFIRINOX, respectively; $P = 0.04$) benefit compared with nal-IRI/FL. Grade 3 neutropenia or higher were more frequently observed in FOLFIRINOX (47.2%) than nal-IRI/FL (35%) ($P = 0.033$). Grade 3 peripheral neuropathy was also common in FOLFIRIONX (5.9%) group compared with nal-IRI/FL (1.0%) ($P = 0.049$). **Conclusions:** In second-line setting for mPC after progression on gemcitabine-based therapy, both nal-IRI/FL and FOLFIRINOX regimen showed comparable efficacy and acceptable safety outcomes. FOLFIRINOX regimen might be preferentially considered in patients with liver metastasis. Research Sponsor: None.

4625 Poster Session (Board #233), Fri, 8:00 AM-11:00 AM

Real-life results from the prospective QoliXane trial of the platform for outcome, quality of life, and translational research on pancreatic cancer (PARAGON) registry. *First Author: Salah-Eddin Al-Batran, University Cancer Center Frankfurt, Institut für Klinisch-Onkologische Forschung and IKF Klinische Krebsforschung GmbH am Krankenhaus Nordwest, Frankfurt, Germany*

Background: Gemcitabine and nab-paclitaxel (NPG) is standard first-line therapy for metastatic pancreatic cancer (mPC), but the pivotal study did not include quality of life (QoL) analyses. **Methods:** The QOLIXANE-PARAGON study started as a prospective, non-interventional, multicenter study conducted in Germany and transitioned into a permanent registry for pancreatic cancer patients (pts) considering all types of treatments. This report focuses on the pts enrolled into the QOLIXANE portion of the study. Pts were recruited from 95 German centers. QoL was prospectively measured via EORTC-C30 questionnaires (prior to and every month thereafter): therapy and efficacy parameters were prospectively collected. QoL and efficacy endpoints were analyzed in the intention-to-treat population (ITT). The primary endpoint was the rate of pts without deterioration of QoL/Global Health Score (QoL/GHS) at 3 months. **Results:** 600 pts were enrolled. Mean GHS/QoL score at baseline was low and was 46.2 (SD 22.8). Median progression-free survival was 5.85 months (95% CI, 5.23 to 6.25). Median overall survival (OS) was 8.91 months (95% CI, 7.89 to 10.19). The KM-analysis showed that 61% and 41% of pts had maintained QoL/GHS after 3 and 6 months, respectively. Median time to deterioration of QoL/GHS was 4.68 months (95% CI, 4.04 to 5.59). Mean QoL/GHS improved from 46.1 (SD 22.7) at baseline to 52.8 (SD 21.3) after 6 months. In the QoL response analysis, 34.6%, 37.4% and 28% of evaluable pts had improved, stable and worse QoL/GHS after 3 months, respectively. In the Cox regression analysis, GHS/QoL scores strongly predicted survival with a HR of 0.86 ($p < 0.0001$). **Conclusions:** QoliXane the largest study on QoL of mPC. It shows that time to deterioration of QoL is short but that a relevant group of mPC in first line have improved or maintained QoL after 3 and 6 months and that QoL is a predictor of pts outcome. Clinical trial information: NCT02691052. Research Sponsor: Celgene.

4626 Poster Session (Board #234), Fri, 8:00 AM-11:00 AM

POLO: Quality-adjusted (QA) progression-free survival (PFS) and patient (pt)-centered outcomes with maintenance olaparib in pts with metastatic pancreatic cancer (mPaC). *First Author: Hyun Kyoo Yoo, AstraZeneca, Cambridge, United Kingdom*

Background: In the Phase III POLO trial (NCT02184195), maintenance olaparib significantly prolonged PFS vs placebo in pts with a germline *BRCA1* and/or *BRCA2* mutation (gBRCAm) and mPaC (median 7.4 vs. 3.8 months). The aim of maintenance treatment is to extend PFS and survival without compromising health-related quality of life due to adverse events. The duration of time spent without symptoms or toxicities (TWiST) and the QA-PFS were assessed in a post hoc analysis of the POLO trial. **Methods:** Patients were randomized 3:2 to receive maintenance olaparib (tablets; 300 mg bid) or placebo. Restricted mean (RM)-PFS was calculated by estimating the area under the Kaplan–Meier PFS curve between randomization and 29.8 months after randomization (maximum follow-up for the placebo arm in POLO). Patient-centered outcomes were assessed by QA-PFS (derived from the product of the EQ-5D-5L single-index utility score from randomization to disease progression and RM-PFS) and TWiST (RM-PFS minus time with toxicity after randomization). **Results:** RM-PFS was significantly longer with olaparib, with a between-treatment difference of 4.8 months (P=0.009; Table). Over this period, no significant or meaningful differences in mean EQ-5D-5L index were observed between treatment groups. The corresponding mean QA-PFS was significantly longer with olaparib vs placebo. TWiST analysis demonstrated a benefit with olaparib over placebo (Table): between-arm difference, 3.8 months (P=0.039) for the primary analysis (criteria 1: grade ≥2 nausea, vomiting or fatigue). Sensitivity analysis (criteria 1 plus abdominal pain, diarrhea, decreased appetite or constipation) also revealed a trend toward benefit with olaparib (difference: 3.4 months, P=0.062). **Conclusions:** Consistent with the primary PFS analysis of the POLO trial, RM-PFS and QA-PFS were significantly longer with maintenance olaparib than with placebo. As demonstrated by the findings of the TWiST analyses, the PFS benefit observed with olaparib in pts with a gBRCAm and mPaC persists even when symptoms of toxicity are considered. Clinical trial information: NCT02184195. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, US.

Endpoints (months)	Placebo N=62	Olaparib N=92	Difference (P)
RM-PFS	7.01	11.78	4.77 (0.009)
Mean EQ-5D-5L*	0.81	0.78	−0.03 (0.28)
Mean QA-PFS	5.65	9.18	3.53 (0.016)
Mean TWiST (primary analysis)	6.89	10.69	3.81 (0.039)
Mean TWiST (sensitivity analysis)	6.80	10.18	3.39 (0.062)

*Higher scores indicate better health status.

4628 Poster Session (Board #236), Fri, 8:00 AM-11:00 AM

Safety and efficacy of biweekly gemcitabine in combination with capecitabine (GemCap) in elderly and frail patients (pts) with resected pancreatic cancer (PC). *First Author: Nausheen Hakim, Northwell Health Cancer Institute, Lake Success, NY*

Background: ESPAC-4 study showed that GemCap conferred a survival benefit over gemcitabine monotherapy in resected PC patients. ESPAC-4 included patients with median age of 65 years (37-81) and ECOG performance status (PS) of 0 (43%), 1 (54%) and 2 (2%) who received a median cumulative dose of gemcitabine of 15,000 mg/m2, capecitabine. Here we present our experience with an adopted biweekly regimen of GemCap in patients who were ≥ 75 years and those who were deemed not suitable for ESPAC-4 regimen. **Methods:** Patients ≥ 75 years with resected PC, ECOG PS of 0-2 and no prior treatments were included. Patients were treated with a modified regimen of gemcitabine (1000-2000 mg/m2) every 2 weeks and capecitabine (800-1000 mg/m2) day 1-7 every 2 weeks. Patients were evaluated for progression-free survival (PFS), overall survival (OS) and sites of recurrence. Toxicities were graded according to NCI CTCAE v5.0. **Results:** Thirty-five (22M, 13F) patients, ≥ 75 (median age 79) treated with biweekly Gem-Cap adjuvant treatment. 7 (28%) patients had ECOG PS of 1 and 28 (72%) had ECOG PS of 2. There were 5, 7 and 16 patients with stage I, II and III disease. Nine patients (25%) had R1 and 26 (75%) had R0 resection. The median PFS and OS were 8.0 months and 22.0 months. Nine (25%) had local recurrence, 21 (60%) had metastatic disease and 3 (8.6%) had NED. Two patients were lost to follow-up. The most frequent toxicities were grades 1-2 anemia (20%), thrombocytopenia (8%) and hand-foot syndrome (HFS) (10%). Grade ≥3 included diarrhea (4%) and HFS (1%) with no treatment-related discontinuations. Treatment compliance was 100%. Delays were necessary in 7% of cases and dose reduction was required in 4% of cases. There was no treatment related death. **Conclusions:** This schedule of biweekly GemCap regimen suggests an acceptable option in for elderly, frail patients with PC and warrants further exploration in patients not suitable for FOLFIRINOX, full dose GemCap or a clinical trial. This regimen required fewer dose reduction, omission or delays and allowed to administer pegylated-filgrastim. Previous studies have also shown decreased toxicity and equal efficacy of 7/7 schedule of capecitabine. Moreover, fewer visits to oncology and related expense do favor towards benefit. Additionally, this tolerable regimen is ideal to be combined with immunotherapy in clinical trials for this patient population. Research Sponsor: None.

4629 Poster Session (Board #237), Fri, 8:00 AM-11:00 AM

Enrichment of alterations in targetable molecular pathways in KRAS wild-type (WT) pancreatic cancer (PC). *First Author: Philip Agop Philip, Karmanos Cancer Institute, Detroit, MI*

Background: Genomic profiling has identified KRAS mutations in 88-90% of PC. KRAS WT tumors represent a molecularly heterogeneous group that may harbor targetable alterations (TA). We studied KRAS WT PC using NextGen sequencing (NGS) and whole transcriptome sequencing (WTS) to characterize the molecular landscape of this unique group and to assess the prevalence of TA. **Methods:** A total of 1164 PC tumors were tested at Caris Life Sciences by NGS (592 genes), WTS (NovaSeq), IHC and fragment analysis. Comparison of KRAS WT vs. mutant (MT) was done by Fisher-Exact or Chi2 and was corrected for multiple tests. **Results:** The KRAS WT cohort included 144 tumors (12.4%). No differences were seen in gender (female: 46% in both WT & MT) and age (median: 66 & 67) compared to KRAS MT. In KRAS WT tumors, targetable fusions tested by WTS and pathogenic mutations by NGS were seen in 22% (32 of 144) and 52% (75 of 144) respectively; potentially targetable amplifications (amp) were seen in 5 additional tumors. No TA were seen in 22% of WT tumors. Key alterations are in Table. Alterations inducing MAPK activation, including BRAF, RAF1, NF1 and GNAS changes were seen in 38 (26%) tumors. Frequent alterations were seen in FGFR genes (11 tumors), MET (4, including 1 exon 14 skip), and ERBB receptor and ligands (10). Fusions in ALK, ROS1, RET and NOTCH1 were seen (8), largely exclusive of other drivers. Wnt, PI3K, chromatin remodeling (CR) and DDR changes were common and sometimes seen concurrent with other alterations. Compared to KRAS MT, no difference of PD-L1 or TMB-H was seen. BRAF, APC, PBRM1, CTNNB1 mutations, MDM2 amp, gene fusions and MSI-H/dMMR were all more frequent in KRAS WT tumors (corrected $p < 0.05$). **Conclusions:** KRAS WT PC is enriched with TA (e.g., BRAF, ALK, ROS1, NRG1, MSI-H). The use of WTS in combination with NGS identifies activated molecular pathways in the majority of KRAS WT tumors. Based on our findings, comprehensive profiling of PC at the DNA and RNA level is recommended to provide patients with therapeutic opportunities beyond standard treatments. Research Sponsor: None.

KRAS WT PC (mutation = M; amp = A; fusion = F).

	Alterations	N
MAPK: 38	BRAF total	27
	BRAF-F	10
	M-class I	6
	M-class II inframe-del I other	4|5
	M- class III	2
	RAF1 F	2
	NF1 M	5
	GNAS M	5
	KRAS A	2
Met: 4	Met A	3
	Met F I exon14 skip	1|1
FGFRs: 11	FGFR2 F I A I M	6|1|1
	FGFR3 F I A	1|1
	FGFR4 A	1
ERBB & ligands: 10	ERBB2 M I A I F	3|2|1
	EGFR A I F	1|1
	NRG1 F	2
Wnt: 19	APC M	8
	CTNNB1 M	5
	RNF43 M	5
	RSPO3 F	1
DDR: 19	BRCA2 I 1 M	9|1
	ATM M	6
	CHEK2 M	1
	PALB2 M	2
PI3K: 9	PIK3CA M	4
	PTEN M	2
	AKT2 I 3 A	2|1
Additional F: 8	ALK F	3
	ROS1 F	1
	RET F	3
	NOTCH1 F	1
CR: 30	PBRM1 M	8
	BAP1 M	3
	ARID1A M	18
	ARID2 M	4

4630 Poster Session (Board #238), Fri, 8:00 AM-11:00 AM

Outcomes and Immunogenicity of pancreatic cancer stratified by the HRDetect score. *First Author: Grainne M. O'Kane, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: The HRDetect score uses whole genome sequencing (WGS) to incorporate patterns of substitution base signatures and structural variation to identify tumours deficient in homologous recombination repair (HRD). HRD-tumours, with a higher mutational burden, may be more immunogenic. **Methods:** We applied HRDetect to 182 resected pancreatic cancers (PDA) and 233 advanced PDA enrolled on the COMPASS trial; both cohorts underwent WGS after tumour enrichment. Patients were classified as high(^{hi}) or low(^{lo}) according to the published score threshold of 0.7; clinical characteristics and survival outcomes were determined. Immunogenicity of the cohorts was explored by analyzing cytolytic activity (CYT) as measured by RNA expression of perforin and granzyme A. **Results:** 14% of resected (25/182) and 14% of advanced cases (32/233) were considered HRDetect^{hi} . The median age at PDA diagnosis was younger in HRDetect^{hi} vs HRDetect^{lo} (61 vs 66 years, p = 0.005), with no difference in sex between groups. Of the 57 cases identified, 37 (65%) were considered true HRD-PDA with inactivation of *BRCA1, BRCA2, PALB2, RAD51C* and *XRCC2*. The remaining 20 cases, were considered false positives for HRD; of these 7 had evidence of a tandem duplicator phenotype with duplications ranging from 10Kbp to 1Mbp in size and 13 had no defining genomic characteristics of the HRD-subtype. In resected PDA, the HRDetect score after adjusting for stage, was not prognostic. In contrast in a multivariable analysis of advanced cases, both HRDetect (HR 0.51, 95% CI 0.30-0.87, p = 0.01) and the Moffitt RNA classifier were highly prognostic (HR 1.99, 95% CI 1.32-3.00, p = 0.0001) with improved survival in HRDetect^{hi} and classical PDA. Of patients receiving platinum in advanced disease (n = 128) HRDetect^{hi} PDA had longer survival compared to the HRDetect^{lo} (15.6 vs. 9.9 months, p = 0.02) although the interaction term between chemotherapy regimen (gemcitabine vs. platinum) and HRDetect score was not significant in this cohort. HRDetect^{hi} tumours had increased cytolytic activity than HRDetect^{lo} PDA; furthermore, within the cohort of HRDetect^{hi} PDA, higher CYT scores were evident in primary lesions compared to metastatic sites sequenced. **Conclusions:** A high HRDetect score is prognostic in advanced PDA where patients treated with platinum have longest survival. HRDetect^{hi} tumours have increased cytolytic activity with differences observed between primary and metastatic lesions. Research Sponsor: Ontario Institute of Cancer Research, Pancreas Cancer Canada.

4631 Poster Session (Board #239), Fri, 8:00 AM-11:00 AM

Paclitaxel protein bound (A) plus gemcitabine (G) plus cisplatin (C), and paricalcitol (P)neoadjuvant therapy for localized pancreatic ductal adenocarcinoma (PDAC). *First Author: Erkut Hasan Borazanci, HonorHealth, Scottsdale, AZ*

Background: Localized PDAC management has recently evolved. Due to concerns over micro metastases at diagnosis the use of neoadjuvant chemotherapy for PDAC has become more common. Typical therapies involve the use of multiagent systemic chemotherapies with or without radiation therapy. In retrospective studies, Cancer Antigen 19-9 (CA 19-9) normalization in borderline resectable (BR) and locally advanced (LA) PDAC has been associated with greater OS. The addition of cisplatin (C) to gemcitabine (G) and paclitaxel protein bound (A), has shown promising clinical data in a previously reported study in advanced PDAC [JAMA Oncol. 2020;6(1):125-132]. We conducted a prospective, phase 2 clinical trial of patients with resectable (R), BR, and LA PDAC utilizing a regimen combining A + G + C + paricalcitol (P) with the primary endpoint of CA 19-9 normalization (NCT03138720). **Methods:** Eligibility criteria include patients with histologically confirmed R, BR, or LA PDAC, elevated CA 19-9, and a KPS $\geq$ 70% with normal end organ function. Doses are A 125 mg/m2, G 1000 mg/m2, C 25 mg/ m2, P at a fixed dose of 25 μg on days 1, 8 of a 21-day cycle (all treatment IV). Primary objective is to evaluate CA 19-9 normalization with the neoadjuvant chemotherapy. Secondary objectives are to assess R0 rate, pathologic complete response (pCR), safety and tolerability, radiologic response rate, and 2 year overall survival (OS) from date of study entry. Exploratory objectives include evaluating imaging biomarkers and vascular involvement by tumor in relation to therapy. **Results:** To date 24 of the planned 24 patients have been enrolled. 13 male, 11 female; age range 49 to 84 yo. Patient classifications is 8 R; 7 BR; 9 LAPC. Median baseline CA 19-9 156 (range 45-3674). Most common drug related grade (gr) 3-4 adverse events (AEs) are: thrombocytopenia gr 3 29%, gr 4 25%, anemia gr 3 45.8%, gr 4 4.2%, and hypophosphatemia gr 3 8.3%. CA 19-9 normalization occurred in 50% (12/24) who have completed at least 1 cycle of treatment. To date, 14 individuals went to surgery, with 13/14 achieving R0, (1 pCR). Overall response rate in measurable patients is 38% (1 CR, 8 PR). Median OS and 2-year survival data are not yet matured. **Conclusions:** In patients with non-metastatic PDAC, the use of A+G+C+P resulted in a CA 19-9 normalization rate in 50% of individuals. The study is ongoing and OS data is maturing. Clinical trial information: NCT03138720. Research Sponsor: HonorHealth Foundatio, Marley Foundation, Stand Up to Cancer, Seena Magowitz Foundation.

4632 Poster Session (Board #240), Fri, 8:00 AM-11:00 AM

Interim data: Phase I/IIa study of EGFR-targeted EDV nanocells carrying cytotoxic drug PNU-159682 (E-EDV-D682) with immunomodulatory adjuvant EDVs carrying α-galactosyl ceramide (EDV-GC) in patients with recurrent, metastatic pancreatic cancer. *First Author: Joanne Lundy, Peninsula and Southeast Oncology, Frankston, VIC, Australia*

Background: Targeted EDV nanocells loaded with doxorubicin and microRNA16a have shown excellent safety profiles in Phase I trials in recurrent glioma and mesothelioma. This planned safety analysis of an ongoing first-in-human, open label Phase I/IIa study in patients with treatment-refractory metastatic pancreatic cancer, assesses safety, biologic and clinical activity of EGFR-targeted EDV nanocells carrying cytotoxic drug PNU-159682, designed to overcome drug resistance, combined with EDV nanocells carrying immunomodulatory adjuvant α-galactosyl ceramide, designed to stimulate anti-tumour immune response. **Methods:** 9 patients with advanced pancreatic cancer enrolled in the dose escalation phase to evaluate safety of the EDV combination. Doses gradually escalated from 2×10^9 EDVs/dose to a maximum of 7×10^9 EDVs/dose in Week 7, with subsequent dosing at the maximum dose achieved in Cycle 1. iRECIST criteria was used to assess tumour response after each cycle, and blood was collected each cycle for cytokine and PBMC analysis. **Results:** Combination EDVs were well tolerated with no DLTs, and no drug related SAEs. A minority of patients experienced G1 infusion reactions, which responded promptly to supportive treatment. PR or SD was achieved at 8 weeks in 8/9 patients (CBR 89%), with responses confirmed at 4 months in 4/5 evaluable patients (80%), with 2 durable responses seen beyond 6 months. Exploratory analyses have revealed elevation of IFN-α and IFN-γ in almost all evaluable patients (6/8). In addition, we observed elevated CD8+ T cells (2/8), iNKT, dendritic and NK cells (3/8), and a reduction in exhausted CD8+ T cells (3/8), suggesting activation of both innate and adaptive immune responses. **Conclusions:** EDVs carrying the cytotoxic drug and immune adjuvant are safe and well tolerated. Early signals point to durable responses, possibly related to the development of an innate and adaptive immune response along with cytotoxic effects on drug resistant tumour cells. The Phase IIa study plans to enrol an additional 35 patients to further evaluate safety and anti-tumour efficacy. Clinical trial information: ACTRN12619000385145. Research Sponsor: EnGeneIC Pty Ltd.

4633 Poster Session (Board #241), Fri, 8:00 AM-11:00 AM

Single-nucleus RNA-seq of frozen archival primary pancreatic ductal adenocarcinoma uncovers multi-compartment intratumoral heterogeneity associated with neoadjuvant treatment. *First Author: William L. Hwang, Harvard Radiation Oncology Program, Boston, MA*

Background: Pancreatic ductal adenocarcinoma (PDAC) remains a treatment-refractory disease and existing molecular subtypes do not inform clinical decisions. Previously identified bulk transcriptomic subtypes of PDAC were often unintentionally driven by "contaminating" stroma. RNA extraction from pancreatic tissue is difficult and prior single-cell RNA-seq efforts have been limited by suboptimal dissociation/RNA quality and poor performance in the setting of neoadjuvant treatment. We developed a robust single-nucleus RNA-seq (sNuc-seq) technique compatible with frozen archival PDAC specimens. **Methods:** Single nuclei suspensions were extracted from frozen primary PDAC specimens (n = 27) derived from patients with (borderline)-resectable PDAC who underwent surgical resection with or without neoadjuvant chemoradiotherapy (CRT). Approximately 170,000 nuclei were processed with the 10x Genomics Single Cell 3' v3 pipeline and gene expression libraries were sequenced (Illumina HiSeq X). **Results:** Distinct nuclei clusters with gene expression profiles/inferred copy number variation analysis consistent with neoplastic, acinar, ductal, fibroblast, endothelial, endocrine, lymphocyte, and myeloid populations were identified with proportions similar to corresponding multiplexed ion beam imaging. Non-negative matrix factorization revealed intra-tumoral heterogeneity shared across patients. Neoplastic cells featured eight distinct transcriptional topics characterized by developmental (epithelial, mesenchymal, endoderm progenitor, neural progenitor) and environmental (anabolic, catabolic, cycling, hypoxic) programs. CAFs exhibited four different transcriptional topics (activated/desmoplastic, myofibroblast, neurogenic, osteochondral). Differential gene expression and gene set enrichment analyses demonstrated that CRT was associated with an enrichment in myogenic programs in CAFs, activation pathways in immune cells, and type I/II interferons in malignant cells. CRT was also associated with a depletion in developmental programs within malignant cells. **Conclusions:** We uncovered significant intratumoral heterogeneity and treatment-associated differences in the malignant, fibroblast, and immune compartments of PDAC using sNuc-seq. Deconvolution of clinically-annotated bulk RNA-seq cohorts and characterization of intercellular interactions with receptor-ligand analysis and spatial transcriptomics are ongoing. Research Sponsor: Lustgarten Foundation, Conquer Cancer Foundation of the American Society of Clinical Oncology, U.S. National Institutes of Health.

4634 Poster Session (Board #242), Fri, 8:00 AM-11:00 AM

A phase I study of nanoliposomal irinotecan and 5-fluorouracil/folinic acid in combination with interleukin-1-alpha antagonist for advanced pancreatic cancer patients with cachexia (OnFX). *First Author: Andrew Eugene Hendifar, Samuel Oschin Cancer Center, Cedars-Sinai Medical Center, Los Angeles, CA*

Background: Interleukin-1-alpha (IL-1α) promotes tumor inflammation by shaping the tumor microenvironment, including tumor infiltrating myeloid cell recruitment, angiogenesis, and skewing and suppression of anti-tumor immunity. IL-1a inhibition in cancer subjects increased lean body mass and decreased fatigue, pain, and appetite loss. We report results of a single site phase 1 trial for an IL-1α antagonist (bermekimab) in combination with nanoliposomal irinotecan (Nal-Iri) and 5-fluorouracil (5FU)/folinic acid (FA) in patients with advanced pancreatic adenocarcinoma and cachexia who have failed gemcitabine-based chemotherapy. **Methods:** A Bayesian adaptive design based on escalation with overdose control was used. Data are presented as frequency (percentage, %) for categorical variables and mean ($\pm$ standard deviation) for continuous variables. Lean body mass (LBM) and fat mass were assessed at cycle 1 and 3, and T-test was used to assess changes. **Results:** Of 21 pts enrolled, 18 were evaluable. Median age was 68. Bermekimab in combination with nanoliposomal irinotecan (70 mg/m2) and 5-fluorouracil (2400mg/m2) was well tolerated at the highest dose level (12mg/kg). 10 pts experienced grade 3/4 toxicities including sepsis, anemia, hypokalemia, neutropenia, or leukopenia. There were no instances of grade 3/4 diarrhea. Ten pts (56%) had weight stability (< 0.1 kg/BMI). Efficacy results include PR (n = 4, 22%), SD (n = 13, 72%), and PD (n = 1, 6%). PFS 7.7 m (95% CI: 4.34-12.73) and OS 10.5 m (95% CI: 5.79-17.70) were reported. LBM and fat mass change was -1.6 kg ($\pm$ 2.0; p-value = 0.003) and -1.4 kg ($\pm$ 1.7; p-value = 0.004). CRP was 20.4 ($\pm$ 35.6) at cycle 1 and decreased significantly (p-value = 0.005). Serum VEGF decreased from C1 to C3 (p-value = 0.007). QLQ-PAN26 domains improved, particularly hepatic function (p = 0.04). FAACT scores improved for functional well-being (p = 0.02). Average daily step counts increased by 589 steps/day (p = 0.29) and resting heart rate decreased by 2.5 beats per minute (p = 0.005), as assessed by actigraphy. **Conclusions:** Bermekimab, nano-liposomal irinotecan and 5-fluorouracil in refractory pancreatic cancer patients with cachexia was well-tolerated with promising efficacy and improvements in patient performance. Clinical trial information: NCT03207724. Research Sponsor: Ipsen.

4635 Poster Session (Board #243), Fri, 8:00 AM-11:00 AM

A single-arm, open-label, phase I study of CPI-613 (Devimistat) in combination with gemcitabine and nab-paclitaxel for patients with locally advanced or metastatic pancreatic adenocarcinoma. *First Author: Angela Tatiana Alistar, Atlantic Health System, Morristown, NJ*

Background: Glycolic and mitochondrial metabolism are aberrant in pancreatic cancer and translate into chemoresistance. Inhibition of glutamine metabolism can potentially synergize with therapies that increase intracellular reactive oxygen species, such as nab-paclitaxel. CPI- 613 is a novel antimitochondrial agent developed by Rafael Pharmaceuticals that showed promising clinical activity in combination with modified FOLFIRINOX in patients with stage IV pancreatic cancer. Preclinical data suggested possible synergy of CPI-613 with nab-paclitaxel. **Methods:** Single arm, open-label, phase I study of CPI-613 with gemcitabine and nab-paclitaxel in patients with locally advanced or metastatic pancreatic cancer to determine MTD, safety, and preliminary efficacy of CPI-613 in combination with chemotherapy. Key eligibility criteria included: histologically documented and measurable locally-advanced or metastatic, PDAC. ECOG performance status 0-2; and first line systemic treatment. CPI-613 was infused intravenously with a starting dose of 500 mg/m^2 followed by modified dose nab-paclitaxel (100mg/m2) and gemcitabine (800 mg/m2) on Days 1, 8, and 15 of a 28-day cycle. The the primary endpoint, the MTD of CPI-613 was determined by a two-stage, dose-escalation schema, with 6-month treatment duration for patients exhibiting treatment response. Secondary endpoints were treatment-related adverse events, complete response (CR) and partial response (PR). **Results:** From February 2018 to 2020, 26 patients were screened, (23 metastatic and 3 locally advanced), 22 patients enrolled and 18 patients underwent a restaging scan. As of the time of submission 3 patients are still on active treatment. Patient demographics were: median age of 65, ECOG was 0-1, The MTD of CPI- 613 was determined to be 1500 mg/m^2. The dose limiting toxicities were not achieved. Overall the treatment was well tolerated with toxicities mainly related to chemotherapy; most common grade 3 and 4 toxicities were hematologic toxicity and neuropathy. 1 patient achieved CR, 9 PR, 8 stable disease and 1 progressive disease for an objective response rate of 50% with a CR rate of 5.5%. **Conclusions:** The results demonstrate that CPI 613 can be safely administered with gemcitabine and nab-paclitaxel at doses up to 1,500 m/g2. Efficacy data suggest synergy with chemotherapy. Further clinical studies of CPI-613 efficacy in pancreatic cancer are in progress. Clinical trial information: NCT03435289. Research Sponsor: Rafael Pharmaceuticals, 1 Duncan Drive, Cranbury, NJ, Atlantic Health System.

4636 Poster Session (Board #244), Fri, 8:00 AM-11:00 AM

Pharmacokinetically-guided 5-FU dose optimization within the preoperative FOLFOXIRI regimen in resectable pancreatic cancer patients. *First Author: Anna Vilalta, Department of Medical Oncology, Clinica Universidad de Navarra, University of Navarra, Pamplona, Spain*

Background: Neoadjuvant therapy is an increasingly used approach in patients with resectable pancreatic cancer (PC). A positive link between chemotherapy dose intensity and patients' outcome has been suggested in PC. The aim of this study was to rule out whether 5-FU pharmacokinetic (PK) parameters correlate with outcome in resectable PC patients treated with preoperative FOLFOXIRI. **Methods:** Patients with resectable and borderline resectable PC treated with Oxaliplatin (85mg/m^2), Leucovorin (400mg/m^2), Irinotecan (150 mg/m^2) and 5-FU (initial dose of 3200 mg/m^2 in 46h infusion and subsequent doses based on PK-guided dose adjustements targeting an AUC of 25-30 mcg*h/ml) were included. 5-FU PK analysis was performed taking two plasma samples during 5-FU infusion in at least two cycles. Drug concentrations were analysed by High-Perfomanced Liquid Chromatography. After induction polychemotherapy (IPCT), patients with no progressive disease received chemoradiation (CRT) (50.4 Gy with concurrent Capecitabine and Oxaliplatin) followed by surgical resection 4 to 6 weeks after the completion of CRT. Subsequent follow-up until disease progression was remained. An exploratory analysis with Log-Rank test was performed to assess progression free survival (PFS) based on 5-FU AUC values. **Results:** From November 2012 to October 2018, 29 patients were retrospectively assessed: median age 63 (46-75); M/F rate 20/9; R0 resection rate of 90% in the intention-to-treat analysis. The pathological response according to CAP classification was 0, 1, 2 and 3 in 14, 58, 19.5 and 8.5%, respectively; and median number of resected lymph nodes was 11 (2-22), with lymph node infiltration (ypN1) in 14% of patients. Grade 3-4 IPCT related toxicities and grade 3 CRT related toxicities were reported in 40 and 30% of patients, respectively. Median PFS was 723 days (24 months) and median 5-FU AUC 28.5 mcg*h/ml (23-53). Median PFS for patients with 5-FU AUC $\geq$27 mcg*h/ml was 29 months versus 15 months in patients with 5-FU AUC $<$ 27 mcg*h/ml (adjusted hazard ratio for disease progression 0.223; 95% CI = 0.059-0.848; p = 0.028; in a model controlled by age, sex and irinotecan dose intensity). **Conclusions:** 5-FU pharmacokinetic parameters achieving a target of AUC $\geq$ 27 mcg*h/ml seem to correlate with longer PFS in this subset of patients. Research Sponsor: None.

4637 Poster Session (Board #245), Fri, 8:00 AM-11:00 AM

Olaparib (O) in patients (pts) with pancreatic cancer with BRCA1/2 inactivating mutations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study. *First Author: Eugene R Ahn, Cancer Treatment Centers of America, Zion, IL*

Background: TAPUR is a phase II basket study evaluating anti-tumor activity of commercially available targeted agents in pts with advanced cancers with genomic alterations. Results in a cohort of pancreatic cancer pts with germline or somatic BRCA1/2 inactivating mutations treated with O are reported. **Methods:** Eligible pts had advanced pancreatic cancer, no standard treatment (tx) options available, measurable disease, ECOG Performance Status (PS) 0-2, and adequate organ function. Genomic testing was performed in CLIA-certified, CAP-accredited site selected labs. Pts received O tablets or capsules dosed at 300 mg (n=27) or 400 mg (n=3), respectively, orally twice daily until disease progression. Simon 2-stage design tested the null disease control (DC) (objective response (OR) or stable disease at 16+ weeks (wks) (SD16+) according to RECIST) rate of 15% vs. 35% (power = 0.85; α = 0.10). If $\geq$2 of 10 pts in stage 1 have DC, 18 more pts are enrolled. If $\geq$7 of 28 pts have DC, the tx is worthy of further study. Secondary endpoints are progression-free survival (PFS), overall survival (OS), and safety. **Results:** Thirty pts with *BRCA1/2* inactivating mutations were enrolled from Nov 2016 to Aug 2019; 20 were previously treated with platinum based therapy. Two were not evaluable and excluded from efficacy analyses. Demographics and outcomes are summarized in Table. One partial response (PR) and 7 SD16+ were observed for DC and OR rates of 31% (90% CI: 18% - 40%) and 4% (95% CI: 0% - 18%), respectively. Seven pts had at least one grade 3 AE or SAE at least possibly related to O including anemia, diarrhea, fever, elevated liver enzymes, enterocolitis, increased bilirubin, and oral mucositis. **Conclusions:** Monotherapy O showed anti-tumor activity in heavily pre-treated pts with pancreatic cancer with germline (5/12 pts with OR or SD16+) or somatic (3/16 pts with OR or SD16+) *BRCA1/2* inactivating mutations extending findings of recent studies of O in pts with advanced pancreatic cancer. Clinical trial information: NCT02693535. Research Sponsor: AstraZeneca, Pharmaceutical/Biotech Company.

Demographics and Efficacy Outcomes (N=30).

Median age, yrs (range)	**60 (44, 78)**
Male, %	63
ECOG PS, %	
0	30
1	57
2	13
Prior systemic regimens, %	
1-2	47
≥3	53
DC rate, % (OR or SD16+) (90% CI)[1]	31 (18, 40)
OR rate, % (95% CI)[1]	4 (0, 18)
Median PFS, wks (95% CI)[1]	8.1 (7.9, 15.1)
Median OS, wks (95% CI)[1]	43.0 (28.1, NA)
1 year OS rate, % (95% CI)[1]	47.2 (19.7, 70.7)

[1]N=28

4638 Poster Session (Board #246), Fri, 8:00 AM-11:00 AM

A phase II trial of preoperative FOLFIRINOX followed by gemcitabine-based chemoradiotherapy in patients with borderline resectable pancreatic ductal adenocarcinoma (BR PDAC). *First Author: Michael Wysota, Montefiore Medical Center, Bronx, NY*

Background: Preoperative (preop) therapy is widely accepted as the standard of care for patients (pt) with BR PDAC with limited evidence for a specific regimen. This study aimed to assess the efficacy of FOLFIRINOX (FOL) chemotherapy followed by gemcitabine-based chemo-radiotherapy (RT) as preop therapy in pt with BR-PDAC. **Methods:** This single arm Simon two stage phase II trial in pt with BR PDAC was conducted in two phases. The first phase included 4 cycles of FOL, and the second included weekly gemcitabine (1000 mg/m2) for 6 cycles with concomitant intensity-modulated RT (50.4 Gy in 28 fractions)(Gem/RT).The primary aim was to compare R0 resection rate (H_0: $\leq$40% vs $H_a \geq$60%) using one-sample one-sided Z test. Secondary outcomes, including overall survival (OS) and progression-free survival (PFS) were assessed using Kaplan-Meier method. **Results:** Of 22 enrolled pt, 18 (81.8%) completed preoperative treatment. Median age at diagnosis was 63.4 years and 12 (54.5%) were female. There were 10 (45.5%) Hispanics, 4 (18.2%) non-Hispanic black, and 8 (36.4%) non-Hispanic white. Tumor location was predominantly head/neck (21, 95.5%), 15 (68.1%) had T2/3, and 9 (40.9%) had N2 (clinical) disease. Fourteen (64.6%) pt, had venous involvement, 5 (22.7%) had arterial, and 3 (13.6%), both. In the first phase, 20 (90.9%) completed 4 cycles of FOL, 6 (27.3%) required dose-reduction and dose was delayed in 12 (54.5%). Stable disease (SD) was achieved in 10 (52.6%), partial response (PR) in 8 (42.1%) and disease progression (PD) in 1 (5.3%) pt. Of 21 pt that entered the second phase, 18 (85.7%) completed 6 cycles of Gem/RT, 5 (26.3%) required dose-reduction and dose was delayed in 6 (31.6%). SD was achieved in 10 (55.6%), PR in 3 (16.7%) and PD in 5 (27.8%). All pt experienced at least one grade 1 adverse event (AE) and 12 (54.5%) at least one grade 3/4 AE, of which neutropenia was the most common-11 (50%). Of the 15 (68.1%) pt who underwent surgical resection, 12 (80%) achieved R0 margins and 5 (33.3%) required vascular reconstruction. The R0 rate among pt that received $>$1 cycle of FOLFIRINOX was 54.5%. Adjuvant chemotherapy was offered to 6/15 pt (40%). The PFS and OS will be reported. **Conclusions:** An R0 resection rate of 54.5% with this limited sample size is significant at the 10% level. Neoadjuvant FOLFIRINOX followed by concomitant Gem/RT was well-tolerated. The study will be amended to include adjuvant FOL in line with the PRODIGE intergroup adjuvant study results. Clinical trial information: NCT01897454. Research Sponsor: None.

4639 Poster Session (Board #247), Fri, 8:00 AM-11:00 AM

FOLFIRINOX de-escalation in advanced pancreatic cancer (aPC): A multicenter real-life study. *First Author: Hortense Chevalier, University of Lille, Lille, France*

Background: FOLFIRINOX (5FU, irinotecan, and oxaliplatin) is a reference first line (L1) of chemotherapy (CT) in fit patients (Pts) with advanced pancreatic cancer (aPC). Limiting toxicities (in particular, neuropathy) are frequent and maintaining quality of life without a lack of efficacy is a crucial need. Modalities and efficacy of maintenance strategy in aPC remain scarcely studied. Our study describes the French practices of a FOLFIRINOX de-escalation and maintenance in a real-life multicentric cohort. **Methods:** We performed a retrospective multicentric study in 5 French centers. Pts receiving FOLFIRINOX L1 for aPC were recruited between January 2011 and December 2018. FOLFIRINOX de-escalation was defined as stopping oxaliplatin and/or irinotecan in patients without tumor progression, after at least 4 cycles of FOLFIRINOX. Maintenance schedules were oral capecitabine or intravenous (IV) 5FU, FOLFOX or FOLFIRI. Primary endpoint was overall survival (OS). Secondary endpoints were first progression-free survival (PFS1) and, in case of reintroduction of FOLFIRINOX, second progression free survival (PFS2). OS and PFS were estimated using the Kaplan-Meier method and compared using the log-rank test. **Results:** Among the 321 patients included, 147 (46%) received a maintenance therapy. Median age was 60.0 (53–66), 35 (24%) had locally advanced PC and 91 (62%) had metastatic PC. The median total number of cycles was 14.0 (11.0–19.0), including 4.5 (2.0–9.0) of maintenance CT. Median OS was 16.1 months (95%CI = 13.7-20.3). Median PFS1 was 8.8 months (95%CI = 8.3-9.7). The preferred maintenance regimen was fluoropyrimidine (FP) in 66 (45%), vs FOLFIRI in 52 (35%) and FOLFOX in 25 (17%). Eighty-two percent of Pts received a second-line chemotherapy. Among 118 Pts who received a maintenance CT with FOLFIRI or FP, there was no difference in PFS1 (median: 9.0 vs 9.3, respectively, p = 0.31) or OS (median: 16.6 versus 18.7, p = 0.60) between the 2 maintenance regimens. After progression under maintenance CT with FOLFIRI or FP, reintroduction of FOLFIRINOX was performed in 16.1% of Pts, with a median PFS2 of 3.4 months (95%CI = 2.5-23.2). As previously reported in the PANOPTIMOX trial, the rates of G3-4 toxicity were significantly higher during FP maintenance CT than with FOLFIRI (41% vs 9%, p = 0.03), especially neuropathy (41% vs 9%). **Conclusions:** FOLFIRINOX de-escalation in aPC is largely used in France. Fluoropyrimidine maintenance chemotherapy appears to be as effective as FOLFIRI. Research Sponsor: None.

4640 Poster Session (Board #248), Fri, 8:00 AM-11:00 AM

A phase Ib study of sEphB4-HSA combined with first-line chemotherapy in patients (pts) with advanced pancreatic (PC) and biliary cancers (BC). *First Author: Diana L. Hanna, Hoag Cancer Center, Newport Beach, CA*

Background: EphB4, a receptor kinase expressed in most epithelial tumors, binds EphrinB2 to affect cancer cell growth, apoptosis and angiogenesis. EphB4 overexpression is associated with advanced stage and shorter survival in multiple cancers. sEphB4-HSA, the albumin-bound extracellular fragment of EphB4, is a first-in-class inhibitor which blocks EphB4-EphrinB2 bidirectional signaling and results in downstream suppression of KRAS, PI3K, and promotes recruitment of CD3 and CD8 T cells into the tumor. The RP2D of sEphB4-HSA is 10 mg/Kg IV q week. Here, we report on sEphB4-HSA in combination with standard first-line chemotherapy. **Methods:** Pts with advanced PC or BC and no prior therapy for metastatic disease were eligible and enrolled into separate cohorts. Pts with PC received gemcitabine 1,000 mg/m2 + nab-paclitaxel 125 mg/m2 on Days 1, 8, 15 of a 28-day cycle. Pts with BC received gemcitabine 1,000 mg/m2 + cisplatin 25 mg/m2 on Days 1, 8 of a 21-day cycle. sEphB4-HSA 10 mg/kg IV was given weekly starting in Cycle 2. Response was assessed every 2 cycles. Primary endpoint was safety and tolerability; secondary endpoints were objective response rate (ORR) by RECIST 1.1, PFS, OS. Expression of EphrinB2 and EphB4 in tumor was examined by IHC and classified as 1+ (weak staining); 2+ (moderate staining); 3+ (strong, uniform staining). **Results:** A total of 44 pts with advanced PC (n = 21) and BC (n = 23; 70% gallbladder cancer) were enrolled. Median age 66 yrs; ECOG 1 (70%), 52% male. Median number of cycles received were 5 (PC) and 7 (BC). Median PFS was 5.6 mo in PC and 5.8 mo in BC (95% CI: 3.1-8.1 [PC]; 2.7-7.0 [BC]). Median OS was 7.9 mo in PC and 9.1 mo in BC (95% CI: 6.5-15.0 [PC]; 5.4-15.0 [BC]). In response evaluable pts (20 PC, 22 BC), ORR was 40% in PC (95% CI: 21%, 63%) and 23% in BC (95% CI: 9%, 45%). Stable disease was noted in 48% of PC and 61% of BC pts. The most common grade 3 or 4 treatment-related AEs in ≥10% of pts in both cohorts combined were hypertension (n = 16; 36%), neutropenia (n = 15; 34%), anemia (n = 14; 32%), thrombocytopenia (n = 7, 16%), fatigue (n = 7, 16%). In the PC cohort, there was an association between EphB4 expression and objective response (p = 0.009). **Conclusions:** sEphB4-HSA has a manageable safety profile in combination with chemotherapy in pts with PC and BC. Clinical activity is manifested by a high disease control rate in both cohorts and a promising RR in PC. Additional biomarker analyses will be presented. Future studies combining chemoimmunotherapy with sEphB4-HSA in pancreatic cancer are planned. Clinical trial information: NCT02495896. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

4641 Poster Session (Board #249), Fri, 8:00 AM-11:00 AM

Comprehensive analysis of KRAS variants in patients (pts) with pancreatic cancer (PDAC): Clinical/molecular correlations and real-world outcomes across standard therapies. *First Author: Andrew Eugene Hendifar, Samuel Oschin Cancer Center, Cedars-Sinai Medical Center, Los Angeles, CA*

Background: Approximately 90% of PDAC tumors are driven by activating KRAS mutations. The biological and clinical impact of common KRAS variants (e.g. G12D, G12V, G12R) and less common variants (e.g. G12C, Q61H, Q61R) remains largely unknown despite the emergence of variant-specific treatment strategies. **Methods:** We retrospectively analyzed real-world outcomes from 1475 PDAC pts who underwent molecular profiling via the Know Your Tumor program. Overall survival (OS) and progression-free survival (PFS) were analyzed by choice of 1st line standard therapies. Outcomes in pts with specific KRAS mutations were compared against the KRAS G12D cohort using Cox regression. Based on our prior data, tumor profiles with actionable molecular findings (DDR mutations or other drivers) were evaluated separately. **Results:** The prognostic/predictive value of specific KRAS variants revealed differences in real-world outcomes (Table). OS was greater in pts with KRAS G12V and G12R variants, as was PFS on 5FU-Based Therapy (e.g. FOLFIRINOX) but not for Gemcitabine/nab-Paclitaxel. Opposing trends were noted for KRAS Q61. Pts with KRAS wild type tumors as well as both actionable subgroups also had an improved OS. **Conclusions:** In this large national dataset, we demonstrate that KRAS mutation status and specific variants appear to be prognostic as well as predictive in pancreatic cancer. Research Sponsor: Pancreatic Cancer Action Network (patient advocacy organization), Perthera (private healthcare company).

Real-world outcomes by KRAS mutation in PDAC.

KRAS Variant (% Prevalence)	OS Since Diagnosis of Advanced Disease (Years)		1st Line Gemcitabine / nab-Pactlitaxel (Months)		1st Line 5FU-Based Regimens (Months)	
	mOS (n)	p-val (HR)	mPFS (n)	p-val (HR)	mPFS (n)	p-val (HR)
G12D (36.9%)	1.24y (324)	**0.011 (1.29)**	7.9m (118)	0.47 (0.88)	8.4m (109)	**0.021 (1.58)**
G12V (27.0%)	1.47 (226)	**0.022 (0.76)**	6.1 (78)	0.12 (1.41)	11.2m (67)	**0.025 (0.59)**
G12R (15.5%)	1.45 (106)	**0.034 (0.73)**	9.9 (32)	0.59 (0.87)	10.1 (39)	**0.021 (0.51)**
G12C (1.2%)	0.62 (8)	0.8 (0.88)	5.4 (1)	0.29 (2.96)	N/R (2)	-
Q61 (5.8%)	1.26 (47)	0.81 (0.95)	9.1 (22)	0.9 (0.96)	4.3 (11)	0.95 (1.03)
Other (1.3%)	1.3 (11)	0.81 (0.88)	2.8 (3)	**0.0071 (5.22)**	2.0 (3)	0.27 (3.16)
Wild Type (12.4%)	2.2 (66)	**0.0018 (0.54)**	8.77 (28)	0.36 (0.75)	N/R (19)	0.18 (0.53)
Actionable (DDR Mutation)	1.96 (165)	**4.3e-07 (0.5)**	8.13 58)	0.25 (1.28)	16.17 (40)	**0.00025 (0.29)**
Actionable (Other Driver)	1.56 (98)	**0.0086 (0.67)**	6.53 (35)	0.099 (1.56)	7.47 (39)	0.71 (1.11)

4642 Poster Session (Board #250), Fri, 8:00 AM-11:00 AM

Cobimetinib plus gemcitabine is an active combination in KRAS G12R-mutated in previously chemotherapy-treated and failed pancreatic patients. *First Author: Bach Ardalan, University of Miami, Miami, FL*

Background: he KRAS proto-oncogene is involved in the RAS/MAPK pathway. Various G12X mutations have been examined with the most common mutations being G12D (40%), G12V (30%), and G12R (15-20%) in pancreatic cancer patients. Throughout the course of studying the G12X mutations, we have observed that not all KRAS mutations are equal. Preclinical data shows G12R is impaired in pI3Kα signaling, as compared to KRAS G12V/D. This mechanism is important in PDAC as it allows tumor growth to be sustained. In preclinical studies, PDX derived tumors were transplanted in mice and were treated with a MEK inhibitor plus chemotherapy, which demonstrated a greater tumor regression than either agent alone. Therefore, we have decided to treat patients with Gemcitabine alongside a 2nd generation MEK inhibitor (Cobimetinib). **Methods:** In our single arm study, 13 KRAS mutated pancreatic patients (KRAS G12D, G12V, and G12R) received the combination of Cobimetinib 20mg BID weekly for three weeks alongside Gemcitabine at 1000mg/m^2 weekly, followed by one week of rest. The above constitutes one cycle. **Results:** Patients were divided into two groups; *Group 1* consists of seven patients that were KRAS G12D/G12V mutated, and *Group 2* included six KRAS G12R mutated patients. In Group 1, seven patients on treatment progressed and died within two months on the study. In Group 2, one achieved PR and others stable disease. Median progression-free survival was 6.0 months (95% CI 3-9.3 months) and median OS has not been reached. All patients are alive at 8 months. Common adverse reactions include rash, fatigue, nausea, and vomiting. Cancer antigen 19-9 decreased in ≥ 50 of all patients in the latter group. We would like to report our positive study to the society. Moreover, we intend to confirm the study in a larger patient cohort. **Conclusions:** Pancreatic cancer patients that demonstrate KRAS G12R mutations are treatable with a new active combination chemotherapy. Research Sponsor: None.

4643 Poster Session (Board #251), Fri, 8:00 AM-11:00 AM

A pilot study to determine the feasibility of a customized low glycemic load diet in patients with stage I-III colorectal cancer. *First Author: Michelle Elizabeth Treasure, Cleveland Clinic Foundation, Cleveland, OH*

Background: Observational evidence associates energy balance factors, particularly diet, with survival in patients with colorectal cancer (CRC). Consumption of a diet with high glycemic indices has been associated with inferior cancer-specific outcomes, but there is limited prospective evidence that alterations in dietary habits improve cancer outcomes. This was a pilot study to determine the feasibility and acceptability of following a low glycemic load (GL) diet in patients with stage I-III CRC and to assess the nutritional resources necessary to follow the diet. **Methods:** 18 patients with stage I-III CRC, who completed definitive cancer therapy and consumed an avg daily GL $>$ 150 participated in a 12 week, tailored, in-person dietary intervention with a target GL of $\leq$102. Compliance was assessed using 24 hour telephone recalls. Acceptability of the diet was assessed using a food acceptability questionnaire, and exploratory correlative laboratories were assessed monthly. **Results:** 67% of patients were compliant with a low GL diet $\geq$ 75% of the time, over a 12 week time period. Majority of participants experienced a decrease in BMI and waist circumference, 28% experienced meaningful weight loss defined as $\geq$ 5%. The nutritionist spent an avg of 6.97 hours (SD 2.18) in-person and 1.58 hours (SD 0.68) by phone with each participant. In the overall group, significant decreases were seen in total cholesterol (7.2% decrease; t = -2.33, p = 0.03), VLDL (26.8% decrease; t = -2.33, p = 0.03) and triglycerides (26.6% decrease; t = -2.29; p = 0.04). All participants were satisfied with the diet; 43% were extremely satisfied. 75% of participants liked the foods they were able to eat "very much" or "extremely". All participants felt the in-person meetings were helpful. 77% did not feel an online video could replace the in-person meetings. 62% of participants did not feel a virtual meeting (e.g skype, etc.) could replace the in- person meeting while 38% felt it could. **Conclusions:** Patients with stage I-III CRC are able to follow a low GL diet with an in-person dietary intervention. Significant decreases in laboratory measures confirm the efficacy of the diet in altering metabolic indices. All participants who completed the study were satisfied with the diet, the majority of whom enjoyed the foods and planned to continue to follow the diet after study completion. The majority felt in-person contact with the nutritionist was essential to their success. This study was an essential step in designing a larger scale trial to evaluate the impact of low GL diet on cancer outcomes. Clinical trial information: NCT02129218. Research Sponsor: Clinical and Translational Science Collaborative of Cleveland 4UL1TR002548-01 from the National Center for advancing Translational Sciences (NCATS) component of the National Institutes of Health and NIH Roadmap for medial research, Other Foundation.

4644 Poster Session (Board #252), Fri, 8:00 AM-11:00 AM

Ramucirumab in patients with advanced HCC and elevated alpha-fetoprotein (AFP): Outcomes by treatment-emergent ascites. *First Author: Andrew X. Zhu, Harvard Medical School, Massachusetts General Hospital, Boston, MA*

Background: REACH and REACH-2 investigated ramucirumab (RAM) vs placebo (PL) in patients (pts) with advanced HCC following sorafenib, with REACH-2 enrolling only pts with baseline AFP $\geq$400 ng/mL. Ascites is common in HCC and associated with poorer outcomes. An exploratory analysis of outcomes by treatment-emergent (TE)-ascites was done. **Methods:** Pts with HCC, Child-Pugh A, ECOG PS $\leq$1, prior sorafenib, and no clinically meaningful ascites were randomized (REACH 1:1; REACH-2 2:1) to RAM 8 mg/kg or PL Q2W. A pooled meta-analysis of independent pt data (stratified by study) from REACH-2 and REACH (AFP $\geq$400 mg/mL) was done. OS and PFS were evaluated by Kaplan-Meier estimator and Cox models. Prognosis of TE-ascites in OS was evaluated by multivariate Cox models (adjusted for baseline ECOG PS, AFP, macrovascular invasion (MVI), and treatment [trt]). **Results:** Baseline characteristics were generally balanced between TE-ascites and non-ascites pts; however, more pts with ascites had MVI at baseline. Any-grade ascites was reported at a higher rate in RAM than PL (66 [21%] vs 33 [15%] pts, respectively), with most being low grade. Rate of Gr $\geq$3 ascites was similar between arms (15 [5%] vs 9 [4%] pts). Median time to onset (43 vs 47 days) and median duration of ascites (13 vs 18 days) were similar in RAM vs PL, with furosemide (22%) and spironolactone (19%) as most common trt and paracentesis (18%) as most common procedure for ascites in both arms. Ascites trended as a prognostic factor for OS after adjustment (with vs without; HR=1.3, 95% CI: 0.99, 1.62). Ascites was more commonly linked with hypoalbuminemia (odds ratio 4.9, 95% CI: 2.5, 9.3), but was not associated with proteinuria or hypertension. TEAEs occurred more frequently in pts with ascites in both arms. The most frequent Gr $\geq$3 TEAE in pts with ascites was hypertension. One RAM pt discontinued trt due to ascites. RAM trt was beneficial irrespective of presence of ascites (Table), and pts with ascites received more post-discontinuation therapy on RAM than PL (18% vs 6%). **Conclusions:** Acknowledging limitations of sample size, RAM provided a survival benefit in pts who did or did not experience TE-ascites. RAM was well tolerated and no new safety findings were observed. Clinical trial information: NCT01400347; NCT02435433. Research Sponsor: Eli Lilly and Company.

Efficacy.

	With Ascites		Without Ascites		Total Pooled Population	
	RAM N=66	PL N=33	RAM N=250	PL N=193	RAM N=316	PL N=226
OS, Median (mos)	6.7	3.4	8.3	5.9	8.1	5.0
HR (95% CI)	0.30 (0.18, 0.49)		0.77 (0.62, 0.95)		0.69 (0.57, 0.84)	
PFS, Median (mos)	4.2	2.0	2.7	1.5	2.8	1.5
HR (95% CI)	0.46 (0.29, 0.74)		0.62 (0.50, 0.77)		0.57 (0.47, 0.69)	

4645 Poster Session (Board #253), Fri, 8:00 AM-11:00 AM

Adjuvant chemoradiotherapy impact on the overall survival of completely resected ampullary and periampullary carcinoma: An updated meta-analysis. *First Author: Philip A. Haddad, Feist-Weiller Cancer Center at LSUHSC-Shreveport, Overton Brooks VAMC, Shreveport, LA*

Background: Ampullary and Periampullary carcinomas (APAC) are uncommon gastrointestinal cancers that are often amenable to surgical resection. The benefit of postoperative adjuvant chemoradiotherapy (ACRT) in patients with completely resected localized AC has been controversial. A meta-analysis which was conducted in 2017 found no associated survival benefit for adjuvant therapies in APAC. However, this meta-analysis was methodologically flawed and combined studies that used adjuvant chemotherapy alone with those that used ACRT. The purpose of this meta-analysis is to evaluate the impact of ACRT on the overall survival (OS) of patients with completely resected APAC incorporating more recent studies. **Methods:** A review of the medical literature was conducted using online databases. Inclusion criteria consisted of resected Ampullary and Periampullary carcinoma, English language, publications from 1999 to the present, comparative studies reporting OS with hazard ratios (HR) or Kaplan-Meier curves of patients that underwent ACRT versus those that did not, and studies that reported the aggregate OS data of adjuvant therapies where the preponderance of the cohort received ACRT. Adjuvant chemotherapy studies and those that reported aggregate OS for a cohort with preponderance of adjuvant chemotherapy were excluded. A meta-analysis was conducted using an inverse variance method with a random-effects model. **Results:** Sixteen retrospective series with a total of 1122 patients were included and analyzed. The majority of APAC patients that received ACRT tended to have high risk features. Four of these studies analyzed their OS data for the high risk APAC patients in addition to the cohort as a whole. Intra-arterial chemotherapy and concomitant radiotherapy was used in one study. ACRT was found to be significantly associated with better OS in patients with completely resected APAC (HR 0.76, 95%CI: 0.65-0.88, p $<$ 0.001). **Conclusions:** This is the first meta-analysis to show that adjuvant chemoradiotherapy is associated with a survival benefit in patients with completely resected high risk Ampullary and Periampullary carcinoma. In the absence of randomized clinical trials, this meta-analysis represents the most compelling data supporting the use of ACRT in this patient population. Research Sponsor: None.

TPS4646 Poster Session (Board #254), Fri, 8:00 AM-11:00 AM

Randomized phase III trial to evaluate omentum preserving gastrectomy for patients with resectable advanced gastric cancer: JCOG1711 (ROAD-GC). *First Author: Takanobu Yamada, Kanagawa Cancer Center, Yokohama, Japan*

Background: Standard surgery for resectable advanced gastric cancer is D2 (standardized extended lymph node dissection) gastrectomy with omentectomy. The reason why omentectomy has been performed is as follows; (1) principal surgery for gastrointestinal cancers is en-block resection of mesothelium including regional lymph nodes. Omentum is a part of the mesothelium of the stomach. (2) Cancer cells implanted into the peritoneal cavity aggregated in the milky-spot of the omentum and formed peritoneal dissemination in an animal model. (3) By special staining, micrometastasis detected in the omentum. There is some arguments for this theory. (1) no prospective study showed survival benefit of omentectomy as compared with omentum preservation. (2) anatomically, milky-spot is found not only in the omentum but also in other mesothelium or Douglas pouch. (3) JCOG1001 phase III study showed no survival benefit of bursectomy against non-bursectomy although bursa is a part of mesothelium of the stomach. (4) Anti-immunity is accelerated by antigen presentation by macrophage in the milky-spot of the omentum. Preservation of the omentum may have several benefits; (1) decrease in blood loss and operation time, (2) preservation of physical function by omentum such as reaction to peritonitis and prevention of adhesion, and (3) overcoming difficulties in laparoscopic omentectomy and avoidance of organ injury during surgery. **Methods:** The study is multicenter randomized phase III trial designed to confirm non-inferiority of omentum preservation to omentectomy for resectable advanced gastric cancer. Patients aged 20-79 years, histologically proven gastric adenocarcinoma, clinical subserosal/serosal invasion, and expected R0 (curative) resection are randomly assigned (1:1) during surgery to either omentum preservation or omentectomy. Total or distal gastrectomy with D2 dissection is performed in both arms. Laparoscopic gastrectomy is not allowed. Intraoperative photographs of the dissected field are centrally reviewed for all patients for quality control. The primary endpoint is relapse-free survival (RFS) and the secondary endpoints are overall survival, blood loss, operation time, and adverse events. Sample size was set at 1050 considering expected 3-year RFS of 77% in both arms with non-inferiority margin of 5%, one-sided alpha of 5%, and power of 80%. Planned accrual and follow up period are 6.5 years and 3 years respectively. The trial was activated in March 2019, and 177 patients are enrolled as of January 2020. Clinical trial information: UMIN000036253. Research Sponsor: None.

TPS4647 Poster Session (Board #255), Fri, 8:00 AM-11:00 AM

POF (paclitaxel/oxaliplatin/5-FU/leucovorin) versus SOX/CAPOX/FOLFOX as a postoperative adjuvant chemotherapy for curatively resected stage III gastric cancer: Study protocol for a randomized controlled trial, FNF-014 trial. *First Author: Liyu Su, Gastrointestinal Medical Oncology, Fujian Cancer Hospital & Fujian Medical University Cancer Hospital, Fuzhou, China*

Background: Postoperative chemotherapy (S-1, CAPOX, or Docetaxel/S-1) is a standard treatment for stage II/III gastric cancer in Asia. With regard to single agent or doublet, the need for improvement has consistently been pointed out because of the relatively poor outcome for patients with stage III gastric cancer. Triplet (FLOT) has shown significant survival benefits in perioperative setting. POF, our regiment similar to FLOT, demonstrated priority to doublet (FOLFOX) in advanced setting (2019 ASCO-GI). We conducted a randomized, multicenter, phase III study to compare triplet to doublet regimens for patients with stage III gastric cancer. **Methods:** This is currently enrolling patients (n = 544) with pathologic stage III gastric cancer after D2 lymph node dissection. Patients are randomized 1:1 and stratified by tumor stage (IIIA, IIIB, or IIIC, AJCC 8th) into POF or SOX/CAPOX/FOLFOX (chosen by the clinicians). SOX: oxaliplatin 130 mg/m2 on day 1, oral S-1 80mg/m2 divided by two on days 1 to 14 every 21 days for 8 cycles. CAPOX: oxaliplatin 130 mg/m2 on day 1, oral capecitabine 1000 mg/m2 twice daily on days 1 to 14 every 21 days for 8 cycles. FOLFOX: oxaliplatin 85 mg/m2, levo-leucovorin 200 mg/m2, and 5-FU 400 mg/m2 bolus on day 1, then 5-FU 2400 mg/m2 continuous infusion over 46 hours, every 14 days for 12 cycles. Three doublets were chosen by the clinicians. POF: paclitaxel 135 mg/m2, followed by FOLFOX omitted 5-FU bolus, every 14 days for 12 cycles. Eligibility criteria: patients aged 18-70 years, primary histologically proven gastric adenocarcinoma (including adenocarcinoma of the gastro-esophageal junction) of stage III with no evidence of metastatic disease, R0 resection with D2 lymph node dissection, good performance status (ECOG PS $\leq$1). Subjects must be able to take orally, and without other concomitant medical conditions that required treatment, initially treated with curative surgery followed by chemotherapy within 42 days. Life expectancy estimated more than 6 months. Adequate organ function. All patients provided written informed consent prior to treatment. Key exclusion criteria: patients with other primary malignancies, gastrointestinal bleeding. The primary end point is 3-year disease-free survival. Secondary end points are 3-year overall survival, 5-year overall survival, 5-year disease-free survival, and adverse events. Clinical trial information: NCT03788226. Research Sponsor: None.

TPS4648 Poster Session (Board #256), Fri, 8:00 AM-11:00 AM

Phase III study of first-line zolbetuximab + CAPOX versus placebo + CAPOX in Claudin 18.2$^+$/HER2$^-$ advanced or metastatic gastric or gastroesophageal junction adenocarcinoma: GLOW. *First Author: Manish A. Shah, Weill Cornell Medical College, New York, NY*

Background: Gastric cancer is the fourth leading cause of cancer death worldwide. Capecitabine + oxaliplatin (CAPOX) is a standard first-line treatment for advanced gastric cancer. Claudin (CLDN)18.2 has emerged as a promising targetable biomarker. In healthy tissue, CLDN18.2, a tight junction protein, is confined to gastric mucosa (ie, cells in the pit and base regions of gastric glands). Upon malignant transformation, structural loss in gastric or gastroesophageal junction (G/GEJ) adenocarcinoma cells may allow antibodies more access to previously unavailable CLDN18.2. Zolbetuximab is a chimeric IgG1 monoclonal antibody that specifically binds to CLDN18.2 and mediates cell death through antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. Results of a phase 2 study (NCT01630083) showed prolonged survival of patients with CLDN18.2-positive (CLDN18.2$^+$) advanced G/GEJ adenocarcinoma treated with zolbetuximab + epirubicin, oxaliplatin, and capecitabine (EOX) vs EOX alone. **Methods:** This phase 3, double-blind, placebo-controlled study (NCT03653507) will enroll ~500 adult patients from global sites. Patients are required to have CLDN18.2$^+$/HER2$^-$ locally advanced unresectable or metastatic G or GEJ adenocarcinoma that is radiographically evaluable per RECIST v1.1. Patients are not permitted to have received prior treatment with chemotherapy for advanced or metastatic G or GEJ adenocarcinoma. Patients will be randomly assigned 1:1 to receive either zolbetuximab plus CAPOX or placebo plus CAPOX. Randomization will be stratified by region (Asia vs non-Asia), number of metastatic sites (0 to 2 vs $\geq$3), and prior gastrectomy (yes vs no). Zolbetuximab will be administered at a loading dose of 800 mg/m^2 IV on Cycle 1 Day 1 followed by 600 mg/m^2 IV every 3 weeks. Central testing of tumor tissue will determine CLDN18.2 and HER2 status (if unknown); patients will be considered CLDN18.2$^+$ if $\geq$75% of tumor cells demonstrate moderate-to-strong membranous immunohistochemical staining. The primary objective is to compare progression-free survival between treatment arms. Secondary endpoints are overall survival; objective response rate; duration of response; and the safety/tolerability, pharmacokinetics, and immunogenicity of zolbetuximab. As of January 31, 2020, 127 sites were active and open to enrollment. Clinical trial information: NCT03653507. Research Sponsor: Astellas Pharma, Inc.

TPS4649 Poster Session (Board #257), Fri, 8:00 AM-11:00 AM

Trial in progress: A phase I study of AMG 199, a half-life extended bispecific T-cell engager (HLE BiTE) immune therapy, targeting MUC17 in patients with gastric and gastroesophageal junction (G/GEJ) cancer. *First Author: Joseph Chao, City of Hope Comprehensive Cancer Center, Duarte, CA*

Background: Prognosis for advanced G/GEJ cancer is poor and new treatment modalities are urgently needed. MUC17 is a transmembrane protein overexpressed and differentially localized on the cell membrane of G/GEJ cancer cells; expression and localization in normal cells is much more limited. AMG 199 is an HLE BiTE immune therapy designed to engage CD3-positive T cells to MUC17-positive G/GEJ cancer cells, mediate redirected tumor cell lysis, and induce T cell activation and proliferation. A clinical trial is being conducted for this novel and targeted immune therapy agent in patients with MUC17-positive G/GEJ cancer. **Methods:** This is a first-in-human phase 1, open-label, dose escalating study (NCT04117958) evaluating AMG 199 in patients with MUC17-positive G/GEJ cancer. Key eligibility criteria include metastatic or locally advanced unresectable MUC17-positive (as determined by IHC using a central laboratory assay) gastric adenocarcinoma or gastroesophageal junction adenocarcinoma ineligible for curative surgery and relapsed or treatment-refractory following $\geq$2 lines including a platinum, a fluoropyrimidine, taxane or irinotecan, and an approved vascular endothelial growth factor receptor antibody or tyrosine kinase inhibitor. Patients eligible for human epidermal growth factor receptor 2 (HER2) directed therapy should have received an approved HER2 targeting antibody. Primary endpoints include: dose-limiting toxicities, treatment-emergent or -related adverse events, vital signs, electrocardiogram (ECG), and laboratory changes. Secondary endpoints include: pharmacokinetics of AMG 199, objective response, duration of response, time to progression, 6-month and 1-year progression-free survival, and 1-year and 2-year overall survival. The dose exploration (n = 30) will estimate the maximum tolerated dose and/or recommended phase 2 dose; this will be followed by a dose expansion (n = 40) and evaluation of the benefit/risk profile of AMG 199. The study began enrolling patients in January 2020 and is ongoing. This is the first clinical trial to investigate MUC17 as a potential anti-tumor target. For more information, please contact Amgen Medical Information: medinfo@amgen.com. Clinical trial information: NCT04117958. Research Sponsor: Amgen.

TPS4650 Poster Session (Board #258), Fri, 8:00 AM-11:00 AM

A randomized phase II/III study of paclitaxel/cisplatin versus cisplatin/5-fluorouracil in neoadjuvant chemoradiotherapy (CRT) followed by surgery for patients with locally advanced esophageal squamous cell carcinoma (ESCC). *First Author: Ta-Chen Huang, National Taiwan University Hospital, Taipei, Taiwan*

Background: Meta-analyses have shown the survival benefit of cisplatin/5-fluorouracil (PF) neoadjuvant CRT over surgery alone for patients with locally advanced ESCC. The CROSS study has demonstrated the statistically significant survival benefit of paclitaxel/carboplatin neoadjuvant CRT for patients with locally advanced esophageal cancer, especially ESCC. A network meta-analysis based on published phase III trials suggested that paclitaxel/platinum might be superior to PF as neoadjuvant CRT in patients with ESCC (Huang et al: Jpn J Clin Oncol. 2015;45:1023–8). However, a direct comparison of two CRT regimens in a prospective randomized clinical trial has not been performed in ESCC. We designed this clinical trial to test the hypothesis that paclitaxel-platinum is superior to PF as neoadjuvant CRT in patients with locally advanced ESCC. **Methods:** This single center open-label phase 2/3 study randomizes patients with histologically confirmed ESCC, T3/4aN0M0 or T1-3N1-3M0 (AJCC 7th edition), in 1:1 ratio, to receive TP (paclitaxel, 50 mg/m2/week; cisplatin 30 mg/m2/week; for 5 weeks) or PF (cisplatin 75 mg/m2, d1; 5-FU 1,000 mg/m2, d1-4; on week 1 and week 5)-neoadjuvant CRT (180 cGy/d, 5 days/week, for 5 weeks). Esophagectomy will be performed 6 to 10 weeks after completing CRT. All patients must be eligible to esophagectomy, with tumor length $\leq$8cm and tumor radial $\leq$5cm, with adequate organ functions, and have ECOG performance status of 0-2. In the phase 2 stage, 128 patients will be enrolled, assuming the pathologic complete response (pCR) rate of TP and PF as 45% and 25%, respectively, with a power of 80% and one-sided 10% significance level. If the primary endpoint of pCR is met, additional 120 patients will be enrolled for the phase III stage with overall survival as the primary endpoint, assuming the hazard ratio of TP versus PF as 0.65 with a power of 80% and a 5% significance level. The trial started patient enrollment in May, 2017. As of Jan of 2020, 52 of planned 128 patients for phase II part have been enrolled. Clinical trial information: NCT03623737. Research Sponsor: Grant for investigator initiated clinical trials.

TPS4651 **Poster Session (Board #259), Fri, 8:00 AM-11:00 AM**

A phase II/III study of perioperative nivolumab and ipilimumab in patients (pts) with locoregional esophageal (E) and gastroesophageal junction (GEJ) adenocarcinoma: A trial of the ECOG-ACRIN Cancer Research Group (EA2174). *First Author: Jennifer Rachel Eads, University of Pennsylvania, Philadelphia, PA*

Background: E/GEJ adenocarcinoma has a high mortality rate despite curative intent treatment. A pathologic complete response (pCR) is associated with better overall survival (OS) but occurs in less than 30% of pts. Immunotherapy is effective in the metastatic setting. Here we aim to evaluate the contribution of immunotherapy in the neoadjuvant and adjuvant settings in pts with locoregional E/GEJ cancer. **Methods:** This is a multi-center, randomized phase II/III trial. Surgical candidates with locoregional E/GEJ adenocarcinoma receive carboplatin AUC 2 IV and paclitaxel 50 mg/m2 IV, both weekly x 5 during concurrent radiation (50.4 Gy) either with or without nivolumab 240 mg IV during weeks 1 and 3, followed by surgery. Pts with no post-operative disease receive nivolumab 240 mg IV every 2 weeks for 12 cycles either with or without ipilimumab 1 mg/kg IV every 6 weeks for 4 cycles. Eligibility criteria include pts with T1-N1-3M0 or T2-3N0-2M0 disease whom are candidates for surgery, no prior chemotherapy or radiation for this disease, no prior immunotherapy, no significant autoimmune disease. Pts must be disease free for adjuvant treatment. Primary neoadjuvant endpoint is pCR rate; primary adjuvant endpoint is disease free survival (DFS). Secondary endpoints include toxicity, DFS and OS. Pre- and mid-treatment diffusion weighted imaging MRI will be conducted during the neoadjuvant portion of the study. A neoadjuvant safety run in of 30 pts is underway. Overall, 278 pts will be needed to detect an absolute improvement of 15% in pCR rate in pts receiving and not receiving neoadjuvant nivolumab and 236 pts will be needed to detect a HR of 0.65 in favor of adjuvant ipilimumab/nivolumab over nivolumab (90% power, one sided alpha of 0.10). Accrual is expected over 34 months at a rate of 8 patients per month. If favorable at interim analysis. Clinical trial information: NCT03604991. Research Sponsor: U.S. National Institutes of Health.

TPS4652 **Poster Session (Board #260), Fri, 8:00 AM-11:00 AM**

A phase II study of selective HDAC6 inhibition with KA2507 for second-line treatment of advanced biliary tract cancer (ABC-11). *First Author: John A. Bridgewater, University College London Cancer Institute, London, United Kingdom*

Background: The ABC-02 trial provided Level A evidence supporting the use of cisplatin plus gemcitabine as first-line chemotherapy for advanced biliary tract cancer (ABC) [Valle, 2010]. In second line therapy oxaliplatin and 5FU and ivosedinib for IDH1 mutated cancers are options [Lamarca, 2019; Abou-Alfa, 2019] however there remains significant unmet need for patients without actionable alterations. Histone deacetylase 6 (HDAC6) is overexpressed in cholangiocarcinoma, reducing primary cilia. This is mediated through increased resorption in normal human cholangiocytes via tubulin deacetylation in the ciliary axoneme. Inhibition of HDAC6 elicits both cell intrinsic and extrinsic anti-cancer activity. HDAC6 inhibition reversed oncogenic loss of ciliation and demonstrated preclinical efficacy in a syngeneic rat orthotopic biliary cancer model [Gradilone, 2013]. KA2507 is a potent and selective small molecule inhibitor of HDAC6. Phase I dose escalation study identified an oral dose of 800mg bid for further development, being well tolerated and showing evidence of selective target engagement. **Methods:** ABC-11 is a Phase II multi-centre, open-label study of KA2507 in 40 evaluable patients with advanced biliary tract cancer previously treated with standard of care chemotherapy. The study follows a single-arm single-stage design using A'Hern's methodology. Eligible patients receive continuous 28-day cycles of fixed daily oral dose of KA2507 until death, disease progression or other pre-defined reason for study drug discontinuation. Tumour assessment is made at baseline and at 8-weekly intervals using RECIST 1.1 criteria until disease progression; primary endpoint is PFS at 4 months. Independent Data Monitoring Committee will review 4 month PFS and other data after first six patients, after a total of 17 patients (futility analysis, corresponding to cut-off of the Simon's minimax 2-stage design; 33% was set as the target 4-month PFS rate expected with KA2507) and at least annually thereafter. Subject to availability of adequate tissue, mandatory pre-treatment and on-study tumour biopsy samples will undergo multiparameter flow cytometry of immune cell subsets, immunofluorescence analysis of immune cell subsets (activation status and topology) and T cell repertoire studies. The study received regulatory and ethical approval to proceed in January 2020 and enrolment is in progress. Clinical trial information: NCT04186156. Research Sponsor: Karus Therapeutics Ltd.

TPS4653 **Poster Session (Board #261), Fri, 8:00 AM-11:00 AM**

Neoadjuvant chemotherapy with gemcitabine plus cisplatin followed by radical liver resection versus immediate radical liver resection alone with or without adjuvant chemotherapy in incidentally detected gallbladder carcinoma after simple cholecystectomy or in front of radical resection of BTC (ICC/ECC): A phase III study utilizing the German Registry of Incidental Gallbladder Carcinoma Platform (GR)—The AIO/CALGP/ACO-GAIN-Trial. *First Author: Thorsten Oliver Goetze, Institute of Clinical Cancer Research, Krankenhaus Nordwest, UCT University Cancer Center, Frankfurt am Main, Germany and Institute of Clinical Cancer Research (IKF) GmbH at Krankenhaus Nordwest, Frankfurt, Germany*

Background: Currently, complete surgical resection represents the only potentially curative treatment option for Biliary Tract Cancer (BTC) including Gallbladder Cancer (GBC). Even after curative resection, 5-year OS is only 20–40%. GBC is relatively rare, but still the fifth most common neoplasm of the digestive tract and even the most frequent cancer of the biliary system. Gallbladder carcinoma is suspected preoperatively in only 30% of all pts, while the majority of cases are discovered incidentally by the pathologist after cholecystectomy for a benign indication. For improving curative rates in BTC and GBC, early systemic therapy combined with radical resection seems to be a promising approach. The earliest moment to apply chemotherapy would be in front of radical surgery. Encouraging results of neoadjuvant/perioperative concepts in other malignancies provide an additional rationale to use this treatment in the early phase of GBC management and even in intrahepatic and extrahepatic cholangiocarcinoma. Especially because data regarding pure adjuvant chemotherapy in BTC`s are conflicting. **Methods:** This is a multicenter, randomized, controlled, open-label phase III study including pts with incidentally discovered GBCs after simple cholecystectomy in front of radical liver resection and pts with resectable/borderline resectable cholangiocarcinomas (ICC/ECC) scheduled to receive perioperative chemotherapy (Gemcitabine + Cisplatin 3 cycles pre- and post-surgery) or surgery alone followed by a therapy of investigator's choice. Primary endpoint is OS; secondary endpoints are PFS, R0-resection rate, toxicity, perioperative morbidity, mortality and QoL. A total of N=333 patients with GBC or BTC will be included. Recruitment has just started; first patient in was on December 6, 2020. EudraCT number: 2017-004444-38. Clinical trial information: NCT03673072. Research Sponsor: Deutsche Forschungsgesellschaft (DFG).

TPS4654 **Poster Session (Board #262), Fri, 8:00 AM-11:00 AM**

Multicenter phase II study of trastuzumab deruxtecan (DS-8201) for HER2-positive unresectable or recurrent biliary tract cancer: HERB trial. *First Author: Akihiro Ohba, National Cancer Center Hospital, Tokyo, Japan*

Background: Biliary tract cancer (BTC) is one of the most lethal cancers with limited treatment options. Early clinical trials showed a hint of activity of HER2 blockade for HER2 positive BTC, the prevalence of which was reported to be from 5% to 20%. Trastuzumab deruxtecan (DS-8201) is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable terapeptide-based linker, and a topoisomerase I inhibitor, which showed durable response in HER2 positive breast cancer as well as in a wide spectrum of cancer subtypes in a phase I study. In addition, preclinical research demonstrated the effectiveness of trastuzumab deruxtecan for HER2 positive BTC patient derived xenograft model. This phase II study is being conducted to evaluate the efficacy and safety of trastuzumab deruxtecan for HER2 positive BTC. **Methods:** The main inclusion criteria are unresectable or recurrent BTC, histologically diagnosed as adenocarcinoma or adenosquamous carcinoma, confirmed HER2-expressing status by central pathological examination, refractory or intolerant to treatment including gemcitabine, and adequate organ function. Patients are registered and receive 5.4 mg/kg trastuzumab deruxtecan every 3 weeks until disease progression or unacceptable toxicities. Primary endpoint is the overall response rate (ORR) in HER2 positive (defined as IHC3+, or IHC2+/ISH+; ISH+ defined as *HER2/CEP17* $\geq$2.0) patients by central imaging review. The ORR in all HER2-expressing patients (including HER2 low expressing defined as IHC/ISH status of 0/+, 1+/-, 1+/+, or 2+/-), progression-free survival, overall survival, and incidence of adverse events are assessed as secondary endpoints. Thirty-two patients will be enrolled, including 24 with HER2 positive BTC as primary cohort and 8 with HER2 low expressing BTC. The study has 80% power for primary endpoint in HER2 positive BTC patients, with one-sided alpha error of 5%; threshold ORR of 15% and expected ORR of 40%. Pharmacokinetics and circulating tumor DNA analyses serially are performed. The study was initiated in May 2019 with enrollment ongoing. A total of 15 patients were enrolled as of January 2020. Funding: Japan Agency for Medical Research and Development, and Daiichi Sankyo. Clinical trial information: JMA-IIA00423. Research Sponsor: Japan Agency for Medical Research, Pharmaceutical/Biotech Company.

TPS4655 **Poster Session (Board #263), Fri, 8:00 AM-11:00 AM**

Perioperative MVT-5873, a fully human monoclonal antibody against a CA 19-9 epitope, for operable CA 19-9 producing pancreatic cancers, cholangiocarcinomas, and metastatic colorectal cancers. *First Author: Shreya Gupta, National Cancer Institute, Bethesda, MD*

Background: Operable hepatopancreatobiliary (HPB) cancers continue to pose significant challenges. Radical resections are rarely curative, and chemotherapy is able to reduce tumor recurrence for only a fraction of patients. Despite the obvious advantages of extirpation of the identifiable tumor(s), the inflammatory milieu that accompanies surgery and the obligate time off cytotoxic agents allows for activation of remote quiescent disseminated tumor cells, leading to metastatic recurrence. We are conducting a study to determine the safety and efficacy of immediate peri-operative MVT-5873, a cytotoxic monoclonal antibody targeting Carbohydrate Antigen 19-9 (CA 19-9), in patients undergoing resections pancreatic cancer, cholangiocarcinoma or metastatic colorectal cancer to the liver. MVT-5873 is a human IgG1 antibody isolated from a patient following immunization with a sLe^a-KLH vaccine. MVT-5873 has demonstrated cell surface binding in sLe^a positive human tumor lines and has been shown to be potent in complement-dependent cytotoxicity assays and antibody-dependent cell mediated cytotoxicity assays. In patients with CA 19-9-producing cancers, MVT-5873 treatment has been shown to decrease serum CA 19-9 levels and prevent tumor progression. This trial may open the door for investigation of additional and/or synergistic agents in the immediate peri-operative period and usher in a new paradigm in the management of surgically treated cancers. **Methods:** This is a prospective, Phase II trial designed to determine the efficacy (increase in 1-yr DFS) and safety of peri-operative MVT-5873 for subjects with operable pancreatic, liver and bile duct cancers with elevated CA 19-9 levels. Patients may receive any standard neoadjuvant regimen prior to enrollment at the NIH Clinical Center in Bethesda, Maryland. Eligible patients will receive a pre-operative dose of MVT-5873 three days prior to the planned operation to remove all demonstrable disease. Following the operation, patients will receive a total of four doses of MVT-5873; the first two doses on postoperative days four and ten. The third dose will be administered on the normally scheduled postoperative clinic visit, followed by a final dose one month after discharge from the hospital and prior to the start of adjuvant treatment. Clinical trial information: NCT03801915. Research Sponsor: U.S. National Institutes of Health.

TPS4656 **Poster Session (Board #264), Fri, 8:00 AM-11:00 AM**

Phase II study of nivolumab (anti-PD1), tadalafil, and oral vancomycin in patients with refractory primary hepatocellular carcinoma or liver dominant metastatic cancer from colorectal or pancreatic cancers. *First Author: M. Cecilia Monge B., National Cancer Institute, National Institutes of Health, Bethesda, MD*

Background: Treatment options for advanced hepatocellular carcinoma (HCC) and liver dominant metastatic disease from colorectal or pancreatic cancers are limited with poor overall survival. Tadalafil has shown to increase anti-tumor immunity by decreasing myeloid derived suppressor cells (MDSC) and impair tumor growth in preclinical HCC models. Oral vancomycin affects bile acid metabolizing gut commensal bacteria leading to increased CXCL16 expression in the liver resulting in NKT mediated liver-selective anti-tumor effects. This study combines immune checkpoint inhibition (ICI) treatment with nivolumab in combination with tadalafil and oral vancomycin. We aim to evaluate the synergy of the antitumor effect induced by the change in gut microbiome with oral vancomycin and the immunomodulatory effect of PDE5 inhibition combined with ICI with nivolumab in advanced liver cancer or liver metastasis. Correlative Studies: Paired liver tumor biopsies are analyzed for genomic analysis (WES, RNA-seq), immune cell infiltration, proteomics and metabolomic studies (bile acids) and chemokine expression. Stool samples are analyzed for microbiota. Blood samples are analyzed for immune monitoring, cytokine profiles and pharmacokinetics of study drugs. Serum bile acid levels are determined in blood in the 2 hour period after test meal ingestion. **Methods:** This is a single-arm study of nivolumab, oral vancomycin and tadalafil. Treatment is delivered in 4-week cycles (C) and continues until off treatment. Imaging is done every 8 weeks. Biopsies are done at baseline and during week 3 of C2. Nivolumab is administered on day (D)1 of each C at a dose of 480 mg IV. Tadalafil is administered orally (PO); 10 mg daily starting on D1 of C1 and continues daily until off study. Vancomycin administration starts on D1 of C1 at 125 mg PO every 6 hours for a total daily dose of 500 mg. Patients will be on vancomycin 3 weeks on, 1 week off per regimen. The study is currently enrolling without DLT. Clinical trial information: NCT03785210. Research Sponsor: U.S. National Institutes of Health.

TPS4657 **Poster Session (Board #265), Fri, 8:00 AM-11:00 AM**

An exploratory study of fruquintinib as second-line treatment for patients with advanced or metastatic biliary tract cancer. *First Author: Qiu Li, West China Hospital , Sichuan University, Chengdu, China*

Background: Biliary tract cancer (BTC) is a relatively uncommon but highly fatal malignancy and most patients with BTC are diagnosed at advanced stages. Currently, no standard second-line treatment has been established following recurrence from the first-line treatment. VEGF is highly expressed in more than 50% of BTC, which indicates anti-angiogenesis might be a potentially effective method to improve the outcome in BTC. Fruquintinib is a novel small molecule tyrosine kinase inhibitor targeting VEGFR1, VEGFR2, and VEGFR3 and is currently being evaluated in clinical trials for multiple cancers including lung cancer, gastric cancer and colorectal cancer, and showed strong anti-tumor activity. However, the effect and safety of fruquintinib has not been investigated in the setting of second-line treatment for BTC. **Methods:** The study is a multicenter, single-arm, phase 2 trial of fruquintinib (5 mg, po, for 3 weeks, followed by 1 week off, 4 weeks for a cycle) for patients with advanced or metastatic BTC who have failed to first-line chemotherapy. The primary endpoint is progression-free survival (PFS) with the null hypotheses of 8 weeks, and the median PFS$\geq$15 weeks as evidence of the study drug activity (α=0.05, 80% power, one-sided). The number of patients required to complete the study is 27. Allowing for 20% expulsion rate, the study needs 33 patients. The secondary endpoints include objective response rate (ORR), disease control rate (DCR), overall survival (OS), safety and quality of life (QoL). Meanwhile, the study also set an exploratory objective to evaluate the mutation status of related genes in plasma (cfDNA) and tumor tissue and explore the interplay between mutation patterns with efficacy. Major eligibility requirements: Age $\geq$18 years; Histologically or cytologically confirmed diagnosis of advanced or metastatic biliary tract adenocarcinoma; First-line chemotherapy failed (tumor progression or intolerable adverse events); No less than 3 months of expected survival; ECOG PS$\leq$1; At least one measurable lesion according to RECIST 1.1 criteria; Adequate organ function. Eligible patients with advanced or metastatic BTC refractory to first-line chemotherapy will be enrolled at 7 medical centers in China. The study is open and actively enrolling at time of submission. Clinical trial information: NCT04156958. Research Sponsor: None.

TPS4658 **Poster Session (Board #266), Fri, 8:00 AM-11:00 AM**

An exploratory study of sorafenib plus toripalimab for unresectable hepatocellular carcinoma with portal vein tumor thrombus. *First Author: Yu Yang, Department of Medical Oncology, Cancer Center, West China Hospital, Sichuan University, Chengdu, China*

Background: Portal vein tumor thrombosis (PVTT) is common among advanced hepatocellular carcinoma (HCC) , resulting in poor prognosis. As the standard first-line treatment, the efficacy of Sorafenib is not satisfactory in HCC with PVTT. Although immune checkpoint inhibitors have made a breakthrough in treatment of advanced HCC, objective response rate (ORR) of anti-PD-1 monoclonal antibody monotherapy is only 17-20%. Recently, PD-1/PD-L1 inhibitors combined with anti-angiogenesis therapy have shown good efficacy in the clinical studies. However, the data on immunotherapy for HCC with PVTT are still limited. Toripalimab is the first Chinese-produced anti-PD-1 monoclonal antibody marketed. We designed the study to evaluate the efficacy and safety of Sorafenib plus Toripalimab as the first-line treatment for unresectable HCC with PVTT. **Methods:** The study is a multicenter, single-arm, phase Ib/II trial. The primary objectives are 6-month progression-free survival (PFS) rate and safety. Secondary objectives include ORR, disease control rate, PFS, overall survival. The escalation stage includes two dose cohorts: Sorafenib 400 mg po qd or 400 mg bid combined with Toripalimab 240 mg iv d1 q3w. 6-12 patients are estimated to evaluate the dose-limiting toxicity within the first 42 days of administration. In the expansion stage, patients are treated with the recommended dose based on the escalation stage, until progressive disease or intolerable toxicity. Assuming Sorafenib plus Toripalimab can improve the 6-month PFS rate to 40% (Sorafenib:20%, β = 0.2 , α = 0.05) and dropout is 10%, this stage need 39 patients. A total of 45-51 patients are enrolled. Major eligibility requirements include: unresectable HCC with diagnoses confirmed histologically or cytologically, or confirmed clinically in accordance with Chinese guideline for HCC diagnosis and treatment (v2017); radiographic evidence of PVTT; age $\geq$18 and $<$ 75 years; at least one measurable lesion according to RECIST 1.1; a predicted life expectancy $\geq$ 3 months; ECOG PS$\leq$1, Child-Pugh class A or B ($\leq$7); no any prior systemic anti-cancer treatment; adequate organ function. Patients with hepatitis B treated with antiviral therapy (viral load $<$ 100 IU/mL) or patients with chronic hepatitis C can be included. The study is open and actively enrolling at time of submission. Clinical trial information: NCT04069949. Research Sponsor: Shanghai Junshi Biosciences Co., Ltd.

TPS4659 Poster Session (Board #267), Fri, 8:00 AM-11:00 AM

Phase II study of pembrolizumab plus olaparib in the treatment of patients with advanced cholangiocarcinoma. *First Author: Aiwu Ruth He, Georgetown University Lombardi Comprehensive Cancer Center, Washington, DC*

Background: Lack of an effective second-line treatment of patients (pts) with advanced cholangiocarcinoma (CC) necessitates the development of new therapies. Preclinical studies suggest CC susceptibility to PARP inhibition (PARPi): *ERCC1* is underexpressed in 74% of CCs, and olaparib is selective for *ERCC1* deficiency, profoundly inhibiting DNA repair. Additionally, PARPi exploits *IDH* mutation-related DNA damage repair deficiency, which is found in about 25% of CCs. Unfortunately, PARPi also upregulates PD-1-PD-L1 receptor-ligand binding, which attenuates anticancer immunity and counteracts the efficacy of PARPi. However, this can be prevented by PD-1 inhibition—blockade of PD-1-PD-L1 acts to re-sensitize cancer cells to T-cell killing. Hence, we hypothesize that the combination of olaparib and pembrolizumab will produce a durable anti-tumor response against CC by synergistically inducing DNA damage and increasing immune response. **Methods:** Thirty-six pts with advanced CC, who either failed to respond to or progressed on first-line therapy, will be enrolled to receive olaparib (300 mg PO bid) daily plus pembrolizumab (200 mg IV Q3 weeks) for 12 months, unless unacceptable toxicities or cancer progression occur, in which cases therapy will cease. MRI or CT tumor assessment will occur just before therapy, every 6 weeks for the first 6 months of therapy, and then every 9 weeks for the next 6 months of therapy (total, 12 months). Three tumor biopsies will be collected: at baseline; at week 4; and at time of progression. In each biopsy, ERCC1, PD-1, and PD-L1 expression, *IDH1/2* mutation status, and immune cell (CD3 and CD8) response will be assessed. The total study duration will be 20-36 months. The primary endpoint will be overall response rate; the secondary endpoints will be PFS, OS, duration of response, and safety and tolerability. It is hypothesized that in pts with advanced CC, second-line therapy with olaparib plus pembrolizumab will improve the response rate from 17.5% to 35%, as well as increase PFS and OS compared to cytotoxic chemotherapy. Study enrollment began in Q1 2020. NCI number pending at time of abstract submission. Clinical trial information: pending at time of submission. Research Sponsor: Merck.

TPS4660 Poster Session (Board #268), Fri, 8:00 AM-11:00 AM

Etctn 10388: A phase I trial of triapine and lutetium Lu 177 dotatate in well-differentiated somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs). *First Author: Aman Chauhan, University of Kentucky, Division of Medical Oncology, Lexington, KY*

Background: Radiolabeled somatostatin analogues provide a means of delivering targeted radiation with a high therapeutic index to NETs that express somatostatin receptors (SSTRs). Radiolabeled somatostatin analogue Lutetium Lu 177 Dotatate (Lutathera) is a beta-emitting radionuclide, recently FDA approved for use in SSTR positive gastroenteropancreatic neuroendocrine tumors (GEPNETS) in the US based on the NETTER-1 Phase III trial. Despite favorable PFS and safety profile, the drug has limited cytoreductive capability with a 17% ORR. We hypothesize that addition of an effective radiation sensitizer could help improve antitumor activity of Lutathera. Ribonucleotide reductase (RNR) is the only enzyme responsible for conversion of ribonucleoside diphosphate to deoxyribonucleotide diphosphate (dNDP), the key building blocks for DNA synthesis. Radiation is a potent inducer of DNA double-strand breaks (DSBs), and RNR is the rate-limiting enzyme in the repair of DNA in this setting. Triapine is an inhibitor of RNR. This study will test the hypothesis that radiation sensitizer triapine can be safely combined with peptide receptor radionuclide therapy and ultimately may improve antitumor activity of Lutetium Lu 177 Dotatate. **Methods:** This study is an investigator initiated, NCI sponsored, multicenter phase 1 trial of triapine and Lutetium Lu 177 Dotatate in well-differentiated somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumor (GEP-NETs) after the failure of at least one line of prior systemic cancer treatment. A total of 29 patients will be enrolled in the dose escalation with help of Bayesian optimal interval design (BOIN) and dose expansion cohorts. The study will be open through the NCI ETCTN (National Cancer Institute Experimental Therapeutics Clinical Trials Network) program. Patients will be treated with 177 lutetium dotatate in combination with triapine. Triapine will be administered orally (100 mg once a day starting dose) from D1-14 with each dose of PRRT [200 mCi]. Primary endpoint is to evaluate recommended phase II dose (RP2D). Secondary endpoints are to evaluate safety, pharmacokinetics, and clinical activity (ORR and PFS). We are also evaluating NETEST, a novel blood based test that evaluates levels of 51 neuroendocrine tumor gene transcripts. In addition, the study will correlate clinical outcome with baseline somatostatin receptor density, somatic tumor mutations and germline mutations. Clinical trial information: 04234568. Research Sponsor: NCI CTEP.

TPS4661 Poster Session (Board #269), Fri, 8:00 AM-11:00 AM

NAPOLI-3: An open-label, randomized, phase III study of first-line liposomal irinotecan + 5-fluorouracil/leucovorin + oxaliplatin versus nab-paclitaxel + gemcitabine in patients with metastatic pancreatic ductal adenocarcinoma. *First Author: Zev A. Wainberg, University of California, Los Angeles, Medical Center, Los Angeles, CA*

Background: Liposomal irinotecan administered with 5-fluorouracil/leucovorin (5-FU/LV) is approved in the USA for metastatic pancreatic ductal adenocarcinoma (mPDAC) following progression with gemcitabine-based therapy. A phase 1/2 study in previously untreated locally advanced/metastatic PDAC showed promising anti-tumor activity with liposomal irinotecan 50 mg/m^2 free base + 5-FU 2400 mg/m^2 + LV 400 mg/m^2 + oxaliplatin (OX) 60 mg/m^2 on days 1 and 15 of a 28-day cycle (Wainberg *et al. Ann Oncol* 2019;30 Suppl 4: SO-005). Herein, we present the design of the phase 3 NAPOLI-3 study investigating the efficacy and safety of this regimen as first-line therapy in patients with mPDAC. **Methods:** NAPOLI-3 (NCT04083235) is a phase 3, open-label, randomized, global study in adults with histologically/cytologically confirmed pancreatic adenocarcinoma not previously treated in the metastatic setting. Patients are required to have one or more metastatic tumors measurable with computed tomography/magnetic resonance imaging and an Eastern Cooperative Oncology Group performance status score of 0–1. Site activation began in Dec 2019 and enrollment is ongoing. Random allocation (1:1) of 750 patients is planned to liposomal irinotecan + 5-FU/LV + OX (regimen as per phase 1/2 study) or nab-paclitaxel 125 mg/m^2 + gemcitabine 1000 mg/m^2 on days 1, 8 and 15 in a 28-day cycle. The primary endpoint is overall survival (OS). Secondary endpoints (progression-free survival [PFS] and overall response rate assessed with Response Evaluation Criteria in Solid Tumors v1.1 criteria) will be compared only if the primary endpoint shows superiority for liposomal irinotecan + 5-FU/ LV + OX over nab-paclitaxel + gemcitabine. Safety assessments include adverse-event monitoring. Patients will continue treatment until disease progression, unacceptable toxicity or study withdrawal, and will then be followed for survival every 2 months until death or study end (when all patients have died, withdrawn consent or are lost to follow-up). Clinical trial information: NCT04083235. Research Sponsor: Ipsen.

TPS4662 Poster Session (Board #270), Fri, 8:00 AM-11:00 AM

A phase II trial of PD-1 inhibition with INCMGA00012 in patients with previously treated unresectable or metastatic adenosquamous pancreatic cancer. *First Author: Christopher Jakubowski, Johns Hopkins Oncology, Baltimore, MD*

Background: Adenosquamous pancreatic cancer (ASQ) constitutes 1-5% of all pancreatic cancers and compared to pancreatic adenocarcinoma (PDAC) has a worse survival. ASQ has glandular and squamous histologic components and given its rarity and aggressiveness, in practice there is no current standard regimens for ASQ. Unfortunately, checkpoint blockade has had an overall disappointing impact on survival in PDAC. In an effort to identify a patient subgroup most likely to respond to immunotherapy, the immune tumor microenviroment (TME) in ASQ was evaluated. Tissue microarrays from archived ASQ samples were first created. Then immunocytochemistry (IHC) staining for immune cells and immune checkpoint proteins was performed. PD-L1 expression and the combined presence of PD-L1+, IDO+, LAG3+, and VISTA+ was seen. All ASQ cases had some degree of tumor infiltrating lymphocytes (TIL, including CD8+ T-cells). Furthermore, PD-L1 and other checkpoint positivity correlated with increased TIL. These findings suggest the presence of adaptive immune resistance. This is in contrast to standard PDAC, in which the expression of immune checkpoints is rarely accompanied by increased effector T-cells. **Methods:** We are conducting a multiple-center, single arm, phase II clinical trial to evaluate PD-1 inhibition with INCMGA00012 in locally advanced unresectable and metastatic ASQ patients. INCMGA00012 is a humanized monoclonal antibody antagonistic to PD-1. The primary objective is to determine the disease control rate at 4 months using RECIST 1.1. The study is planned with 21 evaluable subjects and allows early termination for lack of efficacy. Patients have a pre-treatment biopsy followed by INCMGA00012 500 mg on Day 1 of each cycle (every 4 weeks). A second biopsy will occur eight weeks later. Eligibility criteria includes histologically- or cytologically-proven adenosquamous carcinoma of the pancreas by central pathologic review and patients must have received (or been intolerant to or ineligible for) at least 1 prior line of cytotoxic chemotherapy and received no more than 2 prior systemic treatments. Patients with known MSI-H/dMMR status are excluded. Exploratory objectives include examining changes in the TME checkpoint expression and immune cell infiltrate in the biopsies via IHC and RNA expression studies. The clinical study was activated in February 2020. Clinical trial information: NCT04116073. Research Sponsor: None.

TPS4663 **Poster Session (Board #271), Fri, 8:00 AM-11:00 AM**

Phase I study of proton therapy in adjuvant pancreatic cancer (PROTON-PANC). *First Author: Benjamin Adam Weinberg, Ruesch Center for the Cure of Gastrointestinal Cancers, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC*

Background: Pancreatic adenocarcinoma (PAC) has a poor prognosis, with a 5-year survival rate of 10%. The current standard of care for patients with resectable disease is surgical resection followed by 6 months of adjuvant modified FOLFIRINOX (FFX, leucovorin, fluorouracil, irinotecan, and oxaliplatin). As survival outcomes and distant recurrence improve with the use of FFX, locoregional recurrence remains a cause of morbidity and mortality. We seek to integrate adjuvant short-course proton radiation therapy (PRT) to the surgical bed in between cycles of FFX. While there is limited literature on the combination of short course PRT and FFX, there are analogous experiences using 5 fraction SBRT or IMRT following FFX in routine clinical practice. The ongoing Alliance 021501 trial of preoperative chemotherapy vs. chemotherapy plus radiation (IMRT using 5 Gy X 5 or SBRT 6.6 X 5) in borderline resectable pancreatic cancer mandates that radiation starts 5 days or more following the last dose of FFX. Additionally, at the Lombardi Comprehensive Cancer Center, we routinely combine 5 fraction SBRT after a 10-14 day interval from FFX. **Methods:** This is a phase I, single-arm, open-label study. Eligible pts are $\geq$ 18 years old, have histologically confirmed, resected PAC of the pancreatic head (R0 or R1) on adjuvant FFX, an ECOG performance status of 0-1, and adequate normal bone marrow and hepato-renal function. Exclusion criteria are prior radiation to the upper abdomen (neoadjuvant chemotherapy is allowed). This study will use a 3+3 dose-escalation design to determine the safety and feasibility of combining 5 fractions of adjuvant PRT with FFX using different intervals between cycle 6 of FFX and PRT: dose level 1 uses a 12 day interval, and dose level 2 uses a 5 day interval. The primary endpoint is to determine the RP2D between the 2 proposed schedules. Using a 3+3 dose-escalation schema, 2-12 patients will be required to determine the RP2D. Enrollment began in Q4 2019. Clinical trial information: NCT03885284. Research Sponsor: The Ruesch Center for the Cure of Gastrointestinal Cancers.

TPS4664 **Poster Session (Board #272), Fri, 8:00 AM-11:00 AM**

A randomized phase II study of second-line treatment with liposomal irinotecan, and S-1 versus liposomal irinotecan and 5-fluorouracil in gemcitabine-refractory metastatic pancreatic cancer patients. *First Author: Esther Pijnappel, Amsterdam UMC Location AMC, Amsterdam, Netherlands*

Background: Pancreatic ductal adenocarcinoma (PDAC) is the deadliest form of cancer with a 5-year survival of less than 5% for patients with metastatic disease. Despite improvements over the past years, with the introduction of FOLFIRINOX and gemcitabine plus nab-paclitaxel, the majority has disease progression within 6 months after start of first line treatment. The NAPOLI trial was the first phase III study showing that patients with metastatic pancreatic cancer that progressed after treatment with gemcitabine-based chemotherapy benefitted from second line treatment. Patients received liposomal irinotecan (nal-IRI) either as a single agent or in combination with 5-fluorouracil/leucovorin (5-FU/LV), or 5-FU/LV alone. Patients treated with both nal-IRI and 5-FU/LV experienced a median overall survival (mOS) of 6.1 months versus 4.2 months for the 5-FU/LV group. Recently, two Japanese studies (GEST and JASPAC 01) reported on the use of S-1 in patients with PDAC. In patients with locally advanced or metastatic PDAC, S-1 was non-inferior compared to gemcitabine in terms of mOS (8.8 months for gemcitabine versus 9.7 months for S-1). In the adjuvant setting, S-1 showed superior mOS compared to gemcitabine, 46.5 and 25.5 months respectively, HR for mortality of S-1 compared with gemcitabine was 0.57 (95% CI 0.44–0.72). In view of these results, the objective of this NAPAN study is to compare the progression free survival (PFS) of nal-IRI plus S-1, with nal-IRI plus 5-FU/LV in a Western study population for second line treatment of PDAC. **Methods:** This is a multi-center, open label, randomized phase II trial. Patients $\geq$ 18 years of age with histologically or cytologically confirmed PDAC, previously treated with gemcitabine (-based) therapy, or progression within 6 months of adjuvant gemcitabine-based treatment are eligible. After a safety run-in of the nal-IRI plus S-1 regimen, patients will be randomized between nal-IRI plus S-1 and nal-IRI plus 5-FU/LV. Primary endpoint of the run-in phase is to determine dose limiting toxicity (DLT) and maximum tolerated dose (MTD) of nal-IRI when co-administered with fixed dose S-1. The primary endpoint of the phase II part is to determine the efficacy of the treatment arms in terms of PFS. Secondary endpoints include OS, response rate according to RECIST 1.1, adverse events according to CTC version 5.0 and Quality of life. Until now 2 of the planned 120 patients have been enrolled. Clinical trial information: NCT03986294. Research Sponsor: Servier and Nordic Pharma.

TPS4665 **Poster Session (Board #273), Fri, 8:00 AM-11:00 AM**

PD-1 antibody combined with paclitaxel (albumin bound) and gemcitabine as first-line therapy in patients with metastatic pancreatic cancer. *First Author: Jiujie Cui, Department of Medical Oncology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, Shanghai, China*

Background: Pancreatic cancer is a malignant tumor with limited therapeutic strategies and poor prognosis. About 60% of the patients have metastasis disease at time of diagnosis and lose the opportunity for surgery. Thus, therapy based on drugs becomes a vital part in pancreatic cancer. In 2013, MPACT showed that albumin-bound paclitaxel combined with gemcitabine in the treatment of metastatic pancreatic cancer could increase the mOS from 6.6 months to 8.7 months (HR = 0.72, 95% CI: 0.62-0.83; P $<$ 0.001). Nowadays, the immunosuppressive checkpoint inhibitors acting on PD-1/PD-L1 pathway have shown a significant efficacy in enhancing tumor immune surveillance and anti-tumor immune response. In 2018, two studies reported in ASCO showed the preliminary efficacy of albumin paclitaxel, gemcitabine and PD-1 inhibitor in the treatment of advanced pancreatic cancer. Among patients who have not received treatment before, the disease control rate was even up to 100%. Therefore, this study will further explore the domestic PD-1 antibody combined with albumin-bound paclitaxel and gemcitabine as the first-line treatment of advanced pancreatic cancer among Chinese pancreatic cancer patients. **Methods:** This is a prospective, single-armed, exploratory, investigator initiated trial to explore the efficacy and safety of PD-1 antibody combined with albumin-bound paclitaxel and gemcitabine as first-line treatment of metastatic pancreatic cancer. This study is, to our knowledge, the first one to test the efficacy and safety of PD-1 antibody on metastatic pancreatic cancer patients among Chinese population. Survival index is median survival estimated by Kaplan-Meier and draw the survival curve. The response rate was compared by χ 2 test / Fisher test. All primary and secondary outcomes will be analyzed on the full analysis set. PD-1 antibody, 200mg, D1 administration; paclitaxel (albumin binding type), 125mg/m2, D1, 8 days administration; gemcitabine, 1000mg/m2, D1, 8 days administration, every 21 days as a cycle and PD-1 antibody (200mg, D1, every 21 days) single drug maintenance treatment is given after the completion of 6 cycle chemotherapy. Major eligibility criteria is that each participant must have metastatic pancreatic cancer confirmed by histology or cytology and has never received systemic anti-tumor therapy before. So far, 11 of planned 20 patients have been enrolled. Clinical trial information: NCT04181645. Research Sponsor: HENGRUI MEDICINE.

TPS4666 **Poster Session (Board #274), Fri, 8:00 AM-11:00 AM**

TRYbeCA-1: A randomized, phase III study of eryaspase in combination with chemotherapy versus chemotherapy alone as second-line treatment in patients with pancreatic adenocarcinoma (NCT03665441). *First Author: Pascal Hammel, Hôpital Beaujon (AP-HP), Clichy, and University Paris VII, Paris, France*

Background: Second-line treatment options for advanced pancreatic adenocarcinoma are currently limited. Eryaspase, asparaginase (ASNase) encapsulated in red blood cells (RBCs) is an investigational product under development. Following infusion, asparagine and glutamine are actively transported into RBCs where they are hydrolyzed by the encapsulated ASNase. We have recently reported the outcome of a randomized Phase 2b study inpatients with advanced pancreatic cancer whose disease progressed following first-line treatment(NCT02195180). Eryaspase in combination with gemcitabine monotherapy or FOLFOX combination therapy improved overall survival (OS) and progression free survival (PFS). The safety profile of eryaspase was acceptable. The results of this Phase 2b study provided a rationale for initiating this confirmatory Phase 3 pivotal trial (TRYbeCA-1). **Methods:** TRYbeCA-1 is a randomized, open-label Phase 3 trial (N = ~500) of eryaspase combined with chemotherapy in patients with adenocarcinoma of the pancreas who have failed only one prior line of systemic anti-cancer therapy for advanced pancreatic cancer and have measurable disease. Patients are randomized in a 1:1 ratio to receive gemcitabine/Abraxane or irinotecan-based therapy (FOLFIRI [FOLinic acid-Fluorouracil-IRInotecan regimen] or irinotecan liposome injection/5-fluorouracil/leucovorin) with or without eryaspase, administered as IV infusion on Day 1 and Day 15 of each 4-week cycle. Key eligibility criteria include performance status 0 or 1; stage III-IV disease; documented evidence of disease progression; available tumor tissue; and adequate organ function. The primary endpoint is OS. Key secondary endpoints include PFS and objective response rate, safety, quality of life, pharmacokinetics and pharmacodynamics, and biomarker research. A hazard ratio in OS of 0.725 is being targeted which represents a conservative estimate based on the Phase 2b data and is viewed as being highly clinically relevant. An IDMC is established to review safety at regular intervals andto review efficacy data at the planned interim and final analyses. IDMC last reviewed the trial in October 2019 and suggested the trial continue as planned. Clinical trial information: NCT03665441. Research Sponsor: Erytech.

TPS4667 **Poster Session (Board #275), Fri, 8:00 AM-11:00 AM**

Phase II, open-label, randomized study of first-line zolbetuximab plus gemcitabine and nab-paclitaxel (GN) in Claudin 18.2–positive metastatic pancreatic cancer (mPC). *First Author: Wungki Park, Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY*

Background: Combinations of folinic acid, fluorouracil (5-FU), irinotecan, and oxaliplatin (FOLFIRINOX) along with GN are standard first-line treatment options for mPC. Despite treatment advances, mPC has a poor prognosis with a 5-year survival rate of $< 5\%$, emphasizing an urgent need for new targeted therapeutics. Claudin 18.2 (CLDN18.2) is a tight junction protein restricted to normal gastric mucosa cells; however, in the context of malignant transformation, CLDN18.2 is frequently expressed in carcinomas derived from organs that do not normally express it, such as pancreatic adenocarcinoma (50-70% express CLDN18.2). Zolbetuximab is a chimeric IgG1 monoclonal antibody that specifically binds to CLDN18.2, designed to mediate cancer cell death through antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. **Methods:** This phase 2 study (NCT03816163) with a safety lead-in phase will assess safety and antitumor activity of zolbetuximab plus GN in patients (pts) with histologically confirmed mPC with high CLDN18.2 expression ($\geq$75% of tumor cells demonstrate moderate-to-strong IHC staining). The safety lead-in will assess safety/tolerability of zolbetuximab (n = 3 at 1,000 mg/m^2 on Cycle 1 Day 1 then 600 mg/m^2 Q2W then expand/de-escalate using a 3+3 design) plus GN and confirm the recommended phase 2 dose (RP2D). Dose-limiting toxicities (DLTs), defined as a specified toxicity that occurs during the DLT assessment period and is related to zolbetuximab, will be assessed after Cycle 1 (28 days). After determining the RP2D, approximately 129 pts will be randomly assigned 2:1 to receive either zolbetuximab RP2D Q2W on Days 1 and 15 plus GN on Days 1, 8, and 15 of each cycle (*Arm 1*), or GN alone on Days 1, 8, and 15 of each cycle (*Arm 2*). Randomization will be stratified by ECOG performance status (0 or 1) and liver metastasis (yes or no). Imaging (CT/MRI) will be performed at baseline and every 8 weeks until investigator-assessed disease progression (per RECIST v1.1 criteria) or the start of other systemic anticancer treatment, whichever comes earlier. Primary objectives are to confirm RP2D (safety lead-in), to assess antitumor activity measured by overall survival (randomization phase), and to establish the safety/tolerability profile of zolbetuximab plus GN across the study. Key secondary endpoints in the randomization phase are progression-free survival and objective response rate. As of January 2020, this study is recruiting pts at 74 centers. Clinical trial information: NCT03816163. Research Sponsor: Astellas Pharma, Inc.

TPS4668 **Poster Session (Board #276), Fri, 8:00 AM-11:00 AM**

HGCSG 1803: Single-arm phase II study evaluating efficacy of oxaliplatin, irinotecan and S-1 combination therapy (OX-IRIS) in metastatic pancreatic cancer as first-line treatment. *First Author: Shintaro Nakano, Department of Gastroenterology and Hepatology, Hokkaido University Hospital, Sapporo, Japan*

Background: Combination chemotherapy with oxaliplatin, irinotecan, fluorouracil and leucovorin (FOLFIRINOX) showed improved survival compared to gemcitabine monotherapy for patients with metastatic pancreatic cancer and has become the one of the standard regimens. Despite of its clinical benefit, FOLFIRNIOX needs continuous infusion of 5-FU for 46 hours, which impairs quality of life. In other gastrointestinal cancer, infuser pomp free regimens, in which oral 5-FU drug replace the continuous infusion of 5-FU, have developed as alternative regimen. Therefore, we planned to develop new combination chemotherapy with oxaliplatin, irinotecan and S-1 (OX-IRIS) for advanced pancreatic cancer. We previously conducted the phase I study for assessing the safety and determining the recommended dose of OX-IRIS regimen. **Methods:** To evaluate efficacy and safety of OX-IRIS, HGCSG1803 study staeted as a multicenter, non-randomized, single arm, prospective, phase II study in December 2019. The patients with untreated metastatic or relapsed pancreatic cancer are eligible for this study. OX-IRIS is administered as follows; a 30-min intravenous infusion (IV) of antiemetic, a 2-h IV of oxaliplatin at 85 mg/m^2, a 1.5-h IV of irinotecan at 150 mg/m^2 on day 1 and day 15 of each 4-week cycle, and S-1 (40 mg/m^2) was taken orally twice daily, from after dinner on day 1 to after breakfast on day 15, followed by a 14-day rest, and to be repeated every 2 weeks until disease progression, unacceptable toxicity, or patient refusal. The primary endpoint is response rate, and the secondary endpoints are overall survival, progression-free survival, safety, and dose intensity for each drug. A total of 40 cases are planned for registration from 18 institutions in Japan within 2.5 years. Clinical trial information: jRCTs011190008. Research Sponsor: None.

TPS4669 **Poster Session (Board #277), Fri, 8:00 AM-11:00 AM**

EndoTAG-1 plus gemcitabine versus gemcitabine alone in patients with measurable locally advanced and/or metastatic adenocarcinoma of the pancreas failed on FOLFIRINOX treatment (NCT03126435). *First Author: Li-Tzong Chen, National Health Research Institutes, Tainan, Taiwan*

Background: Pancreatic cancer (PC) is the 3rd deadliest cancer in the United State surpassing breast cancer in 2016, with the overall survival rate of - 9% for those newly diagnosed individuals. The notorious disease is set to become the 2nd leading cause of death from cancer by 2020 in US (National Cancer Institute, NIH). FOLFIRINOX regimen is one of the standard 1st-line treatments for PC patients with good performance status; however, there is currently no standard of care in 2nd-line therapy after FOLFIRINOX failure. EndoTAG-1 is a novel formulation of cationic liposomes embedded with Paclitaxel, which specifically displays antivascular and antiangiogenic activities. By binding and internalizing at tumor endothelial cells after intravenous administration, the cytostatic activity of paclitaxel will be targeted to the activated tumor endothelial cells. **Methods:** Eligible patients with measurable locally advanced and/or metastatic adenocarcinoma of the pancreas failed on FILFIRINOX treatment will be screened and randomized (1:1) into one of the two arms in the study (n=218). The primary endpoint of the study is overall survival (OS), with secondary endpoints include progression-free survival (PFS), objective response rate (ORR), duration of response (DOR) and quality of life (QoL). Arm A: EndoTAG-1 plus Gemcitabine: Patients will receive intravenous injection with EndoTAG-1 (22 mg/m^2) twice weekly plus gemcitabine (1,000 mg/m^2) once weekly for consecutively 3 weeks followed by 1 week rest. The treatment will be repeated every 4 weeks, with 8 weeks per cycle. The treatment will be kept until any one of the following occurs: progressive disease or unacceptable toxicity or withdrawal of consent. Arm B: Gemcitabine: Patients will receive gemcitabine (1,000 mg/m^2) once weekly for consecutive 3 weeks followed by 1 week rest. The treatment will be repeated every 4 weeks, with 8 weeks per cycle. The treatment will be kept until any one of the following occurs: progressive disease or unacceptable toxicity or withdrawal of consent. The phase III trial began enrollment since November 2018. The trial will continue as planned from the last review in January 2020. Clinical trial information: NCT03126435. Research Sponsor: SynCore Biotechnology Co., Ltd., Other Government Agency

TPS4670 **Poster Session (Board #278), Fri, 8:00 AM-11:00 AM**

Adaptive dose optimization trial of stereotactic body radiation therapy (SBRT) with or without GC4419 (avasopasem manganese) in pancreatic cancer. *First Author: Elizabeth Charlotte Moser, Galera Therapeutics, Malvern, PA*

Background: Local progression causes up to 30% of deaths from pancreatic cancer (PC) and is also a significant source of morbidity. Stereotactic body radiotherapy (SBRT) offers the potential for improved therapeutic index over standard fractionation, but current regimens of 5 fractions of 5-7 Gy/fraction are constrained by nearby organ tolerance and offer only palliation without improving survival. Safe dose escalation may be necessary to improve SBRT efficacy. Avasopasem, a superoxide dismutase mimetic, selectively converts superoxide (O2$\bullet$ -) to hydrogen peroxide (H_2O_2) and oxygen. O2$\bullet$ -initiates normal tissue damage due to RT. Avasopasem is in a Phase 3 trial (NCT03689712) to reduce RT-induced oral mucositis in head and neck cancer, based on positive results in a randomized Phase 2 trial for that indication (Anderson, JCO 2019). Avasopasem improved the survival of mice receiving 8.5 Gy x 5 to the upper abdomen. Cancer cells are less tolerant to elevated H_2O_2, and more tolerant to elevated O2$\bullet$ -, than normal cells, and avasopasem demonstrated mechanism-dependent synergy with high dose-fraction RT in a human tumor xenograft with inducible expression of catalase (Sishc, AACR 2018). Thus, adding avasopasem to SBRT may increase both the efficacy and the safety of the latter. **Methods:** 48 patients with locally advanced PC, who have completed medically-indicated induction chemotherapy, are randomized 1:1 to placebo or avasopasem, 90 mg IV, prior to each of 5 consecutive daily (M-F) SBRT fractions. A phase I/II Late Onset Efficacy/ Toxicity tradeoff (LO-ET) based adaptive design adaptive model drives assignment of SBRT dose escalation in each arm based on a dual endpoint (Gr 3-4 GI toxicity or death; local stable disease or better) by 90 days post SBRT. The planned dose levels are 10, 11 and 12Gy x 5 fractions (BED10 = 100,112.5 and 132Gy, respectively) as an integrated boost to the gross tumor volume (GTV). Primary endpoint: Maximum tolerated dose of SBRT with avasopasem or placebo. Secondary endpoints progression-free survival, response rate, and acute (90 day) and late (12 month) radiation toxicity with avasopasem vs placebo. Exploratory correlative studies include ctDNA, tumor exome/transcriptome sequencing, and immune profiling. Clinical trial information: NCT03340974. Research Sponsor: Galera Therapeutics.

TPS4671 **Poster Session (Board #279), Fri, 8:00 AM-11:00 AM**

Phase I study of SEA-CD40, gemcitabine, nab-paclitaxel, and pembrolizumab in patients with metastatic pancreatic ductal adenocarcinoma (PDAC). *First Author: Andrew L. Coveler, Seattle Cancer Care Alliance/University of Washington, Seattle, WA*

Background: SEA-CD40 is an investigational non-fucosylated, humanized IgG1 monoclonal antibody directed against CD40, a co-stimulatory receptor expressed on antigen-presenting cells (APCs). Activation of CD40 on APCs upregulates cytokine production and co-stimulatory receptors, enhancing tumor antigen presentation to T cells. Preclinical data indicate that treatment of PDAC with chemotherapy in conjunction with a CD40 agonist could enhance antigen presentation and initiate an antitumor immune response (Byrne KT and Vonderheide RH, Cell Rep 2016;15, 2719–32). An ongoing Phase 1 study (SGNS40-001) is evaluating SEA-CD40 as monotherapy and in combination with pembrolizumab in patients with advanced solid or hematologic malignancies. A new cohort is enrolling to evaluate the combination of SEA-CD40, gemcitabine, nab-paclitaxel, and pembrolizumab in PDAC. **Methods:** The cohort consists of patients with metastatic PDAC who have had no prior therapy for metastatic disease. Patients must be ≥18 years old, with (neo)adjuvant therapy completed >4 months prior to enrollment, ECOG status ≤1, adequate renal, hepatic, and hematologic function, and measurable disease per RECIST v 1.1 criteria. A standard regimen of gemcitabine and nab-paclitaxel on Days 1, 8, and 15 of each 28-day cycle is administered with SEA-CD40 IV on Day 3. Pembrolizumab is administered every 42 days starting on Day 8. The primary objective is antitumor activity; secondary objectives are safety and tolerability and SEA-CD40 and pembrolizumab pharmacokinetics. Efficacy endpoints are confirmed RECIST ORR per investigator (primary), disease control rate (response or stable disease ≥16 weeks), duration of response, PFS, and OS. Disease is assessed every 8 weeks using RECIST and immune-based RECIST (iRECIST). Treatment continues until occurrence of unacceptable toxicity, progressive disease per iRECIST, consent withdrawal, or study closure. Assessment of dose-limiting toxicity will occur initially in groups of 6 patients to identify the recommended phase 2 dose of SEA-CD40 for the cohort. Enrollment to this cohort began in November 2019. Clinical trial information: NCT02376699. Research Sponsor: Seattle Genetics, Inc.

TPS4672 **Poster Session (Board #280), Fri, 8:00 AM-11:00 AM**

A phase II study of siG12D-LODER in combination with chemotherapy in patients with locally advanced pancreatic cancer (PROTACT). *First Author: Anna M. Varghese, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: KRAS alterations are the most frequent driver alterations identified in pancreas cancer; however, KRAS has remained an elusive therapeutic target. siG12D-LODER is a novel, miniature bio-degradable polymeric matrix encompassing a novel small interfering RNA targeting KRAS G12D and all additional G12X mutations (G12C, G12V...). The siG12D-LODER is inserted directly into the pancreas tumor via endoscopic intervention. A Phase 1/2a dose escalation and expansion study of patients receiving a one-time dose of siG12D-LODER with ongoing chemotherapy demonstrated that the combination was well-tolerated and safe and exhibited promising potential efficacy with 10/12 patients achieving disease control and median overall survival 15.1 months (Golan, Oncotarget 2015). **Methods:** This phase 2 study was initially designed as a randomized, two arm, open label study of gemcitabine and nab-paclitaxel with or without siG12D-LODER for patients with locally advanced pancreas cancer with planned 40 patients in each arm and primary endpoint of progression-free survival. Eighteen patients were enrolled in the chemotherapy alone arm and 18 in the chemotherapy and siG12D-LODER arm. After an interim analysis, the study design has been amended and is now a single arm study in which patients (N=39) with both borderline resectable and locally advanced pancreas cancer will receive investigator's choice of chemotherapy (the combination of gemcitabine/nab-paclitaxel or modified FOLFIRINOX) and all patients will receive up to three doses of the siG12D-LODER administered once every 12 weeks. Primary endpoint is overall response rate after final siG12D-LODER insertion. Secondary endpoints include duration of response, progression-free survival, overall survival, time to response, percentage of patients proceeding to surgical resection, and percentage of patients receiving radiation therapy. Exploratory analyses include evaluation of KRAS mutation status and monitoring of circulating free DNA and circulating tumor cells. The amended protocol is now open for accrual and four patients having been enrolled to date. Trial accrual is anticipated to be completed by December 2020. Clinical trial information: NCT01676259. Research Sponsor: Silenseed.

TPS4673 **Poster Session (Board #281), Fri, 8:00 AM-11:00 AM**

Improving FOLFIRINOX safety in pancreatic cancer patients through multidimensional remote monitoring and proactive care using a domomedecine mobile platform. *First Author: Mohamed Bouchahda, Clinique du Mousseau, Ramsay Générale de Santé, Evry, France*

Background: Pancreatic cancer is a poor prognosis and fast-growing cancer, whose five-year survival is 6% in Europe and the US. FOLFIRINOX has been established as the reference medical treatment for this disease worldwide, yet it also causes leuko-neutropenia, thrombocytopenia, diarrhea, anorexia, asthenia, weight loss, and peripheral sensory neuropathy. Its indication is usually limited to patients having a WHO performance status of 0 or 1. This treatment is often interrupted once Grade 3-4 clinical or hematological toxicities occur, resulting in poor patient performance status and quality of life. Presently, no prospective study monitor and evaluate the qualitative and quantitative effects of FOLFIRINOX on the daily life of pancreatic cancer patients in real-time. Such monitoring would provide early warning signals for the identification of any improvement or deterioration of the patient condition. Whenever necessary, proactive interventions would be triggered to avoid emergency hospitalization for severe adverse events and to enhance treatment compliance. **Methods:** Our study involves the use of the mobile e-Health platform PiCADo (JMIR 2018) to track and analyse circadian rhythms, symptoms, and body weight in real time in 45 advanced pancreatic cancer patients at 4 centres. The patients are continuously telemonitored for rest-activity, temperature and 3D-orientation via a BLE sensor during the six weeks following the first FOLFIRINOX course. Patients weigh themselves daily on a BLE scale and self-rate their symptoms using a touchscreen on GPRS tablet. Alerts are generated according to preset yet modifiable thresholds of automatically computed critical parameters. From these data, we will evaluate the rate of emergency hospital admissions and the admission-free survival, the rates of severe adverse events, patients' symptoms dynamics, and their relations with the disruption of the patients' circadian rhythm. Patient satisfaction and research experience will also be assessed, since engagement is at the core of the success of the approach. The results will guide a future randomized trial comparing standard pancreatic cancer patient care with a personalized FOLFIRINOX approach, including chronotherapy delivery. Support: Ramsay-Sante, Altran. Research Sponsor: Ramsay Générale de Santé.

5000 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

IMvigor010: Primary analysis from a phase III randomized study of adjuvant atezolizumab (atezo) versus observation (obs) in high-risk muscle-invasive urothelial carcinoma (MIUC). *First Author: Maha H. A. Hussain, Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL*

Background: Radical surgery ± cisplatin-based neoadjuvant chemo (NAC) is the mainstay treatment (tx) for MIUC, with no conclusive level 1 evidence for adjuvant chemo (AC). Here we present the primary analysis from IMvigor010, a global, open-label, multicenter, randomized trial of adjuvant atezo (anti–PD-L1; approved in metastatic UC [mUC] settings) in pts with MIUC at high risk of recurrence following primary resection. **Methods:** Pts with MIUC (bladder, upper tract [UT]), ECOG PS 0-2 and resected tissue for PD-L1 testing on immune cells (IC; VENTANA SP142 assay) were enrolled ≤ 14 wks after radical cystectomy/nephroureterectomy with lymph node (LN) dissection. Pathologic stage: 1) ypT2-4a or ypN+ if pts had NAC or 2) pT3-4a or pN+ if pts did not have NAC. No postsurgical radiation or AC was allowed; if no NAC was given, pts must have been ineligible for or declined cisplatin-based AC. Pts were randomized 1:1 to atezo 1200 mg IV q3w or obs for 16 cycles or 1 y (stratification factors: no. of LNs resected, pathologic nodal status, pathologic tumor stage, PD-L1 status, prior NAC). Disease-free survival (DFS) was the primary endpoint (EP). Final DFS, first interim overall survival (OS; secondary EP) and safety are reported. **Results:** The ITT population included 809 pts (median follow-up, 21.9 mo). In the atezo and obs arms, respectively, 48% and 47% had NAC; 7% and 6% had UTUC as primary disease; 48% each had LN+ disease. DFS and OS are in Table. Baseline prognostic/clinical factors did not influence DFS tx benefit; stratified HR was 0.81 (95% CI: 0.63, 1.05) in IC0/1 pts (PD-L1 < 5%; n = 417) and 1.01 (0.75, 1.35) in IC2/3 pts (PD-L1 ≥ 5%; n = 392). 16% of atezo-treated pts had a tx-related G3-4 AE. Skin and gastrointestinal toxicities most commonly led to tx discontinuation. **Conclusions:** IMvigor010, the first phase 3 adjuvant study of a checkpoint inhibitor in MIUC, did not meet its primary EP of DFS. More tx discontinuation due to AEs was seen vs mUC studies. Safety was generally consistent with previous studies. Clinical trial information: NCT02450331. Research Sponsor: F. Hoffmann-La Roche Ltd.

IMvigor010 primary analysis	Atezo (N = 406)	Obs (N = 403)
Final DFS		
No. of Events (%)	212 (52)	208 (52)
Median (95% CI), mo	19.4 (15.9, 24.8)	16.6 (11.2, 24.8)
HR (95% CI)[a]	0.89 (0.74, 1.08); $P = 0.2446$[b]	
First interim OS		
No. of Events (%)	118 (29)	124 (31)
Median (95% CI), mo	NR	NR
HR (95% CI)[a]	0.85 (0.66, 1.09); $P = 0.1951$[c]	

NR, not reached. Data cut off: Nov 30, 2019. [a] Stratified by nodal status, post-resection tumor stage, PD-L1 status. [b] 2-sided *P* value. [c] DFS, then OS tested hierarchically. OS *P* value for descriptive purposes.

5001 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Pembrolizumab plus axitinib versus sunitinib as first-line therapy for advanced renal cell carcinoma (RCC): Updated analysis of KEYNOTE-426. *First Author: Elizabeth R. Plimack, Fox Chase Cancer Center, Philadelphia, PA*

Background: The randomized, open-label, phase 3 KEYNOTE-426 study (NCT02853331) demonstrated that pembrolizumab (pembro) + axitinib (axi) significantly improved OS, PFS, and ORR vs sunitinib as first-line therapy for advanced RCC (aRCC) at the first pre-planned interim analysis (minimum study follow-up of 7 mo). Updated analyses are presented here. **Methods:** Treatment-naive patients (pts) with clear cell aRCC, KPS ≥70%, and measurable disease (RECIST v1.1) were randomly assigned 1:1 to receive pembro 200 mg IV Q3W for up to 35 doses + axi 5 mg orally BID or sunitinib 50 mg orally QD on a 4-wk on/2-wk off schedule until progression, toxicity, or withdrawal. Randomization was stratified by IMDC risk (favorable vs intermediate vs poor) and geographic region (North America vs Western Europe vs rest of world). Primary end points were OS and PFS. Secondary end points were ORR, DOR, and safety. All *P* values are nominal. A post-hoc exploratory analysis was done to evaluate association of depth of response (maximum reduction from baseline in sum of diameters of target lesions) and OS using landmark analysis up to 6 mo after randomization. **Results:** 861 pts were randomly assigned (pembro + axi, n = 432; sunitinib, n = 429). Median (range) duration of follow-up for all pts was 27.0 mo (0.1-38.4). Pembro + axi improved OS (HR, 0.68 [95% CI, 0.55-0.85]; $P < 0.001$; 24-mo OS rate, 74% vs 66%) vs sunitinib. Median (95% CI) OS was not reached with pembro + axi and was 35.7 mo (33.3-NR) with sunitinib. Pembro + axi improved PFS (HR, 0.71 [95% CI, 0.60-0.84]; $P < 0.001$; 24-mo PFS rate, 38% vs 27%) vs sunitinib. For pembro +axi vs sunitinib respectively, median (95% CI) PFS was 15.4 (12.7-18.9) vs 11.1 mo (9.1-12.5); ORR was 60% vs 40% ($P < 0.0001$); CR rate was 9% vs 3%; and median DOR was 23.5 mo (range 1.4+ to 34.5+) vs 15.9 mo (range 2.3-31.8+). In general, the pembro + axi benefit was observed in all subgroups tested, including IMDC risk and PD-L1 expression subgroups. Post-hoc landmark analysis at 6-mo showed that pts on pembro + axi with ≥80% target lesion reduction had OS similar to that of pts with CR per RECIST v1.1 based on Kaplan-Meier curves and HR [95% CI] estimates (0.20 [0.05-0.84] vs. 0.10 [0.01-0.76], respectively) vs pts with 0-30% target lesion reduction. No new safety signals were observed. **Conclusions:** Pembro + axi continued to demonstrate superior and durable antitumor activity vs sunitinib in pts with first-line aRCC with a 27-mo median follow up; no new safety signals were observed. Clinical trial information: NCT02853331. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

5002 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

SAVOIR: A phase III study of savolitinib versus sunitinib in pts with MET-driven papillary renal cell carcinoma (PRCC). *First Author: Toni K. Choueiri, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA*

Background: PRCC is the most common type of non-clear cell RCC, accounting for 10–15% of renal malignancies. As a subset of PRCC cases are MET-driven, MET inhibition may be an appropriate targeted treatment approach. In a single-arm Phase II study, savolitinib (AZD6094, HMPL-504, volitinib), a highly selective MET-tyrosine kinase inhibitor, demonstrated antitumor activity in pts with MET-driven PRCC (Choueiri et al. JCO 2017). The Phase III SAVOIR study (NCT03091192) further assessed savolitinib vs standard of care sunitinib in pts with MET-driven PRCC. **Methods:** In this open-label (sponsor blinded), randomized study, pts with centrally confirmed MET-driven (*MET* and/or *HGF* amplification, chromosome 7 gain and/or *MET* kinase domain mutations), metastatic PRCC were randomized to savolitinib 600 mg once daily (QD), or sunitinib 50 mg QD 4 weeks on / 2 weeks off. Primary objective was progression-free survival (PFS; RECIST 1.1 by blinded independent central review). Secondary objectives included overall survival (OS), objective response rate (ORR), and safety and tolerability. **Results:** After external data on predicted PFS with sunitinib in pts with MET-driven disease became available, study enrollment was closed. At data cutoff (Aug 2019), only 60 of the planned 180 pts were randomized (savolitinib n = 33; sunitinib n = 27). Most had chromosome 7 gain (savolitinib 91%; sunitinib 96%) and no prior therapy (savolitinib 85%; sunitinib 93%). PFS, OS, and ORR were numerically improved with savolitinib vs sunitinib (Table). CTCAE grade ≥3 adverse events (AEs) were reported in 42% and 81% of pts; dose modifications were related to AEs in 30% and 74% of pts with savolitinib and sunitinib respectively. After discontinuation, 36% of all savolitinib and 19% of all sunitinib pts received subsequent anticancer therapy. **Conclusions:** Although pt numbers and follow-up were limited, savolitinib demonstrated encouraging efficacy and an improved safety profile vs sunitinib, with fewer grade ≥3 AEs and fewer dose modifications required. Sunitinib performance was poorer than expected based on external retrospective data. Further investigation of savolitinib as a treatment option for MET-driven PRCC is warranted. Clinical trial information: NCT03091192. Research Sponsor: AstraZeneca.

	Savolitinib (n = 33)	Sunitinib (n = 27)
PFS events, n (%)	17 (52)	20 (74)
Median PFS (95% CI), mo	7.0 (2.8, NR)	5.6 (4.1, 6.9)
HR (95% CI)	0.71 (0.37, 1.36); p = 0.313	
Deaths, n (%)	9 (27)	13 (48)
Median OS (95% CI), mo	NR (11.9, NR)	13.2 (7.6, NR)
HR (95% CI)	0.51 (0.21, 1.17); p = 0.110	
ORR n (%) [95% CI]	9 (27) [13.3, 45.5]	2 (7) [0.9, 24.3]
All partial responses		

NR, not reached

5003 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase II study of the oral HIF-2α inhibitor MK-6482 for Von Hippel-Lindau disease–associated renal cell carcinoma. *First Author: Eric Jonasch, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Patients (pts) with Von Hippel-Lindau disease (VHL) are at risk for several cancers, including clear cell renal cell carcinoma (ccRCC). Inactivation of *VHL* results in constitutive activation of the HIF-2α transcription factor, which drives tumor growth. MK-6482, a potent, selective, small molecule HIF-2α inhibitor, has shown favorable safety and antitumor activity in a phase 1/2 study. We present initial results of the open-label phase 2 study of MK-6482 for treatment of VHL-associated ccRCC (NCT03401788). **Methods:** Adult pts with a pathogenic germline *VHL* variation, measurable localized/nonmetastatic ccRCC, no prior systemic anticancer therapy, and ECOG PS of 0/1 received MK-6482 120 mg orally once daily until progression, intolerable toxicity, or investigator/pt decision to withdraw. Primary end point was ORR of VHL-associated ccRCC tumors per RECIST v1.1 by independent radiology review. Secondary end points were DOR, time to response (TTR), PFS, and safety and tolerability. **Results:** As of December 6, 2019, 61 pts were enrolled; median (range) age was 41 years (19-66) and most pts were male (52.5%) and had ECOG PS of 0 (82.0%). The most common lesions outside the kidney (non-RCC tumors) were CNS hemangioblastomas (80.3%) and pancreatic lesions (50.8%). Median (range) duration of treatment was 9.9 mo (1.9-18.2) and 95.1% of pts remain on therapy. Three pts discontinued (AE, n = 1; death [fentanyl toxicity], n = 1; pt decision, n = 1). There were 17 confirmed responses (ORR, 27.9% [95% CI, 17.1-40.8%]) and 8 (13.1%) unconfirmed (documented at 1 timepoint and to be confirmed at subsequent timepoint) responses; all responses were PRs. Of 61 pts, 53 (86.9%) had decrease in size of target lesions. In 17 pts with confirmed response, median (range) DOR was not reached (2.1-9.0 mo) and median (range) TTR was 5.5 mo (2.7-14.0). Responses were also observed in CNS, retinal, and pancreatic lesions. Median PFS was not reached; 12-mo PFS rate was 98.3%. Treatment-related AEs (TRAEs) occurred in 96.7% of pts, mostly grade 1 (44.3%) or grade 2 (42.6%) and primarily (≥20%) anemia (83.6%; considered an on-target-toxicity), fatigue (49.2%), and dizziness (21.3%). Grade 3 TRAEs occurred in 9.8% of pts, primarily fatigue (4.9%) and anemia (3.3%). There were no grade 4 or 5 TRAEs. One pt discontinued because of a TRAE (dizziness). **Conclusions:** MK-6482 showed promising efficacy and tolerability in pts with VHL-associated ccRCC and responses in other VHL-related lesions. These data support further investigation of MK-6482 in VHL disease. Clinical trial information: NCT03401788. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

5004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Results from a phase II study of bevacizumab and erlotinib in subjects with advanced hereditary leiomyomatosis and renal cell cancer (HLRCC) or sporadic papillary renal cell cancer. *First Author: Ramaprasad Srinivasan, Urologic Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD*

Background: HLRCC is a familial cancer syndrome associated with a type 2 papillary RCC (pRCC) variant. HLRCC is caused by germline mutations in the gene for the Krebs cycle enzyme fumarate hydratase (FH). FH inactivation results in VHL-independent upregulation of hypoxia inducible factor, a reliance on aerobic glycolysis, and activation of the NRF2 pathway, features also shared by some sporadic pRCC tumors. We hypothesized that the metabolic alterations underlying these tumors would be susceptible to targeted therapy with a combination of bevacizumab and erlotinib. **Methods:** Patients with advanced pRCC were eligible to enroll on this phase II study. To enrich for patients with FH deficiency, those with 1) HLRCC and 2) sporadic pRCC were enrolled into parallel, independent cohorts. All patients received bevacizumab 10 mg/kg IV every 2 weeks and erlotinib 150 mg orally daily. Patients who had received no more than two agents targeting the VEGFR pathway were included. Patients remained on treatment until unacceptable toxicity or progression. The primary endpoint was overall response rate (ORR); secondary endpoints were progression free survival (PFS) and duration of response. **Results:** A total of 83 patients with pRCC, including 42 in the HLRCC cohort and 41 in the sporadic cohort were enrolled on study. The majority of patients were IMDC intermediate risk (53/83, 64%) and 27 (33%) had at least one prior treatment. The ORR was 51% (42/83; 95% CI, 40 – 61) in all patients, 64% (27/42; 95% CI, 49 – 77) in the HLRCC cohort, and 37% (15/41; 95% CI, 24 – 52) in the sporadic cohort. The median PFS was 14.2 months (95% CI, 11.4 – 18.6) in all patients, 21.1 months (95% CI, 15.6 – 26.6) in the HLRCC cohort, and 8.7 months (95% CI, 6.4 – 12.6) in the sporadic cohort. The majority of treatment related adverse events (TRAEs) were grade 1 or 2 with the most common being acneiform rash (92%), diarrhea (77%), proteinuria (71%), and dry skin (61%). Grade ≥3 TRAEs occurred in 47% of patients, including hypertension (34%) and proteinuria (13%), with one patient (1.2%) with a grade 5 GI hemorrhage possibly related to bevacizumab. **Conclusions:** The combination of bevacizumab and erlotinib is well tolerated and is associated with encouraging activity in advanced pRCC, particularly in patients with FH deficient tumors. This is the first and largest prospective study in HLRCC and provides the basis for considering bevacizumab and erlotinib as a preferred option in a patient population that has no widely accepted standard. Clinical trial information: NCT01130519. Research Sponsor: U.S. National Institutes of Health, U.S. National Institutes of Health, This research was supported [in part] by the Intramural Research Program of the National Cancer Institute. Funded by the NCI Contract No. [HHSN261200800001E, 75N910D00024, Task Order No. (75N91019F00129)]. Genentech-Roche provided study drug but not funding.

5005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Optimized management of nivolumab (Nivo) and ipilimumab (Ipi) in advanced renal cell carcinoma (RCC): A response-based phase II study (OMNIVORE). *First Author: Rana R. McKay, Dana-Farber Cancer Institute, Boston, MA*

Background: Nivo + Ipi is an established first-line treatment (tx) for advanced RCC. We hypothesized that the addition of CTLA-4 blockade may not be required for all patients (pts). Furthermore, the optimal duration of Nivo maintenance in responding pts is unknown. In this phase II response-adaptive trial, we investigate the sequential addition of 2 doses of Ipi to induce response in Nivo non-responders (NR) and duration of Nivo in responding pts (NCT03203473). **Methods:** We enrolled pts with advanced RCC with no prior checkpoint inhibitor exposure. All pts received Nivo alone with subsequent arm allocation based on RECISTv1.1 response within 6 months (mos) of tx. Pts with a confirmed partial response (PR) or complete response (CR) within 6 months (mos) discontinued Nivo and were observed (Arm A). Arm A pts reinitiated Nivo if they developed progressive disease (PD); Ipi was added to Nivo if PD persisted or recurred. Pts with stable disease (SD) or PD after no more than 6 mos of Nivo alone received 2 doses of Ipi (Arm B). The primary endpoints were the proportion with PR/CR at 1-year (yr) after Nivo discontinuation (Arm A) and proportion of Nivo NR who convert to PR/CR after adding Ipi (Arm B). **Results:** 83 pts initiated tx of whom 99% had ECOG 0-1, 96% clear cell RCC, 51% tx-naïve, and 69% IMDC intermediate/poor risk. Median follow-up was 17.0 mos. 15 pts were not allocated to an arm [7 withdrew for PD, 7 withdrew for toxicity, 1 still on tx with unconfirmed PR (uPR)]. At 6 mos, induction Nivo resulted in a confirmed PR in 11% of pts (n=9/83): 12% (n=5/42) tx-naïve, 10% (4/41) prior tx, 8% (n=1/13) favorable risk, 11% (n=8/70) intermediate/poor risk (Table). 11 pts (13%: 9 PR, 1 uPR, 1 SD) were allocated to Arm A, of whom 5 (45%, 90% CI 20-73%) remained off Nivo at ≥ 1 yr. Of 57 pts (69%) allocated to Arm B, 2 pts converted to a PR (4%, 90% CI 1-11%), both of whom had prior tx and PD as best response to Nivo alone. Grade 3-4 treatment related adverse events (TrAE) occurred in 7% (n=6/83) on induction Nivo and in 23% (n=13/57) on Arm B (Nivo + Ipi). **Conclusions:** We cannot currently recommend a strategy of Nivo followed by response-based addition of Ipi due to the absence of CR and low PR/CR conversion rate (4%). Though a subset of pts treated with Nivo alone can maintain durable responses off tx at 1-yr, early Nivo discontinuation in the absence of toxicity cannot currently be recommended. Investigation into biomarkers to guide tx is ongoing. Clinical trial information: NCT03203473. Research Sponsor: BMS.

	Induction Nivo (n=83)	Ipi Added in NR Arm B (n=57)
PR	9 (11%)	2 (4%)
uPR	3 (4%)	0
SD	36 (43%)	24 (42%)
PD	35 (42%)	23 (40%)
Unevaluable		8 (14%)

5006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase II study of nivolumab and salvage nivolumab + ipilimumab in treatment-naïve patients (pts) with advanced renal cell carcinoma (RCC) (HCRN GU16-260). *First Author: Michael B. Atkins, Georgetown Lombardi Comprehensive Cancer Center, Washington, DC*

Background: Nivolumab (nivo) is FDA approved for pts with VEGFR TKI-resistant RCC and the nivo + ipilimumab (nivo/ipi) combination is FDA approved for treatment naïve pts with IMDC intermediate and poor risk RCC. Little information is available on the efficacy and toxicity of nivo monotherapy in treatment naïve RCC or the efficacy of nivo/ipi salvage therapy in pts with tumors resistant to initial nivo monotherapy. **Methods:** Eligible pts with treatment naïve RCC received nivo 240mg IV q2 wk x 6 doses followed by 360mg IV q3 wk x 4 doses followed by 480 mg q4 wk until progressive disease (PD), toxicity, or completion of 96 wks of treatment (Part A). Pts with PD prior to or stable disease (SD) at 48 wks (pSD) were potentially eligible to receive salvage nivo (3mg/kg) /ipi (1 mg/kg) q3 wk x 4 doses followed by q4 wk nivo maintenance for up to 48 wks (Part B). All pts were required to submit tissue from a metastatic lesion obtained within 12 months (mo) prior to study entry and prior to Part B. Pathology specimens will be analyzed by immunohistochemistry, quantitative immunofluorescence, WES and RNAseq with results linked to clinical outcome. **Results:** 123 pts with clear cell(cc) RCC were enrolled between 5/2017 and 12/2019 at 12 participating HCRN sites. Median age 65 (range 32-86 years); 72% male. IMDC favorable 30 (25%), intermediate 79 (65%) and poor risk 12 (10%). 22 (18%) had a component of sarcomatoid histology (SARC). 117 pts are currently evaluable for response. RECIST defined ORR was: 34 (29.3%)[CR 5 (4.3%), PR 29 (24.8%)], SD 47 (40.2%), PD 36 (30.7%). ORR by irRECIST was 35%. ORR by IMDC was: favorable 12/29 (41.4%), intermediate/poor 22/87 (25.3%) and for SARC 6/22 (27.3%). Median DOR is 13.8 (10.9, NA) mo. Median PFS is 7.4 (5.5, 10.9) mo. 110 pts remain alive. 60 pts (54 PD, 6 pSD) to date were potentially eligible for salvage nivo/ipi (Part B), but 28 did not enroll due to symptomatic PD (17), grade 3-4 toxicity on nivo (8), other (3). 27 of 32 Part B pts are currently evaluable for efficacy and 30 for toxicity. Best response to nivo/ipi was PR (11%), SD (30%), PD (59%). ORR by irRECIST was 19%. Grade 3-5 Treatment-related AEs (TrAE) were seen in 35/123 (28)% on nivo with 1 death due to respiratory failure. Grade 3-4 TrAE were seen in 10/30 (33%) on nivo/ipi with 0 deaths. Correlative studies are pending. **Conclusions:** Nivo monotherapy is active in treatment naïve ccRCC across all IMDC groups. Toxicity is consistent with prior nivo studies. Salvage treatment with nivo/ipi after nivo monotherapy was feasible in 53% of pts with PD/pSD, with 11% responding. Clinical trial information: NCT03117309. Research Sponsor: Bristol Meyers Squibb.

5007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

FRACTION-RCC: Innovative, high-throughput assessment of nivolumab + ipilimumab for treatment-refractory advanced renal cell carcinoma (aRCC). *First Author: Toni K. Choueiri, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA*

Background: The immuno-oncology (I-O) combination nivolumab + ipilimumab (NIVO+IPI) is approved for first-line (1L) and NIVO is approved for second-line treatment post TKI therapy in aRCC. The open-label, randomized, phase 2 Fast Real-Time Assessment of Combination Therapies in Immuno-Oncology (FRACTION-RCC; NCT02996110) platform study has an adaptive design allowing rapid evaluation of I-O therapies, including NIVO+IPI or other investigational combinations. This FRACTION analysis reports preliminary outcomes with NIVO+IPI in aRCC pts after progression on checkpoint inhibitor therapy. **Methods:** All pts, except 1, had previously received and progressed on checkpoint inhibitor treatment. Pts received NIVO+IPI (NIVO 3 mg/kg + IPI 1 mg/kg Q3W ×4, then after 6 weeks, NIVO 480 mg Q4W), up to 2 years or until progression, toxicity, or protocol-specified discontinuation. Primary endpoints were confirmed objective response rate (ORR; per investigator using RECIST v1.1), duration of response (DOR), and progression-free survival probability at week 24. Safety outcomes were reported. **Results:** 46 pts were randomized to NIVO+IPI. Pts had 0 (n = 1), 1 (n = 10), 2 (n = 12), 3 (n = 10), or ≥4 (n = 13) prior lines of therapy. All pretreated pts had prior anti-PD-(L)1-, none had prior anti-CTLA-4- therapy, and 37 had prior TKI-based therapy; 45 pts progressed on anti-PD-(L)1 as the most recent therapy. Most pts had clear cell aRCC (n = 44). After a median study follow-up of 8.9 months, ORR was 15.2%; no pts achieved complete response and 7 achieved partial response. DOR ranged from 2–19+ months (n = 7); 5 pts had ongoing response. Six of 7 responders had received ≥2 prior lines of therapy. Any-grade treatment-related adverse events (AEs) were reported in 36 pts (78.3%; fatigue, rash [both 19.6%], and diarrhea [17.4%] were most common). Grade 3–4 treatment-related AEs were reported in 13 pts (28.3%; diarrhea [8.7%], ↑amylase and ↑lipase [both 6.5%] were most common). Treatment-related immune-mediated AEs of any grade were reported in 22 pts (47.8%; rash [19.6%], diarrhea [17.4%], and ↑alanine aminotransferase [8.7%]). No treatment-related deaths were reported. Updated and expanded results with an additional 3 months of follow-up will be presented. **Conclusions:** These results suggest that NIVO+IPI may provide durable partial response in some pts with prior progression on checkpoint inhibitors, including some heavily pretreated pts. The safety profile of NIVO+IPI in FRACTION pts was similar to historic data in aRCC with this combination. Clinical trial information: NCT02996110. Research Sponsor: Bristol-Myers Squibb.

5008 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase II trial of lenvatinib (LEN) plus pembrolizumab (PEMBRO) for disease progression after PD-1/PD-L1 immune checkpoint inhibitor (ICI) in metastatic clear cell renal cell carcinoma (mccRCC). *First Author: Chung-Han Lee, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: LEN, a multikinase VEGFR inhibitor, plus everolimus is approved for advanced RCC after prior VEGF-targeted therapy. PEMBRO, an anti-PD-1 antibody, plus axitinib is approved as first-line therapy of advanced RCC. We report phase 2 results of the RCC cohort of a phase 1b/2 trial (Study 111/KEYNOTE-146) of LEN + PEMBRO in patients (pts) who progressed after ICI therapy. **Methods:** We performed a multicenter, open-label study of pts with mccRCC, who previously had disease progression by RECIST (confirmed ≥ 4 weeks later) during or following ICI therapy. Pts had measurable disease by immune-related RECIST, and ≥ 1 prior therapy. Pts received LEN 20 mg orally once daily plus PEMBRO 200 mg IV every 3 weeks until disease progression or toxicity. Tumor assessments were performed every 6 weeks (until week 24), then every 9 weeks. The primary endpoint was objective response rate (ORR) at Week 24 by irRECIST. **Results:** 104 pts were enrolled. At data cutoff (January 12, 2020), 71 (69%) pts were still on study treatment. Most pts had ≥2 prior anticancer regimens (58%). 91 of 104 pts were evaluable for response at Week 12 (13 pts NE at Week 12); 46 of 91 pts achieved a confirmed partial response for an ORR of 51% (Table). Median progression-free survival (PFS) was 11.7 months and median duration of response (DOR) was 9.9 months. The most common treatment-related adverse events (TRAEs) were fatigue (49%), diarrhea (44%), proteinuria (37%), hypertension (31%), nausea (31%), dysphonia (29%), stomatitis (29%), and arthralgia (27%). There was 1 grade 5 TRAE (upper gastrointestinal hemorrhage). 43% of pts required dose reduction and 12% of pts discontinued treatment due to TRAEs. Response and safety data will be updated to include all pts evaluable at an April 9, 2020 cut-off. **Conclusions:** LEN + PEMBRO demonstrated promising antitumor activity in pts with mccRCC with disease progression following ICI therapy. No new safety signals were detected. Efficacy outcomes by investigator review per irRECIST. Clinical trial information: NCT02501096. Research Sponsor: Eisai Inc., Woodcliff Lake, NJ, USA, and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., Kenilworth, NJ, USA.

Parameter	LEN + PEMBRO (n=91)[a]
$ORR_{(week\ 12)}$, % (95% CI)	51 (39.9–61.2)
Disease control rate[b], % (95% CI)	91 (83.4–96.1)
Median DOR, months (95% CI)	9.9 (6.9–NE)
Median time to response, months (range)	1.6 (1.2–7.6)
Parameter	**LEN + PEMBRO (n=103)[c]**
Median PFS, months (95% CI)	11.7 (9.5–NE)
Median PFS follow-up time, months (95% CI)	5.7 (5.5–7.8)

[a]Patients followed for ≥12 weeks for response evaluation [b]Complete response + partial response + stable disease (duration ≥ 5 weeks) [c]Total n as of data cutoff

5009 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Biomarker analyses from the phase III CheckMate 214 trial of nivolumab plus ipilimumab (N+I) or sunitinib (S) in advanced renal cell carcinoma (aRCC). *First Author: Robert J. Motzer, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: In CheckMate 214 (NCT02231749), N+I demonstrated superior clinical outcomes vs S in patients (pts) with aRCC. Here, we report exploratory biomarker analyses of pretreatment tumor samples relative to outcomes. **Methods:** Formalin-fixed, paraffin-embedded aRCC samples were characterized by immunohistochemistry (tumor programmed death ligand 1 [PD-L1], n = 992; PD-L1 combined positive score [CPS], n = 980), whole exome sequencing (WES; tumor mutational burden, indel burden, HLA class I zygosity, and *PBRM1* mutation status; n = 481), and RNAseq (n = 213). Gene signature scores were calculated as the median value of Z-scored expression for transcripts. Association with outcome was tested using Fisher s exact test and Cox proportional hazards model. With ≥ 42 mo follow-up, prolonged progression-free survival (PFS) with N+I (< or ≥ 18 mo; n = 82 vs 27, respectively) was analyzed by *limma* and gene set enrichment analysis of Hallmark gene sets (MSigDB). **Results:** PD-L1 CPS did not have improved predictive power over tumor PD-L1. The WES-derived biomarkers were not associated with outcomes in pts treated with N+I or S. For the RNAseq cohort, objective response rates (ORR) for pts with ≥ median scores, and hazard ratios (HR) relative to < median are shown (Table). A higher angiogenesis (Angio) gene signature score was associated with higher ORR and PFS for S; lower Angio score was associated with higher ORR in N+I. Immune signature scores were not predictive for ORR in N+I. Prolonged PFS with N+I (≥ 18 mo, n = 27) was associated with higher expression of Hallmark inflammatory response and Hallmark epithelial mesenchymal transition (EMT) gene sets (both adjusted $P = 0.002$). **Conclusions:** The Angio gene signature was associated with ORR for S (high score) and N+I (low score). Prolonged PFS in 27 pts receiving N+I was linked with inflammation (consistent with findings from PD-1 blockade monotherapy), but associated with EMT-related transcripts (in contrast with findings in other tumor types). Further validation of these exploratory analyses will be required. Clinical trial information: NCT02231749. Research Sponsor: Bristol-Myers Squibb.

	ORR N+I, %	ORR S, %	PFS N+I, HR (95% CI)	PFS S, HR (95% CI)
RNAseq cohort (n = 213)	32	28		
Angio[1]	19[a]	40[a]	1.23 (0.791.92)	0.58[a] (0.370.92)
T-effector[1]	39	27	1.08 (0.691.68)	0.88 (0.551.40)
Myeloid[1]	38	29	0.79 (0.511.23)	1.04 (0.661.65)
TIS[2]	39	29	0.88 (0.571.37)	0.81 (0.511.28)
Javelin[3]	38	30	0.95 (0.611.48)	1.01 (0.641.59)

[a]$P < 0.05$. 1. *Nat Med* 24:749; 2. *J Immunother Cancer* 6:63; 3. *J Clin Oncol* 37(suppl 15): 101.

5010 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Immunogenomic characterization of advanced clear cell renal cell carcinoma treated with PD-1 blockade. *First Author: David A. Braun, Dana-Farber Cancer Institute, Boston, MA*

Background: Immune checkpoint inhibitors targeting the PD-1 pathway have transformed the management of many advanced malignancies, including clear cell renal cell carcinoma (ccRCC), but the drivers and resistors of PD-1 response remain incompletely elucidated. Further, the common paradigm in solid tumor immunology that pre-existing CD8+ T cell infiltration, in combination with high numbers of nonsynonymous mutations (which, in the context of diverse HLA class I alleles, may be presented as neoantigens) drives response to PD-1 blockade, has not been thoroughly explored in ccRCC. **Methods:** We analyzed 592 tumors collected from advanced ccRCC patients enrolled in prospective clinical trials (CheckMate 009, CheckMate 010, CheckMate 025) of treatment with PD-1 blockade (n = 362) or mTOR inhibition (as control arm; n = 230) by whole-exome (n = 454) and RNA-sequencing (n = 311), integrated with CD8 immunofluorescence analysis (n = 219), to uncover the immunogenomic determinants of therapeutic response and survival. Wilcoxon rank-sum test was used to compare somatic alteration burden between clinical benefit (CB) v.s no CB (NCB); Fisher's exact test was used to compare mutations and copy number alteration by infiltration state; and hazard ratio (HR) was calculated from Cox PH model for progression-free (PFS) and overall survival (OS) endpoints. All tests were at a significance level of $p < 0.05$. **Results:** Conventional genomic markers (tumor mutation burden, p = 0.81; neoantigen load, p = 0.47 for CB vs. NCB) and degree of CD8+ T cell infiltration (p = 0.88 for PFS; p = 0.65 for OS) were not associated with clinical response or altered survival with PD-1 blockade. These advanced ccRCC tumors were highly CD8+ T cell infiltrated, with only 22% having an immune desert phenotype and 5% with an immune excluded phenotype. Our analysis revealed that CD8+ T cell infiltrated tumors are depleted of clinically favorable PBRM1 mutations (p = 0.013) and enriched for unfavorable chromosomal losses of 9p21.3 ($p < 0.001$) when compared to non-infiltrated tumors. When found within infiltrated tumors, del(9p21.3) was associated with worse CB rate (36% (9/25) for del(9p21.3) vs. 88% (7/8) for wildtype at that locus, p = 0.017) and worse survival (HR = 2.38, p = 0.01 for PFS; HR = 2.44, p = 0.01 for OS) with PD-1 blockade. **Conclusions:** These data demonstrate how the potential interplay of immunophenotypes with somatic mutations and chromosomal alterations impacts therapeutic efficacy in advanced ccRCC. Research Sponsor: Department of Defense (CDMRP), U.S. National Institutes of Health, Bristol Myers-Squibb.

5011 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Tumor, immune, and stromal characteristics associated with clinical outcomes with atezolizumab (atezo) + platinum-based chemotherapy (PBC) or atezo monotherapy (mono) versus PBC in metastatic urothelial cancer (mUC) from the phase III IMvigor130 study. *First Author: Matt D. Galsky, Mount Sinai Hospital, New York, NY*

Background: Tumor mutational burden (TMB), PD-L1 expression, T-effector gene expression (GE) and a fibroblast TGF-β–response signature (F-TBRS) are associated with clinical outcomes with atezo mono in mUC (Mariathasan, *Nature*, 2018). Here we explore the potential predictive role of these biomarkers and APOBEC mutagenesis in IMvigor130. **Methods:** Pts receiving first-line (1L) mUC treatment (tx) were randomized 1:1:1 to atezo + PBC, atezo mono, or placebo + PBC. Coprimary efficacy endpoints were PFS and OS. Planned exploratory biomarker analyses included PD-L1 expression, TMB (FoundationOne), and T-effector GE (RNA-seq). **Results:** The 851 biomarker-evaluable pts (BEP) were representative of the 1200 ITT pts. Biomarker results are shown in Table. PD-L1 IC2/3 was associated with significantly longer OS for atezo mono vs placebo + PBC and a combination of PD-L1 IC2/3, and high TMB (> 10 muts/Mb) identified a pt subset (≈ 14% of BEP) with particularly favorable outcomes with atezo mono vs placebo + PBC; similar results for PD-L1 and TMB were not seen with atezo + PBC vs placebo + PBC. APOBEC mutagenesis was associated with improved OS with atezo-containing regimens whereas high F-TBRS was associated with inferior OS with atezo mono. **Conclusions:** These results reinforce the potential predictive nature of biomarkers associated with response/resistance to atezo and highlight potentially distinct biology driving benefit with atezo and atezo + PBC. These findings suggest a possible biomarker-directed approach to 1L mUC tx that warrants mechanistic interrogation and prospective validation. Clinical trial information: NCT02807636. Research Sponsor: F. Hoffmann-La Roche.

Interim OS in ITT pts and BEP.

	Interim OS HR (95% CI)[a]; Sample size (n)	
	Atezo + PBC vs PBC	**Atezo vs PBC**
ITT	0.83 (0.69, 1.00); n = 851	1.02 (0.83, 1.24); n = 719
BEP	0.84 (0.67, 1.04); n = 599	0.91 (0.73, 1.15); n = 539
PD-L1 IC2/3[b]	0.73 (0.47, 1.14); n = 167	0.59 (0.36, 0.96); n = 143
TMB^{high} (> 10 muts/Mb)	0.82 (0.58, 1.17); n = 248	0.71 (0.49, 1.03); n = 236
PD-L1 IC2/3 + TMB^{high}	0.88 (0.48, 1.62); n = 94	0.22 (0.08, 0.63); n = 77
$APOBEC^{high}$	0.46 (0.26, 0.84); n = 112	0.42 (0.23, 0.78); n = 109
T-effector GE (top quartile)	0.79 (0.51, 1.24); n = 161	0.58 (0.33, 1.02); n = 132
$F\text{-}TBRS^{high}$ (top quartile)	1.13 (0.73, 1.72); n = 155	1.92 (1.24, 2.99); n = 136

[a]HRs for the BEP are for descriptive purposes only. [b] PD-L1 expression on immune cells (IC; VENTANA SP142 IHC assay) ≥ 5%.

5012 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

DUTRENEO Trial: A randomized phase II trial of DUrvalumab and TREmelimumab versus chemotherapy as a NEOadjuvant approach to muscle-invasive urothelial bladder cancer (MIBC) patients (pts) prospectively selected by an interferon (INF)-gamma immune signature. *First Author: Enrique Grande, MD Anderson Cancer Center Madrid, Madrid, Spain*

Background: Cisplatin-based neoadjuvant chemotherapy (CT) followed by radical cystectomy (RC) is a standard treatment for MIBC. PD-1/L1 inhibitors as single agent induce pathological complete responses (pCR) in this setting. Predictors of response are still ill defined. DUTRENEO trial aimed to prospectively explore the activity of anti-PDL1 + anti-CTLA4 vs CT in pts selected according to a tumor pro-inflammatory IFN-gamma signature (tumor immune score, TIS). **Methods:** Cisplatin-eligible pts with urothelial MIBC (cT2-T4a, N≤1, M0) candidates to RC were classified as "hot" or "cold" according to a tumor TIS determined by Nanostring technology. Patients with "hot" tumors were randomized to DU 1500 mg + TRE 75 mg every 4 weeks x 3 cycles or standard cisplatin-based CT (GEMCIS or MVACdd). Pts in the "cold" arm received standard CT. Primary endpoint was to achieve ≥8 pCR in the DU+TRE arm. PDL1 expression was assessed using immunohistochemistry. **Results:** 61 pts were recruited in 10 sites between oct-2018 and dec-2019. Pts randomized in the "hot" arms received standard CT (n = 22) or DU+TRE (n = 23) and had a pCR rate of 8/22 pts (36.4%) vs 8/23 pts (34.8%), respectively [OR = 0.923 (0.26 – 3.24)]. In the "cold" arm, 16 pts received CT obtaining a pCR rate of 68.8% (11/16 pts). There were more PDL1 low tumors in the "cold" TIS arm (10/12, 83.3%). pCR rate by PDL1 status is shown in the table. One pt in the DU+TRE arm refused RC. Full treatment was delivered to 81.3% of CT "cold" vs 59.1% of CT "hot" vs 73.9% in the DU+TRE arm pts. Grade 3-4 toxicities were more frequent in the CT arms. **Conclusions:** The combination of DU+TRE is safe and active in MIBC patients in the neoadjuvant setting. Nevertheless prospective stratification by a pro-inflammatory IFN-gamma signature failed to select patients more likely to benefit from IO vs CT in this context. Further studies are required to guide treatment selection. Clinical trial information: NCT03472274. Research Sponsor: AstraZeneca.

	COLD: CT (N = 16)	HOT: CT (N = 22)	HOT: DU+TRE (N = 23)
Pathologic complete response	11 (68.8%)	8 (36.4%)	8 (34.8%)
Progressive disease	0 (0.0%)	2 (9.1%)	1 (4.3%)
pCRs in PDL1 high (%)	50.0%	60.0%	57.1%
pCRs in PDL1 low (%)	90.0	60.0%	14.3%
Completed cystectomy	15 (93.8%)	20 (90.9%)	20 (87.0%)
Grade 3-4 toxicities	10 (62.5%)	8 (36.4%)	5 (21.7%)

5013 Poster Discussion Session; Displayed in Poster Session (Board #82), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Cabozantinib in combination with atezolizumab in urothelial carcinoma previously treated with platinum-containing chemotherapy: Results from cohort 2 of the COSMIC-021 study. *First Author: Sumanta K. Pal, City of Hope Comprehensive Cancer Center, Duarte, CA*

Background: Cabozantinib (C), an inhibitor of MET, AXL, and VEGFR, has been shown to promote an immune-permissive environment and has shown promising clinical activity in combination with immune checkpoint inhibitors (ICIs) in solid tumors including renal cell carcinoma and urothelial carcinoma (UC). ICI monotherapy is approved for patients (pts) with locally advanced or metastatic UC with disease progression after platinum-containing chemotherapy. COSMIC-021, a multi-center phase 1b study, is evaluating the combination of C with atezolizumab (A) in various solid tumors (NCT03170960). We report results from Cohort 2 in UC pts with prior platinum-containing chemotherapy. **Methods:** Eligible pts had ECOG PS 0-1 and had progressed on or after a platinum-containing chemotherapy (including pts with disease recurrences < 12 months after the end of perioperative chemotherapy). Pts received C 40 mg PO QD and A 1200 mg IV Q3W. CT/MRI scans were performed Q6W for first year and Q12W thereafter. The primary endpoint is objective response rate (ORR) per RECIST v1.1 by investigator. Other endpoints include safety, duration of response (DOR), PFS, and OS. **Results:** As of Dec 20, 2019, 30 pts with advanced UC were enrolled with a median follow-up of 16.5 mo (range 12, 21). Median age was 66 yrs (range 44, 84), 73% were male, and 60% had ECOG PS 1. Primary tumor sites were bladder (80%), renal pelvis (10%), and ureter (10%); the most frequent metastatic sites included lung (40%) and liver (27%). Fourteen pts (47%) had received ≥2 prior systemic anticancer therapies. The most common treatment-related AEs (TRAEs) of any grade were asthenia (37%), diarrhea (27%), decreased appetite (23%), increased transaminases (23%), and mucosal inflammation (20%). Grade 3/4 TRAEs occurred in 57% of pts, with no grade 5 TRAEs. Confirmed ORR per RECIST v1.1 was 27% (8 of 30 pts), including 2 pts with CR. DCR (CR+PR+SD) was 64%. Median DOR was not reached, with the longest DOR ongoing at 14.3+ mos. Median PFS was 5.4 mo (range 0.0+, 17.3+). **Conclusions:** C in combination with A demonstrated encouraging clinical activity in pts with advanced UC with an acceptable safety profile. Additional cohorts of pts with advanced UC are being explored in the study. Clinical trial information: NCT03170960. Research Sponsor: Exelixis Inc.

5014 Poster Discussion Session; Displayed in Poster Session (Board #83), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Safety and preliminary efficacy of rogaratinib in combination with atezolizumab in a phase Ib/II study (FORT-2) of first-line treatment in cisplatin-ineligible patients (pts) with locally advanced or metastatic urothelial cancer (UC) and *FGFR* mRNA overexpression. *First Author: Jonathan E. Rosenberg, Memorial Sloan Kettering Cancer, New York, NY*

Background: Programmed cell-death ligand 1 (PD-L1) overexpression is a mechanism for immune escape in UC. Rogaratinib, an oral pan-FGFR1-4 inhibitor, showed promising efficacy in a Phase I study in pts with solid tumors, including UC, with *FGFR1-3* mRNA overexpression (Schuler et al. Lancet Oncol 2019). This Phase Ib/II study is evaluating rogaratinib in combination with atezolizumab, a PD-L1 inhibitor, in pts with *FGFR*-positive, locally advanced or metastatic UC (NCT03473756). We report results from the Phase Ib study. **Methods:** Cisplatin-ineligible pts with untreated metastatic UC were eligible if high *FGFR1* or *3* mRNA was detected by RNA *in situ* hybridization of archival tissue (RNAscope). Pts were treated at a starting dose of rogaratinib 800 mg p.o. BID and atezolizumab 1200 mg i.v. on day 1 (21-day cycle). Primary objectives were safety, tolerability, and determination of the recommended Phase II dose. **Results:** 27 pts were treated (rogaratinib 800 mg + atezolizumab, n = 11; rogaratinib 600 mg + atezolizumab, n = 16); 85% were male, median age was 72 years (range 47-83), 37% had an ECOG PS of 1, and 96% had negative/low *PD-L1* expression. Most common treatment-emergent adverse events (TEAEs) were diarrhea (63%), hyperphosphatemia (44%), and urinary tract infection (37%). Dose interruption/reduction due to AEs occurred in 67%/37% of pts; TEAEs lead to discontinuation in 45.5% (800 mg) and 12.5% (600 mg). Most common grade 3/4 TEAEs were increased lipase without pancreatitis (11%), rash, and increased alanine aminotransferase (7% each). Rogaratinib-related unique TEAEs were hyperphosphatemia (44%) and retinal pigment epithelium detachment (4%). The maximum tolerated dose (MTD) was rogaratinib 600 mg BID based on lower overall frequency of AEs. Of 23 evaluable pts (600 mg, n = 13; 800 mg, n = 10), overall 9 (39%) pts had an objective response (RECIST v1.1); 3 (13%) pts had a complete response (600 mg: 2/13 pts), 6 (26%) pts had a partial response (600 mg: 5/13 pts), and 6 (26%) pts had stable disease (600 mg: 4/13 pts). **Conclusions:** Rogaratinib with atezolizumab showed promising efficacy and safety in cisplatin-ineligible pts with tumor *FGFR1 or 3* mRNA-positive UC, with nearly all pts demonstrating low or negative *PD-L1* expression. Pts are being enrolled at the MTD of rogaratinib 600 mg BID plus atezolizumab. Clinical trial information: NCT03473756. Research Sponsor: Bayer AG. Writing support provided by Complete HealthVizion.

5015 Poster Discussion Session; Displayed in Poster Session (Board #84), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

ERDAFITINIB in locally advanced or metastatic urothelial carcinoma (mUC): Long-term outcomes in BLC2001. *First Author: Arlene O. Siefker-Radtke, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Erdafitinib (JNJ-42756493; ERDA) is the only pan-FGFR kinase inhibitor with US FDA approval for treatment of adults with mUC with susceptible FGFR3/2 alterations (alt) and who progressed on ≥ 1 line of prior platinum-based chemotherapy (chemo). Approval was based on data from the primary analysis of the pivotal BLC2001 trial[1]. Here we report long-term efficacy and safety data from the 8 mg/d continuous dose regimen in BLC2001. **Methods:** BLC2001 (NCT02365597) is a global, open-label, phase 2 trial of pts with measurable mUC with prespecified FGFR alt, ECOG 0-2, and progression during/following ≥ 1 line of prior chemo or ≤ 12 mos of (neo)adjuvant chemo, or were cisplatin ineligible, chemo naïve. The optimal schedule of ERDA determined in the initial part of the study was 8 mg/d continuous ERDA in 28-d cycles with uptitration to 9 mg/d (ERD 8 mg UpT) if a protocol-defined target serum phosphate level was not reached and if no significant treatment-related adverse events (TRAEs) occurred. Primary end point was the confirmed objective response rate (ORR=% complete response + % partial response). Key secondary end points were progression-free survival (PFS), duration of response (DOR) and overall survival (OS). **Results:** Median follow-up for 101 patients treated with ERDA 8 mg UpT was ~24 months. Confirmed ORR was 40%. Median DOR was 5.98 mos; 31% of responders had DOR ≥ 1 yr. Median PFS was 5.52 mos, median OS was 11.3 mos. 12-mos and 24-mos survival rates were 49% and 31%, respectively. Median treatment duration was 5.4 mos. The ERDA safety profile was consistent with the primary analysis. No new TRAEs were seen with longer follow-up. Central serous retinopathy (CSR) events occurred in 27% (27/101) of patients; 85% (23/27) were Grade 1 or 2; dosage was reduced in 13 pts, interrupted for 8, and discontinued for 3. On the data cut-off date, 63% (17/27) had resolved; 60% (6/10) of ongoing CSR events were Grade 1. There were no treatment-related deaths. **Conclusions:** With a median follow-up of 2 yrs, ERDA in mUC + FGFR alt showed a manageable safety profile and consistent efficacy, with median OS of 11.3 mos. 31% had a DOR ≥12 mos and 31% were alive at 24 mos. ERDA monotherapy vs. immune checkpoint inhibitor (PD-1) or chemo is being further analyzed in a randomized control study (THOR; NCT03390504).Reference: Loriot Y, et al. *N Engl J Med.* 2019;381: 338-48. Clinical trial information: NCT02365597. Research Sponsor: Janssen Research and Development.

5017 Poster Discussion Session; Displayed in Poster Session (Board #86), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Final results of PEANUT: Pembrolizumab and nanoparticle albumin-bound paclitaxel (nab-paclitaxel) as salvage therapy for metastatic urothelial carcinoma (UC). *First Author: Patrizia Giannatempo, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: Pembrolizumab (pembro) is a new standard of care in chemotherapy (CT) pre-treated patients (pts) with metastatic UC. Nab-paclitaxel demonstrated preliminary activity in advanced UC. In the PEANUT study (NCT03464734) we investigated their combination in advanced UC after CT failure. **Methods:** In an open-label, single-arm, phase 2 trial, pts received 200 mg pembro, intravenously (IV), on D1 and 125 mg/m^2 IV nab-paclitaxel on D1 and D8, every 3 weeks, until disease progression (PD) or unacceptable toxicity. Inclusion criteria were: predominant UC histology, failure of ≤2 platinum-based CT for metastatic disease. Response was evaluated by RECIST v.1.1 criteria every 2 cycles. Biomarkers included PD-L1 combined positive score (CPS) and comprehensive genomic profiling on tumor and blood samples (FoundationONE and FoundationACT assay). The primary endpoint was the progression-free survival (PFS). The target was to detect an improvement in the median PFS from ≤3.0 months (H0) to ≥5.0 months (H1). **Results:** Between 01 and 12/2019, PEANUT study enrolled 65 pts: 24% were female, median age was 69 yrs (IQR: 61-73); 25% had failed > 1 prior systemic therapies; 35% had ECOG-performance status 1; 33% had liver metastases. The median TMB was 6.9 mut/Mb. After median follow-up (FUP) of 5.5 months, 34 pts have relapsed (52.3%). The median PFS was 5 months (95%CI: 3-not reached). The 3-month PFS was 60.7% (95%CI: 49.8-74.1). The confirmed objective response-rate (ORR) was 47.7% (95% CI: 35.2-60.4): 22 partial responses and 9 complete responses (13.8%). The median duration of response was not reached, and 4 pts (6.1%) are long-term responders (> 12 months). Grade 3 treatment-related adverse events (TRAE) were seen in 20 pts (30.7%). Most common any-grade TRAE included alopecia (76%), neutropenia (33.3%) and asthenia (33%). Neither TMB nor CPS were significantly associated with PFS on univariable analyses. In matched tumor/blood samples, objective responses were seen in 8/10 pts with *PI3KCA* mutations (80%); 6/10 pts with *RB1* alterations (60%); 5/12 pts with DNA damage repair gene alterations (41.7%). **Conclusions:** Pembro-nab-paclitaxel, the first salvage CT-immunotherapy combination in UC, demonstrated a good tolerability, promising PFS and a clinically meaningful ORR in II-III line setting of advanced UC. As more mature data on biomarker selection emerges, this combination warrants additional studies in either second-line or earlier disease settings. Clinical trial information: NCT03464734. Research Sponsor: Fondazione IRCCS Istituto Nazionale dei Tumori, Pharmaceutical/Biotech Company.

5018 Poster Discussion Session; Displayed in Poster Session (Board #87), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II study of nivolumab and ipilimumab for advanced rare genitourinary cancers. *First Author: Bradley Alexander McGregor, Dana-Farber Cancer Institute, Boston, MA*

Background: Patients with rare genitourinary malignancies (Bladder cancer of variant histologies (BCVH), adrenal tumors, chemotherapy refractory germ cell tumors (CRGCT), penile carcinoma and prostate cancer of variant histology (PCVH)) have poor outcomes. Nivolumab and ipilimumab has demonstrated safety and efficacy in genitourinary malignancies. In this multicenter, single arm, multi-cohort phase II trial we evaluated the efficacy of nivolumab and ipilimumab in pts with advanced rare genitourinary cancers (NCT 03333616). Herein, we report the results of the fully accrued BCVH, adrenal and other cohorts. **Methods:** Eligible pts had a metastatic rare genitourinary malignancy, ECOG performance status of 0-2 and no prior immune checkpoint inhibitor exposure; aside from CRGCT pts could be treatment naïve. Eligible pts received nivolumab 3 mg/kg and ipilimumab 1 mg/kg intravenously every 3 weeks for 4 doses with continued nivolumab 480 mg IV every 4 weeks. The primary endpoint was overall response rate (ORR) by RECIST 1.1. **Results:** 56 pts were enrolled at 6 institutions between 4/2018 and 7/2019 in 3 cohorts: BCVH (N = 19), adrenal tumors (n = 18) and other tumors (n = 19). Median follow-up was 9.9 (range < 1~21) months. 28(50%) pts received all 4 doses of nivolumab and ipilimumab. 25 pts received nivolumab maintenance at a median of 4 (range 1-18) cycles. ORR in entire cohort was 16% (n = 9: 2 CR 7 PR, Table); 67% of responders (6/9) maintained response greater than 9 months. Median PFS was 2.8 (2.7-5.2) months. 22 pts (39%) developed treatment-related ≥ grade 3 toxicity; 23% required high dose steroids (≥40 mg prednisone or equivalent) and 15 (27%) pts discontinued treatment due to an AE. Grade 5 toxicity occurred in 3 pts; 1 death was treatment related. **Conclusions:** Nivolumab and ipilimumab resulted in objective responses in a subset of pts with rare GU malignancies, especially in BCVH. Biomarkers are being evaluated and an additional cohort exploring the activity in genitourinary tumors with neuroendocrine differentiation is ongoing. This combination warrants further investigation in these pts with substantial unmet needs. Clinical trial information: NCT 03333616. Research Sponsor: BMS.

	CR/PR	SD	PD	NE
BCVH (n = 19): ORR 37%, 80% CI 22-54%				
Adenocarcinoma	1		3	
Plasmacytoid	1			
Small cell	2		1	
Spindle cell			1	
Squamous cell	2	2	2	
Urachal	1	2	1	
Adrenal Tumors (n = 18): ORR 6%, 80% CI 1-20%				
Adrenal cortical carcinoma	1	7	8	
Paraganglioma		1	1	
Other (n = 19): ORR 5%, 80% CI: 1-19%				
PCVH	1		5	
Penile Carcinoma		2	3	1
CRGCT		1	4	
Other		1	1	
Total	9	16	30	1

5019 Poster Discussion Session; Displayed in Poster Session (Board #88), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II neoadjuvant (N-) gemcitabine (G) and pembrolizumab (P) for locally advanced urothelial cancer (laUC): Interim results from the cisplatin (C)-ineligible cohort of GU14-188. *First Author: Hristos Z. Kaimakliotis, Indiana University Simon Cancer Center, Indianapolis, IN*

Background: Patients (pts) with laUC who are C-ineligible have inferior survival compared to counterparts who receive C based N-therapy and have a pathologic response at radical cystectomy (RC). Cohort 2 (C2) of the GU14-188 trial is designed to assess the tolerability and efficacy of N- G and P in laUC pts who are C-ineligible. **Methods:** Eligible pts for C2 were surgical candidates and C-ineligible with cT2-4aN0M0 bladder UC or mixed histology. Enrollment followed a Simon 2-stage design for H_0 of interval futility which was rejected at stage 1, and fully enrolled. Pts were treated with N- G (1000mg/m^2) on days 1, 8, and 15 of a 28 day cycle (cy) for a total of 3 cy, and overlapped with P 200mg every 3wks starting on cy 1 day 8 x 5 doses. Minimum criteria for evaluation of safety: 1 dose of P, and for efficacy: 2 doses P and RC. The primary endpoint of pathologic muscle invasive response rate (PaIR, ≤pT1N0) was assessed at RC and designed for 86% power, 4% significance to detect PaIR difference from 18 to 40%. Molecular subtyping is planned. **Results:** 37 pts were enrolled to C2 with a median (mdn) age of 72, 70% male, 55% > cT2. C-ineligibility was due to renal function (49%), hearing (30%), neuropathy (12%). Mdn per-pt doses given (intended) for P:5(5) and G:9(9). The PaIR was 51.6% (95%CI 0.35, 0.68), P0 (ypT0N0) rate of 45.2%, and neither correlated with baseline PD-L1 score. Downstage to PaIR occurred in 57% of pts with cT2, and 47% of > cT2. Mdn time to RC from last dose was 5.6wks. Six were not included in the primary analysis: 3 (8.1%) did not have RC due to progression (RFS censored), 2 did not receive required protocol therapy, and 1 withdrew consent. At mdn follow up of 10.8mo (4-24), the estimated 12mo RFS, OS, and DSS is 74.9%, 93.8%, and 100%, respectively. Treatment related AE included grade (gr) 3/4 neutropenia (24%), anemia (13%), and platelets (5%). There were no gr 4 non-heme AE, and of 14 (36%) pts with gr 3, 12 did not preclude RC. Of these, there were 4 gr 3 investigator assessed immune related adverse events (IAirAE) of pneumonitis (5%), colitis (3%), and AST elevation (3%). Though IAirAE improved, protocol therapy was discontinued in 3 pts: 2 did not have RC due to progression. **Conclusion:** N- G with P in C-ineligible pts with laUC is feasible with manageable toxicity, and has a pathologic downstage rate comparable to standard of care in the C-eligible population. G and P warrants further study with component contribution as a C- free N- option in laUC. Clinical trial information: NCT02365766. Research Sponsor: Merck & Co.

5020 Poster Discussion Session; Displayed in Poster Session (Board #89), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Biomarker analysis and updated clinical follow-up of preoperative ipilimumab (ipi) plus nivolumab (nivo) in stage III urothelial cancer (NABUCCO). *First Author: Nick Van Dijk, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands*

Background: Encouraging pathological complete response (pCR) rates were observed in trials testing neoadjuvant pembrolizumab or atezolizumab in urothelial cancer (UC). In cT3-4N0 tumors, pCR to atezolizumab was only 17% and restricted to tumors showing characteristics of preexisting T cell immunity. In NABUCCO, we aimed to increase response to pre-operative checkpoint blockade, particularly in high risk patients (pts), by combining ipi plus nivo in stage III UC. We previously reported pCR in 46% and downstaging to no remaining invasive disease in 58% (ESMO2019). Here, we present biomarker analyses and updated clinical follow-up (FU) data. **Methods:** Twenty four stage III (cT3-4aN0 or cT2-4aN1-3) UC pts who were unfit to receive cisplatin-based chemotherapy or refused, were treated with ipi 3 mg/kg (day 1), ipi 3 mg/kg + nivo 1 mg/kg (day 22), and nivo 3 mg/kg (day 43), followed by resection. The primary endpoint was feasibility (resection < 12 weeks). Efficacy (pCR), safety and biomarker analysis were secondary endpoints. Whole-exome sequencing (WES) was done on baseline tumor samples and local lymph node (LN) metastases showing no response. RNA-seq and multiplex immunofluorescence (mIF) for immune cell markers were done pre- and post-therapy. **Results:** After a median FU of 15.6 months, 2 pts relapsed (both non-pCR); 1 of these 2 pts died of metastatic disease. Tumors showing complete response (CR, for biomarker analysis defined as pCR, CIS or pTa) had a significantly higher tumor mutational burden than non-CR tumors. CR to ipi+nivo was independent of baseline CD8 T-cell presence. There was no difference between CR and non-CR tumors in baseline immune gene signatures, such as interferon gamma and T-effector signatures. Surprisingly, exploratory gene expression analysis revealed that non-CR was associated with a baseline B cell immune signature, particularly immunoglobulins and genes involved in B cell receptor signaling. CD20 positive cells (by mIF) and presence of tertiary lymphoid structures (TLS) at baseline were also associated with non-CR. Upon treatment with ipi+nivo, early and mature TLS increased significantly in responding tumors. A subset of pts showed CR in the bladder, but non-CR in a local LN tumor focus. WES revealed that these LN metastases were genetically different from the primary tumor bulk. **Conclusions:** At 15.6 months follow-up, recurrence after pre-operative ipi+nivo was low. Pathological complete response was not restricted to tumors exhibiting preexisting T cell immunity. Clinical trial information: NCT03387761. Research Sponsor: BMS.

5021 Poster Discussion Session; Displayed in Poster Session (Board #90), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase Ib trial of neoadjuvant/adjuvant durvalumab +/- tremelimumab in locally advanced renal cell carcinoma (RCC). *First Author: Moshe Chaim Ornstein, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH*

Background: Effective neoadjuvant and adjuvant therapies are lacking in locally advanced RCC. Given robust activity of checkpoint inhibitors in mRCC, a phase Ib trial of perioperative Durvalumab (D) +/- Tremelimumab (T) in locally advanced RCC was conducted (NCT02762006). **Methods:** Pts with radiographic evidence of high risk localized RCC (clinical stage T2b-4 and/or N1, M0 disease), adequate performance status, and adequate laboratory values were eligible. Primary objective was safety and feasibility of neoadjuvant/adjuvant D +/- T. **Results:** Twenty-nine pts were enrolled. Cohorts, regimens, and immune-related adverse events (irAE) are detailed in the table. In total, 79% male, median age 61 (range, 42-84), 8%/88%/4% clinical T2/T3/T4, 27% positive clinical lymph nodes (LN+), and median time from neoadjuvant dose to surgery was 7 days. On surgical pathology: 5%/14%/77%/5% pathologic T1/T2/T3/T4, and 13% LN+. Median time from treatment to first grade (Gr) >3 irAE or any Gr irAE requiring corticosteroids was 99 days (range, 32-207). There were no treatment-related delays to nephrectomy or surgical complications. Although not meeting the protocol-defined MTD, given higher than expected irAEs, the study was suspended. **Conclusions:** Perioperative durvalumab in locally advanced RCC appears safe. The addition of tremelimumab is associated with higher rates of toxicity. Updated toxicity will be presented. Clinical trial information: NCT02762006. Research Sponsor: AstraZeneca.

Cohorts and toxicity. irAE numbers represent events, not patients. [D = Durvalumab 1500mg; Gr = grade; T = Tremelimumab 75mg].

Cohort	Cohort 1		Cohort 2		Cohort 2a		Cohort 3	
Number of patients	6		6		8		8	
Neoadjuvant Therapy	D (x1)		D + T (x1)		D + T (x1)		D + T (x1)	
Adjuvant Therapy	D (x1 dose)		D (x1 dose)		D (x1 year)		D+T (x 1 dose) then D (x 1 year)	
irAEs	Gr 1-2	Gr 3-4	Gr 1-2	Gr 3-4	Gr 1-2	Gr 3-4	Gr 1-2	Gr 3-4
Elevated lipase/amylase	1		1		2	1	2	1
Rash			1		2		1	1
Elevated AST/ALT					1	1	2	
Hyper/Hypo-thyroidism			1				4	
Arthralgia/Myalgia						2		
Pruritus					1		3	
Pneumonitis							1	
Hypophysitis							1	
Parasthesia						1	1	
Hyperglycemia		1			1			
DKA		1						
Xerostomia			1				1	
Thrombocytopenia				1				
Nephritis							1	

5022 Poster Discussion Session; Displayed in Poster Session (Board #91), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II trial of atezolizumab in BCG-unresponsive non-muscle invasive bladder cancer: SWOG S1605 (NCT #02844816). *First Author: Peter C. Black, Vancouver Prostate Centre, University of British Columbia, Vancouver, BC, Canada*

Background: Radical cystectomy (RC) is the standard of care for patients with BCG-unresponsive high risk non-muscle invasive bladder cancer (NMIBC), but many patients are unfit for surgery or elect bladder preservation. Based on the reported efficacy of atezolizumab in metastatic urothelial carcinoma and the known expression of PD-L1 in NMIBC after BCG therapy, this trial was designed to evaluate the activity of atezolizumab in BCG-unresponsive high risk NMIBC. **Methods:** This single arm phase II registration trial testing systemic atezolizumab (1200 mg IV) every 3 weeks for one year aimed to enroll 135 (70 CIS and 65 non-CIS) eligible patients with histologically proven BCG-unresponsive high risk NMIBC who were unfit for or declined RC. Here we report on the subset with CIS (with or without concomitant Ta/T1) among patients who received at least one protocol treatment. The primary endpoint was pathological complete response (CR) rate at 6 months as defined by mandatory biopsy with a null hypothesis of 30% and alternative of 50% with a 1-sided alpha = 0.05 and 96% power. The 3 month CR rate, defined by cytology, cystoscopy and for-cause biopsy, is reported here as a secondary endpoint, in addition to safety. **Results:** Seventy-five eligible CIS patients were enrolled. Two received no treatment and are not evaluable. Of 73, median patient age was 73.4 years and median number of prior BCG doses was 12. Concomitant Ta/T1 tumor was found in 30 (41.1%) patients, including T1 disease in 16 (21.9%). A CR was observed in 30 (41.1%; 95% CI 29.7%, 53.2%) patients at 3 months and 19 (26.0%; 95% CI 16.5%, 37.6%) at 6 months. Any possibly or probably treatment-related adverse event (AE) was observed in 61 (83.6%) patients. The most frequent AEs were fatigue 36 (49.3%), pruritis 8 (11.0%), hypothyroidism 8 (11.0%), and nausea 8 (11.0%). Grade 3-5 AEs occurred in 9 (12.3%) patients and there was one treatment-related death (myasthenia gravis with respiratory failure and sepsis). **Conclusion:** The observed response to atezolizumab at 3 and 6 months in patients with BCG-unresponsive CIS was similar to that reported in recent similar trials and meets the benchmark for initial CR defined by the FDA guidance. This trial provided no new safety concerns. The duration of response will determine if this is a suitable treatment option for patients with BCG-unresponsive high risk CIS. Clinical trial information: 02844816. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

5023 Poster Discussion Session; Displayed in Poster Session (Board #92), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Evaluation of predictive biomarkers for nivolumab in patients (pts) with metastatic clear cell renal cell carcinoma (mccRCC) from the CheckMate-025 (CM-025) trial. *First Author: Miriam Fícial, Brigham and Women's Hospital, Boston, MA*

Background: We previously showed that levels of CD8+ tumor infiltrating cells (TIC) expressing PD-1 but not TIM-3 and LAG-3 ($CD8^+$ $PD1^+TIM3^-LAG3^-$) were associated with response to nivolumab (nivo) in pretreated mccRCC pts (Pignon et al, 2019). Here, we sought to validate these findings in a randomized Phase III trial of nivo versus everolimus (evero) (CM-025) and explore the association of the biomarker with transcriptomic profiles. **Methods:** Tumor tissues from the CM-025 trial were analyzed (nivo arm: n = 116, evero arm: n = 107). Density/percentage of $CD8^+$ $PD1^+TIM3^-LAG3^-$ TIC was evaluated by immunofluorescence (IF) and PD-L1 expression on tumor cells (TC) was evaluated by IHC. Linear association with outcomes was assessed using binary logistic (ORR, clinical benefit (CB) defined as CR/PR and PFS≥12 months) and Cox PH (PFS, OS) regression models (1-sided p-values shown). Bulk RNA-seq was performed in a subset of samples (n = 71) and data analyzed using ssGSEA and Gene Signature Scores (GSS). **Results:** In the nivo arm, density of $CD8^+$ $PD1^+TIM3^-LAG3^-$ TIC (IF biomarker) was associated with ORR (OR = 1.43, p = 0.03) and CB (OR = 1.54, p = 0.02) while a trend was observed with PFS (HR = 0.87, p = 0.06). At an optimized cutoff, nivo treated pts with high IF biomarker (24/116, 20.7%) had higher ORR (45.8% vs 19.6%, p = 0.01) and CB (33.3% vs 14.1%, p = 0.03) and longer median PFS (9.6 vs 3.7 months, p = 0.03) than pts with low IF biomarker. A significant interaction between the IF biomarker and treatment was seen for both PFS and OS (2-sided p = 0.02 and 2-sided p = 0.08, respectively; significance determined as $p < 0.15$). By bulk RNA-seq, several inflammatory pathways (FDR $q < 0.1$) and inflammatory GSS (FDR $q < 0.05$) were enriched in the high IF biomarker group. When combined with the IF biomarker, TC PD-L1 expression (≥1%) further separated clinical outcomes (ORR, CB and PFS) in the nivo arm. In the evero arm, the IF biomarker was neither prognostic nor predictive of any clinical outcome. **Conclusions:** High levels of $CD8^+$ $PD1^+TIM3^-LAG3^-$ TIC predicted response to nivo (but not to control evero) in mccRCC pts and were associated with activation of inflammatory response. Combination with TC PD-L1 further improved its predictive value, confirming our previous findings (Pignon et al, 2019). Further validation in the setting of first-line anti-PD-1 therapy is ongoing. Research Sponsor: Department of Defense (CDMRP), Pharmaceutical/Biotech Company, U.S. National Institutes of Health.

5024 Poster Discussion Session; Displayed in Poster Session (Board #93), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Association of gene expression with clinical outcomes in patients with renal cell carcinoma treated with pembrolizumab in KEYNOTE-427. *First Author: David F. McDermott, Dana-Farber Cancer Center, Harvard Medical School, Boston, MA*

Background: We assessed the association of baseline RNA-sequencing–based gene expression signatures and DNA alterations with response or resistance to pembrolizumab in patients with advanced renal cell carcinoma in cohorts A (clear cell; n = 110) and B (non-clear cell; n = 165) of the phase 2 KEYNOTE-427 study (NCT02853344). **Methods:** Using RNA-sequencing, we analyzed the association of gene expression signatures (18-gene T-cell–inflamed gene expression profile [GEP]; 10 non–T-cell–inflamed GEP canonical signatures [angiogenesis, gMDSC, glycolysis, hypoxia, mMDSC, MYC, proliferation, RAS, stromal/EMT/TGFβ, WNT]) quantifying tumor microenvironment elements (TME) with objective response rate (ORR) and progression-free survival (PFS). Canonical signatures were derived from 2 databases (TCGA, Moffit) using an algorithm that included genes based on their correlation to reference signatures in the literature. Signature definitions were finalized before linking to the clinical data, and significance was prespecified at 0.10 given the potential for limited power. Canonical signatures were analyzed through regression testing of response for association with consensus signatures after adjusting for T-cell–inflamed GEP and International Metastatic RCC Database Consortium scores in the model. *P* values were adjusted for multiplicity. Using whole exome sequencing, we also summarized the association of renal cell carcinoma driver gene mutations with ORR. Clinical data cutoff: Jan 30, 2019. **Results:** Patient characteristics for this analysis were comparable to the overall population. In cohort A, T-cell–inflamed GEP (n = 78) was statistically significantly associated with a better ORR ($P = 0.021$; AUROC = 0.65) but not PFS ($P = 0.116$). No other TME canonical signatures showed a correlation with ORR or PFS. ORR was estimated for mutations (Table). **Conclusions:** RNA-sequencing–based, T-cell–inflamed GEP was associated with ORR in patients with clear cell renal cell carcinoma receiving first-line pembrolizumab. Precision was limited by sample size for estimating ORR by specific gene mutation status. Evaluation of tissue-based biomarkers in larger studies are planned. Biomarker analyses from patients in cohort B will also be presented. Clinical trial information: NCT02853344. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Gene	n (mutant vs non-mutant)	ORR (95% CI) %, mutant	ORR (95% CI) %, non-mutant
SETD2	18 vs 58	44 (25-66)	24 (15-37)
PBRM1	33 vs 43	30 (17-47)	28 (17-43)
VHL	56 vs 20	30 (20-43)	25 (11-47)
BAP1	14 vs 62	14 (4-40)	32 (22-45)

5025 Poster Session (Board #94), Fri, 8:00 AM-11:00 AM

CD68+ tumor-associated myeloid cells as the target of adenosine-induced gene products and predictor of response to adenosine blockade with ciforadenant (cifo) in renal cell cancer (RCC). *First Author: Martin H Voss, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Adenosine in the tumor microenvironment (TME) is immunosuppressive and may play a role in resistance to immunotherapy. We described an adenosine induced gene expression signature (AS, Fong, Cancer Disc 2020) that correlates with response to therapy with cifo, an adenosine A2A receptor antagonist, as monotherapy or in combination with atezolizumab in refractory RCC. These genes express chemokines that signal through CCR2 and CXCR2 to recruit myeloid cells including immunosuppressive tumor associated-M2 macrophages, which are thought to mediate resistance to anti-PD(L)1 treatment. We now identify tumor infiltrating $CD68^+$ myeloid cells as the effector cell for adenosine mediated immunosuppression. **Methods:** 82 RCC pts have been treated in an ongoing Phase 1/1b trial evaluating cifo (100mg po bid) monotherapy or combination with atezolizumab (840mg IV q 2 weeks). Tumor biopsies, obtained at screening and on therapy, are available for analysis in 32 pts to date. RNA expression was measured in tumors using Nanostring. Immunohistochemistry (IHC) for CD68 was performed on biopsies with CD68+ tumors defined as $>$ 4% tumor area containing CD68+ cells. **Results:** Pt characteristics are median age 63; median prior therapies 3, with 72% failing prior anti-PD(L)1. Gene expression of M2 markers consisting of CD68 ($p = 0.0008$) and CD163 ($p = 0.03$) was higher in baseline samples from AS+ compared to AS- pts. By IHC, 10 pts had CD68+ cells infiltrating the tumor; 9 of 10 AS+. Tumor regression was observed in 6 of 10 CD68+ pts (N = 3 monotherapy and 3 combination) including 4 partial responses (PR, RECIST). No PRs and 2 minor responses were seen in 22 pts who were CD68- ($p < 0.005$). Median time to progression was not reached for CD68+ vs 2 mo for CD68-. Paired biopsies showed a significant reduction in infiltrating CD68+ cells ($p = 0.03$) with treatment including 2 of 2 evaluable PRs. **Conclusions:** Adenosine immunosuppression is mediated by M2 macrophages, which can be reversed by cifo. Enumerating tumor infiltrating CD68+ cells may be a valuable biomarker for identifying pts that will respond to adenosine blockade. Clinical trial information: NCT02655822. Research Sponsor: Corvus Pharmaceuticals.

5026 Poster Session (Board #95), Fri, 8:00 AM-11:00 AM

Clinical outcomes and economic burden for bladder cancer patients: An analysis from a Swedish cancer registry. *First Author: Joaquim Bellmunt, Beth Israel Deaconess Medical Center, Boston, MA*

Background: To investigate the clinical and economic disease burden for patients (pts) with non-muscle invasive bladder cancer (NMIBC), muscle invasive bladder cancer (MIBC), and metastatic urothelial carcinoma (mUC) using a Swedish bladder cancer registry. **Methods:** Pts diagnosed with bladder cancer in the Stockholm Gotland region between 2005-2013 were included and followed until May 31, 2015 or until death. MIBC was classified if a T, N, M at diagnosis was T2, T3, T4, N1, N2, N3, or M1, otherwise pts were classified as NMIBC. All diagnostic and therapeutic interventions were captured and differentiated. Inpatient and outpatient healthcare resource utilization (days) and associated costs (US $) were also analyzed. **Results:** 3587 bladder cancer pts were identified (NMIBC-2728; MIBC-859) with a median observation time of 49.7 (Q1-Q3: 27.8-78.7) versus 17.2 (Q1-Q3: 6.5-39.3) months. 5-year survival for patients with NMIBC at diagnosis was 71.3% (95% CI; 69.5-73.3) and 26.4% (95%CI; 23.4-29.8) for MIBC. By year 1, survival for MIBC-T2, T3, and T4 was 66%, 41.7%, and 28.4%, respectively. Progression from NMIBC to MIBC was estimated in 19.4% (528/2728) of pts. In year 1, 84% (2,275/2,728) of TURBT procedures were performed on NMIBC pts. Over the next 2-10 years of follow-up, 11,035 repeat TURBT procedures were undertaken in this cohort. In the 859 MIBC pts, 607 TURBT procedures and 333 radical cystectomies occurred in year 1. In the same cohort, 28.3% (243/859), 15.5% (78/505), and 8.6% (29/338) received systemic chemotherapy in years 1, 2, and 3, respectively. Total health resource utilization (HRU) cost for the NMIBC and MIBC cohorts is provided in Table. Median HRU cost per person-year was estimated at $30,470 for MIBC versus $9,228 for NMIBC in year 1. For MIBC-T2, T3, and T4, median cost per person-year was $30,154, $33,917, and $38,959 in year 1, respectively. **Conclusions:** This retrospective analysis accomplished its primary purpose to provide a real-world understanding for the clinical and economic impact of bladder cancer over a 10-year period when treatment interventions were relatively consistent. Total HRU Costs for Patients with NMIBC and MIBC per Follow-up Year (Years 1 to 5). Research Sponsor: Janssen.

Diagnosis	Follow-up year	No. of Patients	Person-Years	Total HRU Costs (US $)
NMIBC	1	2,728	2,632	34,811,317
	2	2,531	2,393	14,867,314
	3	2,200	1,972	10,188,457
	4	1,765	1,574	7,323,923
	5	1,399	1,252	5,152,229
MIBC	1	859	666	21,083,790
	2	505	418	4,598,487
	3	338	280	2,082,339
	4	237	203	1,227,474
	5	178	156	693,829

5027 Poster Session (Board #96), Fri, 8:00 AM-11:00 AM

Early results of TROPHY-U-01 Cohort 2: Sacituzumab govitecan (SG) in platinum-ineligible patients (pts) with metastatic urothelial cancer (mUC) who progressed after prior checkpoint inhibitor (CPI) therapy. *First Author: Daniel Peter Petrylak, Yale University School of Medicine, New Haven, CT*

Background: SG is an antibody-drug conjugate consisting of a humanized monoclonal anti–Trop-2 antibody coupled to the cytotoxic agent, SN-38, via a unique hydrolyzable linker. The epithelial cell surface antigen, Trop-2, demonstrates greater expression between UC vs normal tissue, and is a promising target. In a phase 1/2 basket study (IMMU-132-01), SG showed an overall response rate (ORR) of 31% and manageable toxicity in 45 pts with mUC who had a median of 2 (range 1–6) prior therapy lines (Tagawa 2019 ASCO GU). Recent interim results for cohort 1 of the TROPHY-U-01 study in 35 pts with mUC who progressed on platinum and CPI therapy demonstrated an ORR of 29% in pts with a median of 3 prior treatment lines (range 2–6) (Tagawa 2019 ESMO). The most common grade $\geq$3 treatment-related AE (TRAE) was neutropenia. **Methods:** TROPHY-U-01 (NCT03547973) is a global, open-label, phase 2 trial evaluating the antitumor activity of SG (10 mg/kg, days 1 and 8 of 21-day cycles) in pts with advanced UC with measurable disease and ECOG PS 0 or 1. Cohort 2 includes platinum-ineligible pts who progressed after CPI therapy in the first-line metastatic setting. The primary objective is ORR evaluated with RECISTv1.1 by central review. Secondary objectives include progression-free survival, overall survival, and duration of response. **Results:** 18 pts with baseline tumor assessment (50% male; median age 79 y [range 57–87], 67% visceral metastases; 28% liver metastases) received a median of 2 (range 1–5) prior therapies. At a median follow-up of 6 months, ORR was 28% (5/18) with 4 confirmed PRs, and 1 PR pending confirmation. The majority of pts (61% [11/18]) had target lesion reduction. The safety profile was consistent with prior reports. Key grade $\geq$3 TRAEs were neutropenia (39%), fatigue (33%), diarrhea (28%), leukopenia (22%), anemia (17%), and febrile neutropenia (11%). No events of interstitial lung disease, ocular toxicities, or grade $>$ 2 neuropathy were reported. There were no treatment-related deaths. **Conclusions:** In cisplatin-ineligible pts, the ORR for currently approved first-line CPI treatments is ~23–29% (Balar 2017 *Lancet;* Vuky 2018 ASCO). These preliminary data with SG show a manageable safety profile with an encouraging ORR of 28% and support the development of SG in platinum-ineligible pts with mUC who have progressed after CPI therapy. Clinical trial information: NCT03547973. Research Sponsor: Immunomedics, Inc.

5028 Poster Session (Board #97), Fri, 8:00 AM-11:00 AM

Association of molecular subtypes with pathologic response in a phase II study of co-expression extrapolation (COXEN) with neoadjuvant chemotherapy (NAC) for localized, muscle-invasive bladder cancer (SWOG S1314; NCT02177695). *First Author: Seth P. Lerner, Baylor College of Medicine, Houston, TX*

Background: Cisplatin-based NAC is recommended for patients with MIBC prior to radical cystectomy (RC) but the majority will not have a pathologic response. To identify responders the COXEN gene expression model with chemotherapy-specific scores (for DD-MVAC and GC) was developed and in a prospective rPII clinical trial (SWOG S1314) the GC score was associated with path downstaging in the pooled arms. We investigated RNA based molecular subtypes as additional predictive biomarkers for response to NAC in patients treated in S1314. **Methods:** Eligibility required cT2-T4a N0 M0, predominant urothelial, $>$ 5 mm tumor, cisplatin eligible, and plan for RC and PLND. 237 patients were randomized between 4 cycles of ddMVAC and GC. Based on Affymetrix transcriptomic data used to assign COXEN scores, we determined subtypes using 3 classifiers: TCGA (k=5), Consensus (k=6), and MD Anderson (MDA; k=3). Primary objective was to assess subtype association with pathologic response to NAC in the pooled arms and to determine any association with COXEN. TCGA and Consensus classifiers were collapsed into 3 groups for ROC analyses. We tested whether each classifier contributed additional predictive power when added to a model based on pre-defined stratification factors (PS 0 vs. 1; T2 vs. T3, T4a). **Results:** 161 patients had adequate tissue and gene expression results, received at least 3 of 4 cycles of NAC and had pT-N response based on RC. Covariates were 78% PS=0, 89% T2, 84% male, median age 65, 51% randomized to ddMVAC, 49% GC with 33% pT0 and 52% downstaging. Although the TCGA 3 group classifier (Basal-Squamous (BS)/Neuronal, Luminal, Luminal infiltrated) and GC Coxen score yielded the largest AUCs (0.607, 0.610) for pT0 response, neither reached statistical significance ($p=0.20$, $p=0.22$). For downstaging ($<$pT2), the 3 category Consensus classifier (BS/NE-like, Luminal, Stroma-rich) significantly increased the AUC from 0.568 (strat factors alone) to 0.620 ($p=0.044$). The MDA classifier AUC was 0.640 and the GC Coxen score AUC was 0.626, but neither were significant ($p=0.076$, $p=0.14$. The MVAC Coxen score did not improve the AUC beyond the stratification factors. **Conclusions:** The Consensus classifier, which is based in part on the TCGA and MDA classifiers, modestly improved prediction for pathologic downstaging when added to clinical stage and PS. With additional followup, we will assess the association of COXEN scores and subtypes with overall survival. Clinical trial information: NCT02177695. Research Sponsor: U.S. National Institutes of Health.

5029 Poster Session (Board #98), Fri, 8:00 AM-11:00 AM

Outcomes and the impact of genomic characteristics on patients with metastatic urothelial carcinoma enrolled in early phase trials. *First Author: Omar Alhalabi, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: With the recent approvals of checkpoint inhibitors (CPIs), a fibroblast growth factor receptor (FGFR) inhibitor, and an antibody-drug conjugate, patients with platinum-refractory metastatic urothelial carcinoma (mUC) have several treatment options available. However, many patients with platinum-refractory mUC need novel therapies after progressing on current therapies. We assessed the role of early phase trials in treatment of mUC and the impact of genomic alterations on their outcomes. **Methods:** We retrospectively analyzed medical records of patients with mUC who received an investigational therapy at the phase 1 clinic and had CLIA-certified clinical next generation sequencing. Clinical parameters and mutations were abstracted. Progression-free survival (PFS) and overall survival (OS) were calculated using Kaplan-Meier methods. Hazard ratios (HR) were calculated using the Cox proportional hazard model. **Results:** Among the 57 pts enrolled in 41 unique phase 1 trials between 2015 and 2019, 16% (9/57) had variant histology: neuroendocrine carcinoma (n = 3) and urachal carcinoma (n = 6). Median age was 64. Majority were males (72%). 97% received prior platinum therapy and 60% had received prior CPI therapy. Across the pure urothelial carcinoma cohort (n = 48), median PFS was 4.2 months (m), median OS was 9.8 m, and the overall response rate (ORR) was 19%. *TP53, FGFR, TERT, and ARID1A* alterations (alt) were detected in 54%, 41%, 21% and 17% of UC patients, respectively. Patients harboring a *TP53* alt, compared to no alt, had a shorter median PFS of 3.2m vs 9.6 m (HR = 2.738 [1.247 - 6.011], p = 0.0121). On the contrary, median PFS was longer in *FGFR* alt, compared to no alt, 6.3m vs 3.2m (HR = 0.4662 [0.224 - 0.971], p = 0.0415). Of note, 64% of FGFR alt patients were treated under an early phase FGFR targeting trial. Median OS was numerically longer in *FGFR* alt and shorter in *TP53* alt but did not reach statistical significance (table). **Conclusions:** Patients with mUC may derive clinical benefit from enrollment in phase I clinical trials. Patients with TP53 alterations had numerically worse outcomes. Patients with mUC should be considered for an FGFR targeting therapy in the setting of an FGFR alteration. Research Sponsor: None.

	UC	*TP53* alteration vs. no alteration	*FGFR* alteration vs. no alteration
PFS	4.2 m	3.2 m vs 9.6 m	6.3 m vs 3.2 m
HR for PFS (95% Confidence Interval)	--	2.74 (1.25 - 6.01) p = 0.01	0.4662 (0.224 - 0.971) p = 0.0415
OS	9.8 m	5.9 m vs 16.5 m	16.5 m vs 5.3 m
HR for OS (95% Confidence Interval)	--	1.52 (0.73 - 3.15) p = 0.26	0.55 (0.26 - 1.17) p = 0.12

5030 Poster Session (Board #99), Fri, 8:00 AM-11:00 AM

Pathological response rates and quality of life outcomes of neoadjuvant cabazitaxel and cisplatin chemotherapy for muscle-invasive transitional cell carcinoma of the urinary bladder. *First Author: Amarnath Challapalli, University Hospital Bristol NHS Foundation Trust, Bristol, United Kingdom*

Background: Neoadjuvant cisplatin-based combination chemotherapy (NAC) improves survival in muscle invasive bladder cancer (MIBC). However, response rates and survival remain suboptimal. We sought to evaluate the efficacy, safety and tolerability of cisplatin cabazitaxel combination in this patient group. **Methods:** A phase 2 single arm trial (Simon 2 stage), to recruit at least 26 evaluable patients was designed with 80% power to detect the primary endpoint, objective response rate (ORR) of $>$ 35%. ORR was defined as pathological complete response (pCR) plus partial response (pathological downstaging), measured by pathologic staging (T2 or greater at diagnosis, to T1 or less at radical cystectomy). Treatment was with Cisplatin 70mg/m2 and Cabazitaxel 15mg/m2 on day 1 of a 21 day cycle, for 4 cycles prior to surgery. Toxicity was recorded using CTCAE v.4.03. Quality of Life (QoL) data were collected at baseline, prior to each cycle of chemotherapy and at 3-5 weeks after 4th cycle of chemotherapy using EQ-5D and EORTC QLQ-C30, BLM30 questionnaires. **Results:** Objective response was seen in 15 out of 26 evaluable patients, 57.7% and over a third of patients achieved pCR (9/26; 34.6%). 78% (21/27) of patients completed all cycles of treatment, with only 6.7% of the reported adverse events (AEs) being graded 3 or 4. There were 6 treatment related SAEs reported but no SUSARs. In patients who achieved objective response the median progression free (PFS) and overall survival (OS) were not reached (median follow up: 41.5m). In contrast, median PFS (7.2m) and OS (16.9m) were significantly worse (p = 0.001) in patients who did not respond. Response rates for EORTC QLQ-C30, BLM 30 and EQ5D questionnaires was 70.4, 70.4 & 63% respectively, at end of treatment. There was no significant difference in EORTC QLQ C30 summary, global health scores and EQ5D score with treatment. There was a significant decline in mean QLQ C30 domain scores after 1st cycle compared to baseline, but no further deterioration with subsequent cycles of chemotherapy. **Conclusions:** Cabazitaxel with cisplatin as NAC of MIBC can be considered a safe, well-tolerated and effective regimen with higher pCR rate of 34.6%. This compares favorably to that with Cisplatin/Gemcitabine (23-26%). Minimal changes in Global Health & EQ5D observed during NAC further demonstrates the excellent tolerability of this regimen and to our knowledge are the first data regarding QoL in NAC in MIBC. These results warrant further evaluation in a larger phase 3 study. Clinical trial information: 2011 004090 82. Research Sponsor: Sanofi.

5031 Poster Session (Board #100), Fri, 8:00 AM-11:00 AM

Assessing the potential cost-effectiveness of the addition of atezolizumab to first-line platinum chemotherapy in advanced urothelial cancer: Implications for value-based pricing. *First Author: Ali Raza Khaki, University of Washington, Seattle, WA*

Background: Data from interim analysis of IMvigor130 trial showed that 1st line treatment of advanced urothelial cancer (aUC) with atezolizumab (Atezo) + platinum-based chemotherapy (PBC) significantly improved progression-free survival (PFS), but not overall survival (OS), vs PBC. Switch maintenance anti-PD(L)1 after completion of PBC as 1st line therapy is an alternate strategy, recently reported to significantly prolong OS. We aimed to compare cost-effectiveness of combined treatment (Atezo+PBC) vs PBC based on IMvigor130. **Methods:** We used a partitioned-survival model to evaluate the potential cost-effectiveness of treatment with A) Atezo+PBC (gemcitabine with cisplatin or carboplatin) or B) PBC alone with checkpoint inhibitor pembrolizumab at progression (standard-of-care). PFS and OS curves were extracted from IMvigor 130 and parametric models were fit to approximate outcomes with Atezo+PBC with the hazard ratio (HR) from the trial used to project outcomes for PBC alone. We used a health-care payer perspective with a two-year time horizon. Model outputs — costs, life-years, quality-adjusted life years (QALYs) — were used to calculate an incremental cost-effectiveness ratio (ICER). A scenario analysis evaluated the "value-based price" needed for Atezo+PBC to be cost-effective; a one-way sensitivity analysis was also performed. **Results:** Results of the cost-effectiveness analysis are summarized in the table. The mean projected incremental cost of Atezo+PBC compared to PBC was $59,604 for a mean incremental gain of 0.09 life-years and 0.07 QALYs. This resulted in an ICER of $629,755/life-year and $895,800/QALY, respectively. A 33% reduction would be needed in the price of atezolizumab to make Atezo+PBC cost-effective at an ICER of $150,000/QALY. Results were sensitive to cost of pembrolizumab at progression, the cost of Atezo+PBC, and the OS HR between Atezo+PBC and PBC. **Conclusions:** Combined chemoimmunotherapy with atezolizumab and PBC would likely not be cost-effective for the first-line treatment of aUC. However, with a price rebate of 33%, it would approach being cost-effective at a widely used cost-effectiveness threshold. Research Sponsor: U.S. National Institutes of Health.

	PBC	Atezo + PBC	Incremental Results
Costs per person	$92,135	$151,738	$59,604
Life-Years per person	1.27	1.37	0.09
QALYs per person	1.01	1.07	0.07
ICER	QALYs	Life-Years $895,800	$629,755

5032 Poster Session (Board #101), Fri, 8:00 AM-11:00 AM

Comparative effectiveness of second-line (2L) single-agent atezolizumab (A), nivolumab (N), and pembrolizumab (P) in patients (Pts) with locally advanced or metastatic urothelial cancer (aUC) who progressed on platinum-based systemic chemotherapy (plat-chemo): Results from a real-world dataset. *First Author: Umang Swami, Huntsman Cancer Institute at the University of Utah, Salt Lake City, UT*

Background: Five PD-1/L1 inhibitors (PDi) are approved for 2L therapy (Rx) for aUC after progression on plat-chemo, but none compared with each other in randomized trials. Here, we assessed comparative effectiveness of 2L PDi in real-world setting. **Methods:** Pt level data of Pts with aUC were extracted from Flatiron Health EHR-derived de-identified database. Inclusion criteria: 1L Rx with plat-chemo; receipt of single agent PDi in 2L; initiation of 2L PDi 6 mos before data-cut off. Exclusion criteria: $>$90 days from diagnosis to date of next visit to ensure active engagement of Pts with data providing site; initiation of 2L after 7/31/2016 to ensure uptake of PDi for aUC. OS was compared from the date of initiation of 2L Rx. Comparative effectiveness was examined by Cox proportional hazards model, stratified by treatment propensity score. Each Pts' propensity of receiving each 2L PDi was modeled via a random forest based on Pt and disease characteristics potentially driving Rx selection for a PDi (gender, smoking status, race/ethnicity, relapsed vs de novo disease, time between 1L & 2L Rx, cis vs carboplatin in 1L; year of Rx with PDi & following characteristics before 2L Rx: ECOG, Hb, age, ICD codes for liver or CNS mets, albumin & PD-L1 status when available). **Results:** 703 Pts with aUC who initiated 2L Rx between 8/1/2016 to 10/31/2019 were eligible. 2L Rx were A (n=322), N (n=127) & P (n=254). Durvalumab & avelumab were excluded due to low utilization in this dataset. Median follow up from 2L initiation was 4.8 mos. Median OS (mos; 95% CI) with A (6.4 mos; 5-8.7), N (8 mos; 6.3-11.3) and P (8.5 mos; 6.1-11.6) were similar (propensity stratified log rank p=0.19; simple log-rank p=0.34). Over time proportion of Pts receiving 2L A decreased, P increased & N increased then decreased ($p<0.001$). Propensity stratified comparative effectiveness estimates are below. **Conclusions:** In this real-world cohort of Pts with aUC, OS with 2L Rx with A, N, & P were similar on both univariate and propensity stratified analyses. These results agree with prior trial level meta-analysis (PMID 31200951). Strength of this analysis includes large Pt level data from a real world cohort. Limitations include retrospective nature of this study. Research Sponsor: None.

Propensity stratified pairwise comparative effectiveness estimates.

2L	Hazard ratio	95% CI	p value
N vs A	0.82	0.63-1.08	0.16
P vs A	0.82	0.64-1.05	0.11
P vs N	1.00	0.74-1.34	0.99

5033 Poster Session (Board #102), Fri, 8:00 AM-11:00 AM

Early response marker during pembrolizumab treatment in metastatic urothelial cancer: Temporal shift in peripheral CD4 T cells expressing chemokine receptors. *First Author: Maud Rijnders, Erasmus MC Cancer Institute, Erasmus University Medical Center, Rotterdam, Netherlands*

Background: Approval of PD1 blockade greatly improved treatment possibilities for patients with platinum-resistant metastatic urothelial cancer (mUC), however the current response rate for pembrolizumab is less than 25%. Since PD-L1 expression does not have predictive value in this setting, the aim of this study was to identify new markers to improve patient selection. **Methods:** Between Sept 2017 and Jan 2020, 84 mUC patients received pembrolizumab in a prospective biomarker discovery study (NCT03263039). Peripheral blood samples (n = 22) taken prior to and at 6 and 12 weeks after start of treatment were analyzed for frequencies of CD4 and CD8 T cells expressing co-inhibitory, co-stimulatory and chemokine receptors using multiplex flow cytometry. Plasma chemokine levels were determined using ELISA (n = 38), and fresh tumor biopsies obtained prior to and during treatment (n = 26) were analyzed for densities and phenotypes of T cells using multiplex immunofluorescence staining. T cell receptor clonality was analyzed in peripheral blood (n = 10) and tumor biopsies (n = 6) using RNA sequencing. Patients were classified as responder (complete or partial response) or non-responder (progressive disease) according to RECIST v1.1 after 12 weeks of treatment. **Results:** Longitudinal sampling revealed that upon treatment the frequency of CXCR3+ CD4 T cells decreased in responders, whereas the frequency of CXCR3+ CCR1+ CD4 T cells drastically increased in non-responders. Before treatment, the frequency of CD4 T cells co-expressing CXCR3 and CCR1 was already decreased in responders. Notably, in responders, the treatment-related decrease in frequency of CD4 T cells expressing chemokine receptors was accompanied by a decrease in the frequency of CD4 T cells expressing the co-inhibitory receptor PD1, whereas an increase in the frequency of CD4 T cells expressing the co-stimulatory receptor 4-1BB was observed. These findings will be complemented with chemokine levels in plasma, contexture of T cells in tumor biopsies, and T cell receptor clonality analysis. **Conclusions:** mUC patients responding to pembrolizumab treatment demonstrated an on-treatment decrease in frequency of CD4 T cells expressing chemokine receptors that is accompanied by a changed frequency of co-signaling receptor expressing CD4 T cells. These data show that dynamic immune phenotyping can distinguish effective from less effective immune activation by pembrolizumab, and may provide early markers for benefit from PD1 blockade in mUC patients. Research Sponsor: Merck Sharp & Dohme.

5034 Poster Session (Board #103), Fri, 8:00 AM-11:00 AM

First-line pembrolizumab (pembro) monotherapy in advanced non-clear cell renal cell carcinoma (nccRCC): Updated follow-up for KEYNOTE-427 cohort B. *First Author: Jae-Lyun Lee, Asan Medical Center and University of Ulsan College of Medicine, Seoul, South Korea*

Background: KEYNOTE-427 (NCT02853344), a single-arm, open-label, phase 2 study, showed antitumor activity with first-line pembro monotherapy in nccRCC (cohort B). Studies of RCC and immune-oncology have shown that depth of tumor response may correlate with long-term benefit. We present the association between depth of response and OS plus updated efficacy and safety data in cohort B. **Methods:** Pts with histologically confirmed nccRCC, who did not receive prior systemic therapy, and who have measurable disease (RECIST v1.1) received pembro 200 mg IV Q3W for 2 y or until progressive disease, unacceptable toxicity, or withdrawal. End points were ORR (primary), DOR, and PFS (RECIST v1.1); OS; and safety. Association between depth of response, defined as maximum reduction from baseline in sum of target lesions, and OS was evaluated using a Cox proportional hazards model with target lesion reduction group as time-varying covariate. **Results:** Of 165 pts, 72% had papillary histology, 13% had chromophobe histology, and 16% were unclassified. Median time from enrollment to data cutoff was 18.7 mo (range, 9.9-26.0). ORR was 26.1% (95% CI, 19.5-33.5; 10 CRs, 33 PRs). Median (range) DOR was 15.3 mo (2.8-21.0+); 57.3% had DOR ≥12 mo. At 18-mo, PFS rate was 18.9% and OS rate was 67.0%. Most pts (58.8%) had some reduction in target lesions. Pts with a > 30% reduction in target lesions had an increased probability of survival (Table). ORR (95% CI) was similar for papillary (28.0% [20.1-37.0]) and unclassified (30.8% [14.3-51.8]) histology but lower for chromophobe (9.5% [1.2-30.4]). OS rates at 18 mo were 70.8%, 66.7%, and 50.0 in the papillary, chromophobe, and unclassified groups, respectively. Treatment-related AEs (TRAEs) occurred in 67.9% of all pts, primarily pruritus (19%), hypothyroidism (14%), and fatigue (14%). Grade 3-5 TRAEs occurred in 14% of pts; 2 pts died of TRAEs (pneumonia and cardiac arrest). **Conclusions:** First-line pembro monotherapy continued to show antitumor activity in nccRCC with no new safety concerns. In general, for pts who had greater reductions in target lesions, the trend was toward improved OS; pts with reduction of tumor burden ≥80% had comparable long term outcomes to those who achieved a RECIST 1.1 defined CR. Clinical trial information: NCT02853344. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	Association of Depth of Response and Risk for Death N = 165	
	n (%)	HR (95% CI)
Depth of response, %		
CR	10 (6.1)	0 (0.0-NE)
−100 to −80	12 (7.3)	0 (0.0-NE)
< −80 to −60	17 (10.3)	0 (0.0-NE)
< −60 to −30	22 (13.3)	0.66 (0.2-2.0)
< −30 to −0	36 (21.8)	Reference
0 to < 20	36 (21.8)	0.96 (0.4-2.3)
≥20	22 (13.3)	1.66 (0.7-3.8)

5035 Poster Session (Board #104), Fri, 8:00 AM-11:00 AM

Atezolizumab (atezo) therapy for locally advanced/metastatic urinary tract carcinoma (mUTC) in patients (pts) with poor performance status (PS): Analysis of the prospective global SAUL study. *First Author: Daniel Castellano, Hospital Universitario 12 de Octubre, Madrid, Spain*

Background: Pts with PS > 1 have a poor prognosis and are often excluded from clinical trials. The single-arm SAUL study (NCT02928406) evaluated atezo in a 'real-world' population. Overall, safety and efficacy were consistent with prior trials. However, ECOG PS 2 pts had worse overall survival (OS) but fewer adverse events (AEs) than ECOG PS 0/1 pts [Sternberg, 2019], likely reflecting shorter treatment duration and warranting exploration. **Methods:** Pts with mUTC received atezo 1200 mg q3w until loss of clinical benefit or unacceptable toxicity. The primary endpoint was safety. Post hoc analyses compared baseline factors, AEs and efficacy in pts with ECOG PS 2 vs 0/1. In this analysis, AE incidences were restricted to the first 45 days of atezo to adjust for differing treatment exposure. **Results:** None of the baseline factors explored was significantly associated with worse OS or disease control rate (DCR) in ECOG PS 2 pts. However, pts with visceral metastases and ECOG PS 2 had particularly poor outcomes. Safety appeared similar between subgroups. **Conclusions:** ECOG PS 2 pts have a dismal prognosis. The higher proportion with poor prognostic factors despite similar age in ECOG PS 2 vs 0/1 pts may suggest that poor PS was related to disease rather than comorbidities. Risk/benefit should be considered especially carefully when treating pts with ECOG PS 2 due to high-burden/visceral disease. Clinical trial information: NCT02928406. Research Sponsor: F Hoffmann-La Roche Ltd, Basel, Switzerland.

	ECOG PS	
Parameter, n (%)	**2 (n = 101)**	**0/1 (n = 896)**
Median age, y (range)	69 (43–93)	68 (34–92)
Age ≥80 y	10 (10)	68 (8)
Male	78 (77)	694 (77)
Renal impairment	2 (2)	44 (5)
Visceral metastases	52 (52)	322 (36)
Low Hb	32 (32)	118 (13)
Low albumin	46 (47)[a]	183 (21)[b]
Low ALP	45 (45)[c]	207 (23)[d]
PD-L1 IC 2/3	21 (21)[e]	243 (27)[f]
No prior chemo for mUTC	27 (27)	355 (40)
AE, days 1–45		
Any G	75 (74)	656 (73)
G3/4	43 (43)	216 (24)
G5	5 (5)	10 (1)
Treatment related	30 (30)	339 (38)
Special interest	13 (13)	143 (16)
AE leading to atezo withdrawal	2 (2)	25 (3)
Median OS, mo (95% CI)	2.3 (1.6–2.6)	10.0 (8.9–11.2)
Objective response rate [95% CI]	5 (5) [2–11]	130 (15) [12–17]
DCR[g] [95% CI]	14 (14) [8–22]	384 (43) [40–46]

[a]n = 97; [b]n = 873; [c]n = 100; [d]n = 889; [e]n = 91; [f]n = 837. [g]CR/PR or stable disease for ≥4 wks
G = grade

5036 Poster Session (Board #105), Fri, 8:00 AM-11:00 AM

Impact of renal impairment on clinical outcomes in patients (pts) with locally advanced or metastatic (LA/M) urinary tract carcinoma (UTC) treated with atezolizumab (atezo): Analysis of the international SAUL study. *First Author: Margitta Retz, Rechts der Isar Medical Center, Technical University of Munich, Munich, Germany*

Background: Atezo, which targets PD-L1, is an approved therapy for LA/M urothelial carcinoma based on the IMvigor210 and IMvigor211 trials. The single-arm SAUL study (NCT02928406) showed consistent activity and safety in a broader population, including understudied scenarios, eg pts with renal impairment or other IMvigor211 exclusion criteria. **Methods:** Pts with LA/M UTC received atezo 1200 mg q3w until disease progression or unacceptable toxicity. The primary endpoint was safety; secondary endpoints included overall response rate (ORR) and overall survival (OS). Post hoc analyses explored outcomes in pts classified as: chemotherapy (CT) ineligible (calculated creatine clearance [CrCl] 15– < 30 mL/min); cisplatin ineligible and carboplatin eligible (CrCl 30– < 60 mL/min); or cisplatin eligible (CrCl ≥60 mL/min). **Results:** Of 1004 enrolled pts, 46 (5%) were classified as CT ineligible and 420 (42%) as cisplatin ineligible. Results are summarized below. **Conclusions:** These post hoc analyses suggest pts typically considered cisplatin or CT ineligible are candidates for atezo. Pts with renal impairment achieved similar ORR and DCR to pts with CrCl ≥60 mL/min, without increased toxicity. Imbalances in pt characteristics may explain numerical differences in OS. Clinical trial information: NCT02928406. Research Sponsor: F Hoffmann-La Roche Ltd, Basel, Switzerland.

CrCl, mL/min	**15– < 30 (n = 46)**	**30– < 60 (n = 420)**	**≥60 (n = 529)**
Median age, y (range)	75 (48–92)	72 (40–93)	63 (34–86)
Female, n (%)	15 (33)	112 (27)	97 (18)
Visceral metastases, n (%)	18 (39)	161 (38)	194 (37)
No prior CT for LA/M UTC, n (%)	13 (28)	145 (35)	223 (42)
PD-L1 IC 2/3,[a] n (%)	10 (22)	115 (27)	138 (26)
Median atezo duration, mo (range)	3.0 (0.0–18.7)	2.8 (0.0–18.9)	2.8 (0.0–19.0)
Grade ≥3 AEs, n (%)			
Any	21 (46)	188 (45)	239 (45)
Treatment related	3 (7)	51 (12)	73 (14)
Special interest	1 (2)	23 (5)	43 (8)
AE leading to atezo withdrawal, n (%)	3 (7)	22 (5)	32 (6)
Median OS, mo	5.7	8.5	9.4
(95% CI)	(3.4–11.0)	(7.0–10.8)	(8.0–10.4)
ORR, n (%)	6 (13)	62 (15)	67 (13)
[95% CI]	[5–26]	[12–19]	[10–16]
DCR,[b] n (%)	21 (46)	179 (43)	197 (37)
[95% CI]	[31–61]	[38–48]	[33–42]

DCR = disease control rate
[a]≥5% of tumor immune cells express PD-L1
[b]Complete/partial response or stable disease for ≥4 wk

5037 Poster Session (Board #106), Fri, 8:00 AM-11:00 AM

Phase I expansion study of cabozantinib plus nivolumab (CaboNivo) in metastatic urothelial carcinoma (mUC) patients (pts) with progressive disease following immune checkpoint inhibitor (ICI) therapy. *First Author: Daniel da Motta Girardi, National Cancer Institute, National Institutes of Health, Bethesda, MD*

Background: Previous treatment with ICI is more common in clinical practice since recent FDA-approval of 5 ICIs in second-line and 2 in first-line for mUC. There is lack of data regarding the use of ICI after progression on a prior ICI. Cabozantinib has been shown to have immunomodulatory properties and may have synergistic effect with ICI. **Methods:** This is a phase I expansion cohort of mUC pts, who received prior ICI, treated with Cabozantinib 40mg daily and Nivolumab 3mg/kg every 2 weeks until disease progression/unacceptable toxicity. The primary objective was to determine the efficacy and tolerability of CaboNivo. **Results:** Twenty-nine mUC pts were treated. Median follow-up was 14.1 months (mo). The majority of pts were male (75.8%); 27 were White (93.1%), and 2 were Asian (6.9%). Primary tumor was bladder in 21 pts (72.4%) and upper tract in 8 (27.6%). Twenty-two pts (75.9%) had visceral metastasis (mets), 4 (13.8%) had lymph node only mets and 13 (44.8%) had liver mets. The median number of prior lines of treatment for mUC was 2 (range 0-8) with 17 pts (58.6%) receiving 2 prior lines of treatment. The majority of pts (86.2%) received prior chemotherapy for mUC and all pts received prior ICI. The median number of cycles of prior ICI was 7 (range 1-20) and median time between previous ICI and CaboNivo was 2.5 mo (range 1-18). The best response to previous ICI was partial response (PR) in 1 pt (3.4%), stable disease (SD) in 13 (44.9%), progressive disease (PD) in 14 (48.3%) and one (3.4%) was not evaluable (NE). The overall response rate for CaboNivo was 13.8% with 4 pts achieving PR (13.8%), 15 SD (51.7%), 7 PD (24.2%) and 3 NE (10.3%). Responses were seen in the liver, lung, and lymph nodes. Among 4 pts with PR, 2 were primary refractory to previous ICI and 2 had SD. At cutoff date the median duration of response was not reached and 3 PR were still ongoing: 1 had just began and the other 2 were ongoing at 12.3 and 26.4 mo. Among 15 pts with SD, 4 had SD for more than 6 mo and 2 were still ongoing at 8.1 and 25.1 mo. Median progression-free survival was 3.6 mo (95% CI: 2.1 – 5.3 mo) and median overall survival was 10 mo (95% CI: 5.8 – 16.7 mo). Grade 1/ 2 treatment related adverse events (AEs) occurred in 28 pts (97%) and >Grade 3 (G>3) AEs occurred in 14 pts (48%). The most common G>3 AEs were fatigue (14%), hypophosphatemia (14%), lymphocyte count decrease (14%), hypertension (7%) and hyponatremia (7%). **Conclusions:** CaboNivo is clinically active and safe in heavily pretreated pts with progressive mUC following ICI. Clinical trial information: NCT02496208. Research Sponsor: U.S. National Institutes of Health.

5038 Poster Session (Board #107), Fri, 8:00 AM-11:00 AM

Infigratinib and treatment response in advanced/unresectable or metastatic urothelial carcinoma in first-line and later-line treatment settings. *First Author: Yung Lyou, City of Hope Comprehensive Cancer Center, Duarte, CA*

Background: Infigratinib (BGJ398) is a potent and selective FGFR1–3 tyrosine kinase inhibitor (TKI), previously reported to be effective and well tolerated in patients with locally advanced/unresectable or metastatic urothelial carcinoma (mUC) bearing *FGFR3* alterations [Pal et al. Cancer Discovery 2018]. However, this previous study did not examine differences in infigratinib activity based on number of prior lines of treatment (LOT). TKIs studied in other indications (e.g. VEGFRis in renal cell carcinoma) have shown consistent activity in both the first and later LOT. Given the effect seen with other TKIs, we sought to determine if infigratinib showed consistent treatment responses in patients with mUC according to LOT. **Methods:** Eligible patients had mUC and prior platinum-based chemotherapy unless contraindicated and activating *FGFR3* mutations/ fusions. Infigratinib was dosed at 125 mg orally daily (3 weeks on/1 week off). The primary endpoint of objective response rate (ORR: partial response [PR] and complete response [CR]) was assessed, as well as disease control rate (DCR: CR + PR + stable disease [SD]). After classification of LOT for each patient, subgroup analysis of response by LOT was performed. **Results:** 67 patients were enrolled; 81% received ≥1 prior LOT for mUC. 13 patients (19.4%) received infigratinib as 1st LOT for mUC due to ineligibility to receive platinum-based chemotherapy. ORR for the 67 patients was 25% (95% CI 15.5–37.5) and DCR was 64% (95% CI 51.5–75.5). The ORR with 1st-line infigratinib was 31% (95% CI 9.1–61.4) compared with 24% (95% CI 13.5–37.6) for 2nd and later (salvage) LOT. DCR was 46% (95% CI 19.2–74.9) for 1st-line and 69% (95% CI 54.4–80.5) for ≥2 LOT. 13 of the 59 patients with urothelial bladder carcinoma (UBC) received 1st-line treatment with an ORR of 31% (95% CI 9.1–61.4) and 46 patients in ≥2 LOT had an ORR of 20% (95% CI 9.4–33.9). All 8 patients with upper tract urothelial carcinoma (UTUC) received salvage therapy, with an ORR of 50% and a DCR of 100%. An analysis of other outcome measures (e.g. PFS, OS) will be presented. **Conclusions:** These results indicate that infigratinib has activity in patients with mUC regardless of LOT. Additionally, patients with UTUC showed a trend for better ORR and DCR. Taken together, these results support the ongoing adjuvant PROOF 302 study comparing infigratinib with placebo in patients with resected disease, assessing infigratinib in an even earlier setting in a UTUC-enriched population (NCT04197986). Clinical trial information: NCT01004224. Research Sponsor: QED Therapeutics.

5039 Poster Session (Board #108), Fri, 8:00 AM-11:00 AM

Ipilimumab challenge/re-challenge in metastatic urothelial carcinoma (mUC) and other genitourinary (GU) tumors treated with cabozantinib+nivolumab (CaboNivo) or cabozantinib+nivolumab+ipilimumab (CaboNivoIpi). *First Author: Scot Anthony Niglio, National Cancer Institute, National Institutes of Health, Bethesda, MD*

Background: We investigated challenging/re-challenging pts with ipilimumab (ipi) after progression on CaboNivo or CaboNivoIpi. **Methods:** In a phase I expansion study, patients with mUC post-platinum chemotherapy and other GU tumors patients who progressed on Cabo 40 mg daily plus nivolumab, 3 mg/kg every 21 days (CaboNivo) alone or with ipi, 1 mg/kg every 21 days for 4 cycles (CaboNivoIpi)-and achieved a PR or SD≥6 mo, were challenged/re-challenged with ipi, 1 mg/kg every 21 days for up to 4 cycles. Restaging scans were done every 6 wks for the first 12 wks, then every 8 wks and evaluated by RECIST 1.1. **Results:** In total, 24 patients were evaluated: 18 pts (8 UC (5 bladder and 3 upper tract), 4 clear cell renal cell carcinoma (RCC), 3 urachal adenocarcinoma (adeno), 2 bladder adeno, and 1 sarcomatoid clear cell RCC) who progressed on CaboNivo were challenged with ipi. In the challenge group, median (m) follow-up was 21.2 months. One pt achieved a PR in the LNs, but was found to have brain metastases before the next restaging, 13 had SD and 4 had PD. Median duration of PR or SD was 3.6 months (95% CI: 1.4 – 7.8 months). The mOS from start of ipi challenge was 13.9 months (95% CI: 5.8 months- not estimable); mPFS was 4.6 months (95% CI: 1.9 – 8.7 months). Grade 1/2 treatment related adverse events (AEs) occurred in all 18 pts (100%) and ≥Grade 3 (G≥3) AEs occurred in 11 pts (61%). The most common G≥3 AEs were hypophosphatemia (22%), hypertension (6%), adrenal insufficiency (6%), increased AST (6%), and ALT (6%). Six patients (3 bladder UC, 1 penile squamous cell (SCC) carcinoma, 1 urethral SCC, and 1 clear cell RCC with sarcomatoid features) who progressed on CaboNivoIpi were re-challenged with Ipi. On re-challenge, mfollow-up was 20.9 months. There were no PRs, 3 SDs and 3 PDs. mOS from start of re-challenge was 4.0 months (95% CI: 2.2 – 23.3 months) and mPFS was 1.9 months (95% CI: 1.1 – 2.6 months). Grade 1/2 treatment related AEs occurred in all 6 pts (100%) and ≥Grade 3 (G≥3) AEs occurred in 2pts (33%). G≥3 AEs included 1 hypertension (17%) and 1 hyperphosphatemia (17%). **Conclusions:** Ipi challenge/ re-challenge showed low response rates in pts previously treated with CaboNivo or CaboNivoIpi. However, pts treated with CaboNivo who were challenged with ipi had a better OS than patients who had progressed on CaboNivoIpi and were re-challenged with ipi. Larger trials are warranted testing the ipi challenge in pts progressing on CaboNivo. Clinical trial information: NCT02496208. Research Sponsor: U.S. National Institutes of Health.

5040 Poster Session (Board #109), Fri, 8:00 AM-11:00 AM

Recombinant humanized anti-PD-1 monoclonal antibody toripalimab in patients with metastatic urothelial carcinoma: Results of an open-label phase II clinical study Polaris-03. *First Author: Xinan Sheng, Peking University Cancer Hospital and Institute, Beijing, China*

Background: Patients with advanced metastatic urothelial carcinoma (UC) who experience disease progression after standard therapy have limited treatment options. Phase I study of toripalimab in subjects with heavily pretreated metastatic UC had demonstrated an acceptable safety profile and promising clinical activity. Here we report the safety and efficacy result of toripalimab in a phase II clinical study (POLARIS-03) in Chinese patients with metastatic urothelial carcinoma. (Clinical trial ID: NCT03113266). **Methods:** Metastatic UC Patients receive toripalimab 3 mg/kg Q2W until disease progression, unacceptable toxicity or voluntary withdrawal. Clinical response is assessed every 8 weeks. Tumor PD-L1 expression and other biomarkers will be evaluated for correlation with clinical response. **Results:** From May 2017 to September 2019, 204 patients were screened and the study enrollment was completed with 151 patients enrolled from 15 participating centers. The median age was 62 years and 66% were male. 87% patients had visceral metastasis. By the cut-off date of Jan 6, 2020, 92.1% (139/151) patients experienced treatment related adverse event (TRAE) and grade 3 and above TRAE occurred in 35.8% (54/151) patients. Most common TRAE included anemia, triglycerides increased, proteinuria, fatigue, and hyperglycemia. Treatment discontinuation due to a TRAE occurred in 6 (4.0%) patients, while dose delay due to a TRAE occurred in 23 (15.2%) patients. Three patients with major protocol deviations were excluded from efficacy analysis. Among 148 patients assessed by IRC per RECISTv1.1, 2 CR, 36 PR, and 30 SD were observed for an ORR of 25.7% and a DCR of 45.9%. The median DOR was 15.7 months. The median PFS was 1.9 months, and the median OS was estimated 20.8 months. PD-L1 expression results were obtained from 141 patients. PD-L1+ patients (n=46) had significant better ORR than PD-L1- patients (n=95), 41.3% versus 16.8% ($p<0.01$). **Conclusions:** Toripalimab has demonstrated encouraging clinical activity in chemo-refractory UC patients with a manageable safety profile. Patients will be continuously monitored for safety and overall survival. Clinical trial information: NCT03113266. Research Sponsor: Shanghai Junshi Bioscience Co., LTD, Shanghai, China.

5041 Poster Session (Board #110), Fri, 8:00 AM-11:00 AM

Pembrolizumab (pembro) for the treatment of patients with Bacillus Calmette-Guérin (BCG) unresponsive, high-risk (HR) non–muscle-invasive bladder cancer (NMIBC): Over two years follow-up of KEYNOTE-057. *First Author: Arjun Vasant Balar, Perlmutter Cancer Center, NYU Langone Health, New York, NY*

Background: Pembro was recently approved for the treatment of HR NMIBC based on results from the phase 2 KEYNOTE-057 (NCT02625961) study. Herein we present safety, efficacy, and posttreatment outcomes with > 2 y follow-up from KEYNOTE-057 cohort A. **Methods:** Patients with histologically confirmed HR BCG-unresponsive carcinoma in situ (CIS) with or without papillary tumors who received adequate BCG therapy and were ineligible for or opted out of radical cystectomy (RC) received pembro 200 mg Q3W for up to 2 y or until disease recurrence, progression, or unacceptable toxicity. The primary end point was complete response rate (CRR). Key secondary end points were duration of response (DOR) and safety. **Results:** Overall, 102 patients were initially enrolled, and 96 were included in the efficacy analysis. Median time from enrollment to data cut off was 28.4 months (range, 18.2-40.5). CRR was 40.6% (95% CI, 30.7-51.1), and median DOR was 16.2 months (range, 0+ to 30.4+). Among 39 patients with CR, 18 (46.2%) had a DOR ≥12 months. No patient's disease progressed to muscle-invasive or metastatic bladder cancer while on study treatment. Median PFS and OS were not reached. At 12 months, PFS was 82.7% and OS was 97.9%. A total of 36 patients (37.5%) underwent RC after discontinuation from study treatment, which included 9 of 22 patients (40.9%) who had recurrence after initial CR and 27 of 57 (47.4%) nonresponders. Of the 36 who underwent RC, 33 (91.6%) had no pathological upstaging to MIBC and 3 (8.3%) had at least pT2 disease at time of RC. For subsequent treatments other than RC, 27 of 96 (28.1%) patients received additional intravesical therapy (eg, BCG, gemcitabine, or mitomycin), 21 of 96 (21.9%) underwent local procedures (eg, TURBT), and 3 of 96 (3.1%) received systemic therapy (eg, pembro). In 102 patients treated with pembro, treatment-related AEs (TRAEs) occurred in 67 (65.7%) patients; most frequently reported TRAEs were fatigue, pruritus, and diarrhea (10.8% each). Grade 3/4 TRAEs occurred in 13 patients (12.7%), and 21 patients (20.6%) experienced immune-mediated AEs. There were no grade 5 TRAEs. **Conclusions:** After > 2 y of follow-up, durable and clinically meaningful activity of pembro was observed in patients who had HR BCG-unresponsive CIS with or without papillary tumors and who were ineligible for or opted out of RC. Pembro did not seem to limit the opportunity for subsequent therapies, including RC. The safety profile was consistent with what is reported in the literature. Clinical trial information: NCT02625961. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

5042 Poster Session (Board #111), Fri, 8:00 AM-11:00 AM

Thromboembolism (TE) in patients (pts) with bladder cancer treated with checkpoint inhibitors (CPIs). *First Author: Iris Yeong- Fung Sheng, Cleveland Clinic, Cleveland, OH*

Background: Most pts with bladder cancer will be treated with immunotherapy. There is concern for increased TE risk with CPIs in this already high risk population. We present the first analysis of the incidence and outcomes of venous (VTE) and arterial (ATE) thromboembolism in pts with bladder cancer treated with CPIs. **Methods:** Consecutive pts with bladder cancer treated with CPIs at the Cleveland Clinic from 1/2015 to 12/2019 were identified and TE events noted. Overall survival (OS) was estimated using Kaplan-Meier method and the impact of VTE on OS was evaluated using Cox proportional hazards regression. **Results:** Of 274 pts, 72% were men (median age 73.3 years, 89% white), 82% had pure UC, 92% had lower tract disease, and 67% had a Bajorin score ≥1 (median KPS 90, 61% visceral metastases), 59% had prior systemic therapy (median 1, range 0-4) and 36% had prior TE (14% ATE, 19% VTE, 0.4% both). At CPI initiation, 24% were on antiplatelet therapy, and 15% on therapeutic anticoagulation. CPI (median doses 5, range 8.5-59) included: 40% atezolizumab, 3% nivolumab, 57% pembrolizumab. VTE occurred in 14% (n = 37), including 8% DVT, 4% PE, 2% both. DVT locations were 56% lower limb, 26% upper limb, 15% visceral vein, 4% visceral+upper limb. 2% (n = 5) had ATE (1% CVA, 0.4% visceral, 0.4% left subclavian). 92% of VTE and all ATE occurred within 6 months of CPI initiation. The incidence of TE was 10.9% (95%CI 6.6%—15.1%) at 6 months and 19.8% (95%CI 13.3%-26.4%) at 12 months. 82% of VTE (mean 6 days) and all ATE (mean 5 days) resulted in hospitalization. Multivariate analysis showed TE (HR 2.296, 95%CI 1.451-3.632, p = 0.0004), Bajorin score 1 (HR 1.490, 95%CI 1.036-2.142, p = 0.0315), and Bajorin score 2 (HR 3.50, 95%CI 2.14-5.74, p < 0.0001) were independently associated with worse OS. **Conclusions:** CPIs in bladder cancer pts are associated with a high TE risk, especially within six months of initiation. TE is associated with worsened survival. Further investigation into the risk factors for CPI-associated TE is needed to identify if benefits exist from thromboprophylaxis. Research Sponsor: None.

5043 Poster Session (Board #112), Fri, 8:00 AM-11:00 AM

Dissecting outcomes of patients (pts) with <ypT2N0 disease after neoadjuvant chemotherapy (NAC) for muscle invasive bladder cancer (MIBC): Results from a large, international, multicenter collaboration. *First Author: Praful Ravi, Dana-Farber Cancer Institute, Boston, MA*

Background: Pathologic complete response (pCR) after NAC for MIBC is strongly correlated with long-term overall survival. However, there are sparse data on the risk of recurrence based on depth of pathologic response (pT0, pTa, pTis, pT1), and the differential impact of clinicopathologic factors and NAC regimen on recurrence. **Methods:** Baseline data on all pts with cT2-4N0-1 MIBC receiving NAC and who achieved < ypT2N0 disease at radical cystectomy (RC) from 9 international centers were obtained. The key outcome was time to recurrence (TTR) – defined as the time to any recurrence in the urinary tract or regional/distant metastasis, with death (in the absence of recurrence) considered a competing risk. Cox regression analysis was used to analyze the impact of clinical factors on recurrence. **Results:** A total of 506 pts were available. Median age was 66 years (range 33-86) and 78% (n = 396) were male; median follow-up after RC was 2.6 years. The majority of patients had pure urothelial histology (n = 371, 73%), and baseline stage was cT2N0 (n = 368, 73%), cT3-4N0 (n = 95, 19%) and TanyN1 (n = 43, 9%). NAC regimens were gemcitabine-cisplatin (GC, n = 296, 59%), dose-dense methotrexate-vinblastine-doxorubicin-cisplatin (ddMVAC, n = 141, 28%), split-dose GC (n = 29, 6%), MVAC (n = 29, 6%) and non-cisplatin based regimens (n = 11, 2%). At RC, 304 patients (60%) had ypT0N0 disease, 32 (6%) had ypTaN0, 107 (21%) had ypTisN0 and 63 (13%) had ypT1N0. Overall, 43 patients (8%) recurred with a median TTR of 56 weeks (range 7-251); 5-year freedom from recurrence was 87% (95% CI 83-91). The majority (n = 38) recurred outside the urinary tract. On multivariable analysis, ypTa (HR = 3.36 [1.24-9.11]) and ypT1 (HR = 2.88 [1.33-6.22], p = 0.013) disease at RC were predictors of shorter TTR, while female sex was associated with longer TTR (HR = 0.52 [0.27-0.98], p = 0.043). The type of NAC was not predictive of TTR (GC vs. other, HR = 1.49 [0.75-2.97], p = 0.26). **Conclusions:** To our knowledge, this is the largest study to quantify the risk of recurrence in pts achieving pathologic response after NAC and RC for MIBC. 8% of patients undergoing NAC and achieving < ypT2N0 at RC recurred. Residual ypTa and ypT1 disease conferred a significantly higher risk of recurrence, while ypTis did not; female sex was associated with a lower risk of recurrence. Importantly, the type of cisplatin-based NAC regimen used was not an independent predictor of recurrence. Research Sponsor: None.

5044 Poster Session (Board #113), Fri, 8:00 AM-11:00 AM

Study EV-103: Durability results of enfortumab vedotin plus pembrolizumab for locally advanced or metastatic urothelial carcinoma. *First Author: Jonathan E. Rosenberg, Memorial Sloan Kettering Cancer, New York, NY*

Background: Platinum chemotherapy is the standard for patients (pts) with metastatic urothelial carcinoma (mUC) in the first line (1L) setting. PD-1/PD-L1 inhibitors, such as pembrolizumab (P), have shown promising durability in this setting for PD-L1 high patients. Enfortumab vedotin (EV) is an antibody-drug conjugate that delivers the microtubule-disrupting agent MMAE to cells expressing Nectin-4, which is highly expressed in UC. EV recently received FDA accelerated approval based on tumor response rates for adults with locally advanced or mUC who have previously received a PD-1/PD-L1 inhibitor and a platinum-containing chemotherapy. EV is investigational in the 1L setting. Initial EV + P data were previously presented (Hoimes ESMO 2019); this provides durability data and an update on safety/ORR. **Methods:** This multicohort study (NCT03288545) evaluated the safety/activity of EV + P. We report a cohort of 1L cisplatin-ineligible patients treated with EV 1.25 mg/kg + P. In each 3-week cycle, EV was administered on Days 1 and 8 and P on Day 1. The primary endpoint was safety/tolerability; secondary objectives included determination of recommended EV dose, ORR, DCR, DOR/PFS per RECIST v1.1, and OS. **Results:** As of 8 Oct 2019, 45 1L or previously untreated mUC pts (median age 69 yr [51–90]) received a median of 9 (range 1-22) cycles of EV + P. The most common treatment-emergent adverse events (AE) were fatigue (58%, 11% ≥G3), alopecia (53%), and peripheral sensory neuropathy (53%, 4% ≥G3). One pt died due to an AE reported as related (multiple organ failure). With a median follow-up of 11.5 mo, confirmed investigator-assessed ORR was 73.3% (95% CI, 58.1, 85.4) including 15.6% CRs; DCR was 93.3%. The ORR in pts with liver metastasis was 53.3% (8/15). The ORR in pts with available PD-L1 status was 78.6% in PD-L1 high (11/14) and 63.2% in PD-L1 low (12/19). Of the 33 responders, 18 (55%) have ongoing responses including 11 responses beyond 10 months. The median DOR was not reached (range 1.2 to 12.9+ mo); the 12-month DOR rate was 53.7% (95% CI, 27.4, 74.1). The median PFS was 12.3 mo (95% CI, 7.98, -); the 12-month PFS rate was 50.1% (95% CI, 33.0, 65.0). The median OS was not reached (range 0.66 to 19.2+ mo); the 12-month OS rate was 81.6% (95% CI, 62.0, 91.8). **Conclusions:** In 1L cisplatin-ineligible pts with mUC, EV + P, a potential platinum free option, demonstrates promising activity and durability, with a manageable safety profile. Further evaluation of EV + P in mUC and muscle-invasive UC is ongoing. Clinical trial information: NCT03288545. Research Sponsor: Seattle Genetics, Inc, Pharmaceutical/Biotech Company.

5045 Poster Session (Board #114), Fri, 8:00 AM-11:00 AM

Impact of timing of antibiotic use on clinical outcomes in patients with urothelial cancer treated with immune checkpoint inhibitors (ICIs). *First Author: Chana Weinstock, U.S. Food and Drug Administration, Silver Spring, MD*

Background: Although recent evidence has suggested that patients who receive antibiotics (ABX) during the course of ICI treatment might decrease overall survival (OS) (1), our previous analysis did not support a difference in OS in urothelial cancer patients who did and did not use ABX during the course of ICI treatment without regard to timing (2). This updated analysis aims to addresses the question of timing; specifically, use of ABX in the 30-day window pre- or post- initiation of ICI treatment. **Methods:** We pooled data from 7 trials that led to drug approval and which included 1747 patients with advanced urothelial cancer treated with an ICI. Five trials enrolled patients who received prior platinum and 2 enrolled cisplatin-ineligible patients. Concomitant medication datasets were searched for systemic ABX use. The association between ABX use and survival was evaluated using Kaplan-Meier estimates and Cox proportional hazards regression models stratified by study. **Results:** Overall, 56% of patients were exposed to antibiotics (ABX+) and 43% were not exposed (ABX-). In an exploratory analysis, median OS was similar between arms: 9.7 vs. 9.3 months in ABX+ vs. ABX- patients, respectively (HR 0.96). However, OS results differed in the 27% of patients who were exposed to antibiotics in the 30-day window pre- or post- initiation of ICI treatment, for whom median OS was 4.7 months vs. 11.5 months in the ABX+ vs. ABX- patients, respectively (HR 1.8). This remained true after controlling for baseline risk prognostic factors (Bajorin and Bellmunt scores). Similar trends were observed for progression-free survival (PFS). **Conclusions:** Patients treated with ABX while on therapy with an ICI for urothelial cancer had similar OS outcomes to those not treated with ABX. However, in an exploratory analysis looking at ABX use in the 30-day window pre- or post-initiation of ICI treatment, OS appeared decreased in ABX+ vs ABX- patients. Our exploratory analyses appear to show an association of OS/PFS with timing of antibiotics. References: 1) Routy B, Science (2017) 2) Weinstock C, ASCO 2019, abstract. Research Sponsor: None.

	ABX+, no window (N= 986)	ABX-, no window (N= 761)	ABX+ ±30 days (N=482)	ABX- ±30 days (N=1265)
Deaths (%)	671 (68%)	511 (67%)	377 (78%)	805 (63%)
Median OS, months (95% CI)	9.7 (8.2, 11.1)	9.3 (8.1, 10.4)	4.7 (3.9, 5.9)	11.6 (10.9, 13.1)
HR (95% CI)	0.96 (0.85, 1.1)	ref	1.8 (1.6, 2.0)	ref
PFS events	826 (84%)	637 (84%)	428 (89%)	1035 (82%)
Median PFS, months (95% CI)	2.1 (2.1, 2.5)	2.1 (2.0, 2.1)	1.9 (1.7, 1.9)	2.5 (2.2, 2.8)
HR (95% CI)	0.94 (0.85, 1.0)	ref	1.6 (1.4, 1.8)	ref

5046 Poster Session (Board #115), Fri, 8:00 AM-11:00 AM

Detection of urothelial carcinoma using plasma cell-free methylated DNA. *First Author: Pier Vitale Nuzzo, Department of Medical Oncology, Dana-Farber Cancer Institute, Brookline, MA*

Background: Methylation profiling of circulating cell-free DNA (cfDNA) is a promising approach for non-invasive tumor detection due to the presence of tissue-specific epigenetic signatures that are detectable in cfDNA. Cell-free methylated DNA immunoprecipitation and high-throughput sequencing (cfMedDIP-seq) is a sensitive, low-input, cost-effective, bisulfite-free approach to profiling cfDNA methylomes, capable of detecting and classifying various tumor types. We tested the feasibility of cfMeDIP-seq to detect urothelial carcinoma (UC) in plasma samples. **Methods:** We performed cfMeDIP-seq on plasma samples from 43 patients (pts): 18 metastatic UC (UC) pts, 12 pre-cystectomy non-metastatic UC pts, and 13 cancer-free controls. Six (50%) of pre-cystectomy cases were non-muscle invasive UC. cfDNA was immunoprecipitated and enriched using an antibody targeting 5-methylcytosine and PCR-amplified to create a sequence-ready library. The top differentially methylated regions (DMRs) between UC and control samples were used to train a regularized binomial generalized linear model using 80% of the samples as a training set. The 20% of withheld test samples were then assigned a probability of being UC or control. This process was repeated 100 times. **Results:** The average amount (standard deviation) of cfDNA isolated from 1 ml of UC plasma samples was 29.2 (27.4) ng/μL and 8.02 (3.58) ng/μL in cancer-free controls. We identified 9,826 DMRs in plasma samples at an adjusted p-value of < 0.01, which partitioned UC and control samples. Iterative training and classification of held out samples using the top 300 DMRs resulted in a mean AUROC of 0.987. **Conclusions:** cfMeDIP-seq is an interesting new approach for non-invasive detection of UC. cfMeDIP-seq demonstrates high sensitivity to detect UC across all stages of UC, including non-muscle invasive disease. Research Sponsor: Dana Farber Cancer Institute.

5047 Poster Session (Board #116), Fri, 8:00 AM-11:00 AM

Phase Ib/II neoadjuvant (N-) pembrolizumab (P) and chemotherapy for locally advanced urothelial cancer (laUC): Final results from the cisplatin (C)- eligible cohort of HCRN GU14-188. *First Author: Christopher J. Hoimes, Duke Cancer Institute, Durham, NC*

Background: Patients (pts) with laUC who are C-eligible for N- therapy may benefit from combination chemo-immunotherapy. Cohort 1 (C1) of the GU14-188 trial is a phase 1b/2 trial designed to assess the tolerability and efficacy of N- gemcitabine (G), C, and P in pts with laUC. The current standard of care is ddMVAC with a pathologic non-muscle invasive rate (PaIR, ≤pT1N0) of ~44%. **Methods:** Eligible pts for C1 were surgical candidates and C-eligible with cT2-4aN0M0 bladder UC. Enrollment followed a Simon 2-stage design for H_0 of interval futility which was rejected at stage 1, and fully enrolled. Phase 1b (no DLT) /2 treatments were the same: P 200mg q3wks on day 8 x5 doses; with C (70mg/m2) day 1, and G (1000mg/m2) days 1 and 8 of a 21 day cycle (cy), for 4 cy; followed by radical cystectomy (RC). Minimum criteria for evaluation of safety: 1 dose of P, and for efficacy: 2 doses P and RC. The primary endpoint of PaIR was assessed at RC and designed for 86% power with 4% significance to detect a difference from 23 to 48%. Secondary endpoints include relapse free survival and overall survival. **Results:** 43 pts were enrolled to C1 with a median (mdn) age 64, 63% male, 51% > cT2. Mdn per-pt doses given (attempted) for: P:5(5), C:4(4), G:8(8). The PaIR was 61.1% (95%CI 0.45, 0.75), P0 (ypT0N0) rate of 44.4%, and did not correlate with baseline PD-L1 score. Downstage to PaIR occurred in 53% of cT2, and 74% of cT3/4. Mdn time to RC from last dose was 5.3wks. Seven were not included in the primary analysis: 4 (9.3%) without RC, 1 progressed, 1 lost to f/u during C1, 1 did not receive required protocol therapy. There was 1 death on post-RC day 9 due to mesenteric ischemia. Of 4 pts who did not have RC, 3 refused and 1 due to gr4 thrombocytopenic purpura; 4pts are alive and without recurrence at mdn f/u of 32mo. One pt with presumed gr3 MI during cy 4 had a negative inpt cardiac workup and completed therapy and RC without further AE. One gr4 hyponatremia and ten gr3 events did not preclude RC (2-each thromboembolism, elevated creatinine, hyponatremia;1-each: dehydration, emesis, neutropenic fever, infection). Gr 3/4 cytopenias occurred in 57% of pts. At mdn f/u of 34.2mo (3.9-47.4), the estimated 36mo RFS, OS, and DSS is 63%, 82%, and 87%, respectively. **Conclusion:** Neoadjuvant GC with P in laUC has manageable toxicity and has improved pathologic outcomes compared to historic controls. Durable long-term survival in those with- and without -RC is noteworthy in this advanced cohort. KEYNOTE 866, NCT03924856, is a Phase III study of GC with perioperative P. Clinical trial information: NCT02365766. Research Sponsor: Merck & Co.

5048 Poster Session (Board #117), Fri, 8:00 AM-11:00 AM

Outcomes of patients (pts) with metastatic urothelial carcinoma (mUC) following discontinuation of enfortumab-vedotin (EV): Emergence of a new unmet need. *First Author: Catherine Curran, Dana Farber Cancer Institute, Boston, MA*

Background: Enfortumab vedotin (EV) is an antibody drug conjugate recently approved to treat mUC following prior platinum and PD1/L1 inhibitors. The outcomes and patterns of therapy of pts following discontinuation of EV has yet to be studied. We investigated outcomes of pts who completed EV treatment for mUC at multiple institutions in order to identify benchmarks for evaluation of new agents following EV. **Methods:** Clinical data were obtained from mUC patients who had completed EV treatment from collaborating academic institutions. Descriptive stats were performed to describe the overall dataset and compare patient characteristics and outcomes of those who went on to receive further treatment post-EV and those who did not. **Results:** Data were available for 63 patients from 6 collaborating institutions: DFCI, University of Michigan, University of Washington, Moffitt Cancer Center, INT Milan and University of Miami. 17 (27%) were female and 46(73%) were male. The median age was 68 (range 43-83. The primary site of malignancy included bladder, upper tract, and other in 43 (68%), 19 (30%), and 1pt (.02%), respectively. The histologies included pure UC and mixed predominant UC in 49 (78%), and 14 pts (22%), respectively. 32 pts (51%) received further therapy after EV and 31pts (49%) did not. Longer duration of prior EV therapy was associated with receipt of post-EV therapy (p=0.0437). Treatments received post-EV were: trial therapy (n=14), PD1/L1 inhibitor (n=7), pemetrexed (n=4), taxane (n=3), carboplatin (n=2) and unknown in 2 pts. Objective response was observed in 3 of 32 pts (9.4%) who received therapy post-EV. The median duration of time from end of EV to death was 24 weeks. The median overall survival (OS) of those who received post-EV therapy and did not receive post-EV therapy was 37.5 weeks and 12 weeks, respectively. **Conclusions:** Outcomes of mUC following discontinuation of EV are dismal with only 51% receiving subsequent therapy. This study identifies an unmet need setting and establishes benchmarks for the interpretation of activity of new agents evaluated following EV. Research Sponsor: None.

5049 Poster Session (Board #118), Fri, 8:00 AM-11:00 AM

Analysis of chemotherapy-related modulation of the immune microenvironment in muscle invasive bladder cancer. *First Author: Elshad Hasanov, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Novel immune checkpoint inhibitors provide significant clinical benefits for patients with metastatic bladder cancer. It is known that chemotherapy administered to muscle invasive patients prior to radical cystectomy (neoadjuvant chemotherapy) improves survival. However, it is unknown whether immune checkpoint inhibitor therapy in combination with chemotherapy can provide further clinical benefits as neoadjuvant therapy. Here, we test the hypothesis that treatment of bladder cancer with certain chemotherapy agents can modulate bladder tumor immune microenvironment (TIME) for optimal combination with immune checkpoint therapy. **Methods:** Time course and dose response experiments were performed using eight human bladder cancer cell lines (UMUC3, RT4, 253J, RT112, J82, HT1376, T24, and HT1197) and two murine bladder cancer cell lines (MB49, MBT2). Conventional chemotherapy agents and combinations (MVAC, GemCis, PemVin) were used to treat bladder cancer cell lines. Flow cytometry analysis was used to measure immune cell subsets and PD-L1 expression. For *in vivo* studies, the subcutaneous MB49 murine bladder cancer model was used to evaluate responses to chemotherapy and anti-PD-L1 combinations. Pre- and post-treatment bladder tumors from patients who received neoadjuvant MVAC and GemCis are selected to evaluate changes in TIME. **Results:** Our data demonstrate that chemotherapy agents varies in their ability to up-regulate PD-L1 expression on bladder cancer cell lines. Vinblastine, gemcitabine, and pemetrexed treatment each resulted in significant upregulation of PD-L1 expression. Combination regimens with GemCis or PemVin demonstrated induction of PD-L1 across different cell lines. In *in-vivo* studies, GemCis + anti-PD-L1 had a synergistic activity in causing tumor regression. We also found that sequential versus concurrent treatment with chemotherapy and anti-PD-L1 had a similar outcome. Tissue analyses show that combination chemotherapies increased CD4 Th cell infiltration while decreasing Treg cells in TIME. Consistent with the in vitro data, PD-L1 expression was also up-regulated with combination treatment. The evaluation of TIME modulation in human bladder tumors treated with neoadjuvant MVAC or GemCis is ongoing. **Conclusions:** Our data suggest that chemotherapy could favorably modulate TIME and thus, may be combined with immune checkpoint inhibitor to improve anti-tumor responses in the neoadjuvant setting for patients with muscle invasive bladder cancer. Research Sponsor: MD Anderson Physician Scientist Award, Andrew Sabin Family Foundation Award.

5050 Poster Session (Board #119), Fri, 8:00 AM-11:00 AM

Clinicogenomic predictors of extreme responses to anti-PD1/PDL1 checkpoint inhibitors (CPI) in metastatic urothelial cancer (mUC). *First Author: Min Yuen Teo, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Only a subset of mUC patients (pts) derives benefit from CPI. We sought to evaluate potential clinical and genomic predictors, with additional focus on extreme outcomes. **Methods:** CPI-treated mUC with tumor sequencing with MSK-IMPACT (up to 468 genes) were identified. Pre-CPI clinical variables (including hemoglobin [hgb], lymphocyte [lymph], neutrophil [neut] and eosinophil [eos] counts) were extracted. Endpoint was time on treatment (ToT). Poor responders were defined as ToT $\leq$9 weeks and overall survival $\leq$3 months; exceptional responders had ToT $>$20 months. A multivariate Cox model for ToT was performed with clinical variables chosen by stepwise selection minimizing Akaike information criterion. Genomic analyses were adjusted for multiple testing. **Results:** 166/171 identified mUC were evaluable. Median age was 68 years, 78% were male. 72% had bladder primary, while 17%, 35% and 28% had liver, lung and bone metastases (mets). 67% had prior platinum chemo. 24 pts (14%) were poor and exceptional responders, respectively. In univariate analysis, liver mets were associated with shorter ToT while DNA damage repair (DDR) gene alterations, higher body mass index (BMI), eos, hgb and tumor mutation burden (TMB) were associated with longer ToT. No specific genomic alterations achieved q$<$.05. In multivariate model, prior chemo (HR 1.6, p=.01), liver mets (HR 2.4, p$<$.01) and high neut were associated with shorter ToT while urethral primary (HR 0.1, p$<$.01), higher TMB (HR 0.9, p$<$.01) and higher eos (HR 0.1, p$<$.01) were independently associated with ToT. Univariate logistic regression to identify poor and exceptional responders are tabulated. Multivariate results will be reported. **Conclusions:** In addition to validation of various known mUC prognosticators, we observed potential non-linear influence of clinical and genomic factors on extreme outcomes. Research Sponsor: None.

			Exceptional responders		
Poor responders	**Odds ratio**	**p**		**OR**	**p**
Liver mets	1.3	<.01	BMI	1.1	.03
Bone mets	1.2	<.01	Urethral primary	1.5	.04
Upper tract primary	1.1	.05	DDR alterations	1.2	<.01
Eos	0.6	.02	TMB	1.01	<.01
Hgb	0.95	<.01	Eos	1.6	.01
Neut	1.02	<.01	NCOR	1.6	q<.01
CDKN2A del	1.2	q=.03	TET1	1.9	q=.01
CDKN2B del	1.2	q=.03	RICTOR	1.6	q=.04

5051 Poster Session (Board #120), Fri, 8:00 AM-11:00 AM

Maintenance oral etoposide (VP-16) after high-dose chemotherapy (HDCT) for patients with relapsed metastatic germ-cell tumors (mGCT). *First Author: Bilal Anouti, Indiana University Melvin and Bren Simon Cancer Center, Indianapolis, IN*

Background: HDCT and peripheral-blood stem-cell transplant (PBSCT) can cure up to 60% of patients with relapsed mGCT. Maintenance daily oral VP-16 after salvage therapy has been shown effective in inducing remissions (J Clin Oncol 1995;13:1167-9). We evaluate the role of maintenance VP-16 post HDCT+PBSCT compared to observation. **Methods:** The prospectively maintained Indiana University testicular cancer database was interrogated. Patients with relapsed non-seminoma who completed HDCT+PBSCT and achieved serologic remission and hematologic recovery were evaluated. Outcomes of patients who received maintenance VP16 (N = 141) were compared to patients who were observed (N = 252). In this retrospective study, Kaplan-Meier method was used to analyze progression free survival (PFS) and overall survival (OS). Univariable and multivariable cox regression models were used to determine variables associated with PFS. **Results:** 2-year PFS in the maintenance VP-16 versus observation group was 55% vs. 44% (p = 0.008). 2-year OS was 61% vs. 52% (p = 0.01). A multivariable analysis was performed including the factors: primary tumor site (testis vs. mediastinum), IGCCCG risk, platinum refractory, HDCT line of therapy (2^{nd} vs. $\geq 3^{rd}$), tumor marker amplitude at HDCT initiation, and receipt of maintenance VP-16 post HDCT vs. observation. Maintenance VP-16 was confirmed as an independent predictor of improved PFS with HR 0.48 [95% CI, 0.35-0.66] (p $<$ 0.001). **Conclusions:** Maintenance oral VP-16 post HDCT+PBSCT improved PFS and OS. In a multivariable model including known adverse prognostic factors, maintenance VP-16 was an independent predictor of improved PFS. Research Sponsor: Internal funds from Indiana University.

Variable	**Maintenance etoposide N = 141**	**No maintenance etoposide N = 252**	***P***
Median age	27	31	< 0.001
Primary site			
-Testis/RP	130 (93%)	233 (92%)	0.93
-Mediastinum	11 (7%)	19 (8%)	
Metastatic sites			
-Retroperitoneum	118 (84%)	195 (77%)	0.14
-Pulmonary	111 (79%)	171 (68%)	0.02
-NPVM	62 (44%)	100 (40%)	0.41
-Liver	39 (28%)	54 (21%)	0.16
-Bone	9 (6%)	13 (5%)	0.61
-Brain	36 (26%)	50 (20%)	0.19
IGCCCG Risk			
-Good	28 (20%)	80 (32%)	0.03
-Intermediate	17 (12%)	23 (10%)	
-Poor	96 (68%)	146 (58%)	
Platinum refractory	63 (45%)	95 (38%)	0.17
HDCT line of therapy			
-2	124 (88%)	206 (82%)	0.11
-≥3	17 (12%)	46 (18%)	

5052 Poster Session (Board #121), Fri, 8:00 AM-11:00 AM

Multicenter analysis of serum tumor markers, treatment patterns, and relapse in patients with testicular cancer in clinical stage IS. *First Author: Maximilian Peter Johannes Karl Brandt, University Clinic for Urology and Pediatric Urology, Mainz, Germany*

Background: Testicular germ cell tumors (TGCT) in clinical stage I (CSI) are tumors confined to the testis without evidence of metastasis. Around 50% of all TGCT patients present with elevated serum tumor markers (TM) such as alpha-feto protein (AFP), beta-humanochoriongonadotropin (ß-HCG) and lactate-dehydrogenase (LDH). After ablatio testis, TMs usually return to normal according to half-life kinetics, however, in clinical stage IS (CSIS) TMs remain elevated or increase after surgery. Follow-up data on CSIS is scarce and our study aims to assess clinical characteristics and oncologic outcomes in a large TGCT cohort. **Methods:** In this multicenter study we collected data from 5 tertiary referring hospitals in Germany, included patients with CSIS and evaluated TM levels, treatment and the primary outcome relapse-free survival. False CSIS was defined as documented CSIS but TMs that returned to normal after respective half-life kinetics. Differences between predefined groups (chemotherapy, TM, true/false CSIS) was analyzed with fisher's exact and chi-square test. **Results:** Overall, 2616 patient data files were analyzed. Forty-three patients (1.6%) were documented as CSIS of which 27 (63%) were true and 16 (37%) false CSIS. Six (14%) had seminomas and 37 (86%) non-seminomas. In the true CSIS group AFP, ß-HCG, AFP plus ß-HCG and LDH were elevated in 13, 6, 3 and 2 cases. Four true CSIS patients received surveillance, 21 had 3x or 2x courses of BEP (bleomycin, etoposide and cisplatin) and 2 carboplatin. Within the false CSIS group, 2 patients were treated with surveillance, 10 received 3x BEP, one 3x PEI (cisplatin, etoposide and ifosfamid) and 3 had carboplatin. Chi-Square test revealed no difference between true or false CSIS classification in respect to application of chemotherapy (any chemotherapy, p = 0.83). Relapse-free survival after 5 and 10 years was 88.9% and 77.8%, respectively. Three patients in the true CSIS group relapsed (2 seminomas had carboplatin, 1 non-seminoma had surveillance). All relapses were treated with 3 courses of BEP with no documented death in the CSIS population. **Conclusions:** Overall, less than 2% of all TGCT were documented CSIS of which 37% were falsely classified. We report a high proportion of relapse-free survival in CSIS treated with surveillance or BEP with a high heterogeneity in treatment patterns. Correct classification of CSIS remains of critical importance to avoid toxicity for patients that could be safely treated with surveillance. Research Sponsor: None.

5053 Poster Session (Board #122), Fri, 8:00 AM-11:00 AM

Outcome of men with HIV-associated germ cell cancer: Results from an international collaborative study. *First Author: Marcus Hentrich, Red Cross Hospital, University of Munich, Munich, Germany*

Background: Previous studies showed that men with HIV-associated germ cell cancer (HIV-GCC) have a similar cancer-free outcome compared with their HIV-negative counterparts. However, the overall survival (OS) was inferior and little data is available on treatment and outcome of HIV-GCC in the era of combined antiretroviral therapy (cART). **Methods:** Men living with HIV aged ≥ 18 years (yrs) with a diagnosis of histologically proven GCC made from 01/1996 to 07/2018 were included. Primary outcomes were OS and progression-free survival (PFS). Secondary outcomes included characteristics of GCC and HIV-infection, treatment and causes of death. **Results:** Data of 89 men from 23 institutions and 6 countries with a total of 92 HIV-GCC (2 synchronous and 1 metachronous bilateral GCC) were analysed, among them 64 (70%) seminomas and 28 (30%) nonseminomas. 10/89 (11%) cases were primary extragonadal GCC. Median age was 36 yrs (range, 22-52) and median time from HIV to GCC diagnosis was 5 yrs (range, 0-29). Median CD4 count at GCC diagnosis was 420 cells/μl (range, 3-1503) and 83% of pts were on cART. Stage I disease was found in 44/80 (55%) gonadal GCC (metachronous bilateral case included). Of 46 cases with stage II/III/extragonadal GCC 78%, 17% and 4% were assigned to the IGCCCG good, intermediate and poor prognosis group, respectively. Of the 44 stage I cases, 22 (50%) were followed by active surveillance, and 11 (25%) received adjuvant chemotherapy (CT) or radiotherapy. Relapses occurred in 14 pts (6 from stage I, 8 in pts primary disseminated GCC) and CT was applied to 13/14 pts, of which 3 received high-dose CT. Overall, 12/89 (13%) pts have died. Causes of death were refractory GCC (n = 5), an AIDS-defining illness (n = 3) and other (n = 4). After a median follow-up of 6.5 yrs (range, 0.3-20.9), the 5- and 10-year PFS rate was 81% and 73%, and the 5- and 10-year OS rate was 91% and 85%, respectively. There were no significant differences between the good and intermediate prognosis group or between pts with CD4 counts < 200/μl or ≥ 200/μl. **Conclusions:** The 5- and 10-year PFS and OS rates of men with HIV-GCC are similar to those reported for HIV-negative GCC. Pts with HIV-GCC should remain on cART and be managed in an identical fashion to HIV-negative pts. Research Sponsor: None.

5055 Poster Session (Board #124), Fri, 8:00 AM-11:00 AM

Prognostic role of early interim [18F] fluoro-deoxy-glucose positron emission tomography in patients with advanced seminoma undergoing standard treatment. *First Author: Daniele Raggi, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: In patients (pts) with advanced seminoma, efforts are underway to tailor a risk-adapted treatment strategy to the individual pt. Our main objective was to prospectively determine the prognostic value of [18F]fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT2) after two cycles of bleomycin, etoposide and cisplatin (BEP) or EP chemotherapy under standardized treatment and PET evaluation criteria. **Methods:** Pts with advanced-stage seminoma were treated with BEP or EP according to guidelines. PET/CT examinations were performed at baseline, after two cycles in all pts and after chemotherapy at physician's choice. PET/CT response was qualitatively evaluated by two independent nuclear medicine physicians. Contrast-enhanced CT scans were also performed according to the guidelines (at baseline, after treatment, during follow-up). The primary endpoint was the relapse-free survival (RFS). **Results:** From 01/2009 to 01/2017, 75 consecutive pts were enrolled, of whom 70 were evaluable. The clinical stage was IIA-B and IIC-III in 40% and 60% of the pts, respectively. Eight pts (11.4%) received consolidation radiotherapy. By local assessment, 46 PET/CT2 scans (65.7%) were reported as negative, and 46% of these pts presented with stage IIC-III. The median follow-up was 79 months. Five-year RFS of PET/CT2-positive pts was 75% (95%CI: 60-95%) compared with 97.8% (95%CI: 93.7-100%) of PET/CT2-negative pts (p = .002). This significant improvement in RFS was maintained when analyzing only pts with clinical stage IIC-III (p = 0.04) and by excluding those who received consolidation RT (p = 0.02). An increasing linear association was found between the maximum diameter of retroperitoneal lymph nodes and the rate of PET/CT2+. In univariable Cox regression analyses, PET/CT2+ (HR: 12.9, 95%CI: 1.5-106.9, p = 0.02) and elevated HCG levels (HR: 6.3, 95%CI: 1.2-32.3, p = 0.03) were significantly associated with RFS, whereas IGCCCG risk group was not (p = 0.1). PET/CT2 result was also associated with the tumor shrinkage post-BEP (p = 0.009), whereas complete response at CT did not predict the RFS (p = 0.3). **Conclusions:** No residual FDG-uptake after 2 cycles of conventional chemotherapy is prognostic in advanced seminoma, may outperform the utility of standard prognostic risk groups and may be more accurate to predict the RFS compared to standard response criteria. Benchmark RFS estimates for the design of the next clinical trials of chemotherapy de-escalation are offered. Research Sponsor: Fondazione IRCCS Istituto Nazionale dei Tumori.

5056 Poster Session (Board #125), Fri, 8:00 AM-11:00 AM

Persistence of platinum in semen of cisplatin-treated survivors of advanced testicular cancer. *First Author: Eoghan Ruadh Malone, Princess Margaret Hospital, Toronto, ON, Canada*

Background: Cisplatin is highly curative treatment for testicular cancer. Most survivors develop azoospermia immediately after cisplatin with recovery expected in 50% at 2 years and 80% at 5 years. Platinum is a heavy metal that can be detected at low levels in serum many years after treatment, however, it is not known whether platinum also persists in semen and if platinum persistence in semen is associated with impaired fertility. **Methods:** Testicular cancer survivors previously treated with cisplatin were enrolled, relapsed disease treated with salvage chemotherapy was excluded. Semen samples were collected to assess semen quality. Repeat semen collections were performed if azoo- or oligospermia was noted. Serum and semen Platinum levels were determined using HPLC-tandem mass spectrometry. DNA Fragmentation Index (DFI) was measured. **Results:** From 11/2017 to 12/2019, 38 pts (median age 32 years; range: 19-52; median BSA 2.03; range: 1.81-2.61) were enrolled, 31 were treated with 3 cycles of Bleomycin, Etoposide, Cisplatin. Median cumulative cisplatin dose was 300 mg/m^2 (range: 274-404). Median serum platinum concentration was 0.1 ng/mL (range: 0-22.6) at a median of 11 months (range 0.5-36) post treatment completion. Median semen platinum concentration was 0.5 ng/mL (range: 0.2-28.7) at a median of 14 months (range: 1.3-40) post treatment completion. Semen platinum levels were higher in semen than in blood drawn at the same time (p = 0.03). Semen platinum levels were associated with time from last cisplatin dosing (r = -0.34; p = 0.09) but not cumulative cisplatin dose (r = -0.10, p = 0.63). Sperm concentration was correlated with time from last cisplatin dosing (r = 0.58, p < 0.001) but not with semen platinum level (r = -0.15, p = 0.46). DFI was associated with time from last cisplatin dosing (r = 0.55, p = 0.08) but not with semen platinum level (r = -0.32, p = 0.33). In 4 pts with serial semen samples available, semen platinum level decreased with time, sperm concentration and motility increased. **Conclusions:** Platinum can be detected in semen in long-term testicular cancer survivors at higher levels than matched blood samples. Our preliminary findings may have important implications for reproductive health of survivors of advanced testicular cancer, further studies are needed to assess the relationship between platinum persistence in semen and recovery of fertility post chemotherapy. Research Sponsor: Department of Medical Oncology and Hematology Grant (Internal Princess Margaret Hospital).

5057 Poster Session (Board #126), Fri, 8:00 AM-11:00 AM

Model to predict brain metastasis (BM) in patients with metastatic germ-cell tumors (mGCT). *First Author: Ryan Ashkar, Indiana University Simon Comprehensive Cancer Center, Indianapolis, IN*

Background: BM is an independent adverse prognostic factor that can lead to treatment complications and failure in pts with mGCT. We aimed to establish an effective and practical model for prediction of BM in mGCT. **Methods:** 2,256 consecutive pts with mGCT treated at Indiana University between January 1990 and September 2017 were identified. Pts were divided into 2 categories: BM present (N = 144) and BM absent (N = 2112). Kaplan-Meier methods were used to analyze progression free survival (PFS) and overall survival (OS). Logistic regression was used to determine a predictive model for whether BM was present. The data was separated 50/50 into training and validation datasets with equal numbers of events in each. **Results:** Baseline characteristics for 2 groups are listed in Table. 2-yr PFS and OS for pts with vs without BM: 17% vs 66% (p < 0.001) and 62% vs 91% (p < 0.001) respectively. Among the 144 pts with BM, 64 (44%) had radiation only (whole-brain radiotherapy or gamma knife), 21 (15%) had BM-surgery only, 14 (10%) had both radiation and BM-surgery. 45 pts (31%) did not receive local therapy for BM. A stepwise selection was used to determine the best model with p < 0.15 as the entry and staying criteria. The model with the largest ROC AUC was used moving forward. The model was tested in the validation dataset. A model was generated including age at diagnosis≥40 (1 point), presence of pulmonary metastases (3 points), bone metastasis (1 point), pre-chemotherapy hCG≥5000 (1 point), and choriocarcinoma predominant histology (1 point). Patients with 0 points had a 0.4% probability of BM, 1 point: 1%, 2 points: 2.6%, 3 points: 7%, 4 points: 16%, 5 points: 32%, 6 points: 56%, and 7 points: 77%. Details regarding analysis in training and validation datasets will be presented. **Conclusions:** The prediction model developed in this study demonstrated discrimination capability of predicting BM occurrence and can be used by clinicians to identify high-risk pts. Research Sponsor: None.

Variable	BM present N = 144	BM absent N = 2112
Median age at diagnosis (range)	29 (16-49)	30 (13-75)
Primary site		
-Testis	125 (87%)	1966 (93%)
-Retroperitoneum	8 (6%)	81 (4%)
-Mediastinum	10 (7%)	57 (3%)
Histology		
-Seminoma	6 (4%)	381 (18%)
-Non-seminoma	137 (95%)	1721 (82%)
Choriocarcinoma	56 (39%)	90 (4%)
Embryonal carcinoma	30 (21%)	667 (32%)
Yolk sac tumor	12 (8%)	155 (7%)
Teratoma	11 (8%)	223 (11%)
Metastatic sites		
-Retroperitoneal LN	106 (74%)	1788 (85%)
-Pulmonary	134 (93%)	828 (39%)
-Liver	54 (38%)	202 (10%)
-Bone	12 (8%)	54 (3%)
Pre-chemo AFP≥1000 ng/mL	21 (19%)	343 (25%)
Pre-chemo hCG≥5000 mIU/mL	100 (81%)	336 (25%)

5058 Poster Session (Board #127), Fri, 8:00 AM-11:00 AM

Olaparib as salvage treatment for advanced germ cell tumors after chemotherapy failure: Results of the open-label, single-arm, IGG-02 phase II trial. *First Author: Ugo De Giorgi, Department of Medical Oncology, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy*

Background: Therapeutic options for patients with advanced germ cell tumors (GCTs) after multiple relapses or resistant disease are limited. Olaparib is an inhibitor of poly ADP ribose polymerase (PARP), an enzyme involved in DNA repair. We aimed to evaluate olaparib activity in patients with refractory GCT. **Methods:** In this proof-of principle open-label, single-arm, phase II trial of olaparib 300 mg twice daily in patients with relapsed/refractory metastatic germ cell cancer IGG-02 study (NCT02533765), patient eligibility included failure after high-dose chemotherapy or after at least 2 different cisplatin-based regimens. Measurements of serum tumor markers and computed tomography were carried out at baseline and every 6 weeks of olaparib treatment. The study primary endpoint was the overall response rate, the study planned to recruit initially 18 patients and not continue further recruitment until one or more responses were observed. **Results:** Between September 2015 and February 2019, 18 patients, median age 39 years (range, 22-61) were enrolled. The number of prior chemotherapy regimens was: 2 for 3 patients (16.7%), 3 for 5 patients (27.8%), >3 for 10 patients (55.6%). Sixteen cases (89.9%) received prior high-dose chemotherapy with support of hematopoietic progenitor cells. Grade 3-4 adverse events were observed in 5 patients (27.7%). There were no partial responses, 5 cases (27.8%) with stable disease (SD) lasting 3, 4, 4, 7 and 7+ months and 13 (72.2%) progressive disease. The 12-week progression-free survival probability was 27.8% [95% confidence interval (CI): 10.1%-48.9%]. The 12-month overall survival probability was 27.8% (95% CI: 10.1%-48.9%). A germline DNA repair profile panel showed only a BRCA1 mutated case associated with a SD lasted 4 months. **Conclusions:** Olaparib as a single agent has marginal activity in heavily pretreated GCT patients, however, an anecdotic 4-month SD in the only BRCA mutated patient has been reported. Plans for future studies with olaparib are suggested in combination or following salvage chemotherapy in less pretreated and more selected GCT patients. The Study has been conducted with AstraZeneca contribution. Clinical trial information: NCT02533765. Research Sponsor: Astrazeneca.

5059 Poster Session (Board #128), Fri, 8:00 AM-11:00 AM

SBRT versus nephrectomy in the treatment of renal cell carcinoma. *First Author: Mausam Patel, University of Arkansas for Medical Sciences, Little Rock, AR*

Background: Stereotactic body radiotherapy (SBRT) is being increasingly used for renal cell carcinoma (RCC) treatment in non-surgical candidates. However, no studies have compared survival between nephrectomy and SBRT. The National Cancer Database (NCDB) database was used to assess overall survival in patients undergoing SBRT vs nephrectomy. **Methods:** All cases of T1-T4, N0, M0 RCC diagnosed between 2004 and 2016 were extracted from the NCDB. Only patients undergoing either nephrectomy or SBRT, but not both, were included in the final analysis. Primary outcome was overall survival, defined as time in months from diagnosis to death due to any cause. Descriptive statistics were calculated for all variables. Univariate survival analysis was performed using the Kaplan Meier method and log rank test. Multivariate Cox proportional hazards regression models were performed to determine the predictive performance of covariates with respect to overall survival, reported as hazard ratio [HR] with 95% CIs. Nephrectomy patients were propensity score matched to SBRT patients for sub-cohort survival analysis. Comparisons were considered statistically significant at $P < 0.05$. **Results:** There were 243,754 patients meeting inclusion criteria with 243,488 undergoing nephrectomy and 266 undergoing SBRT. Five year OS rates were 53% and 80% for SBRT and nephrectomy, respectively ($P < 0.001$). On multivariate Cox regression, SBRT was associated with an increased risk of death as compared to nephrectomy (HR, 2.05; 95% CI, 1.72 – 2.44; $P < 0.001$). Sex, race, insurance coverage, comorbidity index, tumor grade, lymphovascular invasion status, T-stage, tumor size, and academic status of treatment facility were also independent predictors of survival. After propensity score matching of 266 SBRT patients to 266 nephrectomy patients, there were no significant differences in baseline characteristics between the groups. However, SBRT continued to demonstrate worse survival and an increased risk of death as compared to nephrectomy (HR, 1.85; 95% CI, 1.41 – 2.44; $P < 0.001$). **Conclusions:** Among node-negative, non-metastatic RCC patients, SBRT is associated with inferior survival outcomes as compared to nephrectomy, even after correcting for underlying differences in demographics, tumor characteristics, socioeconomic status, and comorbidities. These results indicate that nephrectomy should remain the standard of care for RCC patients, with SBRT reserved for non-surgical candidates. Research Sponsor: None.

5060 Poster Session (Board #129), Fri, 8:00 AM-11:00 AM

INMUNOSUN-SOGUG trial: A prospective phase II study to assess the efficacy and safety of sunitinib as second-line (2L) treatment in patients (pts) with metastatic renal cell cancer (RCC) who received immunotherapy-based combination upfront. *First Author: Enrique Grande, MD Anderson Cancer Center Madrid, Madrid, Spain*

Background: Immunotherapy (IO)-based combinations have replaced tyrosine kinase inhibitors (TKI) as standard upfront treatment of metastatic RCC pts. Selection of 2L treatment after progression to novel combinations in 1st-line (1L) is mostly based on retrospective series or subgroups analysis of randomized trials. We aim to evaluate the activity and safety of sunitinib in advanced RCC after progression on an IO-based 1L approach. **Methods:** This is a prospective, non-randomized, open-label and multicenter phase II study. Pts with ECOG 0-2 and locally advanced or metastatic RCC after treatment in 1L with a prior PD-1 and/or PD-L1 and/or CTLA-4 inhibitor were included. Sunitinib was administered at 50 mg/day on a 4/2 schedule until disease progression. Primary endpoint was overall response rate (ORR) by RECIST v 1.1 criteria. **Results:** Twenty pts were enrolled in the study. Median age was 66 yo, 70% had intermediate prognosis by Heng's scale, and 88% ECOG 1. 45% of pts received atezolizumab, 30% pembrolizumab, 20% nivolumab and 15% ipilimumab-based regimens as 1L. ORR to 1L treatment was 45%. Median time from end of 1L to sunitinib onset date was 1.1 months (0.3-22.1). Two (10%) pts had partial response with sunitinib and 11 (55%) stable disease for a total disease control rate of 65%. With a median follow-up of 8.8 months, median PFS was 6.8 months (0.0-13.9) and median OS 13.6 months (10.5-16.6). Median duration of treatment was 4 months (0.9-16-2). Most common treatment-related adverse events, all grades, were asthenia (55%), dysgeusia (35%), diarrhea (30%), hypertension (30%), mucosal inflammation (25%), palmar-plantar erythrodysesthesia (25%), anemia (20%), neutropenia (20%) and nausea (15%); grade 3 were asthenia (15%), hypertension (10%) and neutropenia (10%). **Conclusions:** To our knowledge, the INMUNOSUN trial is the first study to evaluate prospectively the activity of a single agent TKI in a pure 2L setting of metastatic RCC pts treated with an IO-based approach upfront. ORR and PFS with sunitinib seem lower than expected when used as a 1L. Consistency in toxicity profile was observed. Clinical trial information: NCT03066427. Research Sponsor: Pfizer.

5061 Poster Session (Board #130), Fri, 8:00 AM-11:00 AM

Association of neutrophil to lymphocyte ratio (NLR) with efficacy from JAVELIN Renal 101. *First Author: Mehmet Asim Bilen, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: The phase 3 JAVELIN Renal 101 trial (NCT02684006) in treatment-naive patients with advanced renal cell carcinoma (aRCC) demonstrated significantly improved progression-free survival (PFS; hazard ratio [HR], 0.69; 95% CI, 0.56, 0.84; $P < 0.001$) and higher objective response rate (ORR; 51.4% vs 25.7%) with avelumab + axitinib vs sunitinib (Motzer RJ, et al. N Engl J Med. 2019;380:1103-15). NLR has emerged as a potential prognostic biomarker in aRCC; elevated NLR is associated with poorer prognosis. Here, we describe the association of NLR with the efficacy of avelumab + axitinib from JAVELIN Renal 101. **Methods:** We examined baseline NLR and its association with efficacy outcomes. PFS, best overall response (per blinded independent central review using RECIST 1.1), and overall survival (OS) data from the avelumab + axitinib arm from the first interim analysis of JAVELIN Renal 101 were analyzed (data cutoff, June 20, 2018). Multivariate Cox regression analyses of PFS and OS were also conducted. **Results:** In the avelumab + axitinib arm, patients with < median NLR (N = 217) had longer observed PFS (stratified HR, 0.85; 95% CI, 0.634, 1.153) and longer observed OS (stratified HR, 0.51; 95% CI, 0.300, 0.871) than patients with ≥ median NLR (N = 217). The ORR was 57.1% in patients with < median NLR vs 47.5% in patients with ≥ median NLR, with complete response in 5.5% vs 1.4%. Multivariate analysis showed that low NLR was associated with longer PFS and OS by treating baseline NLR as either a continuous variable or a binary variable (dichotomized by median). **Conclusions:** Low NLR was associated with better observed treatment outcomes in patients with aRCC who received avelumab + axitinib. Clinical trial information: NCT02684006. Research Sponsor: This study was funded by Pfizer, as part of an alliance between Pfizer and Merck KGaA, Darmstadt, Germany.

5062 Poster Session (Board #131), Fri, 8:00 AM-11:00 AM

TIVO-3: Final OS analysis of a phase III, randomized, controlled, multicenter, open-label study to compare tivozanib to sorafenib in subjects with metastatic renal cell carcinoma (RCC). *First Author: Sumanta K. Pal, City of Hope Comprehensive Cancer Center, Duarte, CA*

Background: Tivozanib (T) is a potent and highly selective VEGFR inhibitor. TIVO-3 is a phase 3 study designed to compare the efficacy and safety of T with those of sorafenib (S) as 3rd and 4th line therapy in patients with metastatic RCC. **Methods:** Subjects with RCC who failed 2 or 3 prior systemic regimens, one of which included a VEGFR TKI other than S or T, were stratified by IMDC risk category and type of prior therapy (two TKIs; TKI plus checkpoint inhibitor (CPI); TKI plus other) then randomized in a 1:1 ratio to T or S. **Results:** The 2 arms were well balanced for demographics and prior cancer history. 60% of subjects had 2 prior lines of therapy and 40% had 3 prior lines. 26% had prior treatment with a CPI. Patients treated with T demonstrated PFS superiority compared to S, 5.6 (95% CI 7.3 - 5.3) v. 3.9 mos (95% CI 5.6 – 3.7; HR 0.73; p=0.02). ORR was 18% for T compared to 8% for S (p=0.02). 44% of T treated subjects experienced a grade 3 treatment-related adverse event compared to 55% for S. The predefined, interim analysis for OS performed two years after enrollment was closed had a HR of 0.99 based on 227 events. The final analysis will be presented based on an estimate of 263 events. **Conclusions:** T is superior to S as measured by PFS; 2-year PFS, and ORR in this heavily-treated/relapsed or refractory RCC population and is better tolerated than S. Final OS data will be updated prior to presentation. Clinical trial information: 02627963. Research Sponsor: AVEO Oncology.

5063 Poster Session (Board #132), Fri, 8:00 AM-11:00 AM

Application of IMDC criteria across first-line (1L) and second-line (2L) therapies in metastatic renal-cell carcinoma (mRCC): New and updated benchmarks of clinical outcomes. *First Author: Shaan Dudani, Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada*

Background: In patients with mRCC, the International mRCC Database Consortium (IMDC) criteria have been validated as a prognostic tool in patients treated with targeted therapy in the 1-4L settings and with 2L Nivolumab (Nivo). However, it is unknown whether the IMDC criteria can be used to risk stratify in recently approved 1L IO combination therapies, including Ipilimumab + Nivolumab (IOIO) and Axitinib + Pembrolizumab/Avelumab (IOVE). We sought to assess the ability of the IMDC criteria to risk stratify with the use of novel 1L IO combinations and provide updated benchmarks for older 1L and 2L treatments. **Methods:** Patients with mRCC starting systemic therapy between 2010-2019 were identified through the IMDC. IMDC risk score was calculated at the time of starting the line of therapy of interest. The primary endpoint was overall survival (OS) from time of initiating the treatment of interest. **Results:** From a total of 6596 unique patients, 5043 treated in the 1L setting and 2498 treated in the 2L setting were included in the analysis. Across the entire cohort, median age was 61, 73% were male, 16% had sarcomatoid features, 79% underwent nephrectomy and 88% had clear-cell histology. IMDC risk groups for 1L and 2L treatment were 17%, 57%, 27% and 10%, 60%, 30% for favourable-, intermediate- and poor-risk disease, respectively. IMDC criteria appropriately risk stratified into 3 prognostic groups in 1L IOIO and 1L IOVE combinations, in addition to older treatments: 1L VEGF TT, 2L VEGF TT, 2L Nivo and 2L Everolimus. Results are displayed in Table. Due to the novelty of 1L IO combinations, median follow up time was shorter and thus landmark OS values are presented. **Conclusions:** IMDC criteria may be used to risk stratify in recently approved 1L IO combination therapies in addition to older 1L and 2L treatments. These data provide contemporary benchmarks for OS that may be used for patient counseling and trial design. Research Sponsor: None.

	Favourable-Risk	Intermediate-Risk	Poor-Risk	P-value (log-rank)
		Median OS (months) by IMDC Risk Group		
1L VEGF TT* (N=4662)	47.8	27.2	8.3	<0.01
2L VEGF TT† (N=1230)	41.0	21.4	7.0	<0.01
2L Nivo (N=586)	NR	28.2	6.7	<0.01
2L Everolimus (N=682)	21.4	14.7	4.8	<0.01
		Landmark OS by IMDC Risk Group		
1L IOIO (N=291)				
1-year OS	96%	83%	56%	<0.01
2-year OS	76%	65%	44%	
1L IOVE (N=90)				0.01
1-year OS	96%	86%	51%	0.01
2-year OS	84%	69%	34%	

*Sunitinib, Pazopanib, Cabozantinib †Sunitinib, Pazopanib, Cabozantinib, Axitinib, Lenvatinib
NR = Not Reached

5064 Poster Session (Board #133), Fri, 8:00 AM-11:00 AM

Immunomodulation by HDAC inhibition: Results from a phase I study with entinostat in combination with atezolizumab and bevacizumab in metastatic renal cell carcinoma patients. *First Author: Roberto Pili, Indiana University, Indianapolis, IN*

Background: Immunosuppressive regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs) limit the efficacy of immunotherapies. We have previously reported that the HDAC inhibitor entinostat has synergistic antitumor effect in combination with immunotherapies in preclinical models by inhibiting Tregs and MDSCs function. The combination of atezolizumab (PD-L1 inhibitor) and bevacizumab (VEGF inhibitor) is active in renal cell carcinoma (RCC). Thus, we have conducted a Phase I study with entinostat, atezolizumab and bevacizumab in patients (pts) with metastatic RCC. **Methods:** The primary objective was to evaluate safety and tolerability. The phase I portion included 3 dose levels of entinostat (1 mg, 3 mg or 5 mg, PO weekly) and fixed, standard doses of atezolizumab (1200 mg IV every 21 days) and bevacizumab (15 mg/Kg IV every 21 days). Pts with any histological type and prior therapies were included. **Results:** Dose levels were completed with up to 1 DLT/dose level. 5 mg was the Phase II recommended dose for entinostat. DLTs included hypertension, encephalopathy, hyponatremia and pruritus. The most common resolved grade 3/4 toxicities were hypophosphatemia (33%), hypertension (17%), and pneumonitis (11%). We have enrolled 18 pts (17 evaluable for ORR by RECIST). 5 pts continue on treatment. 3 pts discontinued treatment because of adverse events, 9 pts for disease progression, and one pt for physician decision. Good risk and intermediate risk pts were 61% and 39%, respectively. Overall ORR was 47.1% (95% CI 23.0-72.2) and median PFS was 7.6 months (95% CI 1.6-16.3). In pts with no prior therapies (12) the ORR was 58.3% (95% CI 27.7-84.8) and median PFS was 13.4 months (95% CI 1.5-28.9). One additional PR was observed by ir-RC but was not confirmed within the data cut-off date of 11/11/19. In pts with prior immune checkpoint inhibitors (ICIs) (5) ORR was 20% (95% CI 0.5-71.6) and median PFS was 7.6 months (95% CI 1.3-NR). Preliminary data show a statistically significant lower % of circulating monocytic MDSC ($HLADR^{-}1CD11b^{+}CD33^{high}CD14^{+}CD15^{-}$) and exhausted T cells ($CD45^{+}CD3^{+}CD8^{+}TIM3^{+}$) following treatment in pts (4) with objective responses as compared to pts (4) with progressive disease. **Conclusions:** The results from this phase I suggest that the combination of entinostat, atezolizumab and bevacizumab is relatively well tolerated and is active in renal cell carcinoma patients, in both ICIs naïve and resistant disease. A phase II portion of this study is currently accruing patients. Clinical trial information: NCT03024437. Research Sponsor: None.

5065 Poster Session (Board #134), Fri, 8:00 AM-11:00 AM

A phase II multicenter study of stereotactic radiotherapy (SRT) for oligoprogression in metastatic renal cell cancer (mRCC) patients receiving tyrosine kinase inhibitor (TKI) therapy. *First Author: Patrick Cheung, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada*

Background: SRT is increasingly considered to delay the need to change systemic therapy in metastatic cancer patients who develop oligoprogression. This prospective phase II study evaluated the use of SRT in the setting of mRCC patients who developed oligoprogression while on 1st or 2nd line TKI therapy. **Methods:** IMDC favourable or intermediate risk mRCC patients (pts) who had previous stability or response on ≥ 3 months of TKI therapy were eligible if they developed radiographic progression of ≤ 5 metastases. The oligoprogressive tumours were treated with SRT while other metastases which were stable or responding to TKI therapy were left alone. TKI therapy was temporarily stopped during SRT, and the same TKI drug then resumed. Endpoints included local control of the irradiated lesions, progression free survival (PFS), overall survival (OS), and cumulative incidence of changing systemic therapy after study entry. **Results:** 37 pts (median age 63, IMDC favourable 12, intermediate 25) with 57 oligoprogressive tumours were enrolled. 35 pts were on sunitinib and 2 on pazopanib. Median duration of TKI therapy prior to study entry was 18.6 months. 4 pts had IL-2 therapy prior to a 2nd line TKI. 21 pts had a solitary oligoprogressive tumour, while 17 pts had 2-3 oligoprogressive tumours treated with SRT. Median biological effective dose (BED_{10}) was 72 Gy, corresponding to an SRT dose of 40 Gy in 5 fractions. Irradiated tumour sites were the following: 21 lung/pleural, 15 bone, 7 lymph node, 4 adrenal, 4 liver, 3 brain, 2 spleen, and 1 pancreas. At a median followup of 11.6 (1.8-53.5) months the median PFS from study entry was 9.6 months (95%CI 7.4-20.5) with the vast majority of progression occurring outside of the irradiated areas. The 2-year local control of the irradiated tumours was 96%. The 2-year OS from study entry was 77%. The cumulative incidence of changing systemic therapy was 47% at 1 year and 75% at 2 years, with a median time to a change in systemic therapy of 12.6 months. There were no grade 3-5 SRT related toxicities. **Conclusions:** To our knowledge, this is the first prospective evaluation of the use of SRT for oligoprogressive metastatic cancer. Local control of irradiated oligoprogressive mRCC tumours was high. After delivering SRT, mRCC patients did not need a change in their systemic therapy for a median of 1 year, effectively increasing the PFS of their TKI therapy. This novel approach should be studied in patients with oligoprogression on immunotherapy. Clinical trial information: NCT02019576. Research Sponsor: Pfizer Canada.

5066 Poster Session (Board #135), Fri, 8:00 AM-11:00 AM

Clinically advanced renal cell carcinoma (RCC) and renal sarcoma (RSC) in young patients: A comprehensive genomic profiling (CGP) study. *First Author: Gennady Bratslavsky, Urologic Oncology Branch, National Cancer Institute at the National Institutes of Health, Bethesda, MD*

Background: We queried whether the landscape of genomic alterations (GA) would differ in patients with metastatic RCC under 40 years of age (under40) and patients 40 years of age or older (over40). **Methods:** FFPE tissues from 2,128 clinically advanced RCC and 25 RSC underwent hybrid-capture based CGP to evaluate all classes of GA. Samples were classified at time of sequencing as the following RCC subtypes: clear cell (ccRCC), papillary (papRCC), chromophobe (chrRCC), medullary (medRCC), collecting duct (cdRC), sarcomatoid (sarcRCC) and NOS (nosRCC). Tumor mutational burden (TMB) was determined on up to 1.1 Mbp of sequenced DNA. Tumor cell PD-L1 expression was determined by IHC (Dako 22C3). **Results:** The male preponderance increased in the over40 patients. The GA/tumor increased in the over40 cohorts except for medRCC. Similarly, TMB was consistently higher in over40 groups. MSI high status was virtually absent. PD-L1 expression, available only in small subsets, was generally absent although 44% high positive staining in sarcRCC was noteworthy. Differences in GA in under40 vs over40 RCC were seen and included increased *PBRM1* and *SETD2* GA in over40 vs under40 ccRCC; increased C*DKN2A/B* and *TERT* and decreased *FH* GA in over40 vs under40 papRCC; increased *TP53* and decreased *VHL*, *BAP1*, *SETD2* and *PTEN* in over40 vs under40 chrRCC; increased *TP53*, *PTEN* and *TERT* GA with decreased NF2 GA in over40 vs under 40 sarcRCC; and increased *TP53*, *VHL* and *TERT* in over40 vs under40 nosRCC. Changes in GA in under40 vs over40 medRCC, cdRCC and RSC were noted but insufficient cases prevented further evaluation. **Conclusions:** When separately evaluated by under/over 40 years of age, CGP of clinically advanced RCC demonstrates differences in genomic landscapes with over40 cases featuring increasing male preponderance, higher GA/tumor, higher TMB and increases in a variety of GA. These findings may play important roles in the planning of future clinical trials designed to personalize the treatment of metastatic RCC. Research Sponsor: Foundation Medicine Inc.

	ccRCC		pRCC		sRCC		nosRCC	
	< 40	>40	< 40	>40	< 40	>40	< 40	>40
Cases	55	1,328	26	279	12	131	11	123
Males	64%	71%	62%	76%	67%	69%	82%	72%
Median age	35	60	30	64	34	60	34	60
GA/tumor	3.2	3.5	1.9	2.9	3.7	4.7	2.5	4.9
TP53	7%	13%	4%	5%	17%	41%	9%	34%
VHL	71%	77%	0%	4%	33%	42%	9%	30%
PBRM1	18%	45%	0%	8%	0%	12%	9%	14%
SETD2	16%	27%	4%	10%	8%	10%	9%	15%
CDKN2A	15%	14%	4%	21%	33%	40%	0%	38%
CDKN2B	13%	11%	0%	15%	33%	30%	0%	28%
FH	2%	.2%	57%	6%	0%	1%	11%	1%
PTEN	13%	12%	0%	1%	0%	13%	0%	7%
NF2	9%	3%	12%	13%	33%	17%	18%	13%
TERT	8%	8%	0%	23%	0%	22%	0%	22%
PD-L1 IHC Low/High +	17%/0%	20%/4%	50%/0%	12%/10%	0%/0%	6%/44%	0%/33%	13%/17%

5067 Poster Session (Board #136), Fri, 8:00 AM-11:00 AM

Quality-adjusted time without symptoms or toxicity (Q-TWiST) of lenvatinib plus everolimus versus everolimus monotherapy in patients with advanced renal cell carcinoma (RCC). *First Author: Chung-Han Lee, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: In the primary analysis of Study 205 phase II trial (NCT01136733), lenvatinib+everolimus (vs everolimus) significantly prolonged progression-free survival (median PFS; 14.6 vs 5.5 months, HR = 0.40, 95% CI [0.24, 0.68]) in advanced RCC patients who received one prior anti-angiogenic therapy. Overall treatment differences were evaluated in a post hoc analysis using a quality-adjusted time without symptoms of disease or toxicity of treatment (Q-TWiST) methodology. **Methods:** Patients' survival time was partitioned into three mutually exclusive health states: time spent with grade 3/4 toxicity (TOX), time prior to disease progression and without grade 3/4 toxicity (TWiST) and time post disease progression (REL). Mean time spent in each state was weighted by a health-state utility associated with that state and summed to calculate the Q-TWiST. Non-parametric bootstrapping method was used to generate 95% CI, which evaluates the between-treatment differences. At base case, utility for TWiST, TOX and REL were assigned as 1.0, 0.5 and 0.5, respectively. A sensitivity analysis was used, applying utilities across the range of 0 (similar to death) to 1.0 (perfect health). A relative gain in Q-TWiST of ≥10% and ≥15% has been established in previous literature as clinically important and clearly clinically important, respectively. **Results:** Patients receiving lenvatinib+everolimus (n = 51) vs everolimus (n = 50) had significantly longer mean time in TWiST (10.9 vs 6.4 months; difference 4.5 [95% CI: 1.4, 7.8]) and numerically longer in TOX (1.9 vs 0.7 months; difference 1.2 [95% CI: -0.3, 3.1]) but shorter in REL (5.8 vs 8.5 months; difference -2.8 [95% CI: -6.2, 0.6]). At base case, lenvatinib+everolimus patients had a significant mean Q-TWiST gain of 3.7 months (14.7 vs 11.0; 95% CI of difference [1.3, 6.3]), with a relative gain of 24% vs everolimus. In a sensitivity analysis using alternative utility values for TWiST (varied from 0.55 - 0.9) with utility of TOX and REL both set as 0.5, absolute mean Q-TWiST gain ranged from 1.7 to 3.3 months, with a relative gain ranging from 11.0% to 21.2% (all significant). With TWiST utility set as 1.0 and utility of TOX and REL varying from 0 to 1.0, Q-TWiST gain ranged from 1.7 to 5.8 months (mostly significant and became non-significant as the REL utility gets closer to 1.0 and TOX utility gets closer to 0). **Conclusions:** Within Study 205, lenvatinib+everolimus resulted in a statistically significant and clinically important gain in Q-TWiST vs everolimus alone. Clinical trial information: NCT01136733. Research Sponsor: Eisai Inc., Woodcliff Lake, NJ, USA, and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

5068 Poster Session (Board #137), Fri, 8:00 AM-11:00 AM

Efficacy of immune-checkpoint inhibitors (ICI) in the treatment of older adults with metastatic renal cell carcinoma (mRCC): An international mRCC database consortium (IMDC) analysis. *First Author: Daniel Vilarim Araujo, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Anti-PD-1/PD-L1 immune-checkpoint inhibitors (ICI) are now a standard of care in metastatic renal cell carcinoma (mRCC). Older adults were underrepresented in registration trials and given that immunological senescence may affect the anti-tumor activity of ICIs, there is uncertainty about the efficacy of ICIs in this population. Here we provide real world data on outcomes of older adults with mRCC treated with ICIs. **Methods:** Patients with mRCC treated with a PD-1/PD-L1 ICI either as monotherapy or as a combination treatment from 2000 to 2019 were included. Older adult was defined as ≥ 70-years at the time of ICI treatment. Descriptive statistics were summarized in means, medians and proportions. Efficacy was assessed by survival analysis, including overall survival (OS), time to treatment failure (TTF), and overall response rate (ORR). Multivariate analyses adjusted for imbalances in IMDC risk factors. $P < 0.05$ was considered statistically significant. **Results:** Of 1427 patients, 397 (28%) were older adults. Mean age of older vs. younger adults was 74 (70-92) vs. 60 (22-69) years. Groups were comparable in terms of gender (Female 28.5% vs. 26.1%, p = 0.36), rates of nephrectomy (21% vs. 18.3%, p = 0.24) and presence of sarcomatoid features (12.3% vs. 17.8%, p = 0.14). Proportion of IMDC risk-groups between older vs. younger adults were as follows: 15.4% vs. 18.2% for favorable, 61.2% vs. 59.1% for intermediate, and 23.4% vs. 22.7% for poor; there was no statistical difference (p = 0.55). ICI was used as 1st line in 40%, 2nd line in 48.5% and 3rd line in 11.5% patients; older adults were less likely to be treated with ICI in 1st line (32.2% vs. 43%, $p < 0.01$). In terms of survival, older adults had poorer median OS (25.1m vs. 30.8m, $p < 0.01$) but similar median TTF (6.9m vs. 6.9m, p = 0.40) compared to younger adults. In multivariate analyses, older age was not a predictor of either worse OS (aHR = 1.02, p = 0.86) or TTF (aHR = 0.95, p = 0.59). Older adults had a lower ORR compared to younger (24% vs. 31%, p = 0.01), which was mainly driven by responses in 1st line (31% vs. 44%, p = 0.02) and not observed in 2nd/3rd line (20% vs. 20%, p = 0.86). **Conclusions:** On multivariate analyses, older adults with mRCC treated with ICI had no difference in OS and TTF when compared to younger adults, despite having lower ORR in 1st line. Our data supports that older age is not an independent risk factor for survival; thus, treatment selection should not be based solely on chronological age. Research Sponsor: None.

5069 Poster Session (Board #138), Fri, 8:00 AM-11:00 AM

First-line pembrolizumab (pembro) monotherapy in advanced clear cell renal cell carcinoma (ccRCC): Updated follow-up for KEYNOTE-427 cohort A. *First Author: David F. McDermott, Dana-Farber/Harvard Cancer Center, Boston, MA*

Background: KEYNOTE-427 (NCT02853344), an open-label, single-arm, phase 2 study, showed clinical activity of first-line pembro monotherapy in patients (pts) with ccRCC (cohort A). Previous studies in RCC and immune-oncology suggest depth of response may correlate with long-term benefit. Association between depth of response and OS, along with updated efficacy and safety for cohort A of KEYNOTE-427, are presented. **Methods:** Pts with histologically confirmed ccRCC, measurable disease (RECIST v1.1), and no prior systemic therapy received pembro 200 mg IV Q3W for 2 y or until progressive disease, unacceptable toxicity, or withdrawal. End points: ORR (primary), DOR, and PFS (RECIST v1.1); OS, and safety. Association between depth of response (maximum reduction from baseline in the sum of target lesions) and OS was evaluated using Cox proportional hazards model with target lesion reduction group as time-varying covariate. **Results:** 110 pts enrolled; median time from enrollment to data cutoff was 23.1 (range, 16.7-27.5) mo. Overall, 38.2% of pts had favorable and 61.2% had intermediate/poor IMDC risk. ORR was 36.4% (95% CI, 27.4-46.1; 3 CRs, 37 PRs); median (range) DOR was not reached (2.3-23.5+ mo); 64.0% had a DOR ≥12 mo. Median PFS was 7.1 mo (95% CI, 5.6-11.0) and median OS was not reached; 18-mo PFS and OS rates were 26.6% and 80.0%, respectively. 69.1% had some reduction in target lesions. Pts with > 60% reduction in target lesions had a greater probability of survival than pts with a ≤60% reduction (Table). ORR observed in IMDC favorable and intermediate/poor risk was 31.0% and 39.7%, respectively; 18-mo OS rate was 95.2% for favorable and 70.5% for intermediate/poor IMDC risk. Treatment-related AEs (TRAEs) occurred in 81.8% of pts, primarily fatigue (29.1%) and pruritus (28.2%). Grade ≥3 TRAEs occurred in 29.1% of pts; 1 pt died of treatment-related pneumonitis. **Conclusions:** First-line pembro monotherapy was tolerable and showed promising antitumor activity in advanced ccRCC. In general, pts who had greater reductions in target lesions demonstrated a trend toward improved OS; pts with reduction of tumor burden ≥80% had comparable long term outcomes to those who achieved a RECIST 1.1 defined CR. Clinical trial information: NCT02853344. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	Association Between Depth of Response and Risk for Death N = 110	
Depth of response, %	**n (%)**	**HR (95% CI)**
CR	3 (2.7)	0 (0.0-NE)
–100 to –80	16 (14.5)	0 (0.0-NE)
< –80 to –60	13 (11.8)	0.39 (0.04-3.54)
< –60 to –30	18 (16.4)	1.57 (0.44-5.65)
< –30 to < 0	26 (23.6)	Reference
0 to < 20	17 (15.5)	1.70 (0.52-5.59)
≥20	14 (12.7)	2.04 (0.61-6.88)

5070 Poster Session (Board #139), Fri, 8:00 AM-11:00 AM

Outcomes of patients with metastatic renal cell carcinoma (mRCC) treated with first-line Immuno-oncology (IO) agents who do not meet eligibility criteria for clinical trials. *First Author: Chun Loo Gan, Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada*

Background: IO combination therapies [including IOIO and IO/vascular endothelial growth factor inhibitor (IOVE) combinations] in mRCC have been approved based on registration clinical trials that have strict eligibility criteria. The clinical outcomes of trial ineligible patients who are treated with first-line IOIO or IOVE combinations are unknown. **Methods:** Metastatic RCC patients treated with first-line IOIO or IOVE were retrospectively deemed ineligible for clinical trials (according to commonly used inclusion/exclusion criteria in IO trials) if they had a Karnofsky performance status (KPS) $< 70\%$, no clear-cell component, brain metastases, hemoglobin (Hb) < 9 g/dL, eGFR < 40 mL/min, platelet count of $< 100{,}000/mm^3$, and/or neutrophil count $< 1500/mm^3$. Time to treatment failure (TTF) and overall survival (OS) were calculated from time of starting first-line IO therapy. **Results:** Overall, 26% (155/592) of patients in the International mRCC Database Consortium (IMDC) were deemed ineligible for clinical trials by the above criteria. Baseline characteristics are listed in Table. The reasons for ineligibility were: no clear-cell component (34%, 53/155), Hb $<$ 9g/dL (28%, 44/155), eGFR $<$ 40 mL/min (19%, 30/155), brain metastases (19%, 29/155), KPS $< 70\%$ (14%, 21/155), platelet $< 100{,}000/mm^3$ (3%, 4/155) and neutrophil count $< 1500/mm^3$ (0%, 0/155). Between ineligible versus eligible patients, the response rate, median TTF and median OS of first-line IOIO or IOVE was 34% vs 46% ($p = 0.02$), 4.2 vs 9.7 months ($p < 0.01$), and 25.3 vs 44.4 months ($p < 0.01$), respectively. When adjusted by the IMDC prognostic categories, the HR for death between trial ineligible and trial eligible patients was 1.50 (95% CI 1.05-2.14). **Conclusions:** The number of patients that are ineligible for clinical trials is substantial and their outcomes are inferior. These data may guide patient counselling and specific trials addressing the unmet needs of protocol ineligible patients are warranted. Research Sponsor: None.

Baseline Characteristics	TRIAL INELIGIBLE (N = 155)	TRIAL ELIGIBLE (N = 437)	P-VALUE
Median Age	62	63	0.24
Male	63% (98/155)	73% (318/437)	0.03
Sarcomatoid histology	25% (29/115)	20% (63/314)	0.25
Nephrectomy	66% (102/155)	75% (326/437)	0.04
IOIO	63% (97/155)	57% (247/437)	0.19
IOVE	37% (58/155)	43% (190/437)	
Received second line therapy	33% (50/155)	34% (148/437)	0.72
IMDC Risk Group			
Favorable	11% (15/138)	19% (74/385)	< 0.01
Intermediate	47% (65/138)	65% (251/385)	
Poor	42% (58/138)	16% (60/385)	

5071 Poster Session (Board #140), Fri, 8:00 AM-11:00 AM

Characterizing sites of metastatic involvement in metastatic clear-cell, papillary, and chromophobe renal cell carcinoma. *First Author: Shaan Dudani, Ottawa Hospital Cancer Centre, University of Ottawa, Ottawa, ON, Canada*

Background: There exists considerable biological and clinical variability between histologic variants of metastatic renal-cell carcinoma (mRCC). Data reporting on sites of metastatic involvement in less common histologies of mRCC are sparse. We sought to characterize the frequency of metastatic site involvement across the three most common histologies of mRCC: clear-cell (ccRCC), papillary (pRCC), and chromophobe (chrRCC). **Methods:** Using the International mRCC Database Consortium (IMDC) database, patients with mRCC starting systemic therapy between 2002-2019 were identified and sites of metastases at the time of systemic therapy initiation were documented. Patients with multiple sites of metastatic involvement were included in analyses of all groups to which they had metastases. The primary outcomes were prevalence of metastatic site involvement and overall survival (OS). Patients with mixed histology were excluded. **Results:** 10,105 patients were eligible for analysis. Median age at diagnosis was 60, 72% were male and 79% underwent nephrectomy. 92%, 7% and 2% of patients had ccRCC, pRCC, and chrRCC, respectively. Frequency of metastatic site involvement across the histologic subtypes is shown in Table. Lung, adrenal, brain and pancreatic metastases were more frequent in ccRCC, lymph node involvement was most frequent in pRCC, and liver metastases were most frequent in chrRCC. Median OS for ccRCC varied by site of metastatic involvement, ranging between 16 months (brain/pleura) and 50 months (pancreas). OS by site of metastatic involvement was compared between histologies for the four most common sites of metastases (lung, lymph nodes, bone, liver). As compared to patients with ccRCC, patients with pRCC had lower OS regardless of site of metastasis ($p < 0.05$). Power was limited and thus differences in OS between ccRCC and chrRCC were not detectable. **Conclusions:** Sites of metastatic involvement differ based on histology in mRCC. These data highlight the clinical and biologic variability between histologic subtypes of mRCC and constitute the largest cohorts of patients with metastatic pRCC and chrRCC to report on sites of metastases. Sites of Metastatic Involvement by Histology. Research Sponsor: None.

Metastatic Site	ccRCC (N=9252)	pRCC (N=667)	chrRCC (N=186)	P-value
Lung	70%	49%	36%	<0.01
Lymph Nodes	45%	69%	51%	<0.01
Bone	32%	29%	33%	0.26
Liver	18%	22%	34%	<0.01
Adrenal	10%	7%	6%	0.02
Brain	8%	3%	2%	<0.01
Pancreas	5%	1%	2%	<0.01
Pleural	4%	3%	0.7%	0.03
Peritoneal	2%	5%	4%	<0.01
Spleen	0.9%	0.6%	0.8%	0.88
Thyroid	0.7%	0.2%	0%	0.25
Bowel	0.7%	0.2%	1.5%	0.24

5072 Poster Session (Board #141), Fri, 8:00 AM-11:00 AM

Baseline and early change of systemic inflammation index (bSII and ΔSII) as prognostic factors in metastatic renal cell carcinoma (mRCC) patients treated with Nivolumab: Final results of the Meet-URO 15 (I-BIO-REC) study. *First Author: Sara Elena Rebuzzi, Medical Oncology Unit 1, IRCCS Ospedale Policlinico San Martino di Genova, Genoa, Italy*

Background: Biomarkers to select mRCC patients most likely to benefit to immunotherapy are still needed. The retrospective multicentre Meet-URO-15 study evaluated the prognostic role of peripheral blood cells in mRCC patients treated with Nivolumab. **Methods:** Complete blood count was collected at the first four cycles of Nivolumab. The primary endpoint was median overall survival (mOS) according to baseline neutrophil-to-lymphocyte ratio. Secondary analyses included bSII defined as platelet x NLR (cutoff = 1375) and ΔSII defined as the difference between SII at 2^{nd}cycle and bSII (median used as cutoff = 383). **Results:** From October 2015 to October 2019, 470 patients started Nivolumab as 2^{nd}(67%), 3^{rd}(22%) and $> 3^{rd}$(11%) line. Median age was 66 years, 71% were male and 83% had clear cell histology. Baseline IMDC group was favorable in 25%, intermediate in 63% and poor in 12%. Lymph-nodes, visceral and bone metastases were present in 54%, 91% and 36%. mOS and progression-free survival (PFS) were 34.8 and 7.5 months. Overall response rate (ORR) and disease control rate (DCR) were 30% and 61%. SII was available in 404 patients: SII $<$ 1375 (82%) correlated with statistically significant improvement of PFS [10.2 *vs* 4.1 months, HR 2.06 (1.54-2.76), $p< 0.001$], OS [46.2 *vs* 9.5 months, HR 3.16 (2.23-4.49), $p< 0.001$], ORR (35% vs 21%, $p= 0.035$) and DCR (67% *vs* 40%, $p< 0.001$). ΔSII was available in 360 patients: ΔSII $<$ 383 (75%) correlated with statistically significant improvement of PFS [11.3 *vs* 4.7 months; HR 1.64 (1.23-2.18), $p= 0.001$] and OS [NR *vs* 21.1 months; HR 1.76 (1.21-2.56), $p= 0.003$], ORR (37% *vs* 24%, $p= 0.023$) and DCR (68% *vs* 53%, $p= 0.01$). Multivariate analyses adjusted for IMDC group, line of therapy and metastatic sites, confirmed the statistically significant correlation of bSII and ΔSII with OS, PFS and DCR. **Conclusions:** Our study showed the statistically significant correlation of lower bSII and early ΔSII with longer OS, PFS and higher DCR in mRCC patients treated with Nivolumab. Research Sponsor: None.

5073 Poster Session (Board #142), Fri, 8:00 AM-11:00 AM

Phase I clinical trials as a therapeutic option for patients with metastatic renal cell carcinoma (mRCC). *First Author: Andrew W Hahn, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Immune checkpoint inhibitors, multi-kinase VEGF agents, and mTOR inhibitors are approved for mRCC. Due to the overlapping mechanisms of action of the twelve approved therapies for mRCC, select patients are referred for phase I clinical trials after progression on multiple lines of treatment. We sought to evaluate the efficacy of phase I trials in patients with mRCC. **Methods:** Patients with all histologies of mRCC were included if they received treatment on a phase I clinical trial at MD Anderson Cancer Center. Baseline clinical characteristics and outcomes data were retrospectively collected. The historical control was a study of 1112 patients with mRCC who received third-line treatment in the IMDC database (PMID: 27318422). Time to event endpoints were calculated using Kaplan-Meier methods. Hazard ratios (HR) were calculated using the Cox proportional hazard model. **Results:** Between 2014 and 2019, there were 106 cases where 82 patients with mRCC were enrolled in a phase I clinical trials (40 unique trials). 30% (32/108) of the cases were in patients with non-clear cell RCC (nccRCC), and the most prevalent nccRCC histologies were papillary (n = 7) and renal medullary carcinoma (n = 7). The median number of prior systemic therapies was 2 (range 0-9). Across the entire cohort, median PFS was 5.9 months (m), median OS was 31.2 m, and the ORR was 23% (Table). In patients who received at least two prior lines of therapy (n = 70), the median PFS was 4.8 m and median OS was 24.9 m. In patients with metastatic nccRCC, median OS, PFS, and ORR were numerically lower, but statistically did not contradict the supposition that these outcomes did not differ from ccRCC (Table). **Conclusions:** In the largest pooled phase I clinical trial experience for patients with mRCC, phase I trials may have therapeutic value when compared to historical controls, where median PFS was 3.9 m, median OS was 12.4 m, and ORR was 10.5%. Patients with all histologies of mRCC may derive clinical benefit from phase I clinical trials, yet patients with ccRCC had numerically better outcomes. Patients with mRCC should be considered for phase I clinical trials. Research Sponsor: None.

	All mRCC	nccRCC	ccRCC	HR	P value
ORR	22%	17%	24%	-	-
CR	2%	0%	3%		
PR	20%	17%	21%		
SD	49%	30%	57%	-	-
PD	29%	53%	19%	-	-
PFS (95% CI)	5.9 m (4.8-9.3 m)	2.5 m (2.1-9.3 m)	7.3 m (5.5-12.4 m)	1.39* (0.86-2.25)	0.19
OS (95% CI)	31.2 m (24.9-38.7 m)	23.9 m (11.4-NR)	31.6 m (27.6-41.5 m)	1.26* (0.71-2.23)	0.44

Table legend: * = HR is for nccRCC versus ccRCC.

5074 Poster Session (Board #143), Fri, 8:00 AM-11:00 AM

CT-based radiomic classifier of primary renal tumors to distinguish between metastatic and non-metastatic disease. *First Author: Sam O Kleeman, Barts Health NHS Trust, London, United Kingdom*

Background: Existing clinicopathological tools are unable to accurately identify renal cell carcinoma (RCC) patients who will develop metastases after surgery. As a result, it is unclear how long and how often to follow-up patients post-operatively. Tumor macropathology, as assayed by CT scanning, represents the sum product of tumor biology and microenvironment. We hypothesized that quantitative tumor features extracted from CT scans (termed radiomics) could discriminate between metastatic and non-metastatic RCCs. **Methods:** This retrospective study incorporated three cohorts of clear-cell RCC patients (n = 279, from TCGA, CPTAC and KiTS19 datasets) treated with nephrectomy. The study cohort was sub-divided into metastatic (n = 54, M1 at diagnosis or recurrence after surgery), high metastatic risk/HMR (n = 85, N1, T3-4, T2G3/4, T1G4) or low metastatic risk/LMR (n = 140, absence of these features) subsets. 3D primary tumor segmentation of arterial contrast CT scans was performed by trained investigators. Features were extracted using pyRadiomics 2.2.0 (n = 839) with gray value and voxel size normalization. For random forest (RF) model training, the cohort was randomly split into training (75%) and validation (25%) sets. **Results:** Multidimensional clustering of radiomic features by t-SNE analysis showed that metastatic and HMR tumors predominantly cluster together, while LMR tumors cluster separately. Consistent with this, there were no differentially regulated radiomic features (DR-features) between HMR and metastatic tumors. In contrast, we identified 26 DR-features (adjusted p-value < 0.05) between presumed-metastatic (n = 139, HMR and metastatic tumors) and LMR tumors, which were then used as input to a RF binary classifier. In the training set, the trained classifier discriminated between presumed-metastatic and LMR tumors with bootstrapped AUC = 0.81. In the validation set, the classifier discriminated subsets with AUC = 0.80. **Conclusions:** High-risk and metastatic tumors have similar radiomic properties, suggesting common biology driving metastasis in RCC. We propose a novel radiomic classifier that accurately distinguishes between presumed-metastatic and low-risk tumors. Further work will assess whether this tool can identify patients with micrometastatic disease at diagnosis, who may benefit from adjuvant therapy or closer, long-term surveillance. Research Sponsor: None.

5075 Poster Session (Board #144), Fri, 8:00 AM-11:00 AM

A phase II study of the selective MET kinase inhibitor INC280 in advanced papillary renal cell cancer. *First Author: Paul Denis Leger, National Institutes of Health, Bethesda, MD*

Background: There are currently no approved systemic agents for patients with advanced type 1 papillary renal cell carcinoma (pRCC). Type 1 pRCC can occur in a hereditary form with germline alterations of *MET* (hereditary papillary RCC: HPRC) or in a sporadic form. Both hereditary and sporadic forms have similar histologic features and somatic *MET* alterations have been found in 15-20% of patients with sporadic pRCC. Furthermore, gain of chromosome 7, where *MET* and the gene for its ligand HGF are located, has been reported in a majority of patients with type 1 pRCC and may represent an alternative means of activating the MET pathway. This is a phase II study evaluating the activity of INC280, a highly selective and potent MET inhibitor, in patients with pRCC. **Methods:** Patients with advanced type 1 pRCC were treated with INC280 at a starting dose of 600mg PO twice daily (capsules). Later in the study course, the capsules were replaced with exposure-equivalent tablets (400mg PO twice daily). Eligible patients had an ECOG PS 0-2, no active brain metastases, and less than 4 prior lines of therapy. The primary endpoint was overall response rate (ORR) assessed by RECIST 1.1. Secondary endpoints included progression-free survival, disease control rate, and tolerability. Exploratory endpoints included the correlation between *MET* alteration/copy number gain and response to INC280. **Results:** Twenty subjects were enrolled from January 2014 to October 2019. Median age was 62 years, 60% of patients were classified as IMDC good risk and 40% as IMDC intermediate risk. Three patients (15%) achieved a confirmed partial response and seven (35%) had stable disease, including 4 (20%) who maintained stable disease for over 6 months. The most common treatment-related adverse events (AEs) were of grade 1-2 including nausea (85%), increased creatinine(70%) diarrhea(60%), fatigue(55%), limb edema(40%), increase in amylase(20%), triglycerides(20%), LFTs(20%), lipase(10%) and leukopenia(10%). INC280-related Grade 3-4 AEs included asymptomatic increased lipase (20%), increased LFTs (10%), increased amylase(5%), leukopenia (5%), lymphopenia (5%) and syncope (5%). **Conclusions:** INC280 demonstrated clinical activity in patients with advanced type 1 pRCC with an acceptable toxicity profile. The correlation between the presence of *MET* alteration and/or copy number gain and response to INC280 is under evaluation. Research Sponsor: Novartis, Other Government Agency.

5076 Poster Session (Board #145), Fri, 8:00 AM-11:00 AM

Genomic and transcriptomic correlates of clinical benefit from immunotherapy and targeted therapy among patients with metastatic renal cell carcinoma (mRCC). *First Author: Nicholas Salgia, City of Hope Comprehensive Cancer Center, Duarte, CA*

Background: Previous studies have delineated *PBRM1* alterations as a prognostic indicator for response to nivolumab in mRCC (Miao *et al* Science 2018). However, further clinically-relevant biomarkers remain elusive in mRCC. Herein, we utilized genomic profiling to detect correlates of clinical benefit (CB) among patients (pts) with mRCC receiving VEGF-directed targeted therapy, immunotherapy, or both. **Methods:** Pts with mRCC who underwent clinical tumor-normal whole exome and whole transcriptome RNA sequencing (Ashion Analytics, Phoenix, AZ) were retrospectively identified at a single institution. Pts' demographics and clinical variables including treatment type, treatment response, and survival outcomes were collected from an institutional mRCC database. Pts who had received immunotherapy or VEGF-directed therapy (or both) were eligible for analysis. CB was defined as pts who experienced a complete response, partial response, or maintained stable disease for at least 6 months on therapy. Two-tailed Fisher's exact test was used to assess characteristics of genomic alterations and clinical benefit. **Results:** Out of 155 mRCC pts with genomic profiling, 58 pts with evaluable response and sufficient follow-up information were included in the analysis. The median age of the cohort was 63 years and 74% were male. The majority (81%) had clear cell histology. 43 pts received targeted therapy and 32 received immunotherapy (17 pts received both). No singular gene was associated with clinical benefit in the targeted therapy cohort. *PBRM1* loss of function mutations were more frequent in pts on immunotherapy who experienced CB ($p > 0.05$). *TERT* promoter mutations were enriched in pts who experienced no CB on immunotherapy ($p = 0.04$). Differential gene expression analysis of the transcriptomes found 135 genes that were significantly upregulated in *TERT*-mutated samples, including *SST, CYSLTR2, WNK2,* and *PTGES* (adjusted p-value < 0.05). ENRICHR analysis found that MYC and KAT2A were key transcription factor pathways significantly enriched in pts with *TERT* mutation who experienced no CB from immunotherapy. **Conclusions:** These data support previous observations regarding the prognostic nature of *PBRM1* in mRCC and offer novel findings associating *TERT* mutations with a lack of CB from immunotherapy. Our transcriptomic analysis implies that MYC-targeting agents and epigenetic modifiers (directed at KAT2A) could overcome immunotherapy resistance. Research Sponsor: None.

5077 Poster Session (Board #146), Fri, 8:00 AM-11:00 AM

Use of immune checkpoint inhibitors (ICIs) after prior ICI in metastatic renal cell carcinoma (mRCC): Results from a multicenter collaboration. *First Author: Praful Ravi, Dana-Farber Cancer Institute, Boston, MA*

Background: Several ICIs are used in first and subsequent lines of therapy for mRCC, either alone or in combination with another ICI or targeted therapy (TT). There are no data on the efficacy and safety of using an ICI in patients who have already received an ICI in a prior line of therapy. **Methods:** We reviewed patients with mRCC at 8 institutions who received 2 separate lines of ICI therapy (ICI-1, ICI-2), including as a single-agent and/or combination with other agents. The primary outcomes were overall response rate (ORR) and time to progression (TTP) with ICI-1 and ICI-2. Immune-related adverse events (irAEs) were graded using CTCAEv5.0. **Results:** 65 patients were included. Median age at diagnosis of mRCC was 60 years (range 30-86) and the majority had clear cell RCC (n=56, 86%). Median follow-up was 3.5 years (95% CI 2.9-4.4). Median lines at which ICI-1 and ICI-2 were received were 1 (1-6) and 3 (2-8) respectively. Reasons for discontinuing ICI-1 were disease progression (n=47, 72%), toxicity (n=15, 23%) or other (n=3, 5%). Therapies received at ICI-2 were single-agent ICI (n=26, 40%), or combinations of ICI with another ICI (n=20, 31%), TT (n=11, 17%) or other agent (n=8, 12%). Responses to ICI-1 and ICI-2 are shown in the Table; ORR to ICI-2 was significantly lower than to ICI-1 (23% vs. 36%, p=0.044). Amongst those who responded to ICI-2 (n=14), 7 (50%) received single-agent ICI, and the remainder received ICI in combination with another ICI (n=4, 29%) or TT (n=3, 21%); 7 patients (50%) had previously responded to ICI-1. The ORR to ICI-2 was higher in responders to ICI-1 (32%) compared to those with SD (17%) or PD (15%) to ICI-1. Median TTP (mTTP) at ICI-2 was shorter compared to ICI-1 (5.3 months vs. 8.5 months, Wilcoxon p=0.024). 29 patients (45%) experienced an irAE with ICI-2; 8 (12%) and 3 (5%) had a grade 3 or 4 irAE respectively, with 3 (30%) of these patients having previously had ≥grade 3 irAE to ICI-1. There were no treatment-related deaths. **Conclusions:** The ORR to ICI-2 was 23%, which is comparable to that seen with ICI after prior TT. Responses were seen even amongst those receiving single-agent ICI at ICI-2 and the likelihood of response to ICI-2 was higher if a patient had previously responded to ICI-1. No increase in toxicity with ICI-2 was apparent. Additional data from prospective studies are needed to determine whether sequential ICI has a role in treatment of mRCC. Research Sponsor: None.

	ICI-1	ICI-2
Partial response (PR)	23/64 (36%)	14/60 (23%)
Stable disease (SD)	28/64 (44%)	23/60 (38%)
Progressive disease (PD)	13/64 (20%)	23/60 (38%)

5078 Poster Session (Board #147), Fri, 8:00 AM-11:00 AM

Randomized prospective trial assessing *Bifidobacterium*-containing probiotic supplementation in metastatic renal cell carcinoma (mRCC) patients receiving vascular endothelial growth factor-tyrosine kinase inhibitors (VEGF-TKIs). *First Author: Nazli Dizman, City of Hope Comprehensive Cancer Center, Duarte, CA*

Background: Studies suggest a link between the gut microbiome and mRCC outcomes, including evidence that mRCC patients (pts) possess a lower abundance of *Bifidobacterium* spp compared to healthy adults (Pal *et al* Clin Cancer Res 2015). The aim of this study was to assess if *Bifidobacterium*-containing probiotics could modulate the gut microbiome and impact rates of clinical benefit (CB) from VEGF-TKIs. **Methods:** Pts initiating VEGF-TKI therapy for mRCC were randomized to probiotic supplemented (PSu) or probiotic restricted (PRe) treatment arms. Pts in the PSu arm consumed two 4 oz servings of Activia daily. Stool samples were collected prior to therapy and at wks 2, 3, 4 and 12. Gut microbiota composition was assessed using whole genome shotgun metagenomic sequencing (Zhu *et al* Microbiome 2018). The primary endpoint was change in *Bifidobacterium* spp with therapy. Microbiome composition was compared across pts with CB (complete/partial response or stable disease) versus no CB (NCB). **Results:** In total, 20 pts were enrolled. The most frequent VEGF-TKIs were cabozantinib (45%), sunitinib (25%) and lenvatinib (25%). Median progression-free survival (PFS) was 6.5 months (95%CI 0.3-12.9) and CB rate was 75%. *Bifidobacterium animalis,* the active ingredient of Activia, reached detectable levels in all pts in the PSu arm, but was only detectable in one pt in the PRe arm. CB rate was not significantly different in PSu vs PRe arms (70% vs 80%, $p > 0.05$), and there was no difference in PFS. LDA effect size (LEfSe) analysis of MetaPhlAn2 data captured 25 enriched species demonstrating an LDA score > 3 in either CB or NCB. Of those with high LDA scores, *Barnesiella intesitinihominis* and *Akkermansia municiphila* were the most significant members ($p = 7.4 \times 10^{-6}$ and $p = 5.6\ 10^{-3}$, respectively). While 92% of *B. intestinihominis* positive pts obtained a CB, only 50% of *B. intestinihominis* negative pts obtained CB ($p = 0.036$). **Conclusions:** This is the first prospective randomized study demonstrating modulation of the gut microbiome with probiotics in mRCC. While microbiome modulation by probiotics did not increase CB rates as intended, consecutive stool specimens allowed us to identify an association between *B. intesitinihominis, A. municiphila* and CB with VEGF-TKIs. In addition to the previously documented association between *A. municiphila* and immunotherapy outcome (Routy *et al*. Science 2018), this species may predict activity with VEGF-TKIs. Clinical trial information: NCT02944617. Research Sponsor: Pfizer Inc.

5079 Poster Session (Board #148), Fri, 8:00 AM-11:00 AM

Prediction of watchful waiting in newly diagnosed metastatic clear cell renal cell carcinoma patients with a good or intermediate prognosis. *First Author: Sarah Verhoeff, Department of Medical Oncology, Radboud University Medical Center, Nijmegen, Netherlands*

Background: In metastatic clear cell renal cell carcinoma (mccRCC), the number of International Metastatic Database Consortium (IMDC) risk factors plus metastatic sites may identify patients with rapid or slow disease progression in a period of watchful waiting (WW) (median WW of 8.4 vs 22.2 months; Rini *et al*. Lancet Oncol. 2016). We aimed to validate this and prospectively assess the added value of baseline PET with [^{18}F]FDG and [^{89}Zr]Zr-DFO-girentuximab to predict the WW-period in the multicenter IMaging PAtients for Cancer drug selecTion (IMPACT)-RCC cohort study. (NCT02228954). **Methods:** Between February 2015 and March 2018, 40 treatment-naïve mccRCC patients with a good (n=13) or intermediate prognosis (n=25) according to IMDC, were enrolled. Following baseline CT, [^{18}F]FDG and [^{89}Zr]Zr-DFO-girentuximab-PET, CT scans (RECIST1.1) were acquired at 2, 4, 6, 9, 12 months and thereafter every 4 months. Primary endpoint was time to radiological and/or clinical disease progression, requiring systemic treatment. Patients were assigned to a favorable (<2 IMDC risk factors and <3 metastatic sites) or unfavorable for WW-group (all others; Rini *et al*). Maximum standardized uptake values (SUV_{max}) were measured in PET-positive lesions measuring $\geq$10mm, or 15mm in lymph nodes. High and low-uptake groups were defined based on median geometric mean (gm) SUV_{max} across patients. A one-sided test was used to validate observations by Rini *et al*; other tests were two-sided. **Results:** The median WW-period was 9.3 months in the unfavorable WW-group (n=19) vs 20.4 months in the favorable WW-group (n=21) (HR 1.89 95%CI 0.94-3.89; p=0.037), confirming observations of Rini *et al*. Patients with high [^{18}F]FDG uptake had a median WW-period of 8.5 months compared to 25.2 months in the low-uptake group (HR 4.08 95%CI 1.89-9.28; p=0.0002). Patients with high [^{89}Zr]Zr-DFO-girentuximab uptake had a median WW-period of 10.7 versus 16.4 months in the low-uptake group (HR 1.37; 95%CI 0.69-2.76; p=0.37). [^{18}F]FDG uptake groups improved a Cox-model for WW based on the prognostic groups of Rini *et al* (p=0.0015); [^{89}Zr]Zr-DFO-girentuximab did not (p=0.98). **Conclusions:** The IMPACT-RCC study validated the observations by Rini *et al.* and shows that adding baseline [^{18}F]FDG PET further improves the prediction of the duration of the WW-period in mccRCC patients. Clinical trial information: NCT02228954. Research Sponsor: Dutch Cancer Society (Alpe d'HuZes Grant RUG 2012-5400).

5080 Poster Session (Board #149), Fri, 8:00 AM-11:00 AM

Axitinib plus pembrolizumab in patients with advanced renal cell carcinoma: Long-term efficacy and safety from a phase Ib study. *First Author: Michael B. Atkins, Georgetown Lombardi Comprehensive Cancer Center, Washington, DC*

Background: Axitinib (AXI) plus pembrolizumab (pembro) showed superior overall survival (OS), progression-free survival (PFS) and response rate compared with sunitinib in a randomized Phase 3 trial in advanced renal cell carcinoma (RCC). Here, we report long-term efficacy and safety data of the combination AXI/pembro from the Phase 1 trial, with almost 5 years of follow-up. **Methods:** 52 treatment-naïve patients with advanced RCC were enrolled between 23 September 2014 and 13 October 2015, and were treated with oral AXI 5 mg twice daily and intravenous pembro 2 mg/kg every 3 weeks. Planned treatment duration was 2 years for pembro and not limited for AXI. Based on International Metastatic Database Consortium (IMDC) criteria, 46.2%, 44.2% and 5.8% of patients were reported as having favourable, intermediate and poor risk. **Results:** At data cut-off date (July 3, 2019), median OS was not reached; 38 (73.1%) patients were alive. 14 (26.9%) patients had died, none were related to treatment. The probability of being alive was 96.1% (95% CI 85.2–99.0) at 1 year, 88.2% (95% CI 75.7–94.5) at 2 years, 82.2 % (95% CI 68.5– 90.3) at 3 years, and 66.8 % (95% CI 49.1–79.5) at 4 years. Median PFS was 23.5 (95% CI 15.4–30.4) months. Median duration of response was 22.1 (95% CI 15.1–not evaluable) months. Median time on treatment with the combination AXI/pembro was 14.5 months (n=52), median time on pembro after AXI discontinuation was 9.0 months (n=10), and median time on AXI after pembro discontinuation was 7.5 months (n=11). After stopping study treatment, 22 patients received subsequent systemic therapy, including nivolumab and cabozantinib (n=6 each). Grade 3/4 AEs were reported in 38 (73.1%) patients. 20 (38.5%) patients discontinued either drug due to AEs: 17 (32.7%) patients discontinued AXI, and 13 (25.0%) patients discontinued pembro with 10 (19.2%) discontinuing both drugs. Dose reduction of AXI due to AEs was reported in 16 (30.8%) patients. The most common AEs reported were diarrhea (84.6%), fatigue (80.8%), hypertension (53.8%), cough (48.1%), and dysphonia (48.1%). Increased alanine aminotransferase and aspartate aminotransferase occurred in 44.2% and 36.5% of patients, respectively. With this longer follow-up, there were no cumulative AEs or new AEs. OS by IMDC risk group will be presented. **Conclusions:** In patients with advanced RCC with almost 5 years of follow-up, the combination of AXI/pembro continues to demonstrate clinical benefit with no new safety signals. Clinical trial information: NCT02133742. Research Sponsor: Pfizer.

5081 Poster Session (Board #150), Fri, 8:00 AM-11:00 AM

FDA pooled analysis of time to treatment discontinuation (TTD) in frontline advanced renal cell carcinoma trials. *First Author: Elaine Chang, U.S. Food and Drug Administration, Silver Spring, MD*

Background: Time to treatment discontinuation (TTD) has been proposed as a potential pragmatic real-world data (RWD) endpoint, and was closely correlated with progression-free survival (PFS) in pooled analyses of non-small cell lung cancer (NSCLC) and breast cancer trials across therapeutic classes (Blumenthal, Ann Onc 2019; Gao, SABCS Abstract P5-14-02). **Methods:** We analyzed data from all randomized patients (pts) in the phase 3 trials submitted to FDA 2016-18 evaluating a combination therapy (Rx) of an immuno-oncology agent and another systemic Rx (IO-X) versus sunitinib (SUN) for treatment-naïve advanced renal cell carcinoma (RCC). Protocols specified treatment until progression, but treatment beyond progression was allowed. TTD was defined as the time from the start of Rx to time of treatment discontinuation of both drugs in combination Rx or SUN. We measured TTD in treatment-defined subgroups (IO-X and SUN) and across all pts, and pt-level correlation (Pearson's *r*) between TTD and PFS and between TTD and overall survival (OS). We also determined rates of disparity between TTD and PFS greater than 3 months. **Results:** Of 3758 pts (IO-X, n=1878; SUN, n=1880), 3190 pts (85%) had a TTD event, and 1899 pts (51%) had a PFS event. Median TTD was longer among pts receiving IO-X than SUN (12.3 versus 8.0 months). Regardless of drug class, more pts had early (TTD shorter than PFS by $\geq$ 3 months) TTD events than late TTD (13.4% versus 6.4%, overall). We found higher correlation between TTD and PFS in pts receiving SUN ($r = 0.89$) than pts receiving IO-X ($r = 0.72$). Overall, TTD was more closely associated with PFS ($r = 0.80$) than with OS (0.61). **Conclusions:** Observed correlations of TTD to PFS were stronger compared to the correlation of TTD to OS. This may be expected because OS is farther removed in time from TTD than is PFS. In contrast to TTD in NSCLC, more than twice as many pts in RCC trials had early TTD than late TTD, regardless of Rx group, which may indicate earlier discontinuation with combination Rx due to additive toxicity. Limitations include the censoring of PFS and OS and the post-hoc nature of this analysis. Research Sponsor: FDA.

	IO-X	SUN	All
N	1878	1880	3758
Median PFS, mo (95% CI)	15.0 (13.9, 15.3)	12.5 (11.5, 13.8)	13.8 (12.7, 14.2)
Median TTD, mo (95% CI)	12.3 (11.5, 12.9)	8.0 (7.8, 9.0)	9.8 (9.3, 10.6)
Corr PFS:TTD (95% CI)	0.72 (0.69, 0.74)	0.89 (0.88, 0.90)	0.80 (0.79, 0.81)
TTD – PFS ≥ 3 mo	8.2%	4.6%	6.4%
PFS – TTD ≥ 3 mo	17.5%	9.4%	13.4%
Median OS, mo (95% CI)	24.4 (23.5, 25.2)	22.2 (21.4, 23.2)	23.5 (22.6, 24.1)
Corr OS:TTD (95% CI)	0.56 (0.53, 0.59)	0.65 (0.62, 0.67)	0.61 (0.59, 0.63)

5082 Poster Session (Board #151), Fri, 8:00 AM-11:00 AM

Immune infiltration and angiogenesis as markers of outcome in the post-nephrectomy setting: Transcriptomic data from patients receiving placebo on a randomized phase III trial (PROTECT). *First Author: A. Ari Hakimi, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Defined stromal and immune features of the tumor microenvironment (TME) have proven relevant for outcomes with systemic therapy in advanced clear cell renal cell carcinoma (ccRCC). We hypothesized that these may matter beyond therapeutic applications and could be relevant much earlier in the disease course. We sought to study the TME in high risk ccRCC patients undergoing definitive surgery. **Methods:** Clinical, pathologic, immunohistochemical, and whole-genome microarray data were acquired on 236 out of 769 patients in the Placebo arm of PROTECT trial (NCT01235962 - pazopanib vs placebo). Transcriptomic scores assessing angiogenesis and myeloid infiltration with individual annotations above/below median were used to categorize patients into four groups (angiogenesis high vs. low; myeloid high vs. low). We tested categorical association with disease free (DFS) and overall survival (OS) using logrank testing and assessed interdependence with relevant clinicopathologic variables, including the UCLA Integrated Staging System (UISS) in a cox regression model. **Results:** Tumors from236 patients were available for analysis. Overall, 37% developed metastatic recurrence and 81% were alive at last follow up. On univariate analysis increasing tumor stage, higher UISS score, and angiogenesis/myeloid subgroups (high – H and low – L) were associated with worse DFS and OS (all p values <0.05). On multivariate analysis TME subgroups remained significant for worse DFS and OS (Table). **Conclusions:** Microenvironmental subgroups stratified into angiogenic and myeloid expression profiles carry independent prognostic significance and should be further explored to guide future biomarker-directed adjuvant trials. Clinical trial information: NCT01235962. Research Sponsor: Novartis, Philantropic.

Variable	Level	HR	Lower 95% CL	Upper 95% CL	P
Angio_Myeloid_Grp	H_L	REF			
	H_H	3.75	1.72	8.21	<0.001
	L_H	6.44	3.06	13.54	<0.001
	L_L	2.12	0.89	5.05	0.09
Stage	T2	REF			
	T3	1.54	0.80	2.94	0.2
	T4	8.69	2.66	28.36	<0.001
UISS Group	2	REF			
	3	0.56	0.24	1.31	0.18
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5083 Poster Session (Board #152), Fri, 8:00 AM-11:00 AM

Patient preferences and expectations of systemic therapy in renal cell carcinoma. *First Author: Dena Battle, KCCure, Alexandria, VA*

Background: In metastatic renal cell carcinoma, the systemic therapy landscape has expanded to include multiple VEGF inhibitors, immunotherapies, and combination therapy. Little is known about patient expectations and preferences when making decisions about systemic therapy. We sought to gather independent data from online kidney cancer patient communities to assess patient perspectives on what matters most when considering treatment options. **Methods:** The KCCure online survey was performed between August 1, and September 30, 2019. Patients were recruited via the KCCure website, social media channels (Twitter, Facebook) and through fliers distributed at cancer centers. Those who agreed to participate were surveyed for demographics (age, gender, race, income, country) and clinical characteristics (date of the diagnosis, disease stage, treatment history). Key questions focused on treatment selection and side effect management. **Results:** Out of 1,136 patients responding, 411 patients were on systemic therapy with a median age of 57 years (range 28-86). 223 (54%) of patients on systemic therapy were male. Patients were primarily from the U.S. (83%). Median duration on therapy was 24.7+/-1.9 months. When asked to select the most important outcome for treatment selection, 58.8 % of patients chose complete response, followed by tumor control (10.2%), low risk of toxicity (5.7%) and the chance to discontinue therapy (3.7%). Patients ranked cost as the least important factor in selecting treatment (2.9%). 10.9% preferred infusion therapy and 42.1% oral therapy, whereas 47% were indifferent about the route of administration. Even if it would be safe to discontinue therapy, 62.8% of patients would be anxious about cancer progression. 23.2% would rather stay on treatment and 39.3% would want increased scanning intervals. Only 34.4% of patients would look forward to having more time off therapy. When asked to define treatment success, 86.3% selected reduction in tumor size, followed by stable disease (71.7%), freedom from symptoms (35.1%) and better quality of life (47.7%). **Conclusions:** Patients rank efficacy as the most important outcome when considering treatment options. Toxicity, time off therapy and cost are not significant priorities for patients. Further data is warranted investigating the impact of communicating treatment options, potential discontinuation of therapy and resulting expectations. Research Sponsor: None.

5084 Poster Session (Board #153), Fri, 8:00 AM-11:00 AM

Patient-reported use of marijuana and cannabinoid (CBD) oil in patients with renal cell carcinoma undergoing systemic therapy. *First Author: Dena Battle, KCCure, Alexandria, VA*

Background: The use of cannabis and cannabinoid related products has become increasingly common among cancer patients. We sought to gather independent data from online kidney cancer patient communities to assess frequency of use of marijuana and CBD-oil and estimate influence on treatment duration and side-effects. **Methods:** The KCCure online survey was performed between August 1, and September 30, 2019. Descriptive statistics were used to characterize patients who self-report using marijuana, their systemic treatments, and interactions with their oncologists. **Results:** Out of 1,136 patients responding, 411 patients were on systemic therapy with a median age of 57 years (28-86). Of the 441 patients with systemic therapy, 223 patients (54%) were male. There was no difference in gender distribution or race among patients who reported using or not using marijuana and or CBD oil. 93 patients (21%) reported using marijuana or CBD oil and 35 patients (8.5%) reported using both. Patients using marijuana and/or CBD oil had a median age of 55.7 +/- 1.1 years compared with patients not using (65.1 +/- 6.9 years). The median treatment duration was 23.9+/-2.4 months for patients using marijuana and/or CBD oil versus 26.4+/- 1.9 months for patients not using these supplements (p=0.437). Patients using marijuana and/or CBD oil were more likely to have bothersome side effects from therapy (p=0.001) and were less likely to talk to their doctor about their situation (p=0.044). The median NCCN distress score in patients using marijuana and/or CBD oil was 49.5+/-25.7 versus 51.4+/-24.0 (p n.s.). No correlation was seen with the use of steroids, anti-diarrhea drugs, anti-nausea-drugs, hormone substitution or other drugs used to manage side effects. **Conclusions:** Marijuana and/or CBD oil are used by a significant number of patients. No benefit/harm on treatment duration and use of concomitant drugs to control side effects and severity was seen. Patients using marijuana and/or CBD oil were more likely to report bothersome treatment related side effects and were more willing to report their side effects to their provider. As cannabinoids become more mainstream and legal in a number of states, more research is needed to better understand the impact these supplements may have on patients. Research Sponsor: None.

5085 Poster Session (Board #154), Fri, 8:00 AM-11:00 AM

Camrelizumab plus famitinib malate in patients with advanced renal cell cancer and unresectable urothelial carcinoma: A multicenter, open-label, single-arm, phase II trial. *First Author: Yuan-Yuan Qu, Fudan University Shanghai Cancer Center, Shanghai, China*

Background: Camrelizumab (SHR-1210) is a humanised anti-PD-1 antibody. Famitinib malate is a tyrosine kinase inhibitor (TKI) against VEGFR-2, PDGFR, c-kit, and FGFR. This is an ongoing, open label, multi-center Phase II study to assess the preliminary efficacy and safety of camrelizumab in combination with famitinib malate in patients (pts) with genitourinary cancers and gynecologic cancers. Here we just report genitourinary cancers results. **Methods:** Eligible pts were aged 18 or older, who had advanced clear-cell renal-cell carcinoma with their primary tumour resected or unresectable urothelial carcinoma, had an ECOG performance status of 0-1and measurable disease. Previous system treatments were allowed (excluding prior PD-1/PD-L1 inhibitors or famitinib treatment). Famitinib 20 mg was administered orally once daily with SHR-1210 200 mg given intravenously every 3 weeks. We assessed antitumour activity and safety in all pts who received at least one dose treatment. The primary end point was objective response rate (ORR) per RECIST v1.1. **Results:** From 23 Jan 2019 to 24 Jun2019, 35 pts were enrolled (25 with RCC, 10 with UC). Median previous treatment line was 1 (range, 1-4), and 50.0% of pts had received ≥2 prior therapies in RCC, all pts received one or more-line therapies in UC. At the data cut-off date (Dec 31, 2019), after at least 6 months follow-up, 22 (63%) pts were still receiving study treatment. The most common reason for discontinuing treatments was disease progression (n = 10). 16 pts achieved a confirmed response, all were partial response, with 8 additional > 24 weeks stable disease. the ORR was 52.0% (13/25, 95% CI 31.3% to 72.2%) in RCC and 30.0% (3/10) in UC, the disease control rate was 84.0% (21/25) in RCC and 70.0% in UC. 13/16 confirmed PR pts were still on treatment, the median duration of response is not reached. The most common grade 3-4 treatment-related AEs (TRAEs) were hypertension (17.1%), proteinuria (11.4%), platelet count decreased (8.6%), hand-foot syndrome (8.6%) and anemia (5.7%). Immune-related adverse events were observed in 7 pts (20%) of 35 pts, 1 pt (2.9%) with grade 3 enteritis. **Conclusions:** The camrelizumab with famitinib combination appeared to show encouraging activity in pts with heavy-treated RCC and UC, and the safety profile of the combination seemed to be manageable and consistent with that of each drug alone. This combination represented a novel potential treatment option for these settings and warranted further investigation. Clinical trial information: NCT03827837. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

5086 Poster Session (Board #155), Fri, 8:00 AM-11:00 AM

Tipifarnib, a farnesyltransferase inhibitor, for metastatic urothelial carcinoma harboring HRAS mutations. *First Author: Jiyun Lee, Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

Background: Tipifarnib is a farnesyltransferase inhibitor known to block RAS signaling and attenuate cancer cell proliferation. We tested the activity and safety of tipifarnib in patients with previously treated urothelial carcinoma (UC) carrying HRAS mutations. **Methods:** In a prospective phase II clinical trial, genetic screening was performed in 224 UC patients; those with missense HRAS mutations or STK11:rs2075606 received study treatment. Eligible patients received oral tipifarnib 900 mg twice daily on days 1–7 and 15–21 of 28-d treatment cycles. The primary endpoint was progression-free survival at 6 mo (PFS6). With two-stage design, at least 18 patients were required. **Results:** Among the 224 patients screened, we found 16 (7%) missense HRAS mutations (G13R, 7; Q61R, 4; G12S, 3; G12C, 2) and 104 (46%) STK11: rs2075606 carriers. In 21 patients enrolled, 14 and 7 patients had HRAS mutations and STK11:rs2075606, respectively. The most frequent adverse events included fatigue and hematologic toxicities. With a median follow-up of 28 months, 4 patients (19%) reached PFS6: 3 had missense HRAS mutations and one patient, enrolled as a STK11 carrier, had HRAS frameshift insertions at H27fs and H28fs rendering a nonsense HRAS mutation. Response rate was 24% (4 missense and one nonsense frameshift HRAS mutation); no response observed in UC patients with wild type HRAS tumors. **Conclusions:** Oral tipifarnib showed a manageable safety profile and encouraging anti-tumor efficacy against treatment-refractory UC containing HRAS mutations. Clinical trial information: NCT02535650. Research Sponsor: Kura Oncology.

5087 Poster Session (Board #156), Fri, 8:00 AM-11:00 AM

Comprehensive genomic profiling (CGP) of histologic subtypes of urethral carcinomas (UrthCa). *First Author: Petros Grivas, University of Washington, Seattle, WA*

Background: UrthCa is an uncommon GU malignancy that can progress to advanced metastatic disease. **Methods:** 127 metastatic UrthCa underwent hybrid-capture based CGP to evaluate all classes of genomic alterations (GA). Tumor mutational burden (TMB) was determined on up to 1.1 Mbp of sequenced DNA and microsatellite instability (MSI) was determined on 114 loci. PD-L1 expression was determined by IHC (Dako 22C3). **Results:** 49 (39%) urothelial (UrthUC), 31 (24%) squamous (UrthSCC), 34 (19%) adenocarcinomas (UrthAC) and 13 (9%) clear cell (UrthCC) were evaluated along with a control cohort of 2,130 bladderUC cases. UrthUC and UrthSCC were more common in men; UrthAC and UrthCC more common in women. Age was similar in all 4 groups. GA in *PIK3CA* were the most frequent potentially targetable GA; MTOR pathway GA in *PTEN* also identified. GA in other potentially targetable genes were also identified including *ERBB2*(6% in UrthUC, 3% in UrthSCC and 12% in UrthAC), *FGFR1-3* (3% in UrthSCC), *BRAF* (3% in UrthAC), *PTCH1* (8% in UrthCC) and *MET* (8% in UrthCC). Higher TMB was seen in UrthUC and UrthCC compared to UrthAC and UrthSCC, possibly reflecting their higher GA/tumor status and suggesting potential for immunotherapy benefit. MSI high status was absent throughout. The bladderUC cases had similar genomic pattern as UrthUC with significantly lower frequency of HPV16/18 positive cases. **Conclusions:** CGP reveals GA that may be predictive of both targeted and immunotherapy benefit in patients with advanced UrthCa and that could potentially be used in future adjuvant, neoadjuvant and metastatic disease trials. Research Sponsor: Foundation Medicine Inc.

	UrthUC	UrthSCC	UrthAC	UrthCC	BladderUC
Number of Cases	49	31	34	13	2,130
Males/Females	78% M/22% F	55% M/45% F	29% M/71% F	9% M/91% F	75%M/25%F
Median age (range)	67 (44-87)	61 (40-76)	64 (22-83)	60 (33-71)	67 (19-88)
HPV16/18	14%	23%	0%	0%	2%
GA/tumor	6.9	10.8	5.6	4.1	7.7
Top Untargetable GA	*TP53 43%*	*TP53 52%*	*TP53 79%*	*CDKN2A 23%*	*TP53 59%*
	TERT 30%	*CDKNA 32%*	*CDKN2A 29%*	*MYC 23%*	*TERT 72%*
	CDKN2A 28%	*TERT 21%*	*SMAD4 24%*	*TP53 23%*	*CDKN2A 37%*
	CDKN2B 22%	*MYC 16%*	*KRAS 24%*	*VEGFA 15%*	*CDKN2B 29%*
	CCND1 16%	*FAT1 14%*	*MYC 18%*	*ARID1A 15%*	*CCND1 14%*
Top Potentially Targetable GA	*PIK3CA 22%*	*PIK3CA 29%*	*PTEN 15%*	*PIK3CA 31%*	*PIK3CA 21%*
	FGFR3 12%	*EGFR 10%*	*ERBB3 12%*	*PTCH1 8%*	*FGFR3 14%*
	BRCA2 8%	*PTEN 7%*	*PIK3CA 12%*	*TSC2 8%*	*BRCA2 10%*
	PTEN 8%	*ERBB2 3%*	*ERBB2 12%*	*MET 8%*	*PTEN 10%*
	ERBB2 6%	*FGFR1 3%*	*NF1 9%*		*ERBB2 7%*
	TSC1 4%	*FGFR3 3%*	*BRCA2 6%*		*TSC1 8%*
	BRCA1 4%	*TSC2 3%*	*EGFR 3%*		*BRCA1 3%*
	KIT 2%	*FGFR2 3%*	*BRAF 3%*		*KIT 1%*
Median TMB (mut/Mb)	5.2	4.3	4.3	5.0	7.0
TMB>10/20 mut/Mb	22%/10%	23%/6%	9%/0%	9%/0%	36%/11%

5088 Poster Session (Board #157), Fri, 8:00 AM-11:00 AM

Impact of human papillomavirus (HPV) infection on the outcome of perioperative treatments for penile squamous-cell carcinoma (PSCC). *First Author: Patrizia Giannatempo, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: PSCC patients (pts) with palpable inguinal lymph node (ILN) disease have a poor overall survival (OS). Multimodal perioperative treatments are usually offered despite the lack of clinically meaningful efficacy. Pending the availability of novel effective systemic therapy, the optimization of conventional treatments in better selected pts is needed. **Methods:** Within an international, multicenter database of 924 PSCC pts who received ILN dissection from USA, Europe, Brazil and China, 494 had information on HPV, and 52 (10.5%) had HPV+ PSCC, predominantly assessed with immunohistochemistry (53%). Multivariable logistic regression analyses evaluated the association between pt factors and HPV status. Multivariable Cox analyses (MVA) assessed predictors of overall mortality (OM), including HPV status, pathologically-involved ILN ratio (ILNR), extranodal extension, margin status, vascular invasion (VI), perioperative RT (pRT) and perioperative chemotherapy (pCT). Comparisons between HPV status and ILNR were performed using interaction tests. Kaplan-Meier method was used to define the OS benefit related in HPV-stratified sub-groups. **Results:** Median age at diagnosis was 58yrs. Overall, pCT and pRT were used in 227 (46%) and 50 (10%) pts. The median follow-up was 62 months. Neither clinical factors nor country were associated with HPV status. On MVA, ILNR (HR: 1.01, p = 0.01) and extranodal extension (HR: 1.5, p = 0.02) were statistically significantly associated with OM, but HPV was not (p = 0.2). However, in the subgroup of pts who received pRT, HPV status was associated with favorable OM (HR: 0.11, 95%CI: 0.03-0.5, p = 0.004) together with negative VI (p = 0.03), and the use of adjuvant CT (p = 0.04). A significant interaction was found on OM between HPV+ status and increasing ILNR, with a cutoff at 50% (p = 0.05). Results are limited by their retrospective nature and small numbers in each subgroup. **Conclusions:** In the largest available dataset of ILND for PSCC, we observed that pRT seemed to be more effective in the subgroup of HPV+ PSCC. These results should be considered as hypothesis-generating and may inspire both the future prospective trials or the ongoing InPACT study. Research Sponsor: Fondazione IRCCS Istituto Nazionale dei Tumori.

5089 Poster Session (Board #158), Fri, 8:00 AM-11:00 AM

A pooled analysis of the efficacy and safety of cabozantinib post immunotherapy in patients with advanced renal cell carcinoma. *First Author: Mototsugu Oya, Department of Urology, Keio University School of Medicine, Tokyo, Japan*

Background: While studies have demonstrated survival benefits of first-line regimens including immuno-oncology agents (IO) in advanced renal cell carcinoma (aRCC), optimal treatment following IO is unknown. In the phase 3 METEOR trial, cabozantinib improved progression-free survival (PFS), objective response rate (ORR), and overall survival (OS) versus everolimus in patients (pts) with aRCC, after VEGFR-TKI therapy. The Japanese phase II C2001 study (NCT03339219), targeting a population similar to that of METEOR, showed similar efficacy and safety results. Here, we present a post-hoc pooled analysis of pts who had received prior IO therapy from METEOR and C2001. **Methods:** A pooled analysis was performed in pts who received 60mg/day of oral cabozantinib once daily enrolled in the METEOR or C2001. Patients were divided into two groups with previous IO treatment (pre-w/ IO subgroup) or without previous IO treatment (pre-w/o IO subgroup). Analyses of ORR, PFS, OS, and safety were performed as measures of clinical outcome in each subgroup. **Results:** 365 pts (pre-w/ IO subgroup: 33 pts, pre-w/o IO subgroup:332 pts) were included for efficacy analysis and 366 pts (pre-w/ IO subgroup: 33 pts, pre-w/o IO subgroup:333 pts) for safety analysis. Minor differences in baseline characteristics were noted between the analysis subgroups but are not expected to substantially affect efficacy outcomes. The ORR was 21.2% (95% CI: 9.0-38.9%) for pre-w/ IO subgroup, and 17.2% (95% CI: 13.3-21.7%) for pre-w/o IO subgroup. PFS rate and OS rate at 6 months pre-w/ IO was 65.5%, 90.8% and pre-w/o IO was 58.3%, 90.6%, respectively. Although there were some differences in the safety profile, almost all AEs were manageable by dose modifications. There were no differences in AEs associated with IO treatment, such as pneumonitis, endocrinolopathy or infusion related reaction. No new safety signals were noted in any subgroups. **Conclusions:** Safety and treatment efficacy of cabozantinib were maintained in the pooled analysis of pts from METEOR and C2001 irrespective of prior IO treatment. Funded by Takeda Pharmaceutical Company Limited, Tokyo, Japan. Clinical trial information: NCT03339219, NCT01865747. Research Sponsor: Takeda Pharmaceutical Company Limited and Exelixis, Inc.

TPS5090 **Poster Session (Board #159), Fri, 8:00 AM-11:00 AM**

A phase II, randomized study of nivolumab (NIVO), NIVO plus linrodostat mesylate, or NIVO plus intravesical bacillus Calmette-Guerin (BCG) in BCG-unresponsive, high-risk, nonmuscle invasive bladder cancer (NMIBC): CheckMate 9UT. *First Author: Noah M. Hahn, Departments of Oncology and Urology, Johns Hopkins School of Medicine, Baltimore, MD*

Background: Immune checkpoint inhibitors, including NIVO (anti–PD-1), have demonstrated favorable tolerability and efficacy profiles, ushering in a new treatment (tx) paradigm for advanced bladder cancer (advBC). However, an unmet need exists for new effective tx options in earlier stages of disease, specifically for patients (pts) with BCG-unresponsive, high-risk NMIBC. Increased IDO and PD-L1 expression in NMIBC tumors (Inman, et al. *Cancer* 2007; Hudolin, et al. *Anticancer Res* 2017), support the combination of anti–PD-1 and IDO1 inhibition in NMIBC. Linrodostat mesylate, a selective, potent, once-daily IDO1 inhibitor, has demonstrated clinical activity in combination with NIVO in pts with immunotherapy-naive advBC who received ≥ 1 prior line of therapy (objective response rate, 37%; Tabernero, et al. *J Clin Oncol* 2018;36(suppl) [abstr 4512]). Furthermore, high levels of PD-L1 expression have been reported in patients not responding to BCG tx. These findings provide a rationale for investigation of NIVO ± linrodostat ± intravesical BCG therapy in BCG-unresponsive high-risk NMIBC. Here we describe a phase 2, randomized, open-label study assessing the safety and efficacy of NIVO ± linrodostat ± intravesical BCG in pts with BCG-unresponsive, high-risk NMIBC (NCT03519256). **Methods:** Pts aged ≥ 18 years with BCG-unresponsive (per February 2018 FDA guidance), high-risk NMIBC, defined as carcinoma-in-situ (CIS) with or without papillary component, any T1, or Ta high-grade lesions, will be enrolled. Pts must have urothelial carcinoma as the predominant histological component (> 50%). Key exclusion criteria include locally advanced or metastatic BC, upper urinary tract disease within 2 years, prostatic urethral disease within 1 year, and prior immunotherapy. Using a novel adaptive-type design, pts will be randomized to 1 of 4 tx arms with NIVO ± linrodostat ± BCG. Primary endpoints include proportion of pts with CIS with complete response (CR) and duration of CR in pts with CIS. Secondary endpoints are progression-free survival and safety. This global study in 14 countries is underway, with a target enrollment of 436 pts. Clinical trial information: NCT03519256. Research Sponsor: Bristol Myers Squibb.

TPS5091 **Poster Session (Board #160), Fri, 8:00 AM-11:00 AM**

A phase III randomized study of neoadjuvant chemotherapy (NAC) alone or in combination with nivolumab (NIVO) ± linrodostat mesylate, followed by adjuvant postsurgical NIVO ± linrodostat, in cisplatin-eligible muscle invasive bladder cancer (MIBC). *First Author: Guru Sonpavde, Department of Genitourinary Oncology, Dana Farber Cancer Institute, Boston, MA*

Background: Immuno-oncology (IO) therapies have revolutionized the treatment (tx) of pts with advanced bladder cancer (advBC). For pts with cisplatin-eligible, muscle invasive BC (MIBC), the recommended tx is cisplatin-based neoadjuvant chemotherapy (NAC) prior to radical cystectomy (RC). However, since only ≈ 30% of pts achieve a pathologic complete response (pCR) translating to improved long-term outcomes with approved regimens, new therapies are needed. PD-L1 expression is associated with aggressive BC and has been shown to increase in BC after NAC, supporting the therapeutic pursuit of the PD-1/PD-L1 axis. Additionally, expression of indoleamine 2,3-dioxygenase (IDO) is higher in BC than in normal bladder tissue and is associated with advanced disease and poor clinical outcome. Linrodostat mesylate, a selective, potent, once-daily oral IDO1 inhibitor that works to reduce kynurenine production, has demonstrated clinical activity in combination with NIVO (anti–PD-1) in pts with IO tx–naive advBC who had ≥ 1 prior line of therapy (ORR, 37%). Taken together, these data provide a rationale for investigating NAC + NIVO + linrodostat in MIBC. Here we describe a randomized, partially blinded, phase 3 study evaluating the efficacy and safety of NAC ± NIVO ± linrodostat followed by RC and continued IO tx in pts with MIBC (NCT03661320). **Methods:** Pts aged ≥ 18 years with previously untreated MIBC (clinical stage T2-T4a, N0, M0), creatinine clearance ≥ 50 mL/min, and predominant UC histology who are eligible for cisplatin-based NAC and RC will be enrolled. Pts with evidence of positive lymph node; metastatic BC; or prior systemic therapy, radiotherapy, or surgery for BC other than TURBT are not eligible. Pts will be randomized to receive NAC (gemcitabine/cisplatin; arm A), NAC + NIVO + oral placebo (arm B), or NAC + NIVO + linrodostat (arm C) followed by RC (all arms); arms B and C will receive continued IO tx. Primary endpoints include pCR after neoadjuvant tx and event-free survival (arms C vs A; arms B vs A). Secondary endpoints are overall survival and safety. This global study in 28 countries began accrual in Nov 2018 and has a target enrollment of 1200 pts. Clinical trial information: NCT03661320. Research Sponsor: Bristol Myers Squibb.

TPS5092 **Poster Session (Board #161), Fri, 8:00 AM-11:00 AM**

Study EV-103: New randomized cohort testing enfortumab vedotin as monotherapy or in combination with pembrolizumab in locally advanced or metastatic urothelial cancer. *First Author: Nataliya Mar, UC Irvine Medical Center, Orange, CA*

Background: Cisplatin-based chemotherapy is the standard for first-line (1L) patients (pts) with locally advanced/metastatic urothelial cancer (LA/mUC). PD-1/PD-L1 inhibitors have promising durability of responses but 1L use is restricted to pts ineligible for cisplatin-containing therapy and whose tumors express PD-L1 (CPS ≥10) or pts ineligible for platinum-containing chemotherapy regardless of PD-L1 status. Enfortumab vedotin (EV), an antibody-drug conjugate, delivers the microtubule-disrupting agent monomethyl auristatin E to cells expressing Nectin-4, which is highly expressed in UC. EV recently received FDA accelerated approval based on tumor response rates for adults with LA/mUC who have previously received a PD-1/PD-L1 inhibitor and a platinum-containing chemotherapy. In the ongoing phase 1b/2 study EV-103/KEYNOTE-869 (NCT03288545), the safety and antitumor activity of EV are investigated as monotherapy (mono) (for the first time in the 1L setting) and in combination with PD-1 inhibitor pembrolizumab (P) +/- chemotherapy in UC. An initial analysis of EV (1.25 mg/kg) + P (200 mg) (both drugs in investigational use here) in this study showed a 73.3% confirmed ORR in 45 1L cisplatin-ineligible LA/mUC pts (dose-escalation + expansion Cohort A) (Rosenberg ASCO 2020). **Methods:** A new Cohort K randomized 1:1 to 1.25 mg/kg EV mono or 1.25 mg/kg EV + 200 mg P provides additional information on EV + P and the contribution of activity from EV in cisplatin-ineligible pts with LA/mUC in the 1L setting. This cohort will enroll 150 adults (≥18 years) with LA/mUC and measurable disease per RECIST v1.1, and exclude pts with prior systemic treatment for LA/mUC, active CNS metastases, ongoing sensory or motor neuropathy (Grade ≥2), or uncontrolled diabetes. Cisplatin-ineligibility in this study is based on ≥1 of the following: ECOG of 2, creatinine clearance of ≥30 and < 60 mL/min, or hearing loss/dysfunction. In each 3-week cycle of this study, EV is administered on days 1 and 8, and P on day 1. The primary endpoint is ORR per RECIST v1.1 by BICR. Secondary endpoints include ORR per RECIST v1.1 by investigator assessment, DOR, DCR, PFS per RECIST v1.1 by BICR and investigator assessment, OS, safety, and tolerability. Sample size is not based on power calculation for formal hypothesis testing but is selected based on ORR estimate precision based on 95% CIs. Efficacy is summarized by treatment arm with no formal statistical comparisons between arms. The study opened in Oct 2017. Cohort K opened in Jan 2020. Clinical trial information: NCT03288545. Research Sponsor: Seattle Genetics, Astellas, Merck.

TPS5093 **Poster Session (Board #162), Fri, 8:00 AM-11:00 AM**

Phase III study of pembrolizumab (pembro) plus chemoradiotherapy (CRT) versus CRT alone for patients (pts) with muscle-invasive bladder cancer (MIBC): KEYNOTE-992. *First Author: Arjun Vasant Balar, NYU Langone Health Perlmutter Cancer Center, New York, NY*

Background: Pembro has shown clinical activity across many stages of bladder cancer (BC), including metastatic BC, MIBC, and NMIBC. Current NCCN and AUA/ASCO/ASTRO/SUO guidelines recommend CRT as a bladder-preserving treatment option for selected pts with MIBC. This phase 3 study was designed to investigate the safety and efficacy of pembro + CRT in pts with MIBC who opt for bladder preservation. Ongoing phase 2 studies (NCT02662062; NCT02621151) have shown that pembro + CRT may be a promising therapeutic option in MIBC. **Methods:** KEYNOTE-992 (NCT04241185) is a phase 3, global, multicenter, double-blind, placebo-controlled, randomized trial to evaluate the efficacy and safety of pembro + CRT versus placebo + CRT in pts with previously untreated MIBC. Adults (≥18 years) opting for bladder preservation with histologically confirmed cT2-T4a, nonmetastatic (NOM0) MIBC after maximal TURBT are eligible. An estimated 636 pts will be randomly assigned 1:1 to receive CRT + either pembro 400 mg IV every 6 weeks (Q6W) or placebo. Treatment will continue with pembro or placebo Q6W for up to 9 doses. CRT regimens will be decided by the investigator before randomization. Accepted radiotherapy regimens are conventional radiotherapy consisting of 64 Gy at 2 Gy/fraction over 6.5 weeks (whole bladder with or without pelvic nodes) or hypofractionated radiotherapy consisting of 55 Gy at 2.75 Gy/fraction over 4 weeks (whole bladder only). Accepted concurrent radiosensitizing chemotherapy regimens are cisplatin monotherapy (35 mg/m^2 IV weekly), 5-fluorouracil (500 mg/m^2 on days 1-5 and days 22-26) + mitomycin C (12 mg/m^2 on day 1), or gemcitabine monotherapy (27 mg/m^2 IV twice weekly). Randomization will be stratified by ECOG PS (PS 0/1 vs 2), PD-L1 combined positive score (< 10 vs ≥10), T stage (T2 vs T3/4), and geographic region (US vs Europe vs rest of world). Pts must provide tissue for biomarker analysis. Efficacy will be assessed by cystoscopy (± biopsy), CT or MRI (with blinded independent central review), and urine cytology at 10 weeks after CRT, then Q12W up to the end of year 2, and then Q24W thereafter. The primary end point is bladder-intact event-free survival, defined as time from randomization to residual/recurrent MIBC, nodal or distant metastasis, radical cystectomy, or death from any cause. Key secondary end points are OS, metastasis-free survival, time to occurrence of NMIBC, and safety. Clinical trial information: NCT04241185. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

TPS5094 **Poster Session (Board #163), Fri, 8:00 AM-11:00 AM**

Phase III study of the hypoxia-inducible factor 2α (HIF-2α) inhibitor MK-6482 versus everolimus in previously treated patients with advanced clear cell renal cell carcinoma (ccRCC). *First Author: Toni K. Choueiri, Dana-Farber Cancer Institute, Boston, MA*

Background: In RCC, the Von Hippel-Lindau (*VHL*) tumor suppressor gene is inactivated in most cases, resulting in the accumulation and overactivation of HIF-2α. HIF-2α is a key oncogenic driver in RCC and is involved in the activation of genes associated with angiogenesis, tumor progression, and metastasis, such as vascular endothelial growth factor A (*VEGFA*), cyclin D1, and *CXCR4*. MK-6482 is a potent and selective small molecule inhibitor of HIF-2α, and it has shown antitumor activity in a phase 1/2 study in patients with previously treated advanced ccRCC. **Methods:** The current study (NCT04195750) is a phase 3, open-label, multicenter, randomized, active-controlled trial to compare the efficacy and safety of MK-6482 with everolimus in patients with previously treated advanced ccRCC. Adults aged ≥18 years will be eligible if they have unresectable, locally advanced, or metastatic ccRCC; have measurable disease per RECIST v1.1; and received ≤3 prior systemic regimens, which must include a PD-1/PD-L1 inhibitor (≥2 doses) and a VEGF-targeted therapy, for locally advanced or metastatic RCC. Approximately 736 patients will be randomly assigned 1:1 to receive MK-6482 120 mg orally once daily or everolimus 10 mg orally once daily. At randomization, patients will be stratified by International Metastatic RCC Database prognostic scores (0 vs 1-2 vs 3-6) and by the number of prior anti-VEGF–targeted therapies received for advanced RCC (1 vs 2-3). Responses will be assessed by CT or MRI per RECIST v1.1 by blinded independent central review at week 9 from the date of randomization, then every 8 weeks through week 49, and then every 12 weeks thereafter. Treatment will continue until documented disease progression, withdrawal of consent, or other discontinuation event. Dual primary endpoints are progression-free survival per RECIST v1.1 and overall survival. Key secondary endpoints include objective response rate, duration of response, patient-reported outcomes, and safety. Clinical trial information: NCT04195750. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

TPS5095 **Poster Session (Board #164), Fri, 8:00 AM-11:00 AM**

PROOF 302: A randomized, double-blind, placebo-controlled, phase III trial of infigratinib as adjuvant therapy in patients with invasive urothelial carcinoma harboring susceptible *FGFR3* alterations. *First Author: Siamak Daneshmand, Keck School of Medicine of USC, Los Angeles, CA*

Background: Radical surgery ± cisplatin-based (neo)adjuvant chemotherapy (NAC) is the mainstay of treatment for invasive urothelial carcinoma of the upper urinary tract (UTUC) or bladder (UBC), but recurrence rates are high. Furthermore, many patients are unable to receive NAC due to cisplatin ineligibility. Fibroblast growth factor receptor 3 (FGFR3) genetic alterations occur in up to 70% of UTUC and up to 20% of UBC and may constitute a potential candidate for targeted therapy. Infigratinib (BGJ398), a FGFR1–3 selective oral tyrosine kinase inhibitor, has shown promising clinical activity and tolerability in patients with advanced urothelial carcinoma having *FGFR3* alterations [Pal et al. Cancer Discov 2018]. PROOF 302 has been designed to investigate the efficacy and safety of infigratinib versus placebo as adjuvant therapy in patients with high-risk invasive urothelial carcinoma and susceptible *FGFR3* alterations. **Methods:** PROOF 302 is a randomized, double-blind, placebo-controlled, phase III study of approx. 218 patients. Adults with high-risk invasive UTUC or UBC with susceptible *FGFR3* genetic alterations (i.e. activating mutations, gene fusions or translocations) who are ≤120 days following surgical resection and ineligible for or refusing cisplatin-based adjuvant chemotherapy or with residual disease after cisplatin-based NAC are eligible. Those who received non cisplatin-based NAC are eligible if they have residual disease and are ineligible for adjuvant cisplatin. Patients receive oral infigratinib 125 mg or placebo (1:1 ratio) once daily on days 1–21 every 28 days for up to 52 weeks or until disease recurrence, unacceptable toxicity or death. Primary endpoint: centrally reviewed disease-free survival (DFS). Secondary endpoints: DFS including intraluminal low-risk recurrence; metastasis-free survival; overall survival; DFS (per investigator); safety and tolerability. Exploratory endpoints include quality of life, pharmacokinetics, cell-free DNA (cfDNA) and/or RNA for resistance mechanisms. The study will involve approximately 120 centers worldwide. The study was initiated in late 2019 and is expected to end in 2024. Clinical trial information: NCT04197986. Research Sponsor: QED Therapeutics.

TPS5096 **Poster Session (Board #165), Fri, 8:00 AM-11:00 AM**

Cell cycLe inhibitiON to target the EVolution of urOthelial cancer (CLONEVO): A single-arm, open-label window-of-opportunity trial of neoadjuvant abemaciclib in platinum-ineligible muscle invasive bladder cancer patients. *First Author: Jones Nauseef, NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY*

Background: The standard of care for clinically localized muscle-invasive bladder cancer (MIBC) is neoadjuvant platinum-based combination chemotherapy followed by radical cystectomy (RC). Up to 40% of patients (pts) are ineligible to receive cisplatin and proceed to RC without any neoadjuvant therapy. We and others have demonstrated enrichment of molecular alterations in cell cycle genes in MIBC, including copy number losses of *CDKN2A* in 41% of pts. Abemaciclib is a unique CDK4/6 inhibitor with single agent activity and a target kinome distinct from other CDK4/6 inhibitors. We have demonstrated that CRISPR knockout of CDKN2A increases susceptibility to abemaciclib in bladder cancer cell lines. Beyond tumor-intrinsic effects, abemaciclib also modulates the tumor microenvironment (TME) via upregulating human endogenous retroviral elements and increasing T cell infiltration. **Methods:** Cell cycLe inhibitiON to target the EVolution of urOthelial cancer (CLONEVO) is a single arm, window-of-opportunity trial of neoadjuvant abemaciclib which will evaluate tumor cell and TME changes in response to abemaciclib. Enrolled pts must be ineligible for platinum-based neoadjuvant therapy for resectable MIBC. Pts receive abemaciclib (200 mg BID PO) for 4 weeks prior to RC. Tumor tissue collected via transurethral resection of bladder tumor (TURBT) and residual tumor at RC undergo single cell RNA sequencing and whole-exome sequencing. Patient-derived organoids and xenografts are generated for a co-clinical trial of abemaciclib alone or in combination. The primary endpoint is the measurement of changes in cell cycle dynamics. Secondary objectives are assessment of toxicity via NCI CTCAE v 5.0 and pathologic downstaging of MIBC. We will perform targeted sequencing of a panel of cell cycle genes in serial plasma and urine cell free DNA to evaluate changes in the variant allele fractions of somatic alterations. The novel design of this trial allows dynamic *in vivo* assessment of tumor changes and creates a new paradigm for studying tumor evolution in real time. Clinical trials information: NCT03837821. Clinical trial information: NCT03837821. Research Sponsor: Lilly.

TPS5097 **Poster Session (Board #166), Fri, 8:00 AM-11:00 AM**

Phase II trial of durvalumab plus tremelimumab with concurrent radiotherapy as bladder-sparing therapy in patients with localized muscle invasive bladder cancer: A SOGUG study. *First Author: M. Andres Cuellar, Catalan Institute of Oncology, Barcelona, Spain*

Background: Several studies have shown that long-term bladder preservation is feasible in selected patients with muscle-invasive bladder cancer, using a multimodal treatment, including transurethral resection (TUR), radiotherapy and chemotherapy. Durvalumab, a fully human monoclonal antibody against PD-L1, has shown activity in patients with advanced pretreated urothelial cancer. A preclinical study showed that the combination of radiation, anti-CTLA4 and anti-PD-L1 overcome- adaptive immune resistance and has superior activity than either therapy alone (Twyman-Saint Victor et al. Nature 2015). The purpose of the present study is to explore feasibility, toxicity and activity in terms of response and bladder preservation of the integration of TUR, immune double checkpoint inhibition with durvalumab and tremelimumab (a fully human monoclonal antibody against CTLA-4), and radiotherapy in the treatment of localized muscle-invasive. **Methods:** This is a multicenter prospective phase II study of multimodal therapy in patients with localized urothelial carcinoma of the bladder in clinical stages T2-4a N0 M0, ECOG 0- 1, without contraindications to immunotherapy, who either wish for bladder preservation or are ineligible for cystectomy. The primary endpoint is pathological response (≤T1) at post-treatment biopsy. A 2-stage sequential design (response rate P0=5, P1=0.7, α=0.10, β=0.20) requires at least 6 responses in the first 12 pts to expand to a second cohort of 20 patients. The treatment consists of initial TUR of the tumor, followed by durvalumab 1500 mg i.v. plus tremelimumab 75 mg i.v., every 4 weeks for 3 doses. Normofractionated external-beam radiotherapy is started 2 weeks later, at doses of 46 Gy to the minor pelvis and 64-66 Gy to the bladder. Patients with pathological response will be candidates to bladder preservation, whereas those with residual muscle invasive tumor will be candidates to salvage cystectomy. At present time, prespecified activity goal for the first stage of accrual was met; second stage accrual began in December 2019. Clinical trial information: NCT03702179. Research Sponsor: None.

TPS5098 Poster Session (Board #167), Fri, 8:00 AM-11:00 AM

Hcrn GU15-215: A phase II trial of atezolizumab (atezo) and bevacizumab (bev) in cisplatin-ineligible patients (pts) with advanced/unresectable urothelial cancer (UC). *First Author: Arjun Vasant Balar, Perlmutter Cancer Center at NYU Langone Health, New York, NY*

Background: Atezolizumab is a standard of care in selected cisplatin-ineligible pts with advanced UC. VEGF targeted therapies have activity in advanced UC and may lead to immune synergy when combined with anti-PD-1/L1 therapy. This phase II study is investigating the combination of bevacizumab and atezolizumab in untreated cisplatin-ineligible pts with advanced UC. **Methods:** HCRN GU15-215 (NCT03272217) is a phase 2, multicenter single arm trial to evaluate the efficacy and safety of atezolizumab and bevacizumab in pts with advanced UC. Cisplatin-ineligible pts (defined as any of estimated CrCl $<$ 60 cc/min, Grade $\geq$ 2 hearing loss or neuropathy, ECOG PS 2 or solitary kidney) with untreated, histologically confirmed locally advanced or metastatic UC irrespective of PD-L1 expression status and with sufficient pre-treatment tumor tissue available for biomarker analysis are eligible. Pts who have received perioperative chemotherapy are eligible, however prior treatment with a checkpoint inhibitor is excluded. Pts with NYHA Class II or greater heart failure, significant cerebrovascular or cardiac disease within 3 months, uncontrolled HTN, persistent gross hematuria, and GI obstruction or perforation within 6 months are excluded. 70 pts will receive treatment with atezolizumab 1200 mg IV plus bevacizumab 15 mg/kg IV every 21 days. All pts will undergo an on-treatment biopsy before cycle 2 if safe and feasible. Peripheral blood samples and stool samples will be collected before treatment and on-treatment for immune-relevant biomarker analyses. Cross-sectional imaging will be performed every 9 weeks on therapy for the first 12 months and then every 12 weeks thereafter to assess for response. Subjects will be eligible to continue treatment until RECIST v1.1 defined progression or unacceptable toxicity for up to 24 months. The primary endpoint is overall survival rate at 1 year and will be analyzed by the Kaplan Meier method. Key secondary endpoints include objective response rate, duration of response, disease control rate, progression-free survival and safety and toxicity as defined by CTCAE version 4.0. Clinical trial information: NCT03272217. Research Sponsor: Genentech.

TPS5099 Poster Session (Board #168), Fri, 8:00 AM-11:00 AM

A phase III, randomized, placebo-controlled trial of nivolumab or nivolumab plus ipilimumab in patients with localized renal cell carcinoma at high-risk of relapse after radical or partial nephrectomy (CheckMate 914). *First Author: Axel Bex, The Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: Surgery is standard treatment for nonmetastatic renal cell carcinoma (RCC). Unfortunately, patients (pts) with stage II or III RCC have high risk of relapse with 5-year disease-free survival rates of ~51%–56%; prevention of recurrence is an unmet need. In CheckMate 214, first-line nivolumab plus ipilimumab (NIVO+IPI) demonstrated significant overall survival improvements in pts with advanced/metastatic RCC, with a manageable safety profile. Moreover, while not yet confirmed in randomized controlled trials, evidence suggests that anti-PD-(L)1 monotherapy may provide sufficient clinical activity in some pts with advanced RCC. These findings indicate a potential for improved clinical outcomes in the early-stage adjuvant RCC setting. As such, the phase 3, double-blind CheckMate 914 study will evaluate NIVO and NIVO+IPI vs placebo in pts with high risk of relapse after nephrectomy (NCT03138512). **Methods:** Key inclusion criteria: radical or partial nephrectomy with negative surgical margins $>$ 4 weeks and $\leq$12 weeks before randomization; predominantly clear cell histology; pathologic TNM staging T2a (grade [G] 3 or 4), T2b (any G), T3 (any G), or T4 (any G) N0M0, or any T (any G) N1M0; Eastern Cooperative Oncology Group performance status $\leq$1; no clinical/radiological evidence of macroscopic residual disease or distant metastases post-nephrectomy; and tumor tissue obtained $\leq$3 months pre-enrollment. Key exclusion criteria: conditions requiring corticosteroid or immunosuppressive systemic treatment, autoimmune disease, prior treatment with drugs specifically targeting T-cell co-stimulation or checkpoint pathways, and prior systemic treatment for RCC. In part A, pts are randomized 1:1 to receive NIVO+IPI or placebo infusions; in part B, pts are randomized 1:1:2 to receive NIVO+IPI, placebo infusions, or NIVO with IPI placebo. All treatments are given for 24 weeks or until disease recurrence, unacceptable toxicity, or withdrawal of consent. Stratification factors: TNM staging and type of nephrectomy procedure. Primary endpoint: disease-free survival per blinded independent central review (part A: NIVO+IPI vs placebo; part B: NIVO vs placebo). Secondary endpoints: overall survival (part A: NIVO+IPI vs placebo; part B: NIVO vs placebo and NIVO+IPI vs NIVO), disease-free survival (part B: NIVO+IPI vs NIVO), and safety. Enrollment in the study is ongoing. Total target enrollment across parts A and B is 1600 pts. Clinical trial information: NCT03138512. Research Sponsor: Bristol-Myers Squibb.

TPS5100 Poster Session (Board #169), Fri, 8:00 AM-11:00 AM

PDIGREE: An adaptive phase III trial of PD-inhibitor nivolumab and ipilimumab (IPI-NIVO) with VEGF TKI cabozantinib (CABO) in metastatic untreated renal cell cancer (Alliance A031704). *First Author: Tian Zhang, Duke Cancer Institute, Durham, NC*

Background: First-line treatment of mRCC has rapidly changed to include IPI-NIVO or CABO, with clinical benefit of each based on the Checkmate 214 and CABOSUN (A031203) trials. Combination immunotherapy with VEGF therapies has shown benefit over sunitinib in the JAVELIN 101 and KEYNOTE 426 trials. It is yet unclear which patients (pts) benefit most from combination immunotherapy-VEGF inhibitors, and the optimal sequence of drugs. **Methods:** In an adaptive, randomized, multicenter phase 3 trial (Alliance A031704, PDIGREE), pts start treatment with induction IPI 1 mg/kg and NIVO 3 mg/kg intravenously (IV) once every 3 weeks. Key inclusion criteria include clear cell mRCC, International Metastatic RCC Database Consortium (IMDC) intermediate or poor risk, Karnofsky performance status $>$ 70, and no prior treatments for mRCC. Based on 3-month radiographic assessment (after completing IPI-NIVO combination), pts with complete responses (CR) undergo maintenance NIVO 480 mg IV every 4 weeks; pts with progression of disease (PD) switch to CABO 60 mg oral daily; pts with non-CR/non-PD are randomized to NIVO 480 mg IV every 4 weeks versus NIVO 480 mg IV every 4 weeks with CABO 40 mg oral daily. Randomization is stratified by IMDC risk criteria and presence of bone metastases. The primary endpoint of the study is overall survival (OS). We hypothesize that 3-year OS will improve to 70% for NIVO-CABO compared to 60% for NIVO alone; to achieve 85% power with a two-sided alpha of 0.05 and exponential distribution, 696 patients will be randomized. Accounting for 30% patients with either CR or PD, and 5% dropout from toxicity, up to 1046 pts will be enrolled. Key secondary endpoints include progression-free survival, 12-month CR rate, overall response rate based on RECIST 1.1 and irRECIST criteria, and toxicity profiles. Quality of life will be assessed based on the FKSI-19, PROMIS-fatigue, and EQ5D-5L questionnaires. Biomarkers associated with CR, tissue-based and plasma-based biomarkers will be assessed. Updated enrollment through May 2020 will be presented. Clinical trial information: NCT03793166. Research Sponsor: U.S. National Institutes of Health.

TPS5101 Poster Session (Board #170), Fri, 8:00 AM-11:00 AM

PROSPER: Phase III randomized study comparing perioperative nivolumab versus observation in patients with renal cell carcinoma (RCC) undergoing nephrectomy (ECOG-ACRIN EA8143). *First Author: Naomi B. Haas, Abramson Cancer Ctr, Philadelphia, PA*

Background: There is no standard adjuvant systemic therapy that increases overall survival (OS) over surgery alone for non-metastatic RCC. Anti-PD-1 nivolumab (nivo) improves OS in metastatic RCC and is well tolerated. In mouse models, priming the immune system prior to surgery with anti-PD-1 results in superior OS compared to adjuvant dosing. Remarkable pathologic responses have been seen with neoadjuvant PD-1 in multiple ph 2 studies in bladder, lung and breast cancers. Phase 2 neoadjuvant RCC trials of nivo show preliminary feasibility and safety with no surgical delays. PROSPER RCC seeks to improve clinical outcomes by priming the immune system with neoadjuvant nivo prior to nephrectomy followed by continued immune system engagement with adjuvant blockade in patients (pts) with high risk RCC compared to standard of care surgery alone. **Methods:** This global, unblinded, phase 3 National Clinical Trials Network study is accruing pts with clinical stage $\geq$T2 or $T_{any}N+$ RCC of any histology planned for radical or partial nephrectomy. Select oligometastatic disease is permitted if the pt can be rendered 'no evidence of disease' within 12 weeks of nephrectomy ($\leq$3 metastases; no brain, bone or liver). In the investigational arm, nivo is administered 480mg IV q4 weeks with 1 dose prior to surgery followed by 9 adjuvant doses. The control arm is nephrectomy followed by standard of care surveillance. There is no placebo. Baseline tumor biopsy is required only in the nivo arm but encouraged in both. Randomized pts are stratified by clinical T stage, node positivity, and M stage. 805 pts provide 84.2% power to detect a 14.4% absolute benefit in recurrence-free survival at 5 years assuming the ASSURE historical control of ~56% to 70% (HR = 0.70). The study is powered to evaluate a significant increase in OS (HR 0.67). Critical perioperative therapy considerations such as safety, feasibility, and quality of life metrics are integrated. PROSPER RCC embeds a wealth of translational studies to examine the contribution of the baseline immune milieu and neoadjuvant priming with anti-PD-1 on clinical outcomes. As of February 2020, 396 patients have been enrolled. Clinical trial information: NCT03055013. Research Sponsor: U.S. National Institutes of Health.

TPS5102 Poster Session (Board #171), Fri, 8:00 AM-11:00 AM

A phase III study (COSMIC-313) of cabozantinib in combination with nivolumab and ipilimumab in patients with previously untreated advanced renal cell carcinoma of intermediate or poor-risk. *First Author: Toni K. Choueiri, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA*

Background: Cabozantinib (C) inhibits tyrosine kinases involved in tumor growth, angiogenesis, and immune regulation, including MET, VEGFR, and TAM kinases (Tyro3, AXL, MER), and may promote an immune-permissive tumor environment, resulting in enhanced response to immune checkpoint inhibitors. C has shown preliminary clinical activity and tolerability in combination with the PD-1 inhibitor nivolumab (N) and as part of a triplet combination with N and the CTLA-4 inhibitor ipilimumab (I) in patients (pts) with advanced renal cell carcinoma (aRCC) (Nadal et al. ASCO 2018). C is approved for pts with aRCC, and N+I is approved as a combination therapy in pts with previously untreated aRCC of intermediate or poor risk. We present the study design of a phase 3 trial of C+N+I vs N+I in previously untreated pts with aRCC of IMDC intermediate or poor risk (NCT03937219). **Methods:** This randomized, double-blind, controlled phase 3 study evaluates the efficacy and safety of C+N+I vs N+I in previously untreated pts with IMDC intermediate or poor risk aRCC. Eligible pts are randomized 1:1 to receive C+N+I or N+I in combination with placebo, stratified by IMDC prognostic score and geographic region. Pts receive C (40 mg oral QD) + N (3 mg/kg IV Q3W) x 4 doses + I (1 mg/kg IV Q3W) x 4 doses, followed by C (40 mg oral QD) + N (480 mg IV flat dose Q4W). Control pts receive C-matched placebo and the same treatment regimen for N+I as the experimental arm. N will be administered for a maximum of 2 years. Eligibility criteria include histologically confirmed metastatic or aRCC with a clear cell component, intermediate or poor risk RCC per IMDC criteria, measurable disease per RECIST 1.1, KPS $\geq$70%, adequate organ and marrow function and age $\geq$18 years. Exclusion criteria include prior systemic therapy for aRCC and uncontrolled significant illnesses. The primary endpoint is PFS per RECIST 1.1 by BICR; the secondary endpoint is OS. Additional endpoints include ORR, safety, correlation of biomarkers with outcomes, and pharmacokinetics of C in combination with N+I. The first patient was enrolled in June 2019 and enrollment is ongoing. Clinical trial information: NCT03937219. Research Sponsor: Exelixis Inc.

TPS5103 Poster Session (Board #172), Fri, 8:00 AM-11:00 AM

A randomized phase II study of nivolumab plus ipilimumab versus standard of care in previously untreated and advanced non-clear cell renal cell carcinoma (SUNIFORECAST). *First Author: Marit Ahrens, Medical Clinic II, University Hospital, Frankfurt Am Main, Germany*

Background: Non-clear cell renal cell carcinomas (nccRCC) are a heterogeneous group of tumors accounting for approximately 25% of RCC patients (pts.). Since most clinical trials focus on clear-cell RCC (ccRCC) only, data on treatment strategies for nccRCC are limited. The combination of Nivolumab and Ipilimumab (IO/IO) has recently been approved for treatment in RCC showing a significant improvement in overall response rate (ORR), progression free (PFS), and overall survival (OS) in intermediate and high-risk pts. compared to sunitinib in a phase-III trial. Furthermore retrospective analysis in nccRCC patients have shown promising results for IO/IO as well in these entities. **Methods:** In this prospective randomized phase-II multicenter European trial adults with advanced or metastatic nccRCC without prior systemic therapy are eligible. Other key inclusion criteria include: available tumor tissue, Karnofsky $>$ 70% and measurable disease per RECIST 1.1. All histological diagnoses are reviewed by a central pathologist. The study plans to randomize ~306 pts. stratified for papillary or non-papillary non-clear cell histology and by the International Metastatic RCC Database Consortium (IMDC) risk score. Pts. will be randomized 1:1 to either i) Nivolumab 3mg/kg intravenously (IV) plus Ipilimumab 1mg/kg IV every 3 weeks for 4 doses followed by Nivolumab fixed dose 240mg IV every 2 weeks or ii) standard of care therapy according to the approved schedule. Treatment will be discontinued in case of unacceptable toxicity or withdrawal of informed consent. Pts may continue treatment beyond progression, if clinical benefit is achieved and treatment is well tolerated. Primary endpoint is the OS rate at 12 months. Secondary endpoints include OS rate at 6 and 18 months, median OS, PFS, ORR and quality of life. The trial is in progress and 122 patients (78 pts with papillary, 37 pts with non-papillary histology) have been enrolled until now. Clinical trial information: NCT03075423. Research Sponsor: Goethe University, Frankfurt, Germany, Pharmaceutical/Biotech Company.

5500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

TheraP: A randomised phase II trial of ^{177}Lu-PSMA-617 (LuPSMA) theranostic versus cabazitaxel in metastatic castration resistant prostate cancer (mCRPC) progressing after docetaxel: Initial results (ANZUP protocol 1603). *First Author: Michael S Hofman, Peter MacCallum Cancer Centre, Melbourne, Australia*

Background: LuPSMA is a radiolabeled small molecule that delivers therapeutic β-radiation to PSMA-expressing tumors. Encouraging efficacy and safety has been shown in non-randomized studies of mCRPC. TheraP is a randomized phase II trial comparing LuPSMA vs cabazitaxel in men with mCRPC progressing after docetaxel. **Methods:** Men with mCRPC, and imaging with ^{68}Ga-PSMA-11 and ^{18}F-FDG PET/CT that confirmed high PSMA-expression and no sites of FDG-positive/PSMA-negative disease, were randomly assigned (1:1) to LuPSMA (6-8GBq q6weeks up to 6 cycles) vs cabazitaxel (20mg/m^2 q3weeks up to 10 cycles); stratified by disease burden (>20 vs ≤20 sites), prior novel antiandrogens (NAA; abiraterone or enzalutamide), and study site. The primary endpoint was PSA response rate (PSA50-RR) defined by ≥50% reduction. Secondary efficacy endpoints included PSA-progression-free survival (PSA-PFS) and overall survival (OS). Data cut-off was 31DEC19 at this first pre-specified analysis. **Results:** 200 (median age 72 y, prior NAA 91%, >20 lesions 78%) of 291 PET screened men were randomised to LuPSMA (N=99) or cabazitaxel (N=101). 17 patients withdrew or died before receiving study treatment (1 LuPSMA vs 16 cabazitaxel). The PSA50-RR was higher in those assigned LuPSMA than cabazitaxel (65/99 [66%; 95%CI 56-75] vs 37/101 [37%; 95%CI 27-46]; P<0.001). At a median follow-up of 11.3 months, LuPSMA significantly improved PSA-PFS (HR 0.63, 95%CI 0.45-0.88, P=0.007; 143 events with next pre-specified analysis planned after 170 events). Efficacy results were similar when analyses were restricted to per-protocol treated men. OS data remains immature (57 deaths). Grade III-IV adverse events (AEs) occurred in 31/98 (32%) LuPSMA-treated men vs 42/85 (49%) in cabazitaxel-treated men. Discontinuations for toxicity occurred in 1/98 (1%) LuPSMA vs 3/85 (4%) cabazitaxel-treated. There were no treatment-related deaths. **Conclusions:** In men with docetaxel-treated mCRPC, LuPSMA was more active (PSA50-RR) than cabazitaxel with relatively fewer G3-4 AEs and PSA-PFS favoring LuPSMA. Clinical trial information: NCT03392428. Research Sponsor: None.

5501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Impact of PSMA-targeted imaging with 18F-DCFPyL-PET/CT on clinical management of patients (pts) with biochemically recurrent (BCR) prostate cancer (PCa): Results from a phase III, prospective, multicenter study (CONDOR). *First Author: Michael J. Morris, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Current imaging modalities are inadequate for localizing and characterizing occult disease in men with BCR PCa, particularly in pts with low PSAs (<2 ng/mL). There is a need for improved diagnostic imaging to better inform treatment planning. ^{18}F-DCFPyL (PyL) is a novel PET imaging agent that binds selectively with high affinity to PSMA, which is overexpressed in PCa cells. **Methods:** Men ≥18 years- with rising PSA after definitive therapy and negative or equivocal standard of care imaging (e.g., CT/MRI, bone scintigraphy) were enrolled. A single 9 mCi (333 MBq) ± 20% dose of PyL was injected, followed by PET/CT 1-2 hours later. Primary endpoint was correct localization rate (CLR), defined as percentage of pts with a 1:1 correspondence between at least one lesion identified by PyL-PET/CT and the composite standard of truth: pathology, correlative imaging, or PSA response. The trial was successful if the lower bound of the 95% confidence interval (LLCI) for CLR exceeded 20% for two of three independent, blinded central PyL-PET/CT reviewers. The secondary endpoint, impact of PyL-PET/CT on clinical management of pts was based on the treating physician's documented clinical plans before and after PyL-PET/CT. **Results:** 208 men (median PSA 0.8 [0.2 - 98.4] ng/mL) underwent PyL PET/CT. The study achieved its primary endpoint: CLR of 84.8% to 87.0% among the three PyL-PET/CT readers; the LLCI for CLR by all three reviewers was >77%. Here we report the clinical impact. Based on local radiology assessment, PSMA-avid lesion(s) were identified in 69.3% (142/208) of pts. 63.9% (131/205) had a change in intended management after PyL-PET/CT, of which 78.6% (103/131) were attributable to positive PyL finding(s) and 21.4% (28/131) to negative PyL scans. Changes included: salvage local therapy to systemic therapy (n=58); observation before initiating therapy (n=49); noncurative systemic therapy to salvage local therapy (n=43); and planned treatment to observation (n=9). PyL was well tolerated with one drug-related SAE (hypersensitivity) and the most common AE being headache (n=4; 1.9%). **Conclusions:** PSMA-targeted PyL-PET/CT detected and localized occult disease in most men with BCR presenting with negative or equivocal conventional imaging. PyL-PET/CT led to changed management plans in the majority of pts, thus providing evidence that clinicians find PSMA PET imaging useful in men with recurrent or suspected metastatic PCa. Clinical trial information: NCT03739684. Research Sponsor: Progenics Pharmaceuticals, Inc.

5502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Accuracy of 68Ga-PSMA-11 for pelvic nodal metastasis detection prior to radical prostatectomy and pelvic lymph node dissection: A multicenter prospective phase III imaging study. *First Author: Thomas A Hope, University of California, San Francisco, San Francisco, CA*

Background: To determine the accuracy of 68Ga-PSMA-11 PET for the detection of pelvic nodal metastases (N1) compared to histopathology at time of radical prostatectomy (RP). **Methods:** This is a prospective multicenter single-arm open-label phase 3 imaging trial. Patients with intermediate to high risk prostate cancer (PCa) considered for RP with lymph node dissection (PLND) were enrolled at the University of California, Los Angeles (UCLA) and at the San Francisco (UCSF) (NCT03368547, NCT02611882, NCT02919111), and underwent one 68Ga-PSMA-11 PET. The primary endpoint was the sensitivity (Se) and specificity (Sp) of 68Ga-PSMA-11 PET for the N1 detection compared to PLND histopathology (reference-standard) on a per patient basis using nodal region-based correlation. Each scan was read by three blinded independent central readers (BICR). Consensus was based on majority rule. **Results:** From December 2015 to August 2019, 633 patients underwent one 68Ga-PSMA-11 PET for primary staging, and 277/633 (44%) subsequently underwent RP and PLND. The median initial PSA was 11.1 [0.04-147]. 75/277 patients (27%) had N1 disease per histopathology. Using a regional based analysis, Se, Sp, positive predictive value (PPV) and negative predictive value (NPV) for N1 detection was 0.40 [0.34, 0.46], 0.95 [0.92, 0.97], 0.75 [0.70, 0.80], 0.81 [0.76, 0.85], respectively. Se was higher for patients with higher PSA: 0.29 [0.24, 0.35] for PSA < 11 ng/ml versus 0.48 [0.42, 0.54] for PSA > 11. Se was higher when the nodes were larger: 0.30 [0.25, 0.36] for nodes < 10 mm versus 0.68 [0.63, 0.74] for nodes > 10. The average node size in true positive patients was 10 mm versus 4 mm in false negative patients. **Conclusions:** In intermediate to high risk PCa patients who underwent RP and PLND, 68Ga-PSMA-11 PET detected pelvic nodal metastases with a sensitivity of 0.40 and a specificity of 0.95. Higher PSAs and larger node size correlated with increased sensitivity. Clinical trial information: NCT03368547, NCT02611882, NCT02919111. Research Sponsor: Prostate Cancer Foundation.

5503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Results of a phase II trial of intense androgen deprivation therapy prior to radical prostatectomy (RP) in men with high-risk localized prostate cancer (PC). *First Author: Rana R. McKay, Dana-Farber Cancer Institute, Boston, MA*

Background: Patients with high-risk localized PC have an increased risk of recurrence and death despite treatment. Abiraterone acetate (AA), a potent CYP17 inhibitor, and apalutamide, a next generation anti-androgen, have each demonstrated improved overall survival in metastatic PC. In this multicenter randomized phase II trial we investigate the impact of intense androgen deprivation on RP pathologic response (NCT02903368). **Methods:** Eligible patients had a Gleason score ≥4+3=7, PSA >20 ng/mL or T3 disease (by prostate MRI) and lymph node <20 mm. During Part 1 of the study, patients were randomized 1:1 to AA + prednisone + apalutamide + leuprolide (APAL) or AA + prednisone + leuprolide (APL) for 6 cycles (1 cycle=28 days) followed by RP. All RPs underwent central pathology review. The primary endpoint was the rate of a pathologic complete response (pCR) or minimum residual disease (MRD, tumor ≤5 mm). Secondary endpoints include PSA response, surgical staging at RP, positive margin rate, and safety. **Results:** 118 patients were enrolled at four sites. Median age was 61 (range 46-72) years. The majority of patients had NCCN high-risk disease [n=111, 94%; T3 n=73 (62%), Gleason 8-10 n=84 (71%), PSA >20 ng/mL n=28 (24%)]. 114 (97%) patients completed 6 therapy cycles followed by RP. Median PSA nadir was <0.01 versus 0.02 ng/mL and time to nadir was 4.2 versus 4.6 months in the APAL and APL arms, respectively. RP outcomes are displayed in Table. The combined pCR or MRD rate was 21.8% in the APAL arm and 20.3% in the APL arm (p=0.85). 13 (11%) patients (8 in APAL; 5 in APL) experienced grade 3 treatment-related adverse events (TrAEs). The most common grade 3 TrAEs were hypertension (5%), elevated ALT (3%) and elevated AST (3%). No grade 4 or 5 TrAE was reported. **Conclusions:** Intense neoadjuvant hormone therapy followed by RP in men with high-risk PC resulted in favorable pathologic responses (<5 mm residual tumor) in 21% of patients. Pathologic responses were similar between the treatment arms. Follow-up is necessary to evaluate the significance of a pathologic response on recurrence rates. Part 2 of this trial will investigate the impact of an additional 12 months of APAL post-RP on biochemical recurrence. A phase 3 trial investigating neoadjuvant apalutamide + leuprolide prior to RP is ongoing. Clinical trial information: NCT02903368. Research Sponsor: Janssen.

Pathologic outcomes at RP.

	APAL (N=55)	APL (N=59)
ypT2	21 (38%)	19 (32%)
ypT3	27 (49%)	34 (58%)
Positive Margins	4 (7%)	7 (12%)
Positive Seminal Vesicles	15 (27%)	16 (27%)
Positive Lymph Nodes	4 (7%)	10 (17%)
pCR	7 (13%)	6 (10%)
MRD	5 (9%)	6 (10%)

5504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Neoadjuvant apalutamide (APA) plus leuprolide (LHRHa) with or without abiraterone (AA) in localized high-risk prostate cancer (LHRPC). *First Author: Eleni Efstathiou, Department of Genitourinary Medical Oncology, Division of Cancer Medicine, Houston, TX*

Background: Novel androgen signaling inhibitors (ASI) with medical castration may improve outcomes in LHRPC. We previously reported relapse free survival association with pathologic measures of tumor regression. However a wide range of persistent cancers was recorded. To build on our findings and test candidate predictors of outcome, we conducted a study examining APA effect in LHRPC. **Methods:** This is a phase II neoadjuvant study of 6 months APA+LHRHa +/- AA (randomized 1:1) in LHRPC ($\geq$ cT2 + Gleason Score $\geq$ 8 or $\geq$ cT2b + Gleason $\geq$ 7 + PSA $>$ 10 ng/mL) followed by radical prostatectomy (RP). We studied treatment effect by pathology measures [path. stage, tumor volume (TV), tumor cellularity % (TC), tumor epithelial volume (TEV: TC x TV)]. Tumor expression of candidate markers of outcome was assessed in the diagnostic biopsy by IHC [AR signaling (AR-N, ARC19, ARV7, PSA), PTEN, glucocorticoid receptor (GR), Ki67, p53, RB] and DNA/RNA seq. A previously identified candidate predictive molecular signature (AR-N overexpression, nARV7 absence, no GR overexpression, Ki67 $\leq$10%) was tested. Univariate (Fisher's exact, Wilcoxon) and multivariate (logistic, linear models) analyses employed. **Results:** Sixty three -of 65 pts enrolled- had RP. PS-ECOG 0, median age 65 (43-77). Treatment was well tolerated with Grade 3 hypertension in 7 (2 APA + LHRHa). Presurgical PSA was $\leq$0.1 in 62/63 (98%). Organ confined disease ($\leq$ypT2N0) found in 13/32(41%) APA+LHRHa vs. 12/31 (39%) APA+AA+LHRHa treated. 2 (3%) had pathologic complete remission (APA+AA+LHRHa), 6 (10%) minimal residual disease (5 on APA +LHRHa). Despite uniformity in PSA response, we recorded heterogeneity in measures of tumor viability: TV (0-11.5cc), TC (1-80%), TEV (0-6.1cc). $\leq$ypT2N0 associates with diagnostic biopsy positivity for the prespecified molecular signature (p $<$0.0001), PTEN expression (p: 0.004), absence of cribriform/ intraductal spread (p 0.002) but not with Gleason Score. On multivariate analysis only the prespecified biopsy signature associates with outcome (p 0.003). Findings were replicated when analyzed by TV, TC and TEV measures. **Conclusions:** Neoadjuvant Apalutamide plus LHRHa is tolerable and results in tumor regression in a subset of LHRPC patients. Dual ASI treatment does not further improve outcomes. Biopsy positive for a prespecified molecular signature, associated with response. Study results emphasize the need to consider biologic heterogeneity and pursue validation of predictors of response in order to improve therapeutic outcomes in LHRPC. Clinical trial information: NCT03279250. Research Sponsor: Prostate Cancer Foundation, Pharmaceutical/Biotech Company, U.S. National Institutes of Health.

5505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase II randomized study of abiraterone acetate plus prednisone (AAP) added to ADT versus apalutamide alone (APA) versus AAP+APA in patients with advanced prostate cancer with noncastrate testosterone levels: (LACOG 0415). *First Author: Fernando C. Maluf, Beneficência Portuguesa de São Paulo, São Paulo, Brazil*

Background: ADT combined with AAP, APA, enzalutamide or docetaxel are among the standard treatment options to patients (pts) with hormone sensitive advanced/metastatic prostate cancer (PC). However, treatment-related adverse events (TRAEs) due to ADT impact negatively on the quality of life of these patients. Effective options with fewer TRAEs are required. **Methods:** LACOG 0415 is a phase II, randomized trial (1:1:1) evaluating the use of AA 1000mg po + prednisone 5mg po BID + ADT versus APA 240mg po alone versus AA 1000mg po + prednisone 5mg po BID + APA 240mg po in patients with advanced PC with noncastrate testosterone levels and indication of ADT (N+ or M+ or biochemical relapse combined with PSA $\geq$ 20 ng/ml or with PSA$\geq$4 ng/ml and PSA doubling-time $<$ 10 months). Stratification factors: metastatic disease (+/-). Primary endpoint was the percentage of pts who achieved PSA $\leq$ 0.2 ng/mL at Week 25, we estimated a PSA response rate of 65% in each of the three arms with a null hypothesis of 45%, power of 80% and alfa 5%, using Fleming one-stage method. Secondary endpoints were percentage of pts with $\geq$ 80% and $\geq$ 50% decline in PSA at week 25, radiographic progression-free survival (rPFS) and safety. **Results:** 128 patients were randomized between Oct 2017 and Apr 2019, and 122 pts were evaluable for PSA response. Median age was 69y (range, 53-88); most pts had ECOG PS0-1(99%). 17% of pts had biochemical relapse only, 9% N+ and 74% M+ disease. At week 25 the PSA was $\leq$ 0.2 ng/mL in 76% of pts in AAP+ADT arm, 59% in APA, and 80% in APA+AAP. All pts had a decline of $\geq$ 50% in PSA at week 25. 97% had a decline of $\geq$ 80% in PSA at week 25: 100% of pts in AAP+ADT arm, 95% in APA and 98% in APA+AAP. A total of 3 pts had clinical progressive disease, one in each arm. Two of them also had radiological progression at week 25, 1 pt in AAP+ADT arm and 1 pt in APA. TRAEs rates of any grade were 71% in AAP+ADT arm, 64% in APA, and 65% in APA+AAP. TRAEs rates of Grade$\geq$3 were 12% in AAP+ADT arm, 9% in APA and 16% in APA+AAP. 9 pts (7%) discontinued the treatment before the week 25, 5(4%) of them due to toxicity: 1 pt from AAP+ADT, 2 pts from APA, and 6 pts from APA+AAP. **Conclusions:** The AAP+ADT and APA+AAP groups showed high effectiveness in terms of PSA response. Radiologic disease control and the decline of $\geq$ 80% in PSA at week 25 were similar among all treatment arms. APA alone had less toxicity. APA+AAP and APA alone are promising regimens in this setting. No new safety signal was detected in the study. Clinical trial information: NCT02867020. Research Sponsor: Janssen.

5506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Baseline circulating tumor cell (CTC) count as a prognostic marker of PSA response and progression in metastatic castrate sensitive prostate cancer (mCSPC): Results from SWOG S1216, a phase III randomized trial of androgen deprivation plus orteronel (cyp17 inhibitor) or bicalutamide. *First Author: Amir Goldkorn, Division of Medical Oncology, Department of Medicine, Keck School of Medicine and Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA*

Background: In mCSPC, androgen deprivation therapy (ADT) combined with chemotherapy or androgen receptor signaling inhibition (ARSI) is the new standard of care. Biomarkers that predict clinical outcomes with these therapies are needed. We hypothesized that CellSearch CTC count, an FDA-cleared biomarker in metastatic castrate resistant PC (mCRPC), may be a valuable biomarker in mCSPC. **Methods:** In S1216, peripheral blood was drawn with informed consent at registration (baseline), and CTCs were enumerated on the FDA-cleared CellSearch platform (Menarini) per standard manufacturer protocol. CTC counts were analyzed centrally for associations with 2 pre-specified trial intermediate endpoints: 7-month PSA (7mPSA) $\leq$ 0.2 ng/ml vs. 0.2–4.0 vs. $>$ 4.0, (intermediate endpoint for overall survival, OS); and progression-free survival (PFS) $<$ vs. $>$ 2 years. Because OS data have not matured, analysis was pooled and equal numbers of samples were analyzed from each treatment arm and outcome measure (7mPSA and PFS) as stipulated by the Data Safety Monitoring Committee. **Results:** From 2014 to 2017, 523 baseline samples were collected. In the 7mPSA analysis (n = 264), CTCs were detected in 38% of men, with a median of 4 CTCs in those with detectable CTCs. In the PFS analysis (n = 336), CTCs were detected in 37% of men, with a median of 3 CTCs in those with detectable CTCs. Adjusting for disease burden (minimal vs. extensive) and ADT status (already initiated or not) at the time of CTC measurement, men with undetectable CTCs were 6.1-fold more likely to attain 7mPSA $\leq$ 0.2 (OR 6.1, 95% CI 2.1-17.2, p $<$ 0.001) and 3.7-fold more likely to achieve $>$ 2 years PFS (OR 3.7, 95% CI 1.7-8.1, p $<$ 0.001) compared to men with baseline CTCs $\geq$ 5. Other cutpoints previously validated in mCRPC studies (CTC $<$ 5 vs. $\geq$5 and CTCs 0 vs. $\geq$1) also strongly discriminated 7mPSA and PFS with statistical significance in this mCSPC cohort. **Conclusions:** CTC count at the start of treatment for mCSPC was highly prognostic of 7-month PSA response (intermediate endpoint for OS) and of PFS at 2 years. To our knowledge, this is the first such strong evidence from a prospective phase 3 trial of this magnitude. Additional analyses are planned when the trial is fully reported. Baseline CTC count may serve as a valuable prognostic marker to discriminate men likely to respond favorably to hormonal therapies from those who may benefit from early alternate interventions. Research Sponsor: U.S. National Institutes of Health.

5507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

The comprehensive methylation landscape of metastatic castration-resistant prostate cancer (mCRPC) identifies new phenotypic subtypes: Results from the West Coast Prostate Cancer Dream Team (WCDT). *First Author: Eric Jay Small, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

Background: While recent studies have delineated the genomic landscape of mCRPC, its epigenomic landscape has not been as well characterized. The goal of this study was to define the comprehensive methylation landscape of mCRPC. **Methods:** mCRPC patients (pts) underwent a metastasis biopsy as part of a multi-institutional study (NCT02432001). Deep whole-genome bisulfite sequencing (mean depth 46x) was performed on fresh frozen tissue from 100 mCRPC patients; data was paired with deep whole-genome and transcriptome sequencing from the same samples. Unbiased hierarchical clustering of the mCRPC methylome was undertaken, and the survival of patients in each cluster was calculated using the Kaplan Meier method. **Results:** Unbiased hierarchical clustering revealed several distinct subtypes. 22% of mCRPC samples exhibited a novel epigenomic subtype associated with hypermethylation. This hypermethylated (HM) cluster was significantly associated with somatic mutations in genes known to be involved in methylation, eg *TET2* and *DNMT3B*, as well as in genes in which mutations have been associated with hyper-methylation in other cancer types (*IDH1* in glioblastoma and *BRAF* in colon cancer). mCRPC survival was 56.1 mos in pts with HM cancers compared to 35.6 mos in non-HM (p = .055). Methylome clustering also identified a unique cluster comprised of all patients with treatment-induced small cell/neuroendocrine cancer, a subtype previously associated with poor survival. **Conclusions:** This integrated study of whole-genome, whole methylome and whole-transcriptome sequencing provides the first comprehensive overview of the important regulatory role of methylation in metastatic castration-resistant prostate cancer, and has identified at least two distinct subtypes. The clinical and therapeutic implications of methylation subtypes should be explored in future studies. Clinical trial information: NCT02432001. Research Sponsor: Prostate Cancer Foundation; Stand Up to Cancer.

5508 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Circulating tumor DNA (ctDNA) dynamics associate with treatment response and radiological progression-free survival (rPFS): Analyses from a randomized phase II trial in metastatic castration-resistant prostate cancer (mCRPC). *First Author: Jane Goodall, The Institute of Cancer Research, London, United Kingdom*

Background: ctDNA can inform on prognosis, treatment response and survival. We evaluated ctDNA in serial plasma samples from patients enrolled in A.MARTIN (NCT01485861), a randomized phase II study of abiraterone with or without ipatasertib in patients with mCRPC. **Methods:** Blood was collected in cell-free DNA Streck tubes from 216 patients at 3 time points; baseline, C3D1 and end of treatment. Cell-free DNA (cfDNA) was extracted from plasma using a Circulating DNA Kit (Qiagen) on a QIASymphony machine (Qiagen). 25ng of extracted cfDNA was used in library preparation, constructed with a custom designed, 58 gene, QIAseq Targeted DNA panel (Qiagen) enriched for PI3K/AR pathway genes. Samples were sequenced to mean depth of 3394x on a NextSeq500 machine. Unless otherwise noted, all analyses combine patients across the 3 study arms, and reported p-values are unadjusted. **Results:** Baseline (BL) ctDNA positivity correlated with radiological progression-free survival (rPFS; HR: 1.8 [95% CI 1.3-2.6], $p < 0.01$); this association with rPFS was maintained in a multivariate cox model with > 5 baseline clinical variables (HR: 1.6 [95% CI 1.1-2.4]; $p = 0.011$). Patients with a C3D1 reduction in ctDNA had superior rPFS compared to patients with a C3D1 increase in ctDNA (HR: 2 [95% CI 1.3-3.2], $p < 0.01$). The rate of ctDNA clearance at C3D1 was higher in the Ipatasertib 400mg arm compared to placebo (56.3% versus 24.4%, $p < 0.01$). We find that changes in ctDNA associated with best confirmed overall response ($p = 0.024$); CR patients had the greatest reduction in ctDNA (mean of -23.4%), followed by PR (-16.3%), then SD (-4.1%), and lastly PD patients (-1.3%). Changes in ctDNA levels correlated with SLD changes ($rs = 0.289$, $p = 0.05$), and also PSA changes ($rs = 0.33$, $p < 0.01$). Changes in ctDNA were associated with rPFS in a multivariate cox analysis that included PSA change ($p < 0.01$), as well as in a separate multivariate analysis that included SLD change ($p < 0.01$). Lastly, we explored CNVs and observed emerging resistance mutations in progression samples, including alterations in *TP53*, *AR*, *FOXA*, *PTEN*, and *PI3K/AKT* pathway genes. **Conclusions:** ctDNA analyses may help (i) identify poorer prognosis disease at baseline, (ii) inform on treatment response (CR/PR/SD/PD) and radiological progression free survival (rPFS) in on-treatment (C3D1) samples, and (iii) can elucidate emerging resistance mechanisms at disease progression. Clinical trial information: NCT01485861. Research Sponsor: Roche.

5509 Poster Discussion Session; Displayed in Poster Session (Board #90), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Prostate cancer relative survival by stage and race/ethnicity, United States, 2001 to 2015. *First Author: David A Siegel, Centers for Disease Control and Prevention, Atlanta, GA*

Background: Prostate cancer is the most common cancer diagnosed and the second leading cause of cancer-related deaths among U.S. men. Incidence rates for distant stage cancer increased during 2010–2014, and survival at all stages was lower for black men than white men. We examined temporal changes in survival by race/ethnicity. **Methods:** Five-year relative survival (RS) (cancer survival in the absence of other causes of death) was calculated for men with prostate cancer aged ≥40 years using National Program of Cancer Registries data (93% U.S. population coverage). Cancers were diagnosed during 2001–2015 with follow-up through 2015. RS was estimated by race/ethnicity (non-Hispanic white, non-Hispanic black, and Hispanic), stage, and year (2001–2007 and 2008–2015). Differences were determined by non-overlapping 95% confidence intervals (CI). **Results:** During 2001–2015, 2,234,233 cases were recorded. Five-year RS was 100% for localized disease in all race/ethnicities and time periods. Overall, RS improved from 29.0% (95% CI, 28.5–29.5) to 31.3% (30.8–31.9) for distant stage and 83.4% (83.0–83.8) to 84.7% (84.2–85.1) for unknown stage. For regional stage, RS improved for white men (table). For distant stage, RS was highest for black and Hispanic men. For unknown stage, RS was highest for white and Hispanic men. **Conclusions:** RS improved for regional, distant, and unknown stage, but disparities by race/ethnicity persist. The disparity between black and white men for distant stage reversed compared to past studies. Further investigation of diagnosis patterns and clinical characteristics of men with distant and unknown stage cancer could inform interventions to address disparities in outcomes. Research Sponsor: None.

Stage	Race/ethnicity	No., 2001–2007	RS (95% CI), 2001–2007	No., 2008–2015	RS (95% CI), 2008–2015
Regional	White	100,214	97.9 (97.7–98.2)	132,175	99.4 (99.1–99.6)
	Black	15,966	98.4 (97.6–98.9)	23,094	99.1 (98.2–99.5)
	Hispanic	7,544	96.8 (95.9–97.5)	11,547	98.1 (97.2–98.7)
Distant	White	36,398	27.5 (27.0–28.1)	53,859	29.4 (28.8–30.1)
	Black	10,784	29.9 (28.9–30.9)	14,774	32.2 (31.1–33.4)
	Hispanic	3,835	35.4 (33.7–37.1)	6,310	38.7 (36.9–40.5)
Unknown	White	83,667	83.2 (82.7–83.6)	61,482	81.1 (80.5–81.7)
	Black	15,645	78.3 (77.2–79.3)	14,914	77.9 (76.7–79.0)
	Hispanic	7,758	81.8 (80.4–83.0)	9,762	86.0 (84.7–87.3)

5510 Poster Discussion Session; Displayed in Poster Session (Board #91), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Assessment and management of cardiovascular risk factors among U.S. Veterans with newly diagnosed prostate cancer. *First Author: Lova Sun, UPHS, Philadelphia, PA*

Background: Cardiovascular disease (CVD) is a leading cause of death in men with prostate cancer (PC). Androgen deprivation therapy (ADT) is associated with increased CVD risk, and American Heart Association guidelines recommend CVD risk factor assessment and management in PC patients starting ADT. We characterized rates of guideline-concordant assessment and management of CVD risk factors for US Veterans with newly diagnosed PC, according to ADT use and prior atherosclerotic CVD diagnosis. **Methods:** We used cross-sectional data from VA Corporate Data Warehouse to identify Veterans with an incident diagnosis of PC from 2001-2017. Primary outcomes were guideline-concordant baseline CVD risk factor assessment (defined as ≥1 blood pressure, cholesterol, and HbA1c or fasting glucose measurement within 1 year prior to 6 months after ADT start or PC diagnosis), CVD risk factor control, and CVD risk-reducing medication use. Risk difference multivariable regression analyses adjusting for age, race, poverty, PC risk category, and year were used to evaluate the effect of ADT on study outcomes. **Results:** Of 191,829 Veterans with newly diagnosed PC, 27% (n = 51,419) were treated with ADT within 1 year of diagnosis, and 18% (n = 34,110) had a pre-existing diagnosis of atherosclerotic CVD. From 2001-2017, annual rates of guideline-concordant CVD risk factor assessment increased from 26% to 77%. In adjusted analyses, pre-existing atherosclerotic CVD diagnosis was associated with higher CVD risk factor assessment rate (64% vs 53%), better control of baseline LDL (94 vs 108 mg/dL), and higher rates of anti-hypertensive (90% vs 66%), lipid-lowering (83% vs 49%), and glucose-lowering (32% vs 20%) medication use. Treatment with ADT was associated with similar to minimally higher rates of CVD risk factor assessment (58% vs 54%), LDL control (104 vs 105 mg/dL), and anti-hypertensive (73% vs 69%), lipid-lowering (55% vs 55%), and glucose-lowering (25% vs 21%) medication use. Sixty percent of men starting ADT had at least one sub-optimally controlled CVD risk factor, and 1 in 4 of these men were not receiving a corresponding risk-reducing medication. One third of men starting ADT had BMI > 30 kg/m2. **Conclusions:** CVD risk factor assessment in Veterans with PC has increased over time. However, ADT does not appear to meaningfully impact CVD assessment or management, despite its known association with CVD risk. Over half of patients initiating ADT had elevated CVD risk factor(s). Multidisciplinary efforts to improve CVD risk mitigation are needed among men initiating ADT. Research Sponsor: U.S. National Institutes of Health, VA Center for Health Equity Research and Promotion.

5511 Poster Discussion Session; Displayed in Poster Session (Board #92), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

PROREPAIR-A: Clinical and molecular characterization study of prostate cancer (PC) patients with and without previously known germline *BRCA1/2* mutations. *First Author: Rebeca Lozano, Spanish National Cancer Research Centre, Prostate Cancer Clinical Research Unit, Madrid, Spain*

Background: Germline *BRCA1/2* (g*BRCA1/2*) mutations are associated with poor clinical outcomes in PC. Previous studies showed that g*BRCA2* carriers present more CNV in several genes associated with more aggressive disease. These aberrations may explain the poor clinical outcomes of these patients, but larger studies are needed to confirm these findings. **Methods:** PROREPAIR-A is a multicenter case-control study in which g*BRCA2* carriers with available diagnostic timor-tissue were matched 1:2 by Gleason and stage at diagnosis (M0 vs M1) with known non-carriers (NC). A minimum of 120 controls-60 cases were required to prove a 5yr Cause Specific Survival (CSS)-rate of 85% vs 60%. The primary endpoint was to confirm the independent prognostic value of g*BRCA2* in PC CSS. In addition, we explored the prognostic role of g*BRCA1* and somatic events in *BRCA2*, *RB1*, *MYC*, *PTEN* and *TMPRSS2-ERG* by FISH. X^2, Kaplan-Meier, log-rank and cox-regression models were carried out to identify associations with baseline characteristics and outcomes: Metastases Free Survival (MFS), Time to Castration-Resistance (TTCR) and CSS. **Results:** A total of 80:160 matched cases-controls were initially included, but tumor tissue and clinical data were only available in 73 g*BRCA2* and 127 NC. 14 g*BRCA1* were also included. At diagnosis, g*BRCA2* were younger (median 62.6 vs 64.5, $p = 0.02$) and had cT3-4 disease more often than NC (31.5% vs 9.4%, $p < 0.01$), but no other significant differences were found. Somatic *BRCA2-RB1* codeletion (40.8% vs 11.8%, $p < 0.01$) and *MYC* amplification (51.4% vs 22.8%, $p < 0.01$) were more frequent in g*BRCA2* compared to NC, but no significant differences in *PTEN* and *TMPRSS2-ERG* were observed. g*BRCA2* mutations as well as somatic *BRCA2-RB1* codel and *MYC* amplif were significantly associated with shorter CSS, MFS and TTCR (Table). MVA model confirmed the independent prognostic value of g*BRCA2* (HR 1.94, $p = 0.03$), *BRCA2-RB1* codel (HR 3.16, $p < 0.01$), *MYC* amplif (HR 2.36, $p < 0.01$), Gleason ≥8 ($p < 0.01$) and M1 at diagnosis ($p < 0.01$) for CSS. **Conclusions:** PROREPAIR-A confirmed the independent prognostic value of g*BRCA2* for CSS. Somatic *BRCA2*, *RB1* and *MYC* aberrations were more frequent in g*BRCA2* carriers. Those alterations are associated with shorter CSS, MFS and TTCR, and may contribute to poor clinical outcomes in g*BRCA2* and NC. Research Sponsor: Prostate Cancer Foundation.

	CSS	MFS	TTCR
g*BRCA2* vs NC	110 vs 211 m $p < 0.01$	105 vs NR m $p < 0.01$	105 vs NR m $p < 0.01$
***BRCA2-RB1* codel vs No**	76 vs 203 m $p < 0.01$	112 vs NR m $p < 0.01$	60 vs NR m $p < 0.01$
***MYC* amplif vs No**	75 vs 211 m $p < 0.01$	114 vs NR m $p < 0.01$	45 vs NR $p < 0.01$

5512 Poster Discussion Session; Displayed in Poster Session (Board #93), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Late toxicities and recurrences in patients with clinical stage I nonseminomatous germ cell tumor after one cycle of adjuvant BEP versus primary retroperitoneal lymph node dissection: A 13-years follow-up analysis of a phase III trial cohort. *First Author: Andreas Hiester, Department of Urology, Heinrich-Heine-University, Düsseldorf, Germany*

Background: One cycle of adjuvant BEP has shown superiority in recurrence free survival over RPLND in patients (pts) with clinical stage (CS) I nonseminomatous germ cell tumor of the testis (NSGCT) (JCO 2008). We report recurrences and late toxicities of this randomized trial after 13 yrs of follow-up (FU). **Methods:** Questionnaires of 382 unselected pts with CS I NSGCT treated within a phase III trial comparing recurrence rate after 1 cycle of adjuvant BEP (arm A) vs. RPLND (arm B) were evaluated regarding recurrences and late toxicity. Overall (OS) and progression free survival (PFS) was calculated by Kaplan-Meier and arms were compared using logrank test. Categorial data were analyzed by chi-square test (PRISM v8). **Results:** In each arm 191 pts were analyzed as intention-to-treat with a median FU of 13.75 yrs (0-22.9 yrs); 3/191 pts (1.6 %) in arm A and 16/191 pts (8.4 %) in arm B had a recurrence. 20-yrs PFS in arm A / B was 97 % (CI 96-99 %) / 92 % (CI 90-95 %), (*p = .0049*). 20-yrs OS in arm A / B was 90 % (CI 86-94 %) / 88 % (CI 86-94 %), (*p = .83*). 23/382 (6 %) pts have died, 22/23 not related to testis cancer, 1/23 died of a recurrence in arm B. 8/191 pts (4.2 %) in arm A and 4/191 pts (2.1 %) in arm B showed metachronous secondary testis cancer (*p = .26*). 5/191 pts (2.6 %) in arm A and 4/191 pts (2.1 %) in arm B developed other malignancies. 170/382 questionnaires were evaluable (arm A: 95; arm B: 75). 45 pts were lost to FU. There were no significant differences comparing both treatment arms regarding potentially treatment-related late toxicities. However, excluding pre-existing complaints, ototoxicity (9/95 (9 %) vs. 4/75 (5 %) pts, *p = .31*) was reported more frequently in arm A. Excluding pre-existing neurological conditions, peripheral neuropathy of all grades was more frequently reported in arm A (15/95 pts; 16 % vs. 9/75 pts; 12 % pts; *p = .48).* Retrograde ejaculation occurred more frequently after RPLND (9/95 pts; 9% vs. 18/75 pts; 24 %, *p = .01*). **Conclusions:** After more than 13 yrs of FU, recurrences in non-risk factor selected pts with CS I NSGCT remain to be significantly more frequent with RPLND. No excess mortality due to secondary malignancies was observed. Late toxicities did not differ between 1 cycle of BEP and RPLND. Only retrograde ejaculation was observed significantly more frequent after RPLND. With long-term observation, 1 cycle of BEP has not only a high efficacy to prevent recurrence but also seems to be tolerated without clinically relevant long-term toxicity. Research Sponsor: None.

5513 Poster Discussion Session; Displayed in Poster Session (Board #94), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Population-based prostate cancer screening using a prospective, blinded, paired screen-positive comparison of PSA and fast MRI: The IP1-PROSTAGRAM study. *First Author: David Eldred-Evans, Imperial Prostate, London, United Kingdom*

Background: The prostate-specific antigen (PSA) test can lead to under- and over-diagnosis of prostate cancer and has not been recommended for population screening. A fast MRI scan might overcome the limitations of PSA. IP1-PROSTAGRAM is the first study to evaluate the performance of a 15-minute non-contrast MRI for prostate cancer screening in comparison to PSA. **Methods:** IP1-PROSTAGRAM was a prospective, population-based, screen-positive paired-cohort study. Men aged 50-69 years in the UK were invited for prostate cancer screening through seven primary care practices or community-based recruitment. Participants underwent a PSA and MRI scan (T2-weighted and diffusion). MRI was scored using PIRADS version 2.0 without knowledge of PSA; screen-positive MRI (defined as either PIRADS score 3-5 or 4-5) were compared against a screen-positive PSA defined as ≥3ng/ml. If any test was screen-positive, a systematic 12-core biopsy was performed with MRI-ultrasound image-fusion targeted biopsy to MRI suspicious areas, as appropriate. Clinically-significant cancer was defined as any Gleason score ≥3+4. The primary outcome was the proportion of screen-positive MRI at different scores; important secondary outcomes were the number of clinically-significant and insignificant cancers detected. **Results:** 2034 men were invited to participate of whom 408 consented and 406 were screened by both PSA and MRI (10/Oct/2018-15/May/2019). The proportion with a screen-positive MRI (score 3-5) was higher than the proportion with a screen-positive PSA (17.7% [95%CI 14.3-21.8] vs. 9.9% [95%CI 7.3-13.2]; $p < 0.001$). A screen-positive MRI (score 4-5) was similar to a screen-positive PSA (10.6% [95%CI 7.9-14.0] vs. 9.9% [95%CI 7.3-13.2], $p = 0.71$). An MRI score 3-5 or 4-5 used to denote a screen-positive MRI, compared to PSA alone, detected 14, 11 and 7 clinically-significant cancers, respectively. There were 7, 5 and 6 clinically-insignificant cancers detected, respectively. No serious adverse events occurred. **Conclusions:** When screening the general population for prostate cancer, MRI using a score of 4-5 to define a screen-positive test, compared to PSA alone at ≥3ng/ml, could lead to more men diagnosed with clinically-significant cancer without increasing the number of men biopsied or diagnosed with clinically-insignificant cancer. Clinical trial information: NCT03702439. Research Sponsor: Wellcome Trust, Other Foundation, The Urology Foundation.

5514 Poster Discussion Session; Displayed in Poster Session (Board #95), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Overall survival (OS) results of phase III ARAMIS study of darolutamide (DARO) added to androgen deprivation therapy (ADT) for nonmetastatic castration-resistant prostate cancer (nmCRPC). *First Author: Karim Fizazi, Institut Gustave Roussy and University of Paris Sud, Villejuif, France*

Background: DARO is a structurally distinct androgen receptor inhibitor with a favorable safety profile, approved for treating men with nmCRPC after demonstrating significantly prolonged metastasis-free survival, compared with placebo (PBO), in the phase III ARAMIS trial: median 40.4 vs 18.4 months, respectively (HR 0.41; 95% CI 0.34–0.50; $P < 0.0001$). We report final analyses of OS and prospectively collected, patient-relevant secondary endpoints, and updated safety results. **Methods:** 1509 patients (pts) with nmCRPC were randomized 2:1 to DARO 600 mg twice daily (n = 955) or PBO (n = 554) while continuing ADT. Secondary endpoints included OS, and times to pain progression, first cytotoxic chemotherapy, and first symptomatic skeletal event. The OS analysis was planned to occur after approximately 240 deaths. Secondary endpoints were evaluated in a hierarchical order. **Results:** Final analysis was conducted after 254 deaths were observed (15.5% of DARO and 19.1% of PBO patients). After unblinding at the primary analysis, 170 pts crossed over from PBO to DARO. DARO showed a statistically significant OS benefit corresponding to a 31% reduction in the risk of death compared with placebo. All other secondary endpoints were significantly prolonged by DARO, regardless of the effect of crossover and subsequent therapies on survival benefit. Incidences of treatment-emergent adverse events (AEs) with ≥5% frequency were generally comparable between DARO and PBO, similar to the safety profile observed at the primary analysis. Incidences of AEs of interest (including falls, CNS effects, and hypertension) were not increased with DARO compared with PBO when adjusted for treatment exposure. AEs in the crossover group were consistent with those for the DARO treatment arm. **Conclusions:** DARO showed a statistically significant OS benefit for men with nmCRPC. In addition, DARO delayed onset of cancer-related symptoms and subsequent chemotherapy, compared with PBO. With extended follow-up, safety and tolerability were favorable and consistent with the primary ARAMIS analysis (Fizazi et al, *N Engl J Med* 2019;380:1235-46). Clinical trial information: NCT02200614. Research Sponsor: Bayer AG and Orion Pharma.

5515 Poster Discussion Session; Displayed in Poster Session (Board #96), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Final overall survival (OS) from PROSPER: A phase III, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with nonmetastatic castration-resistant prostate cancer (nmCRPC). *First Author: Cora N. Sternberg, Englander Institute of Precision Medicine, Weill Cornell Medicine, New York, NY*

Background: PROSPER previously demonstrated a statistically significant and clinically meaningful improvement in metastasis-free survival (MFS) (hazard ratio [HR] 0.29; 95% CI 0.24-0.35; $P < .001$) in men with nmCRPC and rapidly rising prostate-specific antigen (PSA) who received ENZA. When first reported, OS was immature with only 165 of 596 (28%) prespecified deaths. Here we report results from the final OS analysis. **Methods:** Men with nmCRPC, PSA doubling time ≤ 10 mo, and PSA ≥ 2 ng/mL at screening continued androgen deprivation therapy (ADT) and were randomized 2:1 to ENZA 160 mg or PBO. OS treatment effect was assessed using a group sequential testing procedure with O'Brien-Fleming-type alpha spending function ($P \leq .021$ required for statistical significance). Medians were estimated using the Kaplan-Meier method; 95% CIs using a stratified Cox regression model. **Results:** As of Oct 15, 2019 (median follow-up ≈ 48 mo), there were 466 deaths (288 [30.9%] and 178 [38.0%] in the ENZA and PBO arms, respectively). ENZA significantly prolonged OS compared with PBO (HR 0.73; 95% CI 0.61-0.89; $P = .0011$). Median OS was 67.0 mo (95% CI 64.0-not reached) in the ENZA arm and 56.3 mo (95% CI 54.4-63.0) in the PBO arm. Subsequent antineoplastic therapies were initiated after treatment discontinuation by 310 (33%) men in the ENZA arm vs 303 (65%) in the PBO arm. Median duration of treatment was 33.9 mo vs 14.2 mo with ENZA vs PBO, respectively. Grade ≥ 3 adverse events (AEs) were reported by 48% of men in the ENZA arm vs 27% in the PBO arm (16% vs 6% were drug related, respectively). AEs with event rates per 100 patient-yr that were ≥ 2 points higher with ENZA vs PBO were falls (9 vs 4), fatigue (14 vs 12), and hypertension (7 vs 5). **Conclusions:** ENZA treatment resulted in a statistically significant 27% reduced risk of death compared with PBO, demonstrating that initiation of ENZA + ADT before the onset of detectable metastasis improves OS in men with CRPC and rapidly rising PSA. This OS benefit ensues despite crossover from the PBO arm to ENZA and higher rates of subsequent antineoplastic therapies in men from the PBO arm. Safety was consistent with previous clinical trials. This final OS analysis from PROSPER provides prospective validation of MFS as a potential surrogate endpoint for OS in nmCRPC and supports the continued use of ENZA + ADT as a standard of care in men with nmCRPC and rapidly rising PSA. Clinical trial information: NCT02003924. Research Sponsor: Pfizer Inc. and Astellas Pharma, Inc.

5516 Poster Discussion Session; Displayed in Poster Session (Board #97), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Final survival results from SPARTAN, a phase III study of apalutamide (APA) versus placebo (PBO) in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC). *First Author: Eric Jay Small, Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA*

Background: SPARTAN evaluated APA vs PBO in pts with nmCRPC and a prostate-specific antigen doubling time of ≤ 10 mo receiving androgen deprivation therapy (ADT). At primary end point analysis of metastasis-free survival (MFS), APA significantly improved median MFS by 2 yrs, as well as time to metastasis, progression-free survival, and time to symptomatic progression vs PBO (Smith, et al. *NEJM* 2018); overall survival (OS) results were immature. SPARTAN was unblinded upon meeting the primary end point; pts still on PBO were allowed to cross over to APA. Final survival results are reported herein. **Methods:** 1207 nmCRPC pts were randomized 2:1 to APA (240 mg QD) or PBO plus ongoing ADT. At progression, pts could receive open-label sponsor-provided abiraterone acetate + prednisone. After the primary efficacy end point (MFS) was met, 76 PBO pts (19%) crossed over to APA. OS and time to cytotoxic chemotherapy (TTCx) were tested by group sequential testing procedure with O'Brien-Fleming (OBF)-type alpha spending function. Time-to-event end points were analyzed by Kaplan-Meier method and Cox model. A sensitivity analysis for OS, accounting for crossover using a naïve censoring approach, was conducted. **Results:** With follow-up of 52.0 mo, 428 (of 427 required) OS events had occurred. Median treatment duration: APA, 32.9 mo; PBO, 11.5 mo. Median OS was significantly longer with APA + ADT vs PBO + ADT (73.9 vs 59.9 mo), (hazard ratio [HR], 0.784, Table). APA significantly lengthened TTCx (HR, 0.629). Discontinuation rates (APA vs PBO) due to progressive disease were 42.7% vs 73.9%, and due to adverse events (AE) 15.2% vs 8.4%. Safety was consistent with previous reports; grade 3/4 treatment-emergent (TE) AEs of special interest were rash 5.2%, fractures 4.9%, falls 2.7%, ischemic heart disease 2.6%, hypothyroidism 0%, and seizures 0%. 1 TEAE leading to death (myocardial infarction) was considered potentially APA related. **Conclusions:** In pts with nmCRPC, APA + ADT significantly improved OS compared with PBO + ADT, with median OS > 6 yr in the APA + ADT group and 14 mo improvement over PBO + ADT. Benefit from APA was observed despite a 19% crossover from PBO. The safety profile of APA was consistent with prior interim analyses. Clinical trial information: NCT01946204. Research Sponsor: Janssen Research & Development.

End point, median mo	APA + ADT (n = 806)	PBO + ADT (n = 401)	HR	p Value[a]
OS	73.9	59.9	0.784	0.0161[b]
OS (naïve censoring crossover)	73.9	52.8	0.685	0.0002
TTCx	NR	NR	0.629	0.0002

[a]p value from stratified log-rank test.
[b]OBF required p value ≤ 0.046 to be considered statistically significant.
NR, not reached.

5517 Poster Discussion Session; Displayed in Poster Session (Board #98), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

TRANSFORMER: Bipolar androgen therapy (BAT) versus enzalutamide (E) for castration-resistant metastatic prostate cancer (mCRPC). *First Author: Samuel R. Denmeade, Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

Background: Rapid cycling between high and low testosterone (T) (i.e BAT) produces tumor response in mCRPC, and may overcome resistance to newer AR therapies. Here we report a randomized study comparing BAT to E in men with mCRPC progressing on abiraterone (A). **Methods:** In this phase 2 trial, men received either T cypionate 400mg IM (BAT) once every 28 days or daily oral E 160mg. Primary endpoint was clinical/radiographic PFS; crossover was permitted at progression. Secondary endpoints were OS, PSA progression to primary and crossover therapy, PSA and objective responses (OR), time to PSA progression from randomization through crossover (PFS2), quality of life (QoL), and AEs. **Results:** 195 men were randomized (94 to BAT, 101 to E). Results are presented in table. Although diametrically opposed therapies, median PFS and PSA response in the intent-to-treat (ITT) population was not significantly different between BAT and E. OR and OS favored BAT. For those who received BAT and then crossed over to E the PSA50 response was 77.8% and time to PSA progression was 10.9 mo compared to 25.3% and 3.8 mo for those receiving E immediately after A. The sequence of treatment had a significant effect on median PSF2 which was 28.2 mo for men receiving BAT→E vs. 19.6 m for E→BAT. For men who crossed over from BAT to E, OS was 37.3 mo vs. 28.6 months for those receiving E without crossover. AEs were primarily grade 1-2 in the BAT arm and included fatigue, generalized pain, and lower extremity edema. BAT improved QoL (fatigue, physical functioning, sexual function) vs. E. **Conclusions:** BAT could be safely administered to asymptomatic men with mCRPC. BAT produced a comparable PFS to E in A-refractory mCRPC pts. However, PSA50 and OR after crossover, as well as PFS2, were significantly improved in men who received BAT→E versus E→BAT. OS in men receiving BAT→E was 37.3 mo, exceeding historical expectations. These results support the hypothesis that treatment with BAT is safe, has efficacy and can restore sensitivity to antiandrogens. Clinical trial information: NCT02286921. Research Sponsor: Department of Defense Prostate Cancer Research Program.

Prespecified end points (ITT population).

Initial	N =	BAT	N =	E	HR	P Value
Time to clin/radio prog-mo	94	5.7	101	5.7	1.14	0.42
Time to PSA prog.- mo	91	2.8	98	3.8	1.51	0.02
PSA50-no. (%)	85	23 (27.1)	91	23 (25.3)		0.70
OR- no. (%)	33	8 (24.2)	24	1 (4.2)		0.07
OS-mo	94	32.9	101	29.0	0.93	0.74
Crossover		BAT to E		E to BAT		
OS (BAT-Enza vs Enza-BAT)-mo	34	37.3	46	30.2	0.63	0.17
OS (BAT-Enza vs Enza only)-mo	34	37.3	55	28.6	0.50	0.03
Time to PSA prog.- mo	36	10.8	47	1.1	0.26	0.0001
PSA50-no. (%)	36	28 (77.8)	47	11 (23.4)		
OR- no. (%)	35	10 (28.6)	41	3 (7.3)		0.03
PFS2-mo	94	28.2	101	19.6	0.44	0.02

5518 Poster Discussion Session; Displayed in Poster Session (Board #99), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase I, open-label, multicenter study to assess the safety, pharmacokinetics, and preliminary antitumor activity of AZD4635 both as monotherapy and in combination in patients with advanced solid malignancies: Results from prostate cancer patients (NCT02740985). *First Author: Emerson A. Lim, Columbia University-Herbert Irving Comprehensive Cancer Center, New York, NY*

Background: AZD4635 inhibits adenosine 2a receptor (A2aR) signaling and improves immune activation and anti-tumor activity in preclinical models. This phase I study assessed the safety, pharmacokinetics, pharmacodynamics and efficacy of AZD4635 monotherapy (mono) and in combination (combo) with durvalumab (durva) in patients (pts) with refractory solid tumors. Here we present data for immune checkpoint-naïve pts with metastatic castrate-resistant prostate cancer (mCRPC). **Methods:** Pts with refractory mCRPC received AZD4635 mono (75 mg or 100 mg QD oral nanosuspension [(RP2D]) or in combination (75 mg or 100mg QD) with durva 1.5g IV q4wk. **Results:** Between 30Aug16 and 20Jun19 (data cutoff [DCO]) 94 mCRPC pts were treated with mono (n = 49) or combo (n = 45): median age 70.5 yrs; ECOG 0-1 = 99%. The median number of prior treatment regimens was 5 (range = 1-10); 61% of pts (57/94) had prior chemotherapy, 90% had prior new hormonal therapy. PK data suggest AZD4635 concentrations at 75-100 mg QD are above the *in vitro* IC_{50} for A2aR inhibition throughout the dosing interval. Modeling predicts 80-90% A2aR occupancy at steady state for doses at ≥75 mg QD. Most common treatment-related AEs (> 10%) were nausea, vomiting, fatigue, decreased appetite, dizziness, and diarrhea. At the DCO in this ongoing study, 70 pts were evaluable for response by RECIST v1.1 (mono = 33, combo = 37). Confirmed response occurred in 8 pts: mono = ORR 6.1% (2PRs) and combo = 16.2% (2CRs, 4PRs). The duration of response across cohorts ranged from 1-18.5 mo (5 pts ongoing). PSA response (defined as ≥50% decrease from baseline of ≥1ng/ml) was observed in 6.4% (3/47 pts; 95% CI, 1.3-17.5) of mono-treated patients and 20% (9/45 pts; 95% CI, 9.6-34.6) of combo-treated patients. Patients with high adenosine (ADO) gene expression signature (N = 46) in peripheral blood, showed a median PFS of 21 weeks v. 8.7 weeks in ADO signature low patients (N = 46) (HR 0.5, CI 0.3-0.9) (DCO 20Jun19). In addition, baseline TCR clonality and diversity were linked with response. **Conclusions:** In mCRPC pts, AZD4635 alone or in combination with durva was tolerable and associated with clinical benefit. A mCRPC phase II trial is ongoing with continued exploration of predictors of response to treatment. Clinical trial information: NCT02740985. Research Sponsor: Astra Zeneca.

5520 Poster Discussion Session; Displayed in Poster Session (Board #101), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

ProCAID: A randomized double-blind phase II clinical trial of capivasertib (C) in combination with docetaxel and prednisolone chemotherapy (DP) in metastatic castration-resistant prostate cancer (mCRPC). *First Author: Simon J. Crabb, Southampton Clinical Trials Unit, University of Southampton, University Hospital Southampton NHS Foundation Trust and Southampton Experimental Cancer Medicine Centre, Southampton, United Kingdom*

Background: DP extends survival in mCRPC, but clinical benefit is modest. PI3K/AKT/PTEN pathway activation is common in mCRPC contributing to disease progression and DP resistance. C is a pan-AKT inhibitor. Pre-clinical data indicate activity in prostate cancer and synergism with DP. This phase II trial combined C with DP in mCRPC. **Methods:** Key eligibility criteria: histologically or cytologically proven measurable or evaluable mCRPC, suitable for treatment with DP for PSA and/or radiographic disease progression, ECOG performance status 0-1, no prior chemotherapy for mCRPC, not requiring insulin or > 2 oral hypoglycaemic drugs for diabetes mellitus. Treatment: up to 10 cycles of DP (D: 75 mg/m^2 IV, day 1; P: 5 mg bd oral, day 1 – 21) and random assignment (1:1, double blind) to oral C (320 mg twice daily, 4 days on/3 days off, from cycle 1, day 2) or matched placebo to disease progression. Primary endpoint: progression free survival (PFS; comprising PSA, radiographic or clinical progression, new cancer therapy or death; PCWG2 criteria) in the intent to treat (ITT) population. Secondary endpoints included overall survival (OS) and safety. PFS and OS were also assessed by composite biomarker (B) subgroup for PI3K/AKT/PTEN pathway activation status (NGS/IHC on archival tumour, contemporaneous ctDNA). Statistics: designed to detect a 50% increase in median PFS (6 to 9 months (mo)) between the placebo and C arms (90% power, 20% 1-sided alpha) by Cox proportional hazards model. Registration: ISRCTN 69139368. **Results:** 150 patients were randomised to 01/2019. Median follow up 16.77 months (IQR 12.0-26.5). PFS and OS by ITT and B status, are shown in the table (NR, not reached; CI confidence interval). Grade 3–4 adverse events (AE) were equally common between arms (62.2%). The most common AEs were diarrhoea, fatigue and nausea. **Conclusions:** Adding C to DP did not extend PFS. The OS secondary endpoint was significantly increased. PFS and OS results were consistent irrespective of PI3K/AKT/PTEN pathway activation status. Clinical trial information: 69139368. Research Sponsor: Cancer Research UK, Pharmaceutical/Biotech Company.

	C, mo (95% CI)	Placebo, mo (95% CI)	Hazard ratio (95% CI)	p-value
PFS, ITT	7.03 (6.28-8.25)	6.7 (5.52-7.36)	0.92 (0.65-1.31)	0.32
PFS, B +ve (n = 44)	7.75(6.44-9.63)	7.98(5.09-9.82)	1.17(0.61-2.23)	
PFS, B -ve (n = 92)	7.03(4.21-8.25)	6.34(4.76-7.13)	0.89(0.57-1.37)	
OS, ITT	31.15 (20.07-NR)	20.27 (17.51-24.18)	0.54 (0.34-0.88)	0.01
OS, B +ve	26.87(14.59-NR)	20.27(12.91-35.71)	0.62(0.26-1.47)	
OS, B -ve	32.43(18.5-NR)	20.30(16.82-24.18)	0.54(0.30-0.99)	

5521 Poster Session (Board #102), Fri, 8:00 AM-11:00 AM

Molecular determinants of prostate specific antigen (PSA) kinetics and clinical response to apalutamide (APA) in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC) in SPARTAN. *First Author: Fred Saad, Centre Hospitalier de l'Université de Montréal, Université de Montréal, Montréal, QC, Canada*

Background: In SPARTAN, APA + androgen deprivation therapy (ADT) prolonged metastasis-free survival (MFS) and improved PSA kinetics over placebo (PBO) + ADT in high-risk nmCRPC. All molecular subtypes derived benefit in MFS from APA (Feng FY, et al. ASCO GU 2019; abstract 42). We evaluated the association of PSA decline and efficacy outcomes in SPARTAN pts with different molecular subtypes. **Methods:** Gene expression from archival primary tumors (biomarker population) was assessed with the DECIPHER platform (Decipher Biosciences, Inc.) and stratified into genomic classifier (GC) high- and low-to-average risk using GC score > 0.6 and ≤ 0.6, respectively, and ADT-resistant or -sensitive basal or luminal A/B (PAM50 classifier) subtypes. PSA nadir and confirmed PSA decline (Table) were assessed in APA pts overall and at 3, 6, and 12 mo. Associations between molecular subtypes and outcomes were assessed. **Results:** Of 233 available samples, 154 were from APA pts; 49% of APA pts had high GC score and 66% had basal subtype. PSA levels at baseline were similar across all subtypes. Regardless of GC score or basal/luminal subtype, $> 50\%$ of patients achieved $\geq 90\%$ reduction in PSA with APA. PSA declined faster and PSA reduction was deeper at 6 mo (Table) in GC low to average vs GC high risk and luminal vs basal subtypes. Overall, only luminal vs basal subtypes had a significantly higher % of pts with $\geq 90\%$ PSA decline (Chi square p = 0.037). In luminal pts, deeper PSA decline with APA was consistent with improved MFS vs basal pts. In GC high pts, MFS benefit with APA was similar to that in GC low to average pts despite lower PSA decline. Although GC low to average and luminal pts had more rapid and deeper PSA responses than GC high or basal pts, respectively, all pts derived MFS benefit. Association of long-term outcomes with PSA decline in these molecular subtypes will be presented. **Conclusions:** In SPARTAN, all molecular subtypes of pts with nmCRPC treated with APA + ADT had MFS benefit and rapid and sustained PSA decline. PSA responses were deepest and most rapid in GC low to average and luminal subtypes. Clinical trial information: NCT01946204. Research Sponsor: Janssen Research & Development.

PSA kinetics in APA pts at 6 mo.

n (%)	GC high n = 76	GC low to average n = 78	Basal n = 102	Luminal n = 52
PSA decline:				
≥ 50%	71 (93.4)	73 (93.6)	94 (92.2)	50 (96.2)
≥ 90%	39 (51.3)	50 (64.1)	52 (51.0)	37 (71.2)
PSA ≤ 0.2 ng/mL	25 (32.9)	29 (37.2)	31 (30.4)	23 (44.2)
Depth of PSA decline:				
< 50%	5 (6.6)	5 (6.4)	8 (7.8)	2 (3.8)
50%-< 90%	32 (42.1)	23 (29.5)	42 (41.2)	13 (25.0)
≥ 90%	39 (51.3)	50 (64.1)	52 (51.0)	37 (71.2)

5522 Poster Session (Board #103), Fri, 8:00 AM-11:00 AM

A urine exosomal circRNA classifier for detection of high-grade prostate cancer at initial biopsy: A multicenter, retrospective study. *First Author: Liaoyuan Li, Sun Yat-sen University, Guangzhou, China*

Background: The low specificity of prostate-specific antigen (PSA) has resulted in the overdiagnosis and overtreatment of clinically indolent prostate cancer (PCa). We aimed to identify a urine exosomal circular RNA (circRNA) classifier that could detect high-grade (Gleason score [GS]7 or greater) PCa. **Methods:** We did a three-stage study that enrolled eligible participants, including PCa-free men, 45 years or older, scheduled for an initial prostate biopsy due to suspicious digital rectal examination findings and/or PSA levels (limit range, 2.0-20.0 ng/mL), from four hospitals in China. We used RNA sequencing and digital droplet polymerase chain reaction to identify 18 candidate urine exosomal circRNAs that were increased in 11 patients with high-grade PCa compared with 11 case-matched patients with benign prostatic hyperplasia. Using a training cohort of eligible participants, we built a urine exosomal circRNA classifier (Ccirc) to detect high-grade PCa. We then evaluated the classifier in discrimination of GS7 or greater from GS6 and benign disease on initial biopsy in two independent cohorts. We used the sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) to evaluate diagnostic performance, and compared Ccirc with standard of care (SOC) (ie, PSA level, age, race, and family history). **Results:** Between June 1, 2016, and July 31, 2019, we recruited 356 participants to the training cohort, and 442 and 325 participants to the two independent validation cohorts. We identified a Ccirc containing five differentially expressed circRNAs (circ_0049335, circ_0056536, circ_0004028, circ_0008475, and circ_0126027) that could detect high-grade PCa. Ccirc showed higher accuracy than SOC to distinguish individuals with high-grade PCa from controls in both the training cohort and the validation cohorts. (AUC 0.831 [95% CI 0.765-0.883] *vs* 0.724 [0.705-0.852], P = 0.032 in the training cohort; 0.823 [0.762-0.871] *vs* 0.706 [0.649-0.762], P = 0.007 in validation cohort 1; and 0.878 [0.802-0.943] *vs* 0.785 [0.701-0.890], P = 0.021 for validation cohort 2). In all three cohorts, Ccirc had higher sensitivity (range 71.6-87.2%) and specificity (82.3-90.7%) than did SOC (sensitivity, 42.3-68.2%; specificity, 40.1-62.3%) to detect high-grade PCa. Using a predefined cut point, 202 of 767 (26.3%) biopsies would have been avoided, missing only 6% of patients with dominant pattern 4 high-risk GS 7 disease. **Conclusions:** Ccirc is a potential biomarker for high-grade PCa among suspicious men. Research Sponsor: National Natural Science Foundation of China.

5523 Poster Session (Board #104), Fri, 8:00 AM-11:00 AM

Bone metabolism biomarkers (BMB) and progression-free survival (PFS) in men with metastatic hormone-sensitive prostate cancer (HSPC): SWOG S1216, a phase III trial of androgen deprivation therapy (ADT) with or without orteronel. *First Author: Primo Lara, University of California, Sacramento, CA*

Background: We previously reported that baseline BMB are independently prognostic for overall survival (OS) in men with castration resistant prostate cancer. We correlated BMB with outcomes in mHSPC as part of S1216, a phase III trial of ADT +/- the novel CYP17 inhibitor orteronel. **Methods:** Blood was obtained at study entry for bone resorption [C-telopeptide(CTx) & Pyridinoline(PYD)] & formation markers [C-terminal collagen propeptide(CICP) & bone alkaline phosphatase(BAP)]. With prior DSMC approval, patients were sampled to mask potential treatment effect. Logistic regression was used to assess if BMB elevation above median was prognostic for a PFS event w/in 2 years across pooled study treatment arms, adjusting for baseline variables (including disease extent, PSA, age, pre-randomization ADT, & presence of bone mets). An additional interaction term between BMB elevation & presence of bone mets was included; if significant, separate models were developed for men +/- bone mets. **Results:** Of 1,313 men, 656 were included in this analysis. All 4 BMB levels were higher in men with a PFS event w/in 2 years vs. those with no PFS event. The odds ratio (OR) for a PFS event was significantly higher in men w/ elevated baseline BMB (see table). For BAP, a significant interaction between marker elevation and bone mets was seen (p = 0.003); men w/ bone mets and BAP elevation had an OR of 1.83 for a PFS event in 2 years. **Conclusions:** In men with newly diagnosed HSPC, elevated baseline levels of BMB were significantly associated with PFS, with about a two-fold increased risk of a progression event w/in 2 years. For CICP, CTx, & PYD, this association was independent of the presence of bone metastases. Baseline BMB levels have strong prognostic value in the mHSPC context. Correlative analysis of BMB & OS is planned. Clinical trial information: NCT01809691. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

Bone metabolism biomarker	Population	Odds Ratio (95% CI)	p-value	Bone marker X presence of bone mets interaction p-value
CICP	Full cohort	1.73 (1.21, 2.47)	0.003	0.73
CTx	Full cohort	1.90 (1.35, 2.69)	0.0003	0.66
PYD	Full cohort	2.22 (1.56, 3.14)	< 0.0001	0.34
BAP	Full cohort	---	---	0.003
	Men with bone mets	1.83 (1.23, 2.73)	0.003	---
	Men without bone mets	0.47 (0.22,1.02)	0.06	---

5524 Poster Session (Board #105), Fri, 8:00 AM-11:00 AM

Ability of cell-cycle progression score to predict risk for progression to metastatic disease and disease-specific mortality in prostate cancer patients after prostatectomy. *First Author: Gregory P. Swanson, Baylor Scott and White Health, Temple, TX*

Background: Prostate cancer treatment aims to prevent metastatic disease (METS) and disease-specific mortality (DSM). A major challenge is to identify those at highest risk so additional intervention can be initiated earlier when it has a better chance of success. Pathologic parameters alone have limited ability to predict METS and DSM, but data suggests biomarkers can improve risk discrimination. **Methods:** Eligible patients had: (1) prostate cancer treated with radical prostatectomy (RP; 1988-1995); (2) available tissue for cell-cycle progression (CCP) testing that resulted in a valid score; (3) preoperative prostate-specific antigen (PSA); (4) no neoadjuvant therapy; and (5) clinical follow-up (N = 360). Cancer of the prostate risk assessment post-surgical (CAPRA-S) was combined with CCP into a combined cell-cycle risk score (CCR = $0.38 \times$ CAPRA-S + $0.57 \times$ CCP). **Results:** Median follow-up was 23.5 years for patients alive at last follow-up. Overall, 11% (41/360) developed METS and 9% (33/360) had DSM. CCP score added significant information to CAPRA-S when predicting METS (p = 0.001) and DSM (p = 0.001). CCR score was also a significant predictor of METS and DSM (p-values $< 1\times10^{-8}$). CCP and CCR scores were prognostic of METS in patients with rising post-RP PSA. Of patients with biochemical recurrence (BCR), 25% (41/163) developed METS. CAPRA-S alone was predictive of these events (p = 0.01) but was significantly improved with the addition of CCP (Hazard Ratio [HR] = 1.69 [95% Confidence Interval (CI) 1.13, 2.52], p = 0.014). CCR was also highly prognostic (HR = 1.56 [95% CI 1.20, 2.03], p = 0.001). CCR score discriminated risk of METS both post-RP and after post-RP BCR (Table). **Conclusions:** Overall, the CCR score significantly predicted METS and DSM in prostate cancer post-RP and was also highly prognostic in those with a post-RP rising PSA. It is therefore a useful tool for determining who is at greatest risk of treatment failure and may benefit from earlier intervention. Research Sponsor: Myriad Genetics.

Kaplan-Meier estimates (95% CI) of 15-year risk of METS or DSM post-RP or after post-RP BCR.

CCR	Risk of METS Post-RP (%)	Risk of DSM post-RP (%)	CCR	Risk of METS post-BCR (%)	Risk of DSM post-BCR (%)
(-1, 1] n = 156	4.7 (0.9, 8.3)	2.5 (0, 5.2)	**(-1, 1] n = 39**	24.9 (7.9, 38.8)	16.1 (1.7, 28.4)
(1, 2] n = 109	6.6 (0.8, 12.1)	4.4 (0, 9.2)	**(1, 2] n = 48**	15.1 (1.5, 26.9)	9.9 (0, 20.2)
(2, 3] n = 60	26.9 (11.8, 39.3)	17.3 (4.6, 28.4)	**(2, 3] n = 47**	34.3 (15.4, 48.9)	27.9 (9, 42.9)
(3, 6] n = 35	35.7 (16, 50.8)	30% (11.2, 44.8)	**(3, 6] n = 29**	46.2 (22.5, 62.6)	34.8 (13.2, 51)

5525 Poster Session (Board #106), Fri, 8:00 AM-11:00 AM

***HSD3B1* (1245A>C) polymorphism and clinical outcomes in metastatic castration-resistant prostate cancer (mCRPC) patients treated with abiraterone acetate (AA) and enzalutamide (ENZA): Results from two prospective studies.** *First Author: Isabel Aragon, Genitourinary Cancer Traslational Research Unit, Institute of Biomedical Research in Málaga (IBIMA), Málaga, Spain*

Background: The common HSD3B1 (1245A > C) germline variant is associated with increased *de-novo* synthesis of androgens and worse outcomes in men treated with androgen-deprivation therapy in metastatic hormone sensitive prostate cancer. The aim of this study is to determine the role of this polymorphism on treatment outcomes for AA and ENZA in patients with mCRPC. **Methods:** A total of 547 patients treated with AA or ENZA for mCRPC from two prospective cohorts; cohort 1 included 202 from British Columbia (Canada) and cohort 2 enrolled 345 patients from the Spanish study PROREPAIR-B. HSD3B1 genotype was determined by targeted sequencing in cohort 1 and by Taqman SNP genotyping assay in cohort 2. Associations between HSD3B1 genotypes and (TTPP), time to progression (TTP) and overall survival (OS) were evaluated via univariate COX regression. Multivariate analysis was performed to determine the independent association of each covariate. **Results:** The proportions of patients with a homozygous wild-type HSD3B1 (AA), heterozygous (AC) and homozygous variant (CC) genotype were respectively 45.6%, 39.4% and 15%. As expected, known prognostic factors for mCRPC such as hemoglobin, alkaline phosphatase (ALP), LDH, PSA at baseline as well as site of metastasis were significantly associated with TTPP and TPP. In the combined cohort, HSD3B1 (CC) genotype was associated with worse TTP (HR 1.31, 95%CI 1.02-1.67, p = 0.032) and PSA response rates (48% for CC vs 62% and 65% for AA and AC, respectively (p = 0.019, χ^2)). Similar trend was observed for TTPP (HR 1.28, 95%CI 0.99-1.66, p = 0.064). OS was not different among genotypes, but was significantly shorter for patients with CC genotype in cohort 1 (HR 1.97, 95%CI 1.14-3.40, p = 0.016). There was no association between HSD3B1 genotype and time to castration-resistance in either of the two cohorts. Multivariable analysis showed that LDH, ALP, hemoglobin and use of AA or ENZA as first-line therapy for mCRPC were independent prognostic factors for TTP and TTPP; non-significant association was observed for genotype and TTP. **Conclusions:** HSD3B1 homozygous variant genotype (CC) was associated with shorter TTP and lower PSA response rate in mCRPC patients treated with AA or ENZA. However, the CC genotype did not provide prognostic information beyond that conferred by standard clinical variables, suggesting that it may not be a suitable stand-alone biomarker in mCRPC. Research Sponsor: BC Cancer Foundation, Other Foundation, Other Government Agency.

5526 Poster Session (Board #107), Fri, 8:00 AM-11:00 AM

Biomarker analysis from the KEYNOTE-199 trial of pembrolizumab in patients (pts) with docetaxel-refractory metastatic castration-resistant prostate cancer (mCRPC). *First Author: Emmanuel S. Antonarakis, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD*

Background: In the phase II KEYNOTE-199 study (NCT02787005), pembrolizumab monotherapy demonstrated antitumor activity in pts with docetaxel-refractory mCRPC (n = 258). Here we evaluated the association between prespecified molecular biomarkers and clinical outcomes. **Methods:** Cohorts 1 (C1) and 2 (C2) enrolled pts with RECIST-measurable PD-L1–positive (combined positive score [CPS] ≥1 using immunohistochemistry) and PD-L1–negative (CPS <1) disease, respectively. C3 enrolled pts with nonmeasurable, bone-predominant disease, irrespective of PD-L1 status. Biomarkers evaluated in this analysis were tumor mutational burden ([TMB; mutations/exome] n = 155), PD-L1 CPS (n = 255), tumor microenvironment–based 18-gene RNA expression profile ([GEP] n = 196), and microsatellite instability ([MSI] as determined by Promega PCR analysis; n = 147). Outcomes evaluated for C1 and C2 (n = 200) were ORR, disease control rate (DCR), and radiographic PFS (rPFS) per blinded, independent central review per PCWG-modified RECIST v1.1. Outcomes evaluated for C1-C3 (n = 258) were prostate-specific antigen (PSA) response, time to PSA progression, and OS. Significance of continuous biomarkers (CPS; TMB; GEP) was prespecified at 0.05 for one-sided *P* values from logistic (ORR; DCR; PSA response) and Cox proportional hazard regression (rPFS; OS; PSA progression) adjusted for Eastern Cooperative Oncology Group performance status. Binary biomarkers (MSI) were analyzed using Fisher's exact test (ORR; DCR; PSA response). Clinical data cutoff date: Jun 24, 2019. **Results:** Median TMB was 53.0 (interquartile range [IQR], 40.5 to 78.0), median CPS was 1 (IQR, 0 to 5), and median GEP was –0.64 (IQR, –0.88 to –0.46); 6 pts (2.3%) had MSI-high tumors. In C1-C3, TMB was associated with PSA response (one-sided nominal *P* = 0.0016) and time to PSA progression (one-sided nominal *P* = 0.00092). In C1-C3, PD-L1 CPS was associated with PSA response (one-sided nominal *P* = 0.046) and time to PSA progression (one-sided nominal *P* = 0.021). In C1-C3, GEP was not significantly associated with response. In C1-C3, MSI was associated with PSA response (one-sided nominal *P* = 0.019). **Conclusions:** In this biomarker analysis from KEYNOTE-199 C1-C3, TMB and PD-L1 CPS were associated with better PSA response; however, small pt numbers limit definitive conclusions on ORR, DCR, and OS. Further evaluation of molecular biomarkers in pts with mCRPC treated with pembrolizumab is warranted. Clinical trial information: NCT02787005. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

5527 Poster Session (Board #108), Fri, 8:00 AM-11:00 AM

Association of BRCA alteration (alt) type with real-world (RW) outcomes to PARP inhibitors (PARPi) in patients (pts) with metastatic castrate-resistant prostate cancer (mCRPC). *First Author: Emmanuel S. Antonarakis, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD*

Background: Inactivating alts in *BRCA1/2* result in homologous recombination deficiency and are predictive of PARPi response in mCRPC. *BRCA* reversion mutations, which restore the protein function, are frequently observed in acquired resistance to PARPi. In tumors harboring homozygous gene deletions (*BRCA*del) reversions cannot develop; thus, we hypothesize that *BRCA*del pts may have prolonged benefit from PARPi compared to pts harboring other BRCA alterations. **Methods:** Pts were included from the Flatiron Health (FH)-Foundation Medicine (FMI) de-identified clinico-genomic database (CGDB). Inclusion criteria were diagnosis of mCRPC, treatment in the FH network and an FMI comprehensive genomic profiling result between 1/1/2011 - 9/30/2019. Time to therapy discontinuation (TTD) and overall survival (OS) from start of PARPi were estimated with Kaplan-Meier analysis and unadjusted/adjusted (age at PARPi initiation, line number, practice type) hazard ratios (HR/aHR) from Cox proportional hazards models adjusted for survival bias. **Results:** Out of 829 mCRPC cases, *BRCA1/2* alts were detected in 15 (1.8%) and 71 (8.6%) respectively, with 2 cases included in both groups. 26% of *BRCA*alts were *BRCA*del, 67% were coding mutations, and 7% were genomic rearrangements. 25 (28%) *BRCA*alt pts were treated with PARPi, 11/25 in the 1st or 2nd line setting including 43% of *BRCA*del and 44% of other *BRCA*alt cohorts. Median age at PARPi initiation was 70 yrs and 88% were treated in community practices. TTD was significantly longer in the *BRCA*del (n = 7) cohort vs. other *BRCA*alt cohort (n = 18) (22.7 vs. 9.2 months; HR: 0.16 [0.03-0.74]; aHR: 0.13 [0.02 – 0.92]) while a statistically nonsignificant difference in median OS was observed (31.5 vs. 11.9 months; HR: 0.20 [0.02-1.58]; aHR: 0.24 [0.02-3.15]). In comparison, no statistically significant difference in TTD was observed for *BRCA*del (n= 7) vs. other BRCAalts (n=19) pts treated with 1st line hormonal therapies (abiraterone or enzalutamide) (3.4 vs. 5.7 months; HR: 1.16 [0.45-2.98]; aHR: 0.72 [0.25-2.10]). Follow up analysis with more pts and somatic/germline status and zygosity of *BRCA*alts will be presented. **Conclusions:** These data suggest a differential benefit from PARPi therapy across *BRCA*alt subgroups. This observation may in part be explained by the inability to develop reversion mutations to restore BRCA function in tumors with *BRCA*del. Further studies are warranted to fully assess the association of *BRCA*alt type with outcomes to PARPi-based treatments. Research Sponsor: Foundation Medicine, Inc.

5528 Poster Session (Board #109), Fri, 8:00 AM-11:00 AM

Association of polymorphisms in androgen production, uptake, and conversion chain (APUC) genes with mortality of prostate cancer patients. *First Author: Sean Thomas McSweeney, University of Minnesota Medical Center, Minneapolis, MN*

Background: Genes involved in APUC may affect prognosis in PC. We tested the association of four SNPs involved in the APUC pathway: hydroxy-delta-5-steroid dehydrogenase, 3 beta-and steroid delta-isomerase 1 (*HSD3B1*), 5α reductase enzyme (*SRD5A*), and solute carrier organic ion (*SLCO2B1*) with all-cause and PC mortality 596 in the Atherosclerosis Risk in Communities (ARIC) study. **Methods:** Between 1987 & 2015 596 men were diagnosed with PC. Median age at diagnosis was 70 (range 53-86) years; 21% of all PC patients were African American. After diagnosis, follow-up was median 8.4 years (max 26.7 years) until PrC death (N = 60), death from any cause (N = 253), or end of 2015. SNPs were genotyped using the Affymetrix Genome-Wide Human SNP Array 6.0 and imputed to the 1000 Genomes Phase 3 reference panel. To examine survival, we used Kaplan-Meier curves and Cox proportional hazards regression. Hazard ratios (HR) and 95% confidence intervals (CI) were adjusted for age, field center, stage and grade at diagnosis. We also controlled for confounding by ancestry by adjusting for genetic principal components. The analyses were conducted in all PrCa patients and in Whites PrCa patients only. Polymorphisms tested included rs1047303 (A = > C, also called 1245C); rs523349 (C = > G); and rs1789693 (A = > T) and rs12422149 (G = > A), located in the aforementioned genes. **Results:** The A allele for *SLCO2B1* rs1789693 (A = > T) was significantly associated with an increased risk of PC mortality (versus T): multivariable-adjusted HRs (95%CI) were (2.06, 1.14-3.74; p = 0.02) and all-cause mortality (1.29, 1.00-1.66; p = 0.05) among Whites. The associations were similar when Whites and African-Americans were combined and when accounting for ancestry. The C allele for *HSD3B1* rs1047303 (C = > A) was not statistically significantly associated with either PC or all-cause mortality in the whole cohort (which included localized disease), although HRs were increased for men diagnosed with stage 4 disease (n = 35) in both additive and dominant models. For carriers of the C allele (gain of function) versus AA, HRs were 5.32 (1.16-24.33; p = 0.03) and 6.13 (1.51-24.86; p = 0.01) for PC and all-cause mortality, respectively. All associations with *SRDA2* (rs12422149) and *SLCO2B1* (rs12422149) were not significant. **Conclusions:** The gain of function allele in *HSD3B1* rs1047303 (1245C) was associated with increased PC and all-cause mortality in men diagnosed with metastatic PC, paralleling prior findings. Associations with *SLCO2B1* SNP rs1789693 require validation in larger studies. Research Sponsor: None.

5529 Poster Session (Board #110), Fri, 8:00 AM-11:00 AM

AR enhancer and locus genomic alterations as cell-free DNA biomarkers of primary resistance to AR-directed treatment of metastatic prostate cancer. *First Author: Chris Maher, Washington University in St. Louis, St. Louis, MO*

Background: Predicting primary resistance to androgen receptor (AR)-directed therapies is critical for personalizing treatment of metastatic prostate cancer (mPCa). Analyses of liquid biopsies are potential tools but remained underutilized due to limited sensitivity. We developed a cell-free DNA (cfDNA) assay (EnhanceAR-Seq) to monitor genomic alterations in mPCa including *AR* enhancer duplication, a resistance marker recently discovered in ~81% of mPCa patients. Here we show that applying EnhanceAR-Seq to plasma cfDNA to monitor alterations of *AR* gene and enhancer (*AR*/enhancer) predicted primary resistance with high sensitivity and outperformed the clinically validated CTC AR-V7 assay. **Methods:** Forty mPCa patients were prospectively enrolled at the Washington University School of Medicine Siteman Cancer Center with plasma cfDNA analyzed by EnhanceAR-Seq. Twenty-five of them also had the Oncotype DX AR-V7 Nucleus Detect CTC assay performed at a similar timepoint at the discretion of the treating oncologist. All patients received AR-directed therapy (eg. abiraterone, enzalutamide) and underwent standard-of-care clinical and laboratory follow-up. Primary resistance was defined as PSA progression, change of treatment or death within 4 months of treatment initiation, or radiographic progression within 6 months. **Results:** Median clinical follow up after diagnosis was 50 months. EnhanceAR-Seq detected alterations targeting *AR*/enhancer in 18 patients (45%), *TP53* in 8 patients (20%), and *PTEN* in 6 patients (15%). We found that *AR*/enhancer alterations (copy gain, tandem duplication, and point mutation) in cfDNA were strongly predictive of primary resistance to AR-directed therapy (PPV = 100%, Sens. = 89%). Our assay outperformed the CTC AR-V7 assay, which was positive in only two patients (PPV = 50%, Sens. = 6%). Furthermore, patients with *AR*/enhancer alterations had significantly worse progression-free survival (P = 0.0015; HR = 11.5) and overall survival (P = 0.0002; HR = 6.8). Finally, serial cell-free DNA analysis of 10 patients showed that *AR*/enhancer copy number gain was maintained or acquired in 5 of 6 AR-resistant cases, and neutrality maintained in 4 of 4 AR-sensitive cases. **Conclusions:** cfDNA-based *AR*/enhancer locus genomic alterations could potentially be used to predict primary resistance to AR-directed therapy with higher sensitivity than the clinically validated CTC AR-V7 assay, be used for serial timepoint monitoring and guiding personalized clinical decision-making. Research Sponsor: American Cancer Society and Siteman Cancer Center.

5530 Poster Session (Board #111), Fri, 8:00 AM-11:00 AM

Clinical analysis of the extracellular vesicle-fingerprint score blood test to refine the prediction of clinically significant prostate cancer and avoid prostate biopsy. *First Author: Adrian S. Fairey, University of Alberta, Edmonton, AB, Canada*

Background: The accuracy of the extracellular vesicle-fingerprint score (EV-FPS) test to predict clinically significant prostate cancer (PCa; Gleason grade (GG) ≥ 3) from indolent disease (GG ≤ 2) and avoid unnecessary prostate biopsies was determined at the point of prostate biopsy decision. **Methods:** Clinical data, health information, and blood samples were collected from a prospective validation cohort of 415 men, without prior PCa diagnosis, referred to urology clinics for prostate biopsy or transurethral prostate surgery (June 2014-Dec 2016). The patient's EV-FPS risk score was calculated by combining machine learning model-analyzed microflow cytometry data from EV biomarkers with logistic regression-analyzed patient-centric clinical features. The plasma-derived EV biomarkers were prostate-specific membrane antigen, polysialic acid and ghrelin-growth hormone receptor. The patient clinical features were; age, ethnicity, PCa family history, PSA levels, abnormal digital rectal examination (DRE) and prior negative prostate biopsy. Together, the biomarkers and clinical features provided specificity for clinically significant PCa. **Results:** The EV-FPS test identified clinically significant PCa patients with high accuracy (0.81 area under curve) at 95% sensitivity and 97% negative predictive value. Using a 7.85% probability cut-off after test validation; 95% of the patients with GG ≥ 3 would have been found before biopsy, 35% biopsies would have been avoided and diagnosis of GG ≥ 3 PCa would have been missed in only 5% of the cohort. **Conclusions:** This minimally invasive EV-FPS test accurately predicted clinically significant PCa in men with high EV-FPS risk scores, high PSA level and/or abnormal DRE. Therefore, men with low EV-FPS risk scores could potentially avoid unnecessary prostate biopsies. Clinical care cut-offs to calculate the number of biopsies that could have been avoided, and the percentage of GG ≥ 1 to GG ≥ 3 PCa that could have had a delayed diagnosis. Research Sponsor: Alberta Cancer Foundation, Other Foundation.

PCPTRC + EV-FPS cut-off	Biopsies		GG ≥ 1 PCa		GG ≥ 2 PCa		GG ≥ 3 PCa	
	Performed (%)	Avoided (%)	Found (%)	Missed (%)	Found (%)	Missed (%)	Found (%)	Missed (%)
0%	415 (100%)	0 (0%)	258 (100%)	0 (0%)	168 (100%)	0 (0%)	73 (100%)	0 (0%)
≥ 5%	384 (93%)	31 (7%)	248 (96%)	10 (4%)	164 (98%)	4 (2%)	73 (100%)	0 (0%)
≥ 7.5%	294 (71%)	121 (29%)	203 (79%)	55 (21%)	143 (85%)	25 (15%)	69 (95%)	4 (5%)
≥ 7.847%	271 (65%)	144 (35%)	190 (74%)	68 (26%)	139 (83%)	29 (17%)	69 (95%)	4 (5%)
≥ 10%	200 (48%)	215 (52%)	143 (55%)	115 (45%)	106 (63%)	62 (37%)	61 (84%)	12 (16%)

5531 Poster Session (Board #112), Fri, 8:00 AM-11:00 AM

Prevalence and tissue concordance of BRCA2 copy number loss evaluated by single-cell, shallow whole genome sequencing of circulating tumor cells (CTCs) in castration-resistant prostate cancer (CRPC). *First Author: Ethan Barnett, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Genomic studies have shown that up to 25% of prostate cancer tissue specimens harbor alterations in DNA Damage Repair (DDR) genes, which may sensitize the tumor to poly ADP-ribose polymerase inhibitors (PARPi). Trials evaluating PARPi in patients with DDR deficiencies have shown varied response rates and differences regarding which genomic alterations predict for sensitivity to these agents, with the majority of objective responses seen in BRCA2-altered tumors. These results highlight the need to develop biomarker assays which can predict benefit from PARPi therapy. Tissue and cell-free DNA (cfDNA) have been the most utilized sources of tumor material for analysis in this setting, but success rates of obtaining sufficient tumor for analysis from bone are low and detecting tumor-derived copy number variants (CNVs) in cfDNA is challenging. Circulating tumor cells (CTCs) represent an alternate source of genetic information, for which assays are available to isolate and sequence individual cells in a manner that eliminates background noise from stroma and healthy cells, while capturing inter-cellular heterogeneity. **Methods:** Blood samples, collected from 138 progressing metastatic CRPC patients within 30 days of a pre-treatment biopsy intended for sequencing using MSK-IMPACT, were sent to EPIC Sciences for CTC analysis. Detected CTCs underwent single cell, low pass whole genome sequencing. Prevalence and concordance of BRCA2 copy-loss, regardless of whether single copy or homozygous, was compared in matched tissue and CTC samples. **Results:** BRCA2 copy-loss was identified in 21% (23/108) and 50% (58/115) of successfully sequenced tissue and CTC samples, respectively. In the 58 patients with CTC-detected BRCA2 loss, BRCA2 loss was detected in 36% (220/565) of the sequenced CTCs, representing a median of 46% (range 4-100%) of CTCs found in each individual sample. When both sequencing assays were successful, BRCA2 loss was detected in CTCs in 84% (16/19) of the tissue-positive cases, whereas tissue sequencing detected BRCA2 loss in 35% (16/46) of CTC-positive cases. **Conclusions:** Data from this study supports the notion that single-cell CTC sequencing can detect BRCA2 copy-loss at a high frequency, including cases that were negative in tissue, while also characterizing inter-cellular heterogeneity. Further studies will investigate whether CTC BRCA2 copy-loss can predict the likelihood of response to PARPi. Research Sponsor: EPIC Sciences.

5532 Poster Session (Board #113), Fri, 8:00 AM-11:00 AM

Comparative effectiveness of systemic treatments for metastatic castration-sensitive prostate cancer: A parametric survival network meta-analysis of randomized controlled trials. *First Author: Lin Wang, Johns Hopkins School of Public Health, Baltimore, MD*

Background: Treatment decision-making for metastatic castration-sensitive prostate cancer (mCSPC) is complicated by the unclear comparative effectiveness and widely varying costs of competing strategies. Objective: To compare the effectiveness and safety of systemic treatments for mCSPC. **Methods:** We searched bibliographic databases, regulatory documents, and trial registries for randomized controlled trials testing active drugs added to androgen deprivation therapy (ADT) for mCSPC. We used Cochrane risk-of-bias tool (version 2) to assess trial quality and Bayesian network meta-analysis (NMA) to estimate the relative effects of competing treatments. In addition to combing published time-invariant hazard ratios (HRs), we reconstructed survival data from Kaplan Meier curves to enable parametric survival NMA that allows time-varying HR. **Results:** Seven trials with 7,236 patients were included comparing six treatments (Table). Risk of bias is a concern for trials with open label (N=4), missing data (N=3), or unprespecified analysis (N=3). Ordered from the most to the least effective, treatments significantly improving overall survival (OS) include abiraterone acetate, apalutamide, and docetaxel; treatments significantly improving radiographic progression-free survival (rPFS) include enzalutamide, abiraterone, apalutamide, and docetaxel. (see HRs in Table) Allowing time-varying HR produced similar treatment rankings. Serious adverse events (SAE) were substantially increased for docetaxel (odds ratio [OR] 104.17, 95% credible interval [CI] 24.85-1012.32) and slightly increased for abiraterone (OR 1.42, 95% CI 1.11-1.83). **Conclusions:** Abiraterone provided the largest OS benefit with slightly increased risk of SAE. Apalutamide offered comparable OS benefit with abiraterone without increasing SAE risk. Although enzalutamide delayed rPFS to the greatest extent, longer follow-up is needed to examine its OS benefit. Research Sponsor: None.

Treatment rankings based on overall survival and radiographic progression-free survival.

Treatment strategy (plus ADT)	HR of OS vs ADT (95% CI)	Median rank for OS	HR of rPFS vs ADT (95% CI)	Median rank for rPFS
Abiraterone acetate	0.62 (0.54-0.71)	1	0.45 (0.40-0.51)	2
Apalutamide	0.67 (0.51-0.88)	2	0.48 (0.39-0.59)	3
Docetaxel	0.80 (0.71-0.89)	3	0.68 (0.61-0.75)	4
Enzalutamide	0.81 (0.53-1.23)	4	0.39 (0.30-0.51)	1
Standard non-steroid antiandrogen (bicalutamide, nilutamide, or flutamide)	1.21 (0.74-1.97)	5	0.97 (0.70-1.35)	5

5533 Poster Session (Board #114), Fri, 8:00 AM-11:00 AM

Phase I study of a novel S1P inhibitor, NOX66, in combination with radiotherapy in patients with metastatic castration-resistant prostate cancer. *First Author: Paul L. de Souza, University of Western Sydney School of Medicine, Liverpool, Australia*

Background: NOX66 is a new formulation of the small molecule, idronoxil. The primary mechanism of action of idronoxil stems from its binding to the transmembrane enzyme ENOX2 expressed on cancer cells, resulting in reduced S1P and increased ceramide levels, thereby promoting apoptosis. Additional intracellular effects include the inhibition of DNA repair mechanisms. There is growing evidence that S1P is a promotor of tumour resistance to immune cell infiltration, highlighting NOX66's potential to modulate the immune response against cancer. **Methods:** This two-part phase 1b open-label study enrolled patients with late-stage progressive mCRPC. Part 1 was a dose-escalation safety assessment of three doses of NOX66 (400 mg, n = 4; 800 mg, n = 6 and 1200 mg, n = 15) administered daily for 14 days with radiation therapy (20 Gy) delivered in 5 fractionated doses to one or more symptomatic lesion/s. Part 2 was an expansion cohort with NOX66 at 1200 mg in conjunction with radiation therapy. The primary endpoint of safety was assessed by the frequency and grade of treatment-emergent adverse events (TEAEs). At 6 weeks, 3- and 6-month follow up, treatment response was assessed radiographically by RECIST1.1 and by PSA >50% reduction. **Results:** 25 patients received and completed treatment. TEAEs considered related to NOX66 alone were mild (Grade 1) cases of dry mouth and oral mucositis; mild (Grade 1) fatigue was considered related to both NOX66 and radiation. None of the 21 Grade ≥3 TEAEs were considered related to NOX66. At 6 months, of the 15 evaluable patients by RECIST1.1, 9 had SD and 1 had PR and these same patients had maintained this response from 3 months. Five of the 16 PSA-evaluable patients achieved a PSA response (61-98% PSA reduction) at 6 months, which again was maintained from 3 months. **Conclusions:** NOX66 in combination with low-dose radiation therapy was found to be safe and well tolerated with promising signals of durable efficacy in patients with late-stage mCRPC. Responses of lesions outside the radiation field are being reviewed. Clinical trial information: NCT03307629. Research Sponsor: Noxopharm Limited.

5534 Poster Session (Board #115), Fri, 8:00 AM-11:00 AM

Contrasting genomic profiles in post-systemic treatment metastatic sites (MET), pretreatment primary tumors (PT), and liquid biopsies (LB) of clinically advanced prostate cancer (PC). *First Author: Andrea Necchi, Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: Comprehensive genomic profiling (CGP) was done on pre-systemic treatment (pre) PT, post-treatment (post) MET sites and LB in PC to uncover differences in genomic alterations (GA) and potential impact on therapy selection. **Methods:** 1,294 PC tissues and 782 LB underwent hybrid-capture based CGP. PT biopsies and resections were compared with post-treatment MET biopsies from bone (BO), liver (LIV), lung (LU), brain (BN), lymph node (LN) and soft tissue (ST) sites and LB. TMB was determined on up to 1.1 Mbp of sequenced DNA for tumor samples. Tumor cell PD-L1 IHC was measured (Dako 22C3). **Results:** Differences in alteration frequencies between PT, MET and LB for selected genes are shown in the Table. *TMPRSS2:ERG* fusion frequencies were similar between PT and MET (35% vs 33%) but varied between MET sites (27% in BO and ST to 40% in LN). GA in *AR* were lowest in pre PT (2%) and highest in MET (24% in LU to 50% in LIV). BN had the highest GA/tumor (8) and the most *PTEN* GA. *BRCA2* GA frequency varied from 0% in BN to 15% in LI. Potential predictors of IO response included *CDK12* GA (16% in LU) and MSI high status (29% in BN). High PD-L1 expression was found in only two cases (LN) and low PD-L1 expression was relatively uncommon. *ERBB2* amplifications were increased in MET compared with PT. *RB1* GA were increased in LIV cases. LB GA had a similar increase in *AR* and *TP53* GA to MET and appeared to be a blend of MET site biopsies across alteration frequencies. **Conclusions:** CGP of PT, MET and LB in PC demonstrates differences most likely associated with exposure to systemic therapies. Differences identified in the MET GA landscape suggest that liquid biopsies may capture a broader range of therapeutic opportunities for PC patients. Research Sponsor: Foundation Medicine Inc.

	Pre	Post						
	PT	BO	LIV	LU	BN	LN	ST	LB
Cases	770	127	34	25	7	205	126	782
Median age (range)	64 (39-89+)	68 (44-89+)	69 (48-84)	70 (50-86)	75 (58-84)	68 (39-89+)	68 (44-89+)	71 (45-89+)
GA/sample	3.8	5.0	5.1	4.2	8.0	4.8	5.0	-
TMPRSS2:ERG	35%	27%	32%	32%	29%	40%	27%	-
AR	2%	31%	50%	24%	43%	33%	31%	32% (n = 290)
TP53	37%	41%	56%	28%	57%	50%	41%	50%
PTEN Copy Number Alterations	16%	25%	24%	28%	57%	33%	25%	-
PTEN Short Variants	6%	10%	15%	4%	29%	7%	10%	7%
BRCA2	9%	8%	15%	8%	0%	7%	8%	8%
ATM	6%	6%	0%	24%	0%	5%	6%	15% (n = 290)
PIK3CA	7%	6%	3%	8%	14%	6%	6%	5%
RB1	4%	9%	30%	0%	0%	5%	9%	5% (n-290)
CDK12	5%	10%	0%	16%	0%	5%	10%	4% (n = 290)
BRAF	4%	3%	6%	0%	0%	3%	3%	3%
ERBB2	0.6%	5%	3%	8%	0%	2%	5%	1%
MSI-High	2%	5%	7%	0%	29%	2%	5%	1% (n = 290)
Median TMB	1.3	2.5	2.5	2.5	7.5	2.5	2.5	-
TMB > 10 mut/Mb	5%	7%	9%	0%	43%	4%	7%	-
TMB > 20 mut/Mb	3%	4%	3%	0%	29%	2%	4%	-
PD-L1 IHC Low (> 1%) Positive	8%	3%	15%	13%	0%	4%	3%	-

5535 Poster Session (Board #116), Fri, 8:00 AM-11:00 AM

Molecular determinants of outcome for metastatic castration-sensitive prostate cancer (mCSPC) with addition of apalutamide (APA) or placebo (PBO) to androgen deprivation therapy (ADT) in TITAN. *First Author: Felix Y Feng, Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

Background: In TITAN, addition of APA to ADT improved radiographic progression-free survival (rPFS) and overall survival (OS) versus PBO plus ADT in patients (pts) with mCSPC. In this post hoc analysis, we performed transcriptome-wide profiling of tumor samples and assessed association of molecular subtypes with rPFS. **Methods:** The DECIPHER platform (Decipher Biosciences, Inc.) was used to assess gene expression in archival primary prostate tumors from TITAN. Samples were classified into high versus low to average risk of metastases (DECIPHER genomic classifier [GC] > 0.6 and ≤ 0.6, respectively), basal and luminal A/B (PAM50 classifier), and androgen receptor activity (AR-A) signature high and low. Associations between subtypes with rPFS were assessed with Cox proportional hazards model. **Results:** The biomarker population included 222 pts (APA, 110; PBO, 112). Benefit in rPFS from APA in the biomarker population (HR [95% CI]; p value; 0.49 [0.31-0.78]; 0.002) resembled that in the overall study population (0.49 [0.40-0.61]; < 0.0001). The majority of TITAN pts had GC high scores (n = 166, 75%). GC high risk subtype in the PBO group had poorer prognosis for rPFS than GC low to average risk subtype (median rPFS 18.2 mos for GC high vs not reached [NR] for GC low to average, 0.28 [0.11-0.69]; 0.006), but there was no difference in prognosis between high and low to average GC risk subtypes in the APA group (GC high NR vs GC low to average NR; 0.81 [0.35-1.89]; 0.625). Pts were further stratified based on basal/luminal and AR-A signatures. Basal (n = 112, 50%) and AR-A low (n = 96, 43%) subtypes, known to be nonresponsive to ADT, both showed significant benefit from APA vs PBO (0.30 [0.16-0.57]; < 0.001 and 0.25 [0.12-0.52]; < 0.001, respectively). The majority of AR-A low subtype (74%, 71/96) overlapped with basal subtype. Further conclusions for risk of rPFS in GC low, luminal, and AR-A high subtypes and OS across all subtypes will be assessed as more events occur. **Conclusions:** In TITAN, addition of APA to ADT improved rPFS for all subtypes of pts with mCSPC. APA overcame the poor prognosis of GC high risk subtype and prolonged rPFS in ADT-resistant AR-A low and basal molecular subtypes, suggesting APA is beneficial especially for the highest risk molecular subtypes. Clinical trial information: NCT02489318. Research Sponsor: Janssen Research & Development.

5536 Poster Session (Board #117), Fri, 8:00 AM-11:00 AM

Clinical, genetic, and pathologic determinants of prostate cancer brain metastasis. *First Author: Mira Patel, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Prostate cancer (PCa) brain metastasis (BM) is a rare event occurring in 0.16-0.63% of PCa patients. Current clinical data on this phenomenon is limited to small retrospective cohorts and our understanding of it is incomplete. We sought to identify clinical and molecular predictors of PCa BM in a large retrospective cohort treated at our institution. **Methods:** Men diagnosed with Pca from 1995-2017 with ≥6 months of follow-up were included. Data was collected on clinical and tumor characteristics at diagnosis, PCa treatment, brain and bone metastasis, and tumor genetic profile based on Integrated Mutation Profiling of Actionable Cancer Targets (IMPACT) analysis. Results were examined using Kyoto Encyclopedia of Genes and Genome (KEGG) pathway. Genes altered in ≥5% of patients were included. Time to brain metastasis (TTBM) and overall survival (OS) were analyzed with univariable (UVA) Fine-Gray competing risks regression and Cox proportional hazards. TTBM and OS were landmarked at 6 months after PCa diagnosis. False discovery rate (FDR) adjustment accounted for multiple comparisons. **Results:** 27,887 men met inclusion criteria; 74 developed BM. Clinical variables associated with increased hazard of TTBM in UVA were high-clinical and pathologic-* (p<.001) T stage, node-positive disease* (p<.001), primary* and total* Gleason (p<.001), receipt of abiraterone* (HR 52.51 (95% CI 7.1-389.8), p<.001), and receipt of leuprolide* (HR 3.0 (95% CI 1.7-5.4), p<.001). Tumor alterations associated with BM include mutations in BRCA2 (HR 2.94 (95% CI 1.1-8.0), p=.04), MYC (HR 3.41 (95% CI 1.2-9.5), p=.02), PTEN (HR 2.90 (95% CI 1.2-6.9), p=.02), RB1 (HR 3.09 (95% CI 1.2-8.0), p=.02), and pathways involving homologous recombination (HR 2.70 (95% CI 1.1-6.4), p=.02), Fanconi anemia* (HR 4.22 (95% CI 1.8-10.0), p<.001), Ras signaling* (HR 4.6 (95% CI 1.5-13.9), p=.006), mTOR signaling (HR 2.88 (95% CI 1.1-7.9), p=.04), VEGF signaling* (HR 3.60 (95% CI 1.5-8.8), p=.005), and GnRH signaling* genes (HR 3.93 (95% CI 1.6-9.6), p0.003). Variables associated with increased hazard of BM after FDR adjustment are denoted with an asterisk. Variables associated with reduced OS after FDR adjustment were neuroendocrine or blastoma histology, node-positive disease, high-T stage, high initial PSA, receipt of leuprolide, and alterations in AR, TP53, and CDK12 genes. **Conclusions:** PCa BM is significantly associated with high-stage and grade disease, receipt of androgen deprivation agents such as abiraterone and leuprolide, and alterations in the Fanconi anemia, Ras, VEGF, and GnRH pathways. Research Sponsor: None.

5537 Poster Session (Board #118), Fri, 8:00 AM-11:00 AM

Overall survival (OS) with docetaxel (D) vs novel hormonal therapy (NHT) with abiraterone (A) or enzalutamide (E) after a prior NHT in patients (Pts) with metastatic prostate cancer (mPC): Results from a real-world dataset. *First Author: Umang Swami, Huntsman Cancer Institute at the University of Utah, Salt Lake City, UT*

Background: NHT (A and E) are approved first-line (1L) treatment (Rx) for mPC. After progression on NHT, Rx include either alternate NHT or D. However, OS from a randomized trial comparing NHT vs D after progression on 1L NHT has not been reported. **Methods:** Pts data were extracted from the Flatiron Health EHR-derived de-identified database. Inclusion: diagnosis of mPC; 1L Rx with single agent A or E only, single-agent Rx with alternate NHT (E or A) or D in second line (2L). Exclusion: > 180 days between date of diagnosis of mPC and date of next visit to ensure Pts were actively engaged in care at data-providing site; Rx with NHT in non-metastatic setting, any prior exposure to D. OS was compared using Cox proportional hazards model stratified by Rx propensity score. Each Pts' probability of receiving D (rather than NHT) was modeled via a random forest based on Pts and disease characteristics which may drive treatment selection. These included pre-2L Rx ECOG scores, PSA, LDH, ALPH, Hb, age, ICD codes for liver metastasis, diabetes, neuropathy, and heart failure; insurance payer, year of start of 2L Rx, time on 1 L NHT, Gleason score, PSA at the original diagnosis of mPC. Subgroup analyses included 1L Rx duration < 12 mos. **Results:** 1165 Pts between 2/5/2013 to 9/27/2019 were eligible. Median follow up 8 mos (range 0.1-64.5). Median OS after 1L A was higher with E as compared to D (15.7 vs. 9.4 mos). Median OS after 1L E was higher with A as compared to D (13.3 vs. 9.7 mos) (table). Propensity distributions were overlapping among Rx arms and showed only modest imbalance. In 2L, D had a worse adjusted hazard ratio of 1.29 and 1.35 as compared to E and A respectively ($p < 0.05$). Similar results were seen with 1L Rx duration of < 12 mos ($p < 0.05$). **Conclusions:** These hypothesis-generating data provide real-world OS estimates with 2L D & NHT in mPC. In propensity-stratified analyses, mPC Pts who progressed on NHT had a worse OS with 2L D as compared to alternate NHT. Results were consistent in unadjusted analysis & subgroup analyses of 1L Rx < 12 mos. Results are subject to residual confounding and missingness. After prospective validation these data may aid in Rx sequencing, Pts counselling, and design of future clinical trials in this setting. Research Sponsor: None.

Propensity score adjusted OS analyses.

	A-->D vs E	E-->D vs A
Overall no. of Pts	206 vs 514	137 vs 308
HR; 95% CI, p-value	1.29; 1.04-1.60, 0.02	1.35; 1.03, 1.77, 0.03
No. of Pts with 1L <12 mos	172 vs 344	108 vs 192
HR; 95% CI, p-value	1.33; 1.07-1.65, 0.01	1.36; 1.01-1.82, 0.04

5538 Poster Session (Board #119), Fri, 8:00 AM-11:00 AM

Impact of olaparib vs physician's choice of new hormonal agent (pcNHA) on burden of pain in metastatic castration-resistant prostate cancer (mCRPC): PROfound. *First Author: Fred Saad, Centre Hospitalier de l'Université de Montréal/CRCHUM, Montreal, QC, Canada*

Background: In the Phase III PROfound study (NCT02987543) olaparib significantly improved radiographic progression-free survival (primary endpoint) vs pcNHA (enzalutamide or abiraterone) in patients (pts) with mCRPC and homologous recombination repair (HRR) gene alterations. In pts with alterations in *BRCA1*, *BRCA2* and/or *ATM* (cohort A), time to pain progression was also significantly improved by olaparib vs pcNHA. We report additional pain analyses evaluated in the overall study population (cohort A and B). **Methods:** Pts were randomized to olaparib tablets (300 mg bid; n=256) or pcNHA (n=131). Pts completed the Brief Pain Inventory-Short Form (BPI–SF) questionnaire (electronic administration) every 4 weeks up to 6 months after progression or treatment crossover. Responses were analysed to determine time to progression to worst pain, pain severity and first opiate use for cancer-related pain (Kaplan-Meier), and also pain interference in daily activity (mixed model for repeated measures). **Results:** 85% and 76% of olaparib pts were free of pain progression (worst pain item) compared with 75% and 51% in the pcNHA arm, respectively at 6 and 12 months. The proportion of pts without pain progression (overall pain severity) also favoured olaparib (Table). Median time to first opiate use was significantly prolonged in olaparib arm compared with pcNHA arm; 18 months for olaparib vs 9 months for pcNHA (Table). BPI-SF pain interference scores were also more favourable for olaparib than pcNHA; difference in overall adjusted mean change from baseline score −0.75 (95% CI: −1.14, −0.36) *P*=0.0002. Further pain burden results for cohort A will also be presented. **Conclusions:** Olaparib reduced the burden of pain and time to first opiate use in pts with mCRPC and HRR gene alterations vs pcNHA, demonstrating a clinical and symptomatic patient benefit. Clinical trial information: NCT02987543. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Time to pain progression and first opiate use (overall population).

	Endpoint	Events n (%)	6-month event free rate (%)	12-month event free rate (%)	Median (m)	HR (95% CI)	*P* value (nominal)
Time to progression in worst pain	olaparib (N=256)	32 (12.5)	85.2 74.7	76.3 50.5	NR NR	0.64 (0.35, 1.21)	0.149
	pcNHA (N=131)	16 (12.2)					
Time to progression in pain severity	olaparib (N=256)	24 (9.4)	88.7 81.5	81.0 65.2	NR NR	0.71 (0.35, 1.54)	0.411
	pcNHA (N=131)	11 (8.4)					
Time to first opiate use*	olaparib (n=175)	65 (37.1)	74.8 61.0	58.8 47.7	18.0 9.0	0.67 (0.46, 0.99)	0.023
	pcNHA (n=92)	44 (47.8)					

Overall questionnaire compliance rate: 92.6% olaparib; 93.1% pcNHA. *pts not on opiates at baseline

5539 Poster Session (Board #120), Fri, 8:00 AM-11:00 AM

Health-related quality of life (HRQoL) for olaparib versus enzalutamide or abiraterone in metastatic castration-resistant prostate cancer (mCRPC) with homologous recombination repair (HRR) gene alterations: PROfound. *First Author: Antoine Thiery-Vuillemin, Centre Hospitalier de Besancon, Besancon, France*

Background: In the randomized Phase III PROfound trial (NCT02987543), olaparib significantly prolonged radiographic progression-free survival compared with physician s choice of new hormonal agent (pcNHA, enzalutamide or abiraterone) in men with mCRPC and HRR gene alterations, whose disease had progressed on prior NHA. Olaparib significantly improved time to pain progression in Cohort A. We report additional patient reported outcome measures of HRQoL in the overall study population (Cohorts A+B). **Methods:** HRQoL was assessed in the overall study population using the Functional Assessment of Cancer Therapy-Prostate (FACT-P) questionnaire, comprising 5 subscales: physical wellbeing (PWB), functional wellbeing (FWB), emotional wellbeing, social wellbeing, and prostate cancer subscale (PCS). The Trial Outcome Index (TOI; PWB+FWB+PCS) and FACT Advanced Prostate Symptom Index (FAPSI-6: derived from 6 FACT-P items) were also calculated. Adjusted mean change and time to deterioration in scores were statistically analyzed. **Results:** Baseline FACT-P total score was similar for both treatment arms. FACT-P total and subscale scores during treatment were all higher for olaparib vs pcNHA, with clinically meaningful differences between treatment arms in the adjusted least square (LS) mean changes from baseline in all but FWB and FAPSI-6 (Table). The time to deterioration in FACT-P total and TOI, FAPSI-6, PWB and PCS scores favored olaparib but were not statistically significant, with hazard ratios ranging from 0.68 to 0.94. Further HRQoL results for cohort A will also be presented. **Conclusions:** Olaparib delayed deterioration in HRQoL scores vs pcNHA and was associated with better HRQoL functioning over time compared with pcNHA in men with mCRPC and HRR gene alterations. Clinical trial information: NCT02987543. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Comparison of change from baseline.

	LS means		
	Olaparib N = 162	**pcNHA N = 74**	**Difference in LS means**
FACT-P total	**-8.01**	**-14.67**	**6.67**
TOI	**-5.05**	**-12.21**	**7.16**
FAPSI-6	**-0.54**	**-2.92**	**2.38**
FWB*	**-1.94**	**-3.53**	**1.59**
PWB	**-2.10**	**-4.30**	**2.20**
PCS	**-0.99**	**-4.32**	**3.33**

*Olaparib n = 160. A clinically meaningful change was an increase (improvement) or decrease (deterioration) of ≥6 (FACT-P total), ≥5 (TOI), ≥3 (FAPSI-6, PCS), or ≥2 points (PWB, FWB)

5540 Poster Session (Board #121), Fri, 8:00 AM-11:00 AM

Radium-223 (Rad) and niraparib (Nira) treatment (tx) in castrate-resistant prostate cancer (CRPC) patients (pts) with and without prior chemotherapy (chemo). *First Author: William Kevin Kelly, Sidney Kimmel Cancer Center at Thomas Jefferson University, Philadelphia, PA*

Background: Despite multimodality txs such as surgery, radiotherapy, hormonal tx and chemo, metastatic CRPC (mCRPC) prognosis remains poor. Research suggests PARP-1 is a key regulator of androgen receptor (AR) signaling and transition to lethal CRPC. Nira is a safe, potent and selective PARP-1/2 inhibitor that has shown single agent clinical activity in CRPC, and Rad is an alpha particle emitter. Addition of PARP inhibition may further enhance the clinical benefit of Rad. Nira has a favorable safety profile however, data on safety, tolerability and efficacy of Nira plus radiotherapy is limited. We hypothesize that targeting the PARP-1/AR axis in combination with radiation is safe and will improve mCRPC management. **Methods:** This is a phase (ph) Ib dose finding study (NCT03076203) of pts with progressive mCRPC using Time-to-Event Continual Reassessment Method (TITE-CRM). The primary objective is to determine the optimum ph II dose of Nira plus Rad (55 kBq/kg of body weight) in pts with and without prior chemo. Secondary endpoints include PSA reduction at 12 weeks (wks) and radiographic progression-free survival at 6 months. Pts enrolled to one of three dose levels of Nira (100, 200, and 300 mg PO daily). After completing 6 cycles of Rad, pts continued on Nira alone until objective progression, tx intolerance or pt decision. TITE-CRM identifies the maximum tolerated dose (MTD) based on toxicities observed over 12 wks of tx. **Results:** Between Oct 2017 and Jan 2020, 30 pts were enrolled (15 per stratum). Median age was 70 years; ECOG performance status was 0. The MTD of Nira was 100 mg in the chemo-exposed arm and 200 mg in the chemo-naïve arm. 19 Grade ≥ 3 adverse events were possibly related to tx: lymphocyte count decrease (n = 4, 13%), neutrophil count decrease (n = 3, 10%), anemia (n = 3, 10%), hypertension (n = 3, 10%), platelet count decrease (n = 2, 7%), creatinine increase (n = 1, 3%), hydronephrosis (n = 1, 3%), nausea (n = 1, 3%), white blood cell count decrease (n = 1, 3%). Tx duration and PSA response are shown in the table. **Conclusions:** Nira plus Rad was determined to be safe and tolerable. The MTD of Nira was identified and is pending ph II investigation. Managed by: Prostate Cancer Clinical Trials Consortium; Funded by: Janssen Scientific Affairs and Bayer Healthcare Pharmaceuticals, Inc Clinical trial information: NCT03076203. Research Sponsor: Janssen Scientific Affairs, Pharmaceutical/Biotech Company.

Cohort	**Median Tx Duration (wks)**	**Proportion of Pts with ≥50% PSA Decline at 12 wks (%)**
100 mg Chemo-naïve (n = 3)	21	33
Chemo-exposed (n = 10)	18	0
200 mg Chemo-naïve (n = 7)	25	14
Chemo-exposed (n = 5)	15	0
300 mg Chemo-naïve (n = 5)	24	20
All Pts (n = 30)	19	10

5541 Poster Session (Board #122), Fri, 8:00 AM-11:00 AM

Prostate-specific antigen (PSA) kinetics in patients (pts) with advanced prostate cancer treated with apalutamide: Results from the TITAN and SPARTAN studies. *First Author: Kim N. Chi, BC Cancer and Vancouver Prostate Centre, Vancouver, BC, Canada*

Background: The phase III TITAN and SPARTAN studies demonstrated improved outcomes with the addition of apalutamide (APA) to androgen deprivation therapy (ADT); outcomes included prolonging overall survival and radiographic progression-free survival (rPFS) in metastatic castration-sensitive prostate cancer (mCSPC) in TITAN, and metastasis-free survival (MFS) in nonmetastatic castration-resistant PC (nmCRPC) in SPARTAN. A post hoc analysis of PSA kinetics in pts from both studies is reported. **Methods:** Baseline PSA at randomization, time to PSA nadir, and proportion of pts achieving a PSA decline of ≥ 90% (PSA90) and of pts achieving a PSA ≤ 0.2 ng/mL at 3 and 12 months and at any time after treatment in the APA arms of the TITAN and SPARTAN studies were evaluated. Within each study, rPFS/MFS were compared between pts achieving a PSA90 or PSA ≤ 0.2 ng/mL response vs not. **Results:** 525 TITAN pts and 806 SPARTAN pts treated with APA were included in the analysis. Median baseline PSA, time to PSA nadir, median PSA nadir, and maximum percentage changes from baseline PSA are shown in the table. PSA90 and confirmed PSA ≤ 0.2 ng/mL were evident as early as 3 months in both TITAN and SPARTAN, and percentage of confirmed response continued to increase at 12 months. Pts treated with APA who achieved PSA90 were at lower risk of rPFS events in TITAN and of MFS events in SPARTAN, with a hazard ratio (95% confidence interval) of 0.46 (0.321-0.653) and 0.36 (0.271-0.489) in each respective study (both $p < 0.0001$), compared with APA pts who did not achieve PSA90. Pts with confirmed PSA ≤ 0.2 ng/mL had similar rPFS and MFS benefits. **Conclusions:** Pts with advanced PC, whether mCSPC or nmCRPC, treated with APA + ADT demonstrated rapid PSA declines that continued over time. There was a high rate of pts with PSA90 and with PSA ≤ 0.2 ng/mL responses, with a majority of pts reaching PSA90 by 12 months. Pts achieving PSA90 and/or PSA nadir of ≤ 0.2 ng/mL had a prolonged rPFS and MFS in TITAN and SPARTAN, respectively. Clinical trial information: NCT02489318; NCT01946204. Research Sponsor: Janssen Research and Development.

	TITAN (mCSPC) N = 525	SPARTAN (nmCRPC) N = 806
Median baseline PSA, ng/mL	5.97	7.78
Time to PSA nadir (median), mo	5.55	7.36
Median PSA nadir, ng/mL	0.03	0.37
Maximum decrease from baseline (median), %	98	94
90% PSA rate, %		
3 mo	58	46
12 mo	71	61
Overall	72	62
Confirmed PSA ≤ 0.2 ng/mL, %		
3 mo	51	21
12 mo	64	35
Overall	67	38

5542 Poster Session (Board #123), Fri, 8:00 AM-11:00 AM

Safety and overall survival (OS) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) treated with radium-223 (Ra-223) plus subsequent taxane therapy. *First Author: Celestia S. Higano, Department of Medicine, University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA*

Background: Ra-223, a targeted alpha therapy, showed a survival benefit and favorable safety profile over 3 years' (yrs) follow-up in mCRPC pts (ALSYMPCA trial). REASSURE (NCT02141438) is a global, prospective, single-arm, observational study of long-term Ra-223 safety in routine clinical practice in mCRPC pts (planned 7-yr follow-up). **Methods:** This analysis, based on the second prespecified interim analysis (data cutoff 3-20-2019) of REASSURE (N = 1465), evaluated safety/OS in the pt subset that was chemotherapy-naïve at Ra-223 administration but received subsequent taxane therapy any time after Ra-223 completion. **Results:** 182 pts received taxane therapy after Ra-223. Most (58%) had unresected primary tumors, 69% had ≥6 metastases, 99% received prior systemic anticancer therapy (Table). 143 (79%) completed 5 or 6 Ra-223 injections. Subsequent anticancer therapies included docetaxel (95%), enzalutamide (25%), cabazitaxel (24%), abiraterone (12%), lutetium-177-prostate-specific membrane antigen (4%), and sipuleucel-T (1%). During/up to 30 days after taxane therapy, 15 pts (8%) had grade 3/4 hematologic adverse events: anemia (erythropenia) (n = 11, 6%), neutropenia (n = 3, 2%), and thrombocytopenia (n = 2, 1%). Median OS was 24.3 (95% CI: 20.9–27.5) months from Ra-223 initiation and 11.8 (95% CI: 10.6–14.1) months from subsequent taxane initiation. **Conclusions:** In this cohort where Ra-223 was integrated prior to taxane therapy, most pts received multiple subsequent anticancer therapies. It appears that sequencing of multiple treatment modalities with different mechanisms of action may contribute to improved OS. Taxane therapy in routine clinical practice in pts previously treated with Ra-223 had acceptable hematologic safety/tolerability profiles. Clinical trial information: NCT02141438. Research Sponsor: Bayer.

	N = 182
Median age, yrs	70
Eastern Cooperative Oncology Group performance status 0–1, n (%)	160 (88)
Median time, months, from:	
Initial diagnosis to CRPC (n = 85)	36
CRPC to study entry (n = 104)	11
Diagnosis of bone metastases to study entry (n = 133)	22
Extent of disease, n (%)	
< 6 lesions	43 (25)
6–20 lesions	85 (50)
> 20 lesions	26 (15)
Superscan	6 (4)
Median laboratory values	
Prostate-specific antigen, ng/mL	33
Alkaline phosphatase, U/L	106
Lactate dehydrogenase, U/L	228
Hemoglobin, g/dL	13
Prior anticancer therapies, n (%)	
Abiraterone acetate	95 (52)
Enzalutamide	66 (36)
Sipuleucel-T	22 (12)
Fractures, n (%)	11 (6)
OS from start of:	
Ra-223, months	24.3
Subsequent taxane, months	11.8

5543 Poster Session (Board #124), Fri, 8:00 AM-11:00 AM

KEYNOTE-199 cohorts (C) 4 and 5: Phase II study of pembrolizumab (pembro) plus enzalutamide (enza) for enza-resistant metastatic castration-resistant prostate cancer (mCRPC). *First Author: Christopher J. Hoimes, Duke Cancer Institute, Durham, NC*

Background: Initial evidence suggests activity of pembro + enza in patients (pts) resistant to enza. We present results from the multicohort phase II study KEYNOTE-199 (NCT02787005) in chemotherapy-naive pts with mCRPC treated with pembro + enza after progression with enza and who had RECIST-measurable (C4) or bone-predominant (C5) disease. **Methods:** Pts who did or did previously receive abiraterone and for whom enza treatment failed after clinically meaningful response received pembro 200 mg Q3W, with continuation of enza for up to 2 y or until progression, toxicity, or withdrawal. End point was ORR per RECIST v1.1 (C4) by blinded independent central review (primary); DOR (C4), time to PSA progression, rPFS, OS, and safety. **Results:** A total of126 pts (C4, 81; C5, 45) were treated. Median (range) PSA was 31 ng/mL (0.4-1667) in C4 and 19 ng/mL (1-1750) in C5.Median (range) time from enrollment to data cut off was 15 mo (7-21) in C4 and 19 mo (7-21) in C5. In C4, ORR (95% CI) was 12% (6-22; 2 CRs, 8 PRs) and median (range) DOR was 6 mo (3+ to 13); 60% of pts had DOR ≥6 mo. DCR (CR + PR + SD) was 51% in C4 and C5. Median (95% CI) time to PSA progression was 4 mo (4-4) in C4 and 4 mo (4-4) in C5. Median (95% CI) rPFS was 4 mo (3-6) for C4 and 4 mo (3-6) for C5; 12-mo rPFS rate was 17% in C4 and 23% in C5. Median (95% CI) OS was NR (16-NR) in C4 and 19 (14-NR) mo in C5; 12-mo OS rate was 70% in C4 and 75% in C5. Shorter median OS was more associated with prior enza treatment <6 mo than with prior enza treatment ≥6 mo. Liver metastasis was associated with shorter median OS however, median OS in visceral disease subgroups appeared longer than expected. Any-grade/grade ≥3 treatment-related AEs occurred in 75%/26% of pts in C4 and 69%/24% in C5. Two pts in C5 died of immune-related AEs (Miller Fisher syndrome and myasthenia gravis). Any-grade/grade 3/4 rash (regardless of relatedness) was higher than that in prior reports for individual agents (33%/6%). **Conclusions:** Pembro + enza after enza resistance had manageable safety and showed antitumor activity for RECIST-measurable and bone-predominant mCRPC. This combination is being evaluated in an ongoing phase III combination trial. Clinical trial information: NCT02787005. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

OS by Subgroup	C4+C5 (N=126)	
	Median OS, mo (95% CI)	OS at 12 mo, %
Visceral disease		
With liver	n=15 11 (6-NE)	40
Without liver	n=25 NR (6-NE)	59
None	n=86 NR (18-NE)	82
Prior enza use		
<6 mo	n=16 11 (5-16)	40
≥6 mo	n=110 NR (18-NE)	77

5544 Poster Session (Board #125), Fri, 8:00 AM-11:00 AM

Pembrolizumab (pembro) plus olaparib in patients (pts) with docetaxel-pretreated metastatic castration-resistant prostate cancer (mCRPC): KEYNOTE-365 cohort A efficacy, safety, and biomarker results. *First Author: Evan Y. Yu, University of Washington, Seattle, WA*

Background: Pembro + olaparib has shown antitumor activity and acceptable safety in docetaxel-pretreated pts with mCRPC enrolled in cohort A of the phase I/II KEYNOTE-365 study (NCT02861573). Updated results with new biomarker data are reported. **Methods:** Pts with docetaxel-pretreated mCRPC who progressed within 6 mo of screening received pembro 200 mg IV Q3W + olaparib 400-mg capsule or 300-mg tablet PO BID. Pts might have received 1 other chemotherapy and ≤2 second-generation androgen-receptor targeted therapies. Primary end points: PSA response rate (decrease ≥50% from baseline, confirmed by a second value ≥3 wks later), ORR per RECIST v1.1, and safety. Key secondary end points: DCR, DOR, rPFS, and OS. Biospecimens (eg, blood, tissue) were collected for biomarker analysis (tissue PD-L1 expression, androgen receptor variant 7 [AR-v7] expression in circulating tumor cells [CTCs], and a T-cell–inflamed gene expression profile [GEP]). ctDNA was analyzed by Guardant Health 360 (GH360) and Omni (GH Omni) assays. FFPE tissue was analyzed by FoundationOne CDx (F1CDx) assay. **Results:** 84 of 87 enrolled pts were treated; 48/84 (57.1%) had measurable disease. Median (range) time from enrollment to data cutoff was 3.6 mo (0.0-29.2) for all pts and 26.7 mo (21.2-29.2) for 41 pts with ≥27 wks' follow-up. Confirmed PSA response rate was 9% (95% CI, 3.5-16.8) in 82 pts with a baseline PSA assessment. Median time to PSA progression: 3.8 mo (95% CI, 2.9-4.4). In 24 pts with measurable disease and ≥27 wks' follow-up, ORR was 8.3% (95% CI, 1.0-27.0; 2 PRs) and DCR ≥6 mo was 20.8% (95% CI, 7.1-42.2). Median (range) DOR was NR (12.0+ to 21.4+ mo); 2 pts had DOR ≥12 mo. In all pts, median rPFS was 4.3 mo (95% CI, 3.4-7.7) and median OS was 14.4 mo (95% CI, 8.1-18.5). Grade ≥3 TRAEs occurred in 29 pts (35%); 2 pts died of TRAEs (1 myocardial infarction, 1 unknown). Overall, 26% had PD-L1$^+$ tumors (combined positive score ≥1). Of 31 pts with CTC data, 12.9% were AR-v7$^+$. No *BRCA1/2* mutation was detected by GH360 (n=42). Of 57 pts analyzed by GH Omni, 2 had *BRCA2* mutations, 1 had a *BRCA1* mutation, 4 had *ATM* mutations, 1 had a *CHEK1* mutation, and 6 had *CDK12* mutations. Of 49 pts analyzed by F1CDx, 4 had *BRCA* mutations; 1 pt had a copy number loss mutation not detected by ctDNA analysis. GEP was not associated with ORR or PSA response. **Conclusions:** Pembro + olaparib continued to show activity and acceptable safety in pts with docetaxel-pretreated mCRPC. A phase III study of this combination is ongoing (KEYLYNK-010, NCT03834519). Clinical trial information: NCT02861573. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

5545 Poster Session (Board #126), Fri, 8:00 AM-11:00 AM

Pembrolizumab (pembro) plus enzalutamide (enza) in patients (pts) with abiraterone acetate (abi)-pretreated metastatic castration-resistant prostate cancer (mCRPC): KEYNOTE-365 cohort C efficacy, safety, and biomarker results. *First Author: Henry Jacob Conter, University of Western Ontario, Brampton, ON, Canada*

Background: Pembro + enza (cohort C) has shown antitumor activity and acceptable safety in abi-pretreated pts with mCRPC in the phase I/II KEYNOTE-365 study (NCT02861573). Updated results with new biomarker data from cohort C are reported. **Methods:** Pts who became intolerant to or for whom ≥4 weeks of abi failed in the prechemotherapy mCRPC state and who progressed within 6 mo of screening were enrolled. Pts received pembro 200 mg IV Q3W + enza 160 mg/day orally. Primary end points were PSA response rate (PSA decrease ≥50%; confirmed by a second value ≥3 weeks later), ORR per RECIST v1.1 by blinded independent central review, and safety. Key secondary end points were DCR per RECIST v1.1 (CR+PR+SD or non-CR/non-PD ≥6 mo), DOR per RECIST v1.1, radiographic PFS (rPFS) per PCWG-modified RECIST v1.1, and OS. Biospecimens (eg, blood, tissue) were collected at baseline and during the study for biomarker analysis, including tissue PD-L1 expression, androgen receptor variant 7 (AR-v7) expression in circulating tumor cells (CTCs), and a T-cell-inflamed gene expression profile (GEP). **Results:** Of 103 enrolled pts, 102 were treated; 39% of treated pts had measurable disease. Median (range) time from enrollment to data cutoff was 19.1 mo (1.1-28.8) for all pts and 21.4 mo (15.1-28.8) for pts with ≥27 wks' follow-up (n=69). Confirmed PSA response rate was 22% in 101 pts with a baseline PSA assessment. Median time to PSA progression was 3.5 mo (95% CI, 2.9-4.0). In pts with measurable disease and ≥27 wks' follow-up (n=25), confirmed ORR was 12% (2 CRs, 1 PR) and DCR was 32%. Median DOR was not reached (range, 0.0+ to 24.4+ mo); 2 pts had a response for ≥6 mo. In all pts, median (95% CI) rPFS was 6.1 mo (4.4-6.5) and median OS was 20.4 mo (15.5-NR). At 6 mo, rPFS rate was 55.1% and OS rate was 88.2%. Treatment-related AEs occurred in 92 pts (90%); most frequent (≥20%) were fatigue (38%), nausea (22%), and rash (20%). Grade 3-5 treatment-related AEs occurred in 40 pts (39%). Three pts died of AEs (1 AE was treatment related [cause unknown]). Of all pts, 29% had PD-L1$^+$ tumors (combined positive score ≥1). Of 51 pts with AR-v7 data, 13.7% were AR-v7$^+$ and 86.3% were AR-v7$^-$. GEP was not significantly associated with ORR or PSA response. **Conclusions:** Pembro + enza continued to show activity in pts with abi-pretreated mCRPC. Safety of the combination was consistent with the known profiles of pembro and enza. A phase III study of this combination is ongoing (KEYNOTE-641, NCT03834493). Clinical trial information: NCT02861573. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

5546 Poster Session (Board #127), Fri, 8:00 AM-11:00 AM

Use of plasma androgen receptor (AR) testing to optimize docetaxel chemotherapy in castration-resistant prostate cancer (CRPC): A multicenter biomarker study. *First Author: Vincenza Conteduca, IRCCS-IRST (Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori), Meldola, Italy*

Background: Plasma *AR* status has been identified as a potential biomarker of response in CRPC patients receiving docetaxel or the *AR*-targeted therapies abiraterone or enzalutamide. However, the relevance of plasma *AR* in the overall management of CRPC patients (pts) receiving docetaxel at different dose due to the toxicity profiles and physician-patient preferences is unknown. **Methods:** This was a multi-institution study of associations between baseline plasma *AR*-copy-number status assessed by droplet digital PCR and outcome in 325 CRPC pts. Between September 2011 and July 2019 pts started treatment with docetaxel administered at standard regimen 75mg/m^2 every three weeks or adapted regimen (75-80% of standard recommended dose or 30mg/m^2 weekly administration) at the discretion of the treating physician. Patients were assigned randomly into 2 sets with a ratio 2:1 to either training (n=217) and internal validation (n=108) cohorts. **Results:** In our study, adapted regimen of docetaxel was administered in 68 (31.3%) and 35 (32.4%) of training and validation cohorts, respectively. Based on plasma *AR* status, 67 (30.9%) and 39 (36.1%) validation and training set pts were classified as *AR* gain, respectively. In men treated with standard docetaxel regimen, no difference in progression-free/overall survival (PFS/OS) was seen between plasma *AR* normal and gain in both cohorts. In patients treated with adapted docetaxel regimen, we observed a significantly shorter median PFS (3.9 vs. 6.4 months, HR 4.77, 95%CI 1.48-3.80, p=0.0003) and median OS (11.2 vs. 20.4 months, HR 2.87, 95%CI 1.73-2.13, p=0.0008) in the training cohort. This finding was confirmed in the validation cohort (median PFS: 4.8 vs. 7.4 months, HR 2.54, 95%CI 1.40-4.58, p=0.005, and median OS: 11.8 vs. 26.4 months, HR 5.00, 95%CI 2.59-9.65, p<0.0001). In addition, *AR*-gained patients were less likely than *AR* normal to have a PSA decline when receiving an adapted regimen in both cohorts (p=0.010 e p=0.003, respectively). **Conclusions:** This study suggests that plasma *AR* may improve clinical decision making in choosing not only between *AR*-directed therapies and taxanes, but also between adapted and standard regimen of docetaxel in first- and subsequent-therapy lines, providing promising clinical implications to select the proper timing and dose of docetaxel. Prospective trials to validate these findings are warranted. Research Sponsor: None.

5547 Poster Session (Board #128), Fri, 8:00 AM-11:00 AM

Efficacy of enzalutamide (ENZA) + androgen deprivation therapy (ADT) in metastatic hormone-sensitive prostate cancer (mHSPC) by pattern of metastatic spread: ARCHES *post hoc* analyses. *First Author: Neal D. Shore, Carolina Urologic Research Center, Myrtle Beach, SC*

Background: ENZA + ADT significantly reduced the risk of radiographic progression or death in men with mHSPC (NCT02677896). Here, we assess how pattern of metastatic spread impacts the efficacy of ENZA + ADT in patients enrolled in ARCHES. **Methods:** Patients with mHSPC were randomized 1:1 to ENZA (160 mg/day) + ADT or placebo (PBO) + ADT, stratified by disease volume and prior docetaxel treatment. The primary endpoint was radiographic progression-free survival (rPFS). Secondary endpoints included time to prostate-specific antigen (PSA) progression, time to first symptomatic skeletal event (SSE), time to castration resistance, and time to initiation of new antineoplastic therapy. *Post hoc* analyses were performed by pattern of metastatic spread at study entry. **Results:** Of the overall population with known metastases at screening (n=1146), the largest patient subgroups were those with bone metastases only (n=513) and those with bone and soft-tissue metastases only (n=351); there were fewer M0 patients or patients with soft-tissue metastases only (n=154) and patients with visceral ± bone metastases (n=128). ENZA + ADT reduced the risk of rPFS and other secondary endpoint measures versus PBO + ADT across all subgroups, with greater relative efficacy observed in patients without visceral metastases (Table). **Conclusions:** ENZA + ADT provides improvements in rPFS and other secondary endpoints versus PBO + ADT in patients with mHSPC regardless of pattern of metastatic spread, particularly in patients without visceral metastases. These results highlight the importance of patient/physician discussion regarding the use of ENZA in the treatment of mHSPC. Clinical trial information: NCT02677896. Research Sponsor: This study was funded by Astellas Pharma Inc. and Pfizer Inc., the co-developers of enzalutamide. Medical writing and editorial assistance were provided by Lianne Young, BSc (Hons), and Jane Beck from Complete HealthVizion, funded by the study sponsors.

Endpoint, HR (95% CI)	Bone only (n=268;[b] n=245[c])	Bone and soft tissue only (n=164;[b] n=187[c])	M0[a] or soft tissue only (n=74;[b] n=80[c])	Visceral ± bone (n=64;[b] n=64[c])
rPFS	0.33 (0.22, 0.49)	0.31 (0.21, 0.47)	0.43 (0.16, 1.20)	0.94 (0.51, 1.73)
Time to PSA progression	0.12 (0.07, 0.22)	0.24 (0.15, 0.39)	0.07 (0.01, 0.54)	0.39 (0.17, 0.90)
Time to first SSE	0.51 (0.27, 0.96)	0.45 (0.22, 0.92)	NE (0.00, NR)	0.45 (0.11, 1.81)
Time to castration resistance	0.25 (0.17, 0.36)	0.26 (0.18, 0.39)	0.33 (0.13, 0.82)	0.49 (0.26, 0.92)
Time to new antineoplastic therapy	0.31 (0.19, 0.49)	0.16 (0.08, 0.33)	0.31 (0.07, 1.52)	0.68 (0.28, 1.61)

[a]Assessed as M0 by independent central review after investigator assessment as M1 at study entry; [b]ENZA + ADT; [c]PBO + ADT NE, not estimable; NR, not reached

5548 Poster Session (Board #129), Fri, 8:00 AM-11:00 AM

Prognostic markers for overall survival and outcome to LuPSMA radionuclide treatment in patients with metastatic castration-resistant prostate cancer. *First Author: Andrei Gafita, University of California, Los Angeles, CA*

Background: The aim of this international multicenter retrospective analysis was to identify prognostic markers for the clinical outcome in late-stage mCRPC patients treated with ^{177}Lutetium-prostate-specific membrane antigen (LuPSMA) radionuclide treatment. **Methods:** Patients with progressive mCRPC treated with LuPSMA at six centers in Germany, USA, and Australia were considered for inclusion. Eligible patients had 24 predefined, pretherapeutic covariates (demographics, prior mCRPC treatments, and PSMA PET/CT derived parameters) and survival data available. Endpoints included overall survival (OS) and PSA progression-free survival (PSA-PFS). Covariates were tested using univariate and mulitvariate proportional hazards regression Cox models. **Results:** 267/414 (64%) patients met inclusion criteria and were analyzed. 113 patients participated in clinical trials (ACTRN12615000912583, NCT03042312), while 154 were enrolled in compassionate-access programs. After a median follow-up of 22.5 months, median OS was 13.0 months (95%CI 11.6-14.4); 83% of the patients died. Median PSA-PFS was 4.0 months (95%CI 3.2-4.7). In the multivariate analysis, factors associated with shorter OS were: shorter time since diagnosis of prostate cancer (HR=2.04; p=0.002), lower number of prior systemic therapies (≤3; HR=1.56; p=0.006), prior exposure to chemotherapy (HR=1.42; p=0.05), lower hemoglobin levels (HR=1.13; p=0.002), higher number of lesions (≥20: HR=1.53; p=0.009), multiple sites of metastases (bone/LN only vs. bone + LN; HR=1.39; p=0.03) and visceral involvement (M1c) (HR=1.45; p=0.01). Factors associated with longer PSA-PFS were: longer time since diagnosis of prostate cancer (HR=0.44; p<0.001), higher hemoglobin levels (HR=0.32; p=0.03), presence of pelvic lymph nodes (LN) metastasis (N1) (HR=0.68; p=0.01), no distant lymph node metastases (M1a) (HR=0.66; p=0.01), no skeleton involvement (HR=0.44; p=0.01), no visceral metastases (M1c) (HR=0.51; p<0.001), higher PSMA-positive tumor volume (HR=0.87; p=0.04), and higher SUVmean (HR=0.94; p=0.002). **Conclusions:** This retrospective analysis identified prognostic factors for survival and treatment response to LuPSMA. Along with the conventional risk factors in mCRPC, PSMA PET/CT can be a useful tool for stratifying patients and guide patient's selection for LuPSMA radionuclide treatment. Research Sponsor: Prostate Cancer Foundation.

5549 Poster Session (Board #130), Fri, 8:00 AM-11:00 AM

Overall survival after ^{177}Lu-PSMA-617 molecular radiotherapy in patients with metastatic castrate-resistant prostate cancer: Post-hoc analysis of a prospective phase II trial. *First Author: Jeremie Calais, University of California, Los Angeles, CA*

Background: This was an open-label randomized prospective bi-centric single-arm phase II clinical trial of ^{177}Lu-PSMA-617 molecular radiotherapy in patients with progressive metastatic castrate-resistant prostate cancer (mCRPC) conducted at University of California Los Angeles (USA) and Excel Diagnostics & Nuclear Oncology Center (Houston, TX, USA) (NCT03042312). The study was investigator-initiated under an investigational new drug approval protocol (IND#133661) with authorization of charging for investigational drug (cost-recovery, Title 21 CFR 312.8). We report here the post-hoc analysis of overall survival (OS) in a single-study site cohort (UCLA). **Methods:** Patients with progressive mCRPC (biochemical, radiographic, or clinical) after ≥1 novel androgen axis drug (NAAD), either chemotherapy (CTX) naïve or post-CTX, with sufficient bone marrow reserve, normal kidney function, and sufficient PSMA-target expression by PET were eligible. Patients received up to 4 cycles of ^{177}Lu-PSMA-617 every 8±1 weeks and were randomized into 2 treatment activities groups (6.0 or 7.4 GBq). Efficacy was defined as serum PSA decline of ≥50% from baseline and served as primary endpoint (hypothesis: ≥40% of responders after 2 cycles). **Results:** 43 patients were randomized to the 6.0 GBq (n= 14) and 7.4 GBq (n=29) treatment arms. 11/43 (26%) were CTX naïve while 10/43 (23%), 12/43 (28%), 5/43 (12%) and 5/43 (12%) had received 1, 2, 3 or 4 CTX regimens. Median baseline PSA was 29.2 ng/ml (mean 228.8, range 0.5-2082.6). 21/43 (49%) completed 4 cycles of ^{177}Lu-PSMA-617 whereas 4/43 (9%), 13/43 (30%) and 5/43 (12%) underwent 1, 2 and 3 cycles. PSA decline of ≥50% was observed in 11/43 of patients (26%) after 2 cycles and in 16/43 (37%) at any time (best PSA response). 9/43 (21%) had a PSA decline of ≥90% and 23/43 (53%) had any PSA decline (>0%). After a median follow-up of 19.5 months the median OS was 14.8, 15.7 and 13.5 months in the whole cohort, the 6.0 GBq and 7.4 GBq treatment arms, respectively (p=0.68). Patients showing a PSA decline of ≥50% after 2 cycles and at any time had a longer OS: median 20.1 months vs. 13.6 (p=0.091) and 20.1 vs. 11.6 (p=0.002), respectively. **Conclusions:** In this post-hoc analysis of a single-site cohort of 43 patients included in a prospective phase II trial the median OS after 177Lu-PSMA-617 molecular radiotherapy in patients with progressive mCRPC was 14.8 months. There was no difference of efficacy between the 6.0 GBq and 7.4 GBq treatment arms. Clinical trial information: NCT03042312. Research Sponsor: None.

5550 Poster Session (Board #131), Fri, 8:00 AM-11:00 AM

Pembrolizumab (pembro) plus docetaxel and prednisone in patients (pts) with abiraterone acetate (abi) or enzalutamide (enza)-pretreated metastatic castration-resistant prostate cancer (mCRPC): KEYNOTE-365 cohort B efficacy, safety and, biomarker results. *First Author: Srikala S. Sridhar, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Pembro + docetaxel and prednisone (cohort B) has shown anti-tumor activity in pts with mCRPC in the phase I/II KEYNOTE-365 study (NCT02861573). Updated efficacy and safety and new biomarker data from cohort B are reported. **Methods:** Pts who received at least 4 wk of abi or enza in the prechemotherapy mCRPC setting and whose disease progressed within 6 mo of screening were eligible. Pts received pembro 200 mg IV + docetaxel 75 mg/m^2 IV Q3W and prednisone 5 mg orally twice daily. Primary end points were PSA response rate (PSA decrease ≥50%; confirmed by a second value ≥3 weeks later), ORR per RECIST v1.1 by blinded independent central review, and safety. Key secondary end points were DCR per RECIST v1.1 (CR+PR+SD or non-CR/non-PD ≥6 mo), DOR per RECIST v1.1, radiographic PFS (rPFS) per PCWG-modified RECIST, and OS. Biospecimens (blood, tissue) were collected for biomarker analysis, including tissue PD-L1 expression, androgen receptor variant 7 (AR-v7) expression in circulating tumor cells, and a T-cell-inflamed gene expression profile (GEP). **Results:** Of 105 enrolled pts, 104 were treated, and 50% had measurable disease. Median (range) time from enrollment to data cutoff was 19.9 mo (1.4-27.8) for all pts and 21.8 mo (17.9-27.8) for pts with ≥27 wks follow-up (n=72). Confirmed PSA response rate was 28% in 103 pts with a baseline PSA assessment. Median time to PSA progression was 6.2 mo (95% CI, 3.7-7.4). In pts with measurable disease and ≥27 wks follow-up (n=39), ORR was 18% (7/39, all PRs) and DCR was 51%. Median DOR was 6.7 mo (range, 3.4-9.0+ [+ indicates ongoing responder]); 5 pts had a response for ≥6 mo. In all pts, median rPFS was 8.3 mo (95% CI, 7.6-10.1) and OS was 20.4 mo (16.9-NR). At 6 mo, the rPFS rate was 72.8% and OS rate was 95.3%. Treatment-related AEs (TRAEs) occurred in 96% of all pts; most frequent were alopecia (39%), diarrhea (38%), and fatigue (38%). Grade 3-5 TRAEs occurred in 40% of pts; 2 pts died of TRAEs (pneumonitis). Overall, 24% of pts were PD-L1$^+$ (combined positive score ≥1). Of 57 pts with AR-v7 data, 17.5% were AR-v7$^+$, 77% were AR-v7$^-$, and 5% were undetermined. GEP was not significantly associated with ORR or PSA response. **Conclusions:** Pembro + docetaxel and prednisone showed activity in pts with abi or enza-pretreated mCRPC. Safety of the combination was consistent with the known profiles of the individual agents. A phase 3 study of this combination is ongoing (KEYNOTE-921, NCT03834506). Clinical trial information: NCT02861573. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

5551 Poster Session (Board #132), Fri, 8:00 AM-11:00 AM

Prostate cancer biomarker enrichment and treatment selection (PC-BETS) study: A Canadian cancer trials group phase II umbrella trial for metastatic castration-resistant prostate cancer (mCRPC). *First Author: Kim N. Chi, BC Cancer and Vancouver Prostate Centre, Vancouver, BC, Canada*

Background: Genomic characterization of mCRPC has identified commonly occurring alterations but also recurrently mutated genes at much lower frequencies. To efficiently evaluate anti-tumor activity of novel targeted therapies in mCRPC patients (pts) we initiated an umbrella trial using circulating tumour DNA (ctDNA) to enrich accrual for cancers with alterations that may predict response. **Methods:** mCRPC pts that have progressed after treatment with a next generation AR-pathway inhibitor (ARPI) were enrolled to this multi-center, multi-arm, 2-stage phase II trial. Plasma cell-free DNA was subjected to targeted sequencing and pts allocated to a treatment arm by a Tumor Board (TB) based on *a priori* criteria (biomarker positive, BM+) or by randomization if biomarker negative (BM-). Primary objective was to determine the clinical benefit rate (CBR: PSA decline ≥50% (PSA50), CR/PR, or stable disease ≥12 weeks). We report on 1st-stage activity of arms evaluating inhibitors of CDK4/6 (palbociclib), WEE1 kinase (adavosertib), cMET (savolitinib) and the AR inhibitor darolutamide. Additional planned arms include inhibitors of AKT (ipatasertib), Polo-like Kinase 4 (CFI-400945), immune checkpoints (durvalumab, tremelimumab) and carboplatin. **Results:** 250 pts were screened from two sequential trials over 29 months at 11 centers. Median time from blood draw to TB decision was 35 days. 169 pts (68%) had detectable ctDNA (≥1%) with a mean ctDNA fraction of 24% (range 1-95%). Commonly detected genomic alterations involved AR (49% gain, 24% mutation), TP53 (49%), PTEN/PI3K pathway (35%), DNA repair (23%: mismatch repair (5%), BRCA2 (8%), ATM (3%), CDK12 (5%), other (2%)) and CTNNB1/APC (14%). To date, 46 BM+ pts and 37 BM- patients were enrolled: median age 70 years (53-88), 100% had prior ARPI, 45% had prior docetaxel, 17% with visceral metastases. Accrual and CBR are presented in table. Adverse events were as expected. **Conclusions:** Prospective centralized screening of ctDNA to stratify mCRPC pts into a precision oncology trial is feasible. Activity was seen in 4 of 7 evaluable cohorts with darolutamide and adavosertib, meeting the threshold for expansion of these arms. Clinical trial information: NCT03385655, NCT02905318. Research Sponsor: Canadian Cancer Clinical Trials Network, Other Foundation, Pharmaceutical/Biotech Company, Canadian Cancer Society.

	Palbociclib		Adavosertib		Savolitinib		Darolutamide		
	BM+	BM-	BM+	BM-	BM+	BM-	BM+ AR gain	BM+ AR mut	BM-
Pts Enrolled (N)	6	10	10	9	3	9	17	10	9
Pts with CBR (N)	0	0	0	1	0	0	2	3	1

5552 Poster Session (Board #133), Fri, 8:00 AM-11:00 AM

First-in-human phase I study of HPN424, a tri-specific half-life extended PSMA-targeting T-cell engager in patients with metastatic castration-resistant prostate cancer (mCRPC). *First Author: Johanna C. Bendell, Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN*

Background: HPN424 is a first-in-class, prostate-specific membrane antigen (PSMA)-targeting T-cell engager designed as a small, globular protein to enable efficient solid-tumor penetration with prolonged half-life. HPN424 is derived from the TriTAC platform (Tri-specific T-Cell-Activating Construct) and engineered with three binding domains: anti-PSMA for tumor cell engagement, anti-albumin for half-life extension and anti-CD3 for T-cell engagement. **Methods:** This Ph I study is evaluating HPN424 in progressing mCRPC patients (pts) who have received >2 prior systemic therapies. Primary endpoints are safety, tolerability and determination of MTD/RP2D. Secondary objectives are pharmacokinetics (PK), pharmacodynamics, immunogenicity, and preliminary anti-tumor activity. HPN424 is administered IV once weekly. Tumor assessments include PSA, CT, and bone scans every 9 weeks. **Results:** As of 1/17/20, 27 pts were dosed in 8 cohorts ranging from 1.3 to 72ng/kg. Pts received a median of 6 prior systemic regimens, including >1 novel AR therapy, and 59% received prior chemotherapy for mCRPC. Median PSA at baseline was 251 ng/mL (range: 0.05 – 5000). No DLTs have been observed. The most common grade >3 TRAEs were cytokine release syndrome (CRS) (3 pts) and transient elevated liver transaminases (2 pts) that occurred concurrently with CRS. All CRS events resolved and pts were successfully re-treated. Short-term steroid premedication was effective in limiting CRS and allowing long-term weekly treatment. HPN424 demonstrated dose proportional increase in Cmax and AUC with a geometric mean T1/2 of 30.5 hours. Dose-dependent, transient increases in peripheral cytokine and chemokine levels were observed. Reduction in circulating tumor cells (CTCs) was seen in 11 of 19 pts with measurable CTC at baseline. Six pts had PSA decreases from baseline ranging from -3.8% to -76%, including 2 pts with PSA decline ≥50%. Ten of 20 pts (50%) with > 18 weeks follow-up remained on study beyond week 18 and includes 8 pts on study > 24 weeks. **Conclusions:** HPN424 represents a novel half-life extended PSMA-targeting T-cell engager that can be safely administered once weekly. AEs have been transient and manageable. Cytokine increases indicate T-cell activation. CTC reductions in subset of pts suggest target engagement. Early signs of clinical activity include PSA reductions and time on study, including 8 pts on study > 24 weeks. Dose escalation is ongoing, including exploration of step dosing. Clinical trial information: NCT03577028. Research Sponsor: Harpoon Therapeutics.

5553 Poster Session (Board #134), Fri, 8:00 AM-11:00 AM

Primary analysis of a phase II study of metastasis-directed ablative therapy to PSMA (^{18}F-DCFPyL) PET-MR/CT defined oligorecurrent prostate cancer. *First Author: Rachel Glicksman, Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada*

Background: Despite maximal local therapies (MLT) (radical prostatectomy followed by radiotherapy [RT]), 20-30% of men will progress to incurable prostate cancer (PCa). Most recurrences in this scenario are characterized by rise in PSA with negative bone scan (BS) and computed tomography (CT). We conducted a phase II trial for men with rising PSA after MLT using ^{18}F-DCFPyL (PSMA) PET-MR/CT followed by metastasis-directed therapy (MDT) to PET positive foci. We report the results of our primary analysis. **Methods:** Patients with rising PSA (0.4-3.0 ng/mL) after MLT, negative BS/CT and no prior salvage ADT were eligible. All patients underwent PSMA PET-MR and PET-CT. Those with limited disease burden amenable to MDT underwent either stereotactic ablative RT (SABR) or surgery (lymph node dissection). No ADT was used. The primary endpoint was biochemical response rate (complete [undetectable PSA] or partial [PSA decline ≥50% from baseline]) following MDT. A Simon's two-stage study design was employed. Estimated time of delay in salvage ADT was calculated using the Kaplan-Meier method. Toxicity was prospectively recorded (CTCAE v4.0). **Results:** After a median of 63 months (range 3-180) post MLT, 72 patients underwent PSMA PET-MR/CT with median PSA 0.98 ng/mL (range 0.4-3.1). Sixteen patients had negative and 56 had positive PET-MR/CT scans, of which 37 (51%) were amenable to MDT. The median number of treated lesions was 2 (range 1-5). Of the treated patients, 30 (81%) had miT0N1M0 disease, 2 (5.5%) had miT0N1M1a, 2 (5.5%) had miT0N0M1a and 3 (8%) had miT0N0M1b. Twenty-seven patients underwent SABR (median 30 Gy in 3 fractions) and 10 had surgery. At a median of 11 months (range 1-29) post MDT, 8 patients (22%) had complete (CR) and 14 (38%) had partial (PR) responses. Among the 8 CRs, 5 had surgery and 3 had SABR; of the 14 PRs, 2 had surgery and 12 had SABR. The estimated median delay in salvage ADT for the entire cohort, PR and CR subgroups was 13 months (IQR 8-20), 16 months (IQR 13-20) and 30 months (IQR not reached), respectively. Two grade 2+ toxicities were observed, both in surgical patients: deep venous thrombosis and ureteric injury requiring stent placement. **Conclusions:** ^{18}F-DCFPyL PET-MR/CT has high detection rates (78%) in men with rising PSA after MLT. We observed a favorable therapeutic index with MDT (60% response rate) for patients with metachronous PSMA-unveiled oligometastatic PCa following MLT. Phase III studies using validated intermediate clinical endpoints are needed before integration into routine practice. Clinical trial information: NCT03160794. Research Sponsor: Terry Fox Canadian Comprehensive Cancer Centre Network (TF4CN) Pilot Project, Terry Fox Research Institute (TFRI); Abbvie CARO Uro-Oncologic Radiation Awards (ACURA); Astellas Prostate Cancer Innovation Fund, University of Toronto, Other Foundation.

5554 Poster Session (Board #135), Fri, 8:00 AM-11:00 AM

Cabazitaxel versus enzalutamide/abiraterone in CARD eligible mCRPC patients with or without germline HRR defects. *First Author: Nuria Romero-Laorden, Hospital Universitario La Princesa, Madrid, Spain*

Background: The CARD trial proved that in mCPRC patients (pts), previously treated with docetaxel and an androgen-receptor signaling inhibitor (ARSi), cabazitaxel (CBZ) significantly improves progression-free (PFS) and Overall Survival (OS) compared with the alternative ARSi. Concurrently, the PROFOUND study showed the superiority of olaparib vs. ARSi in pts with similar prior treatment history and genetic alterations in Homologus Recombination DNA repair related genes (HRR). **Methods:** PROREPAIR-B (NCT03075735) is a prospective study which aimed to demonstrate the prognostic role of germline deleterious mutations in (g)HRR genes and the benefit of first (1L), second (2L) and subsequent therapy lines for mCRPC. Outcomes with 1-2L have been previously reported. Here we evaluated radiographic (r)-PFS, clinical (c)-PFS, and OS in PROREPAIR-B pts who meet CARD study eligibility criteria and who received CBZ and/or ARSi. Survival analysis were performed using Kaplan Meier method and Cox regression models. **Results:** 95 out of 419 mCRPC pts included in PROREPAIR-B meet CARD eligibility criteria and received CBZ (n=60) or ARSi (n=35) including 14 gHRR carriers, 8/6 treated with CBZ/ARSi, respectively. Visceral metastases were more frequent among pts treated with CBZ (p=0.01). ECOG 2, M1 at diagnosis, Abiraterone as 1st ARSi and prior radiographic PD (all $p<0.05$) were more frequent in our pts than in the CARD study. Overall, CBZ was superior to ARSi in terms of rPFS (median 6.0 vs. 3.7 months (m), p=0.03), cPFS (median 4.4 vs. 3.4 m, p=0.01) and PSA50 responses (39% vs. 17%, p=0.027). Differences in OS were not observed, although approximately 60% of patients in ARSi had crossed to CBZ at the time of the analyses. Results of subgroups analyses were similar to those reported by CARD. In this series, gHRR carriers had a significant worse prognosis (OS HR 1.9; rPFS HR 2.4; cPFS HR 2.6) than non-carriers. In gHRR carriers CBZ was not superior to ARSi in terms of rPFS (2.5 vs. 3.0 m, p=0.8), cPFS (2.5 vs. 2.4 m, p=0.8) and OS (4.5 vs. 3.7, p=0.8). Cox MVA models adjusted for unbalances and CARD grouping factors confirmed a significant interaction between treatment and gHRR status for rPFS and cPFS, suggesting that the benefit of CBZ was not observed in gHRR. **Conclusions:** Our results confirm the benefit of CBZ treatment over a second ARSi (either abiraterone or enzalutamide) in unselected mCRPC population. However, the outcomes in gHRR carriers are poor with either CBZ or ARSi supporting the need of novel therapies in this setting. Clinical trial information: NCT03075735. Research Sponsor: Spanish Society of Medical Oncology (SEOM), Spanish Oncology Genitourinary Group (SOGUG), Pharmaceutical/Biotech Company.

5555 Poster Session (Board #136), Fri, 8:00 AM-11:00 AM

Detection of prostate cancer and determination of its significance using explainable artificial intelligence. *First Author: Okyaz Eminaga, Department of Urology, Stanford University School of Medicine, Stanford, CA*

Background: The variation of the human perception has limited the potential of multi-parametric magnetic resonance imaging (mpMRI) of the prostate in determining prostate cancer and identifying significant prostate cancer. The current study aims to overcome this limitation and utilizes an explainable artificial intelligence to leverage the diagnostic potential of mpMRI in detecting prostate cancer (PCa) and determining its significance. **Methods:** A total of 6,020 MR images from 1,498 cases were considered (1,785 T2 images, 2,719 DWI images, and 1,516 ADC maps). The treatment determined the significance of PCa. Cases who received radical prostatectomy were considered significant, whereas cases with active surveillance and followed for at least two years were considered insignificant. The negative biopsy cases have either a single biopsy setting or multiple biopsy settings with the PCa exclusion. The images were randomly divided into development (80%) and test sets (20%) after stratifying according to the case in each image type. The development set was then divided into a training set (90%) and a validation set (10%). We developed deep learning models for PCa detection and the determination of significant PCa based on the PlexusNet architecture that supports explainable deep learning and volumetric input data. The input data for PCa detection was T2-weighted images, whereas the input data for determining significant PCa include all images types. The performance of PCa detection and determination of significant PCa was measured using the area under receiving characteristic operating curve (AUROC) and compared to the maximum PiRAD score (version 2) at the case level. The 10,000 times bootstrapping resampling was applied to measure the 95% confidence interval (CI) of AUROC. **Results:** The AUROC for the PCa detection was 0.833 (95% CI: 0.788-0.879) compared to the PiRAD score with 0.75 (0.718-0.764). The DL models to detect significant PCa using the ADC map or DWI images achieved the highest AUROC [ADC: 0.945 (95% CI: 0.913-0.982; DWI: 0.912 (95% CI: 0.871-0.954)] compared to a DL model using T2 weighted (0.850; 95% CI: 0.791-0.908) or PiRAD scores (0.604; 95% CI: 0.544-0.663). Finally, the attention map of PlexusNet from mpMRI with PCa correctly showed areas that contain PCa after matching with corresponding prostatectomy slice. **Conclusions:** We found that explainable deep learning is feasible on mpMRI and achieves high accuracy in determining cases with PCa and identifying cases with significant PCa. Research Sponsor: Department of Defense.

5556 Poster Session (Board #137), Fri, 8:00 AM-11:00 AM

Prospective evaluation of ^{18}F-DCFPyL PET/CT in biochemically recurrent prostate cancer: Analysis of lesion localization and distribution. *First Author: Hong Song, Stanford University, Stanford, CA*

Background: ^{18}F-DCFPyL, a promising PET agent targeting prostate specific membrane antigen (PSMA), is prospectively evaluated in a single academic center for detecting recurrent lesions in prostate cancer patients with biochemical recurrence (BCR). **Methods:** We prospectively enrolled 150 men (51-91 years old, mean ± SD: 70.3±7.5) with biochemical recurrence (PSA median 2.38 ng/mL, range 0.12 to 698.4) after primary definitive treatment with prostatectomy (65%), radiotherapy (35%) or both (19%). The ^{18}F-DCFPyL positive lesions compatible with prostate cancer were evaluated by two independent readers. Impact of ^{18}F-DCFPyL PET/CT on patient management was recorded from clinical chart review. **Results:** ^{18}F-DCFPyL PET/CT had an overall positivity rate of 83% (125 scans), which increased with higher prostate specific antigen (PSA) levels (ng/mL): 63% (PSA $<$ 0.5), 75% (0.5≤PSA $<$ 1), 91% (1≤PSA $<$ 2), 95% (2≤PSA $<$ 5) and 98% (PSA≥5), respectively. In the cohort who underwent prostatectomy, ^{18}F-DCFPyL PET/CT had higher positivity rate in patients with shorter PSA doubling time (PSAdt) (94% in PSAdt 0-3 months vs. 53% in PSAdt $>$ 12 months, $P<0.01$). No difference of ^{18}F-DCFPyL positivity rate was observed in post-radiation patients with different PSAdt, nor were there differences between patients with low grade (Gleason 6) or higher-grade prostate cancer (Gleason 7-10). 20 patients (13%) had lesions in the prostate bed only and 41 patients (27%) had oligometastatic disease (1-3 lesions), making them candidates for locally targeted therapy. We identified a total of 1455 ^{18}F-DCFPyL positive lesions, including 51 lesions in the prostate bed, 271 pelvic and 463 extrapelvic lymph nodes, approximately 585 osseous lesions, including 5 patients with diffuse osseous metastases, and 85 lesions in other organs (most commonly in the lungs). 91 out of 150 patients (61%) had change in treatment after ^{18}F-DCFPyL PET and, most noticeably, 48 of these patients (32% total) had lesions only localized on ^{18}F-DCFPyL PET/CT despite negative conventional imaging. **Conclusions:** ^{18}F-DCFPyL PET/CT holds great potential to be a "one-stop shop" diagnostic tool in the work-up of BCR prostate cancer, with high (61%) impact on the management of these patients. Clinical trial information: NCT03501940. Research Sponsor: Progenics provided DCFPyL as part of a research access program. No other financial support.

5557 Poster Session (Board #138), Fri, 8:00 AM-11:00 AM

Updated results of a phase I/II prospective dose escalation trial evaluating safety and efficacy of combination ^{177}Lu PSMA 617 and idronoxil in men with mCRPC post androgen signalling inhibition and taxane chemotherapy (LuPIN trial). *First Author: Louise Emmett, Department of Theranostics and Nuclear Medicine, St. Vincent's Hospital, Sydney, Australia*

Background: There is no established standard of care post cabazitaxel in men with mCRPC. Ongoing trials in ^{177}LuPSMA-617 have demonstrated good efficacy and safety, but synergistic combinations may further improve treatment responses. Idronoxil (NOX66) inhibits external NADH oxidase type 2 with downstream pro-apoptotic actions including radio-sensitization. Herein we present updated results and an additional cohort of a prospective single arm phase I/II dose escalation/expansion trial of LuPSMA-617 and NOX66 in mCRPC. **Methods:** Men with progressive mCRPC post androgen signalling inhibition (ASI) and 2 lines of taxane chemotherapy were considered eligible. Key inclusion criteria included PSMA PET/CT intensity SUV max > 15 with no discordant disease on FDG PET/CT, Hb >10, Platelets >100 and GFR >40mls/min. Enrolled patients received up to 6 doses of ^{177} Lu-PSMA 617 (7.5Gbq) day 1 every 6 weeks in combination with NOX66 days 1-10 each cycle. Cohort 1 (n=8) received 400mg NOX66. Cohorts 2 and 3 subsequently received 800mg and 1200mg of NOX66, respectively, following safety reviews. Data regarding safety, efficacy, pain scores, and QOL were collected. **Results:** 32 men were enrolled in cohorts 1&2 (November 2017 – June 2019) and 24 in cohort 3 (August 2019-February 2020). To date there have been no dose-limiting toxicities. Data for cohort 3 are immature. For cohorts 1 & 2: 31/32 men received ≥2 cycles, with 12/32 (47%) completing 6 cycles. Any PSA response was seen in 84% (27/32), with a PSA response > 50% in 62.5% (20/32). Median PSA PFS is 6.1 months Of men with increased baseline pain scores ≥3 (24/32), 50% (12/24) had a clinically significant reduction in pain indicators. Adverse events are summarized below. Updated results for cohorts 1 and 2 and preliminary results of cohort 3 will be presented. **Conclusions:** Combination LuPSMA-617 + NOX 66 appears safe and efficacious in men with heavily pre-treated end stage mCRPC. Clinical trial information: ACTRN12618001073291. Research Sponsor: Noxopharm.

5558 Poster Session (Board #139), Fri, 8:00 AM-11:00 AM

Pain progression at initiation of cabazitaxel in metastatic castration-resistant prostate cancer (mCRPC) is associated with a poor prognosis: a post-hoc analysis of PROSELICA. *First Author: Nicolas Delanoy, Department of Medical Oncology, Georges Pompidou European Hospital, Paris, France*

Background: PROSELICA phase III trial (NCT01308580) showed that cabazitaxel 20 mg/m2 (C20) is non-inferior to C25 in mCRPC patients (pts) post-docetaxel (DOC) *(Eisenberger JCO 2017)*. Pts enrolled were symptomatic or not. This post-hoc analysis evaluates the influence of progression type at randomization on outcomes. **Methods:** Progression type at randomization was defined as follows: PSA progression only (PSA-p; no radiological progression (Radio-p), no pain), Radio-p (± PSA-p, no pain) or pain progression (pain-p, ±PSA-p, ±Radio-p). The relationship between progression type and overall survival (OS), radiological progression-free survival (rPFS) and PSA response (confirmed PSA decrease ≥ 50%) was analyzed. **Results:** All patients randomized (n = 1200) had received prior DOC and 25.7% had received prior abiraterone or enzalutamide. Progression type was evaluable in 1065 pts (PSA-p = 24.5%, radio-p = 20.9%, pain-p = 54.6%). Pain progression was associated with clinical and biological features of aggressive disease and worse outcomes (decreased PSA response, rPFS and OS) vs PSA-p or radio-p (Table). The survival (rPFS and OS) on C25 was numerically higher than on C20 in pts with radio-p and pain-p. Conversely, C20 and C25 equally benefited pts with PSA-p only. In multivariate analysis (all arms combined), pain progression was an independent predictor of poor OS. **Conclusions:** This post-hoc analysis of PROSELICA shows that pain progression at initiation of cabazitaxel in mCRPC pts previously treated with DOC is prognostic. The activity of C25 was numerically higher than C20 in patients with radiological or pain progression. Clinical trial information: NCT01308580. Research Sponsor: None.

	Progression type			
	PSA-p N = 261	Radio-p N = 223	Pain-p N = 581	Global p°
PSA response				
- Overall	35.9%	43.7%	31.3%	p = 0.02
- C20	31.2%	33.7%	26.0%	p = 0.49
- C25	41.8%	53.9%	36.0%	p = 0.02
rPFS				
- Overall	10.0 [9.3; 11.3]	8.1 [7.0; 8.8]	7.8 [6.9; 8.4]	p < 0.001
- C20	10.0 [9.0; 11.3]	7.2 [5.3; 8.3]	7.1 [6.0; 8.3]	p < 0.001
- C25	9.8 [8.9; 14.7]	8.7 [7.2; 9.8]	8.2 [7.2; 8.9]	p < 0.001
OS from mCRPC diagnosis				
- Overall	47.8 [42.6; 53.3]	41.6 [38.0; 45.9]	37.1 [34.5; 40.0]	p < 0.001
- C20	49.1 [40.1; 55.1]	41.6 [37.1; 47.6]	36.0 [31.7; 39.7]	p < 0.001
- C25	45.7 [39.0; 62.5]	41.0 [35.0; 46.6]	38.3 [34.7; 41.2]	p = 0.001
OS from randomization				
- Overall	18.4 [15.9; 21.1]	16.8 [14.3; 18.4]	12.0 [11.1; 12.8]	p < 0.001
- C20	18.5 [15.1; 22.3]	14.7 [11.1; 17.7]	11.6 [10.1; 12.5]	p < 0.001
- C25	17.9 [14.7; 21.9]	18.7 [15.1; 21.1]	12.5 [11.1; 14.4]	p < 0.001

*median [95% CI], months; °Log rank test for rPFS and OS

5559 Poster Session (Board #140), Fri, 8:00 AM-11:00 AM

Efficacy and safety in older patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) receiving cabazitaxel (CBZ) versus abiraterone (ABI) or enzalutamide (ENZ) in the CARD study. *First Author: Cora N. Sternberg, Englander Institute of Precision Medicine, Weill Cornell Medicine, New York, NY*

Background: In the CARD (NCT02485691) study, radiographic PFS (rPFS), PFS and OS were significantly improved with CBZ vs. androgen-signaling-targeted agents (ARTA; ABI or ENZ) in pts with mCRPC who had received docetaxel (DOC) and progressed within 12 months (mo) on an alternative ARTA. This analysis evaluated the impact of age (< 70 vs. ≥ 70 years) on the efficacy and safety of CBZ and ARTAs in CARD. **Methods:** 255 pts with mCRPC were randomized 1:1 to CBZ (25 mg/m^2 IV Q3W + prednisone [P] + G-CSF) vs. ABI (1000 mg PO + P) or ENZ (160 mg PO) until disease progression, unacceptable toxicity or pt request. Pts were eligible if they had received ≥ 3 cycles of DOC and progressed ≤ 12 mo on the previous alternative ARTA. Primary endpoint was rPFS. Subgroup analysis of older (≥ 70 years; n = 135) and younger (< 70 years; n = 120) pts was pre-specified for rPFS; others were post hoc. **Results:** rPFS was significantly improved vs. ARTA in both older (median 8.2 vs. 4.5 mo; HR 0.58; 95% CI 0.38–0.89) and younger pts (median 7.4 vs. 3.2 mo; HR 0.47; 95% CI 0.30–0.74). Median OS for CBZ vs. ARTA was 13.9 vs. 9.4 mo (HR 0.66; 95% CI 0.41–1.06) in older pts and 13.6 vs. 11.8 mo (HR 0.66; 95% CI 0.41–1.08) in younger pts. PFS, tumor, PSA and pain responses also favored CBZ, regardless of age. Grade ≥ 3 adverse events (AEs) occurred in 57.8% vs. 49.3% of older pts receiving CBZ vs. ARTA and 48.4% vs. 42.1% in younger pts. AEs leading to death were more frequent with ARTA, mainly due to disease progression. **Conclusions:** CBZ had improved efficacy outcomes vs. ARTA in pts with mCRPC previously treated with DOC and the alternative ARTA, regardless of age. Grade ≥ 3 cardiac AEs were more frequent in older pts treated with ARTA. A higher rate of AEs was reported in older vs. younger pts, for ARTA and CBZ. CBZ and ARTA had different safety profiles in older compared with younger pts. Clinical trial information: NCT02485691. Funding: Sanofi. Research Sponsor: Sanofi.

	< 70 years		≥ 70 years	
AEs, %	CBZ n = 62	ARTA n = 57	CBZ n = 64	ARTA n = 67
Serious AE	32.3	33.3	45.3	43.3
AE leading to death	1.6	7.0	9.4	13.4
Any grade ≥ 3 AE	48.4	42.1	57.8	49.3
Infection	9.7	5.3	4.7	7.5
Cardiac disorder	1.6	0.0	0.0	9.0
Asthenia or fatigue	1.6	3.5	6.3	1.5
Spinal cord/nerve-root disorder	1.6	3.5	3.1	4.5
Febrile neutropenia	3.2	0.0	3.1	0.0

5560 Poster Session (Board #141), Fri, 8:00 AM-11:00 AM

Phase I dose-escalation study of PSMA-targeted alpha emitter ^{225}Ac-J591 in men with metastatic castration-resistant prostate cancer (mCRPC). *First Author: Scott T. Tagawa, Weill Cornell Medicine, New York, NY*

Background: Antibodies (Abs) or small molecules can target PSMA with different biodistribution. Certain sites of PSMA expression (e.g. salivary/lacrimal glands, kidneys, small bowel) are not accessible to Abs. Given radiosensitivity of PC and potency of alpha emitters plus the ability to minimize targeting off tumor PSMA+ sites with J591, we performed a 1st in human study of ^{225}Ac-J591. **Methods:** Men with progressive mCRPC following at least 1 potent AR-pathway inhibitor (ARPI) and chemo (or unfit/refuse) without limit of # prior therapies (Ra-223 and ^{177}Lu-PSMA allowed) with ECOG PS 0-2 and adequate organ function were eligible. Baseline ^{68}Ga-PSMA11 PET was performed, but not used for eligibility. Initially 1-subject cohorts treated until transition to 3+3 at dose level 5 (predicted by dosimetry to have moderate toxicity) with a single infusion of ^{225}Ac-J591 (13.3 KBq/kg with planned escalation up to 93.3 KBq/kg). Dose-limiting toxicity (DLT) defined as attributable grade (Gr) 4 heme toxicity or Gr 3/4 non-heme tox. Imaging, genomic, patient-reported outcomes (PRO), and immune correlates embedded. **Results:** 22 men treated on 7 dose levels; median age 72.5 (range 58-89), PSA 147 (5-7168); 82% with >2 prior ARPI, 64% chemo, 23% Ra-223, 55% ^{177}Lu-PSMA. 1 (5%) CALGB (Halabi) good prognostic risk, 10 (45%) intermed, 11 (50%) poor risk. 1 of 6 in cohort 6 (80 KBq/kg) had DLT (Gr 4 anemia and platelets); no others had attributable Gr > 2 non-heme or Gr > 3 heme AE (including 0 of 6 at the highest dose level 93.3 KBq/Kg). Gr 1/2 AE's: 17 (77%) fatigue, 11 (50%) pain flare, 10 (45%) anemia (+1 Gr 3), 10 (45%) platelets, 6 (27%) nausea, 6 (27%) xerostomia (5 of 6 with prior ^{177}Lu-PSMA), 5 (23%) neutropenia, 4 (18%) AST elevation. Despite prior treatment including ^{177}Lu-PSMA and no selection for PSMA expression, 14 (64%) with any PSA decline, 9 (41%) with > 50% PSA decline. 15 (68%) had initial PSA rise followed by decline from peak (delayed effect). 2 with response > 1 year despite prior ^{177}Lu-PSMA. Of 15 with paired baseline and 12-wk CTC counts, 8 declined, 4 remained undetectable, 3 increased. In subset with complete PRO data (baseline to 12 wks), pain was improved or absent by BPI-SF in 63% and by FACT-P in 89%. Social and emotional well-being domains of FACT-P improved or stabilized in majority; physical well-being improved in most responders. **Conclusions:** Alpha-emitter ^{225}Ac targeting PSMA via J591 Ab is tolerable with early evidence of clinical activity in a pre-treated population with favorable PRO's. Enrollment to expansion cohort being completed. Clinical trial information: NCT03276572. Research Sponsor: Weill Cornell Medicine, Other Foundation, Other Government Agency, U.S. National Institutes of Health.

5561 Poster Session (Board #142), Fri, 8:00 AM-11:00 AM

Safety outcomes of darolutamide versus apalutamide and enzalutamide in nonmetastatic castration-resistant prostate cancer (nmCRPC): Matching-adjusted indirect comparisons. *First Author: Shan Jiang, Bayer U.S. LLC, Whippany, NJ*

Background: Randomized nmCRPC trials comparing darolutamide (D), apalutamide (A) and enzalutamide (E) have not been reported. Safety of these therapeutics has important implications in assessing patient risk-benefit concerns. Matching-adjusted indirect comparison (MAIC) is a method to perform indirect treatment comparisons adjusting for cross-trial heterogeneity. Objective: To compare the safety outcomes of D vs. A or E using MAIC. **Methods:** Data from the ARAMIS (D vs. placebo [PBO]), SPARTAN (A vs. PBO) and PROSPER (E vs. PBO) trials were used. Key safety outcomes including adverse events (AEs) that have central nervous system relevance were compared using anchored MAIC. Individual patient level data (IPD) from ARAMIS were selected and re-weighted to match the inclusion criteria and baseline characteristics published in SPARTAN and PROSPER (no access to their IPD). The Benjamini-Hochberg approach was applied to adjust for multiplicity. The D vs A MAIC matched on 7 covariates: age, prostate-specific antigen (PSA) level and doubling time, Eastern Cooperative Oncology Group (ECOG), Gleason score, bone-sparing agent use and prior surgery. Sensitivity analyses were conducted matching on different sets of covariates. D vs. E were matched on age, region, PSA level and doubling time, ECOG, Gleason score and bone-sparing agent use. Risk difference (RD) ([DARO – PBO_{ARAMIS}] – [ENZA – $PBO_{PROSPER}$]) and odds ratio (OR) ($OR_{ARAMIS}/OR_{PROSPER}$) were calculated. RD<0 or OR<1 indicate lower AE risk for D. **Results:** For D vs. A, the effective sample sizes (ESS) of D and its placebo (PBO) arm were 604 and 391 after matching. Fall, fracture, and rash were statistically significantly lower for D vs. A (Table). For D vs. E, the ESS of D and PBO arm were 580 and 395, respectively. Fall, dizziness, mental impairment, hypertension, fatigue and severe fatigue were statistically significantly lower for D vs. E. **Conclusions:** After adjusting for trial differences, D showed favorable safety profile in fall, dizziness, mental-impairment, hypertension, rash, fatigue, and fracture. Research Sponsor: Bayer U.S. LLC.

AEs [a]	D minus A % [RD]	D/A [OR]	D minus E % [RD]	D/E [OR]
Fall	-6.3*	0.6	-6.3*	0.4**
Dizziness	-1.0	1.0	-4.9*	0.5
Mental-impairment	-2.6	0.4	-3.5*	0.3**
Hypertension	-2.4	1.2	-3.9**	0.7
Rash	-16.0*	0.5	NR	NR
Fatigue	-4.4	0.9	-12.8*	0.6**
Severe fatigue	-0.7	0.3	-2.2*	0.2
Fracture	-6.2*	0.4**	NR	NR

[a] All grades AEs with the exception of severe fatigue (grade 3+) * Raw and multiplicity adjusted p-value <0.05 ** Raw p-value <0.05 NR=not reported in PROSPER

5562 Poster Session (Board #143), Fri, 8:00 AM-11:00 AM

Association of detectable levels of circulating tumor DNA (ctDNA) with disease burden in prostate cancer (PC). *First Author: Gerhardt Attard, University College London Cancer Institute, London, United Kingdom*

Background: PC is characterized by a relatively low prevalence of recurrent somatic point mutations. ctDNA is shed from PC and can be analyzed to profile somatic point mutations and copy number changes. We evaluated a computational approach to detect ctDNA (ie. ctDNA+) in PC based on allele frequencies of polymorphisms and mutations. We then sought to confirm the association of this biomarker with disease burden and clinical outcome. **Methods:** Customized, hybrid capture, high-depth next-generation sequencing was performed on pre-treatment (PT) plasma samples from a phase 2 line 3+ metastatic castration-resistant PC (mCRPC) study (NCT02854436, GALAHAD) and PT and end of treatment (EOT) samples from randomized Phase 3 study in non-metastatic (nm) CRPC (NCT01946204, SPARTAN) and from metastatic castration-sensitive PC (mCSPC) (NCT02489318, TITAN). Associations of ctDNA+ with bone lesions (number), visceral metastases (+/-), circulating tumor cells count (CTCc), and serum prostate specific antigen (PSA), alkaline phosphatase (AP) and lactate dehydrogenase (LD) were tested. Also, associations of ctDNA+ with overall survival (OS) and second progression free survival (PFS2) were evaluated in randomized studies using Cox regression. **Results:** ctDNA+ at PT was 7.5% in nmCRPC, 23.7% in mCSPC and 66% in heavily pre-treated mCRPC. ctDNA+ increased from PT to EOT in nmCRPC (7.5% to 27%) and mCSPC (23.7% to 63.6%). Disease burden metrics were evaluated in ctDNA+ vs ctDNA- patients. ctDNA+ was associated with higher disease burden in mCRPC (Table), nmCRPC and mCSPC. At EOT, ctDNA+ patients had shorter OS and PFS2 in nmCRPC (HR [95% CI] OS: 2.73 [1.83, 4.08], $p < 0.0001$; PFS2: 2.00 [1.38, 2.90], $p = 0.0002$) and mCSPC (HR [95% CI] OS: 7.59 [3.22, 17.91], $p < 0.0001$; PFS2: 4.84 [2.47, 9.47], $p < 0.0001$). **Conclusions:** ctDNA+ assessed using our novel, composite biomarker increases with advanced disease state and disease progression, is significantly associated with disease burden and poor clinical outcome in PC and could be a clinically relevant metric for monitoring response to therapy. Clinical trial information: NCT02854436. Research Sponsor: Janssen Research and Development, LLC.

Galahad Study	ctDNA+	ctDNA-	p-value
> 10 bone lesions (%)	70	41	0.0145
Liver metastases (%)	20	4	0.08
CTCc (median)	44	2	6.1E-9
PSA (median)	191	32	0.0003
AP (median)	201	75	8.8E-7
LD (median)	272	188	2.5E-5

5563 Poster Session (Board #144), Fri, 8:00 AM-11:00 AM

Results of the randomized phase II study of sipuleucel-T (Sip-T) +/- Radium-223 (Ra-223) in men with bone-metastatic castration resistant prostate cancer. *First Author: Catherine Handy Marshall, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD*

Background: It has been suggested that immune modulation can be augmented by radiation, possibly by enhancing tumor-antigen display. SipT-induced antigen-specific immune responses in mCRPC patients correlate with survival. We hypothesized that the combination of Ra223 and SipT would enhance SipT-related immune response and improve outcomes compared to SipT alone. **Methods:** Patients with asymptomatic, bone-predominant mCRPC, without visceral mets >1.0 cm, were randomized (1:1) to SipT alone or with 6 doses of Ra223 (NCT02463799). Men in the SipT+Ra223 arm started SipT between the 2nd and 3rd dose of Ra223. The primary immunologic endpoint was PA2024-specific T-cell proliferation 6 wks after the first SipT infusion. Secondary immune endpoints were PA2024-specific ELISPOT response, PAP-specific proliferation and ELISPOT, humoral responses against both antigens, and antigen spread. Clinical endpoints were radiographic PFS, PSA response (≥50% decline), AlkPhos response (≥30% decline), and safety. **Results:** 32 men were randomized, 16 per arm. Baseline characteristics in SipT+Ra223 and SipT arms were similar: age (median 71 vs. 70 yrs), Gleason (8-10: 69% vs. 69%), baseline PSA (med 25 vs. 33 ng/mL), AlkPhos (med 89 vs. 92 U/L) and ECOG score (≥1: 31% vs. 19%). There was no significant difference in prior use of abi/enza (38% vs. 44%), or chemo (0% vs. 25%). At 6 weeks, absolute PA2024-specific T-cell proliferation was 2.1-fold higher in the Sip-T arm compared to the SipT+Ra223 arm (35.6 vs. 16.6; *P*=0.03) and remained higher through week 26. Relative to baseline, the 6-week PA2024-specific T-cell proliferation change was 3.6 times greater in the Sip-T arm compared to the SipT+Ra223 arm (*P*=0.007) and remained higher through week 14. There were no significant differences in antigen spread or humoral responses. Median radiographic PFS was longer in the SipT+Ra223 arm (9.3 vs. 3.2 months; HR 0.26, 95% CI 0.11–0.61; *P*=0.007). PSA and AlkPhos responses were better in the SipT+Ra223 arm (PSA50: 5/15=33% vs. 0/14=0%; *P*=0.04; AlkPhos30: 9/15=60% vs. 1/15=7%; *P*=0.01). There was no difference in SREs (13% vs. 7%). **Conclusions:** SipT+Ra223 was associated with improved clinical outcomes and a higher rate of PSA responses compared to SipT alone, although surprisingly, the SipT arm demonstrated higher peripheral PA2024-specific T-cell proliferation. Since neither agent reliably induces PSA responses alone, these data suggest a synergistic effect of the combination. Larger randomized studies of this combination are planned. Clinical trial information: NCT02463799. Research Sponsor: Dendreon, Bayer.

5564 Poster Session (Board #145), Fri, 8:00 AM-11:00 AM

Cabozantinib in combination with atezolizumab in patients with metastatic castration-resistant prostate cancer: Results of cohort 6 of the COSMIC-021 study. *First Author: Neeraj Agarwal, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT*

Background: Cabozantinib (C) may enhance response to immune checkpoint inhibitors (ICIs) by promoting an immune-permissive microenvironment and has shown encouraging activity in combination with ICIs in tumor types including RCC and HCC. C and atezolizumab (A) have shown low objective response rates as monotherapy in metastatic castration-resistant prostate cancer (mCRPC) (Smith JCO 2012; Kim JCO 2018). COSMIC-021 (NCT03170960), a multinational phase 1b study, is evaluating the combination of C + A in various solid tumors. We report results for Cohort 6 in mCRPC. **Methods:** Eligible patients (pts) were required to have radiographic progression in soft tissue after enzalutamide and/or abiraterone, measurable disease, and an ECOG PS of 0 or 1. Prior chemotherapy for mCSPC was permitted. Pts received C 40 mg PO QD and A 1200 mg IV Q3W. CT/MRI scans were performed Q6W for the first year and Q12W thereafter. The primary endpoint is ORR per RECIST 1.1. Other endpoints include safety, ORR per irRECIST, duration of response (DOR), PFS, and OS. Results are presented for the first 44 pts enrolled. **Results:** Median follow-up as of Dec 20, 2019 was 12.6 mo (range 5, 20) for the 44 mCRPC pts. Median age was 70 y (range 49, 90), 50% had ECOG PS 1, 34% had visceral metastases, and 61% had extrapelvic lymph node metastases. 27% had prior docetaxel and 52% had 2 prior novel hormonal therapies. The most common any grade treatment-related adverse events (TRAEs) were fatigue (50%), nausea (43%), decreased appetite (39%), diarrhea (39%), dysgeusia (34%), and PPE (32%). One grade 5 TRAE of dehydration was reported in a 90 y/o. Median duration of treatment was 6.3 mo. ORR per RECIST 1.1 among all 44 pts was 32% (2 CRs [4.5%] and 12 PRs [27%]); 21 (48%) pts had SD resulting in a disease control rate of 80% in all pts. One pt with PD per RECIST 1.1 had an irPR per irRECIST. ORR per RECIST 1.1 was 33% in 36 pts with high-risk disease (visceral and/or extrapelvic lymph node metastases). Median DOR for all pts with response per RECIST 1.1 was 8.3 mo (range 2.8, 9.8+). 17 (50%) of 34 pts with post-baseline PSA evaluation had a decrease in PSA. In 12 responders with post-baseline PSA evaluation, 8 (67%) had a PSA decrease ≥50%. Tumor PD-L1 expression will also be reported. **Conclusions:** The combination of C + A had a tolerable safety profile and demonstrated clinically meaningful activity with durable responses in men with mCRPC. Given the encouraging activity in these pts, especially in those with high-risk disease, further evaluation of C + A in men with mCRPC is being pursued. Clinical trial information: NCT03170960. Research Sponsor: Exelixis Inc.

5565 Poster Session (Board #146), Fri, 8:00 AM-11:00 AM

Safety and clinical activity of atezolizumab (atezo) + radium-223 dichloride (r-223) in 2L metastatic castration-resistant prostate cancer (mCRPC): Results from a phase Ib clinical trial. *First Author: Michael J. Morris, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: mCRPC patients (pts) tend to have a poor prognosis and limited treatment (tx) options, especially those with concomitant bone metastases (mets). We explored the ability of combination tx with atezo (anti–PD-L1) and r-223 (α-particle emitter) to stimulate anti-tumor immunity in mCRPC pts. **Methods:** This Phase Ib study evaluated the safety and tolerability of atezo + r-223 in pts with mCRPC and multiple bone mets, visceral mets and/or lymphadenopathy who progressed after androgen pathway inhibitor tx. The initial cohort phase evaluated the safety and tolerability of a concurrent dosing schedule (CDS), in which atezo and r-223 were administered on the same day. Following assessment of CDS, pts were randomized 1:1:1 to CDS or 1 of 2 staggered dosing schedules (atezo or r-223 introduced a full cycle before the other). This was followed by an expansion of enrollment (randomized 1:1:1). Pts got atezo 840 mg IV q2w and r-223 at 55 kBq/kg IV 6 times at 4-wk intervals until unacceptable toxicity or loss of clinical benefit. Exploratory measures of efficacy included investigator-assessed ORR (RECIST 1.1), PSA response rate, time to PSA progression, radiographic PFS (rPFS; PCWG2 criteria) and OS. Biopsy samples were collected at baseline and prior to cycle 2 to evaluate changes in the tumor microenvironment during tx. **Results:** As of Oct 4, 2019, 45 pts were enrolled and 44 had evaluable data. Baseline characteristics were generally similar across groups. All 44 evaluable pts had $\geq$ 1 all-cause AE; 23 (52.3%) had Gr 3-4 AE. Eight pts (18.2%) had Gr 5 AE as per protocol reporting of deaths; 4 (9.1%) were from disease progression. Median follow-up was 13.9 mo (range, 1.7–34.2). Confirmed ORR was 6.8% (95% CI: 1.43, 18.66). Confirmed PSA response rate was 4.5% and median time to PSA progression was 3.0 mo (95% CI: 2.8, 3.3). Median rPFS was 3.0 mo (95% CI: 2.8, 4.6) and median OS was 16.3 mo (95% CI: 10.9, 22.3). Changes in PD-L1 and CD8 IHC were consistent with the known mechanism of action of atezo, as were changes in alkaline phosphatase with radium. **Conclusions:** No dose-limiting toxicities, safety signals, or changes in serum biomarkers were observed beyond the known safety profiles of atezo and r-223. This Phase 1b study did not seem to show clinical benefit from combination tx. Ongoing subgroup and biomarker analyses may provide additional insights. Studies of PD-1/PD-L1 targeted therapies in combination with tumor-directed radiation in molecularly selected mCRPC pts are planned or underway. Clinical trial information: NCT02814669. Research Sponsor: F. Hoffmann-La Roche, Ltd.

5566 Poster Session (Board #147), Fri, 8:00 AM-11:00 AM

TALAPRO-1: Phase II study of talazoparib (TALA) in patients (pts) with DNA damage repair alterations (DDRm) and metastatic castration-resistant prostate cancer (mCRPC) – updated interim analysis (IA). *First Author: Johann S. De Bono, The Royal Marsden Hospital and The Institute of Cancer Research, London, United Kingdom*

Background: PARP inhibitors (PARPi) show antitumor activity in mCRPC/DDRm pts treated with novel hormonal therapy (NHT). TALAPRO-1 is an open-label study evaluating TALA (potent PARP inhibitor/trapper) in men with mCRPC/DDRm. We report a planned IA (Dec 2019). **Methods:** TALAPRO-1 (NCT03148795) is enrolling pts (N $\approx$ 100) with measurable soft tissue disease, progressive mCRPC, and DDRm likely to sensitize to PARPi (*ATM*, *ATR*, *BRCA1/2*, *CHEK2*, *FANCA*, *MLH1*, *MRE11A*, *NBN*, *PALB2*, *RAD51C*), who received 1–2 chemotherapy regimens ($\geq$1 taxane-based) for metastatic disease and progressed on $\geq$1 NHT (enzalutamide/abiraterone acetate) given for mCRPC. DDRm are defined as known/likely pathogenic variants or homozygous deletions. Pts receive oral TALA 1 mg/day (moderate renal impairment 0.75 mg/day) until radiographic progression, unacceptable toxicity, consent withdrawal or death. Primary endpoint is objective response rate (ORR). Secondary endpoints: time to OR; response duration; PSA decrease $\geq$50%; circulating tumor cell (CTC) count conversion (to CTC = 0 and $<$5 per 7.5 mL blood); time to PSA progression; radiographic PFS (rPFS); overall survival; safety. A planned efficacy/safety IA was done when 60 pts with DDRm and measurable disease completed $\geq$6 months of TALA/no longer followed (DDR population [DDRp]). Radiographic responses are based on investigator assessments. **Results:** 113 pts received TALA (cutoff Dec 12, 2019); 75 pts were DDRp, had measurable disease, received $\geq$16 wk treatment, and were evaluable for ORR (54.7% *BRCA1/2*, 4.0% *PALB2*, 22.7% *ATM*; 18.7% other DDRm).All DDRp pts had prior docetaxel; 45.3% cabazitaxel. Confirmed ORR, rPFS, and composite response (investigator-assessed) in pts who received TALA for $\geq$16 weeks are in the table. Most common treatment-emergent adverse events: anemia (42.5%); nausea (32.7%). **Conclusions:** TALA monotherapy has encouraging antitumor activity in docetaxel-pretreated mCRPC pts with *BRCA1/2* alterations and was generally well tolerated. Clinical trial information: NCT03148795. Research Sponsor: Pfizer Inc.

	BRCA1/2 N=46	*PALB2* N=4	*ATM* N=18	Other N=18	Total N=86
[a,b]ORR, % (response/n)	43.9 (18/41)	33.3 (1/3)	11.8 (2/17)	0	28.0 (21/75)
[b]rPFS, mths (95% CI)	9.3 (8.1-13.7)	7.4 (2-7.4)	5.5 (1.7-8.2)	3.7 (1.7-3.9)	-
[b,c]Composite response, % (response/n)	76.1 (35/46)	50.0 (2/4)	27.8 (5/18)	11.1 (2/18)	51.2 (44/86)

[a]Measurable soft tissue disease per investigator at screening; [b]DDR deficient population; [c]OR and/or PSA response $\geq$50% and/or CTC conversion (from CTC $\geq$5 to $<$5)

5567 Poster Session (Board #148), Fri, 8:00 AM-11:00 AM

Olaparib (O) in patients (pts) with prostate cancer with BRCA1/2 inactivating mutations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study. *First Author: Evan P. Pisick, Cancer Treatment Centers of America, Zion, IL*

Background: TAPUR is a phase II basket study evaluating anti-tumor activity of commercially available targeted agents in pts with advanced cancers with genomic alterations. Advanced prostate cancer (PC) pts with germline or somatic BRCA1/2 inactivating mutations treated with O are reported. **Methods:** Eligible pts had advanced PC, no remaining standard treatment (tx) options, measurable disease, ECOG Performance Status (PS) 0-2, and adequate organ function. Tumor genomic testing was performed in CLIA-certified, CAP-accredited site selected labs. Pts received O tablets or capsules dosed at 300 mg (n=24) or 400 mg (n=5), respectively, orally twice daily until disease progression. Simon 2-stage design tested the null disease control (DC) (objective response (OR) or stable disease at 16+ weeks (wks) (SD16+) according to RECIST) rate of 15% vs. 35% (power = 0.85; α = 0.10). If $\geq$2 of 10 pts in stage 1 have DC, 18 more pts are enrolled. If $\geq$7 of 28 pts have DC, the tx is worthy of further study. Pts had radiographic evaluations at 8 and 16 wks and then every 12 wks. Secondary endpoints are progression-free survival (PFS), overall survival (OS) and safety. **Results:** 29 pts with *BRCA1/2* inactivating mutations were enrolled from Aug 2016 to Jul 2019; 4 were identified as ineligible after enrollment due to bone only disease and removed from analyses. Demographics and investigator-reported outcomes are summarized in the Table. Nine pts with OR and 8 with SD16+ were observed for DC and OR rates of 68% (90% CI: 53% - 77%) and 36% (95% CI: 18% - 57%), respectively. Six pts had at least one grade 3 AE or SAE at least possibly related to O including anemia, aspiration, dehydration, diabetic ketoacidosis, fatigue, and neutropenia. **Conclusions:** Monotherapy with O showed anti-tumor activity in heavily pre-treated PC pts with germline (1/2 pts with OR or SD16+) or somatic (16/23 pts with OR or SD16+) *BRCA1/2* inactivating mutations. These findings extend results from recent trials of O in advanced prostate cancer pts with germline only BRCA1/2 mutations. Clinical trial information: NCT02693535. Research Sponsor: AstraZeneca, Pharmaceutical/Biotech Company.

Demographics and efficacy outcomes (N=25).

Median age, yrs (range)	**65 (40, 90)**
Male, %	100
ECOG PS, %	
0	44
1	56
Prior systemic regimens, %	
1-2	40
≥3	60
DC rate, % (90% CI)	68 (53, 77)
OR rate, % (95% CI)	36 (18, 57)
Median PFS, wks (95% CI)	41.0 (16.3, 53.1)
Median OS, wks (95% CI)	75.4 (49.4, NA)
1 year OS rate, % (95% CI)	79.4 (47.6, 93.1)

5568 Poster Session (Board #149), Fri, 8:00 AM-11:00 AM

Comparison of germline mutations in African American and Caucasian men with metastatic prostate cancer. *First Author: Elisa Marie Ledet, Tulane University Cancer Center, New Orleans, LA*

Background: The relevance of germline mutations in metastatic prostate cancer is well established; however, comparison of germline genetics in African American (AA) versus Caucasian (CA) men with metastatic prostate cancer (PCa) is limited. **Methods:** Germline data from self-identified AA and CA metastatic PCa patients (pts) were collected from 5 academic cancer centers. Various commercial cancer-specific germline testing panels were used to evaluate 12-86 genes. Pathogenic (P) or likely pathogenic (LP) mutations, and variants of unknown significance (VUS), were reported according to ACMG guidelines. Self-reported family history (FH) was annotated for 99% of pts. Statistical analyses included Chi-squared and Fischer's exact tests. **Results:** A total of 821 metastatic PCa pts were assessed: 152 AAs and 669 CAs. For P/LP alterations, AAs had a frequency of 11.2% (17/152) as compared to a frequency of 14.6% (98/669) in CAs (p = 0.302). AA pts were more likely to have a VUS than CA pts, 61% vs 43% respectively (OR = 2.09, 95%CI [1.45, 2.99], p $<$ 0.001). BRCA mutations were similar between races, but AA were more likely to have a BRCA1 P/LP alteration (OR = 6.00, 95% CI [1.33, 27.09], p = 0.025). AA pts were less likely to have a P/LP alteration in a non-BRCA gene (OR = 0.34, 95% CI [0.15, 0.80], p = 0.013). Among DNA repair genes, there were no significant difference between AA and CA pts (p = 0.574); however, there was a trend toward AA pts having fewer P/LP alteration in a non-BRCA DNA repair genes (OR = 0.26, 95% CI [0.06, 1.08], p = 0.071). In pts with $>$1 first degree relative (FDR) with ovarian cancer, P/LP germline alterations were more likely in CAs (OR = 2.33, 95% CI [1.05, 5.17], p = 0.043); but there were no significant differences in AAs (p = 0.098). Those with $>$2 FDRs with PCa were more likely to have a P/LP change in CAs (OR = 2.32, 95% CI [1.04, 5.15], p = 0.043), but there were no difference in AAs (p = 0.700). In pts with $\geq$2 FDRs with breast cancer, P/LP germline alterations were more likely in both AAs (OR = 9.36, 95% CI [1.72, 50.84], p = 0.019) and CAs (OR = 3.92, 95% CI [1.79, 8.59], p = 0.001). **Conclusions:** We did not observe a difference in the overall frequency of germline P/LP alterations between AA and CA men with metastatic PCa but VUSs were more common in AA men. These AA men have an overall frequency of BRCA mutations similar to CA men; however, BRCA1 mutations were more prevalent in these AAs. Non-BRCA P/LP mutations are significantly less frequent in AA pts. A positive family history of $>$2 FDRs with breast cancer was associated with P/LP alterations in both AA and CA pts. Research Sponsor: None.

5569 Poster Session (Board #150), Fri, 8:00 AM-11:00 AM

CARD: Overall survival (OS) analysis of patients with metastatic castration-resistant prostate cancer (mCRPC) receiving cabazitaxel versus abiraterone or enzalutamide. *First Author: Bertrand F. Tombal, Institut d Recherche Clinique, Université Catholique de Louvain, Brussels, Belgium*

Background: The CARD trial (NCT02485691) compared cabazitaxel vs. an androgen receptor targeted agent (ART; abiraterone/enzalutamide) in mCRPC previously treated with docetaxel and the alternative ART (abiraterone/enzalutamide), in any order. These post hoc analyses assessed OS from various time points and the impact of prognostic factors. **Methods:** Patients with mCRPC previously treated with docetaxel and progressing ≤ 12 months on prior abiraterone/enzalutamide were randomized 1:1 to cabazitaxel (25 mg/m^2 IV Q3W + daily prednisone + prophylactic G-CSF) vs. abiraterone (1000 mg PO + daily prednisone) or enzalutamide (160 mg PO). OS was calculated from date of diagnosis of metastatic disease, date of mCRPC, and start of 1st, 2nd or 3rd life-extending therapy (LET). A stratified multivariate Cox regression analysis assessed the impact of 14 prognostic factors on OS using a stepwise model selection approach with a significance level of 0.10 for entry into the model and 0.05 for removal. **Results:** In the CARD study (N = 255), median OS was longer with cabazitaxel vs. abiraterone/enzalutamide (13.6 vs 11.0 months; HR 0.64, 95% CI 0.46–0.89; p = 0.008). OS was numerically improved for cabazitaxel vs. abiraterone/enzalutamide when assessed from the time of diagnosis of metastatic disease or mCRPC, or from start of 1st or 2nd LET (Table). In the multivariate analysis, low hemoglobin, high baseline neutrophil to lymphocyte ratio, and high PSA values at baseline were associated with worse OS. In presence of these factors, the OS benefit observed with cabazitaxel versus abiraterone/enzalutamide remained significant (HR 0.63, 95% CI 0.42–0.94, p = 0.022). **Conclusions:** Cabazitaxel numerically improved OS vs. abiraterone/enzalutamide in patients with mCRPC previously treated with docetaxel and the alternative ART (abiraterone/enzalutamide), whatever the time point considered. The robustness of this OS benefit was confirmed by stratified multivariate analysis. Sanofi funded. Clinical trial information: NCT02485691. Research Sponsor: Sanofi.

	Median OS, months	
OS from time of	Cabazitaxel n = 129	Abiraterone/enzalutamide n = 126
Metastatic disease diagnosis	54.7	42.5
mCRPC diagnosis	40.9	31.3
1st LET	36.4	30.5
2nd LET	24.2	21.9
3rd LET	13.6	11.0

5570 Poster Session (Board #151), Fri, 8:00 AM-11:00 AM

Survival outcome in patients with metastatic castration-resistant prostate cancer according to first-line treatment. *First Author: Marine Gross-Goupil, University Hospital, Bordeaux, France*

Background: Therapeutic strategy in metastatic castration-resistant prostate cancer (mCRPC) has evolved significantly with the introduction of abiraterone acetate in association with prednisone/prednisolone in first-line treatment in December 2012. This work aimed to compare the effectiveness of abiraterone acetate and docetaxel as first-line treatments for mCRPC, in real-life setting. **Methods:** Patients with mCRPC were identified in the main scheme of the National Healthcare System database (SNDS), which covers about 86% of the French population, and capturing all reimbursed healthcare expenditures and hospital discharge summaries. Those initiating docetaxel or abiraterone acetate in 1st line in 2014 were included and 1:1 matched on the previous prostate cancer stage before mCRPC status, the delay from the date of initial diagnosis and a high-dimensional propensity score. The 36-month overall survival and the 36-month discontinuation-free survival (i.e. survival time until treatment switch or death) were compared using Cox proportional hazards risk model. **Results:** In 2014, out of the 12,951 patients with prevalent mCRPC, 1,214 initiated docetaxel in 1st line and 2 444 initiated abiraterone. A total of 716 patients per group were matched with good comparability (C-statistic = 0.6). The median duration of docetaxel–defined as the time between the first and the last infusion–was 7.3 months with a median of 6 infusions. The median duration of abiraterone acetate–corresponding to the period covered by the dispensed drug–was 9.1 months. Near 70% of the docetaxel and 62% of the abiraterone acetate patients received a 2nd line of treatment. Results related to the main survival outcomes are presented in the table below. **Conclusions:** First-line treatment with abiraterone acetate in mCRPC patients results in a better 36-month overall survival and discontinuation-free survival compared to docetaxel in real-life setting. Research Sponsor: JANSSEN.

	Docetaxel n=716	Abiraterone acetate n=716	*p-value*
Overall Survival			
36-month survival probability, % [95%CI]	27.9 [25.0 – 31.2]	34.6 [31.5 – 38.1]	<0.003
Median survival, months [95%CI]	18.5 [17.1 – 20.7]	25.5 [23.0 – 27.3]	
Discontinuation-Free Survival			
36-month survival probability, % [95%CI]	2.9 [2.1 – 4.1]	13.8 [11.7 – 16.4]	<0.001
Median survival, months [95%CI]	7.4 [7.0 – 8.0]	10.8 [10.1 – 11.7]	

5571 Poster Session (Board #152), Fri, 8:00 AM-11:00 AM

Clinical significance of CTC enumeration on the Epic Sciences platform in metastatic castration-resistant prostate cancer (mCRPC) patients treated with AR signaling inhibitors (ARSi). *First Author: Joseph Schonhoft, Epic Sciences, Inc., San Diego, CA*

Background: Circulating Tumor Cell (CTC) number, enumerated using the analytically valid FDA cleared Cell Search (Menarini Silicon Biosystems) platform has been shown to be prognostic for survival pre- and post-therapy, and used as an aid to monitoring breast, colorectal and prostate cancers. The assay uses antibody-based capture and defines a CTC as an EpCAM+ and CD45- intact cell. In contrast, with the Epic sciences CTC detection platform red blood cells are first lysed and all nucleated cells deposited on pathology slides, fixed, and imaged. There is no affinity selection and CTCs for this analysis were defined *in silico* as any cytokeratin (CK)+, CD45- cell with an intact DAPI+ nucleus. Here we report the prognostic significance of the CK+ CTCs detected on the EPIC Sciences platform in mCRPC patients prior to treatment with an AR signaling inhibitor. **Methods:** A pre-treatment blood sample was collected from 181 unique patients with progressing mCRPC about to start an ARSI as 1st, 2nd or 3rd line therapy at MSKCC. CTCs were enumerated on the Epic Sciences platform and verified by a trained human technician. **Results:** At least 1 CTC was detected (median = 1, 0-711 CTCs/ml) in 134 (74%) of cases, with higher counts observed in patients with visceral or multiple osseous sites relative to those with lymph node only disease. Counts increased by line of therapy. The table shows the associated risk of death for CTCs modeled as a continuous variable. **Conclusions:** The results support the clinical validity of CTC number determined on the Epic Sciences platform as a significant baseline prognostic factor. In multivariate modeling CTC number was found to be the most significant blood-based predictor of poor OS with each doubling representing a 20% greater risk of death observed with adjustment for therapy line, LDH, PSA, and ALK. Research Sponsor: Epic Sciences, Other Government Agency.

Cox proportional hazards models for assessing the prognostic value of CTCs detected on the Epic Sciences platform with association to overall survival.

Model	PSA		CTC		CTC + PSA		ALK + LDH + PSA		ALK + LDH + PSA + CTC	
Continuous Blood Based Measurement	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
CTC	1.4 (1.3, 1.6)	<0.0001	-	-	1.3 (1.2, 1.5)	<0.0001	-	-	1.2 (1.1, 1.4)	0.002
PSA	-	-	1.3 (1.2, 1.4)	< 0.0001	1.2 (1.1, 1.3)	0.0002	1.1 (1.0, 1.3)	0.0168	1.1 (1.0, 1.2)	0.064
ALK	-	-	-	-	-	-	1.3 (1, 1.6)	0.0614	1.2 (0.9, 1.6)	0.13
LDH	-	-	-	-	-	-	1.9 (1.4, 2.7)	0.0001	1.6 (1.1, 2.3)	0.012

Each continuous covariate was log2 transformed and all models adjust for line of therapy and patient age.

5572 Poster Session (Board #153), Fri, 8:00 AM-11:00 AM

Circulating tumor cells (CTCs) with small-cell like pathology are prevalent in metastatic castration-resistant prostate cancer (mCRPC) and show selective pharmacodynamic reductions in patients treated with platinum but not ARSI or taxane. *First Author: Howard I. Scher, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: The increasing availability and earlier use of life prolonging drugs targeting the androgen receptor signaling axis (ARSI) has resulted in an increase in the frequency of late state tumors with "small cell/neuroendocrine (NESC) phenotypes" similar to small-cell lung cancer (SCLC). Definitive pathologic criteria to diagnose the "entity" are lacking, and the eligibility criteria across trials are inconsistent, limiting the ability to relate outcomes between studies. We hypothesized that an analytically valid assay for a rigorously defined "small-cell CTC" phenotype might serve as a unifying biomarker for the presence of NESC-like tumors in an individual for use in clinical trials. **Methods:** Using the WHO guidelines for small-cell diagnosis in tissue as reference, we defined an equivalent set of single-cell CTC criteria for defining a CTC with small-cell histology: a small and circular CD45-, CK+ cell with high N/C ratio lacking detectable nucleoli. Small-cell subtype pharmacodynamic changes were studied in 233 patients with progressing mCRPC about to start an AR signaling inhibitor ARSi (N=111), taxane (N=89), or platinum (N=33). **Results:** CTCs with small-cell morphology had lower AR protein expression compared with non-small-cell CTCs (P<0.0001) and increased with therapy line. The small-cell CTC subtype decreased in number from baseline to on-therapy in patients treated with platinum but not in those treated with ARSi or taxane (Table). **Conclusions:** Digital pathology analysis of CTCs defined a CTC subtype consistent with that of small-cell carcinoma that were only reduced in number with platinum-based therapy. The tracking of CTC subtypes after treatment with different drug classes may help assess drug activity in heavily treated patients that often have heterogeneous disease that of which may not be captured using standard measures of response. Research Sponsor: Epic Sciences, Other Government Agency.

Percent of patients with small-cell/neuroendocrine (NESC) CTCs by therapy class.

	CTC/mL > 0; Number of patients (N)	NESC/mL > 0; Number of patients (N)	CTC/mL > 0; Number of patients (N)	NESC/mL > 0; Number of patients (N)	P-value for decrease from Baseline to On-therapy (unadjusted/ Bonferonni adjusted), paired test
TimePoint	Baseline		On-therapy		Change
ARSi (N=111)	90 (81%)	35 (32%)	76 (68%)	29 (26%)	0.29 / 0.87
Taxane (N=89)	76 (85%)	37 (42%)	68 (76%)	23 (26%)	0.09 / 0.28
Platinum (N=33)	30 (91%)	14 (42%)	25 (76%)	7 (21%)	0.015 / 0.045

5573 Poster Session (Board #154), Fri, 8:00 AM-11:00 AM

Clinical outcomes and markers of treatment response in a randomized phase II study of androgen deprivation therapy with or without palbociclib in RB-intact metastatic hormone-sensitive prostate cancer (mHSPC). *First Author: Phillip Lee Palmbos, University of Michigan Rogel Cancer Center, Ann Arbor, MI*

Background: Targeted therapies based on tumor molecular markers are not currently used in mHSPC. Palbociclib, a CDK4/6 inhibitor, blocked proliferation and promoted G1 arrest in a Rb-and Cyclin D-dependent manner in preclinical models of HSPC. We hypothesized that co-targeting AR (ADT) and cell cycle (palbociclib) would improve outcomes in mHSPC pts. **Methods:** mHSPC pts with Rb intact tumors based on IHC of metastatic tumor biopsy were stratified and randomized (1:2) to Arm A: ADT or Arm B: ADT+ palbociclib (125mg 3 weeks on, 1 week off). Primary endpoint was confirmed PSA RR (≤ 4 ng/mL) after 28 weeks of therapy. Secondary endpoints included safety/tolerability, PFS, PSA and radiographic RR. Metastatic biopsy and primary tumors were subjected to whole exome and transcriptomic sequencing where available. CTC's were enumerated at various time points. **Results:** 72 eligible pts (median age 67 years, PSA 73ng/mL) with newly diagnosed mHSPC were registered and underwent biopsy. 97% retained RB expression (IHC). 62 pts were stratified by disease extent and early initiation of ADT, and randomized. 60 pts initiated therapy (Arm A: 20; Arm B: 40). Adverse events were reported previously. 80% of pts (Arm A: 16/20, Arm B: 32/40; p = 0.87) on both arms met primary PSA endpoint (≤4ng/mL at 28 weeks). PSA undetectable rate at 28 weeks was Arm A: 50% (10/20) and Arm B: 43% (17/40; p = 0.5). Measurable disease RR: Arm A: 89% and Arm B: 89%. 12-month biochemical PFS was Arm A 69% (95%CI: 44-85%), Arm B 74% (95%CI: 57-85%). 41 patients on trial underwent sequencing of metastatic biopsy and 10 patients had matched primary prostate tumor sequencing results. CCND1 amp, 8q gain, PTEN and KMT2C mutations were each observed in metastatic, but not paired prostate primary tumors. TP53, PIK3 pathway (PIK3CA, AKT1, PTEN) mutations and 8q gains were associated with reduced PSA PFS [HR (95%CI): 3.0 (1.2-7.2), p = 0.018; 3.2(1.03-10),p = 0.044; 4.96 (1.8-12), p = 0.001, respectively]. Pretreatment CTCs were associated with lower PSA CR (p = 0.04) and shorter PFS (12-month PFS: 58% vs. 86%, p = 0.031). **Conclusions:** A tissue based biomarker preselected trial is feasible in mHSPC. ADT + palbociclib did not impact outcomes. Pretreatment CTC counts, TP53 and PIK3 pathway mutations, and 8q gain may offer prognostic value in mHSPC. Support: Movember-PCF Challenge Award, Pfizer. Clinical trial information: NCT02059213. Research Sponsor: Movember-PCF Challenge Award, Pharmaceutical/Biotech Company.

5574 Poster Session (Board #155), Fri, 8:00 AM-11:00 AM

A blood-based multi-mRNA liquid biopsy with >90% accuracy for diagnosis and assessment of prostate cancers. *First Author: Kambiz Rahbar, University Hospital Münster, Münster, Germany*

Background: There are a paucity of blood-based biomarkers with clinical utility for prostate cancer (PCa). We developed a circulating mRNA (27-gene) prostate cancer signature to diagnose and manage PCa. **Methods:** Gene identification: Publicly available PCa transcriptome sets (n= 1,159 samples) were evaluated and compared with normal blood-based transcriptomes using gene co-expression network enrichment, differential expression and functional enrichment analyses to identify candidate markers. Gene expression evaluation: Seven PCA cell lines and two normal prostate epithelial lines were used to assess candidate genes. Marker genes were determined in PCa tumor tissue (n= 50) and validated in the TCGA-PRAD (n= 500) dataset. Blood gene expression: Set #I: PCA: n= 132, BPH: n= 44, controls n= 55. Set #II: n= 50 (biochemical recurrence [BCR]). We constructed an artificial intelligence PCa model using classification algorithm analyses. Scoring: normalized algorithmically analyzed gene expression (0 to 100), positive score >20. PSA: BPH (n= 44) and PCa (n= 132). Clinical score assessment: Surgical cohort: (n= 47), samples: pre-surgical and post: 1 week - 14 months. Statistics: Kruskal-Wallis, Pearson-correlation, Fisher's and AUROC analyses (Mean±SEM). **Results:** Transcriptomic analysis identified 27 candidates. Cell lines/tissue: Expression levels were significantly elevated ($p< 0.001$, 2.1-35.8-fold) in cell lines and PCa surgical samples. All 27 markers were confirmed in TCGA-PRAD samples (average TPM: 58 to 10,366). *Blood*: In Set#I, levels in PCa were 47±2 ($p< 0.0001$) compared to BPH (19±1) and controls (18±0.5); AUROC: 0.92 (BPH) and 0.94 (controls), with an accuracy of 85-88%, a sensitivity of 86% and specificities 82 and 93%. For PSA, the AUROC (PCa vs. BPH) was 0.51 (p= 0.88). PSA was positive in 86% of BPH and was > 10ng/ml in 30%. PSA was positive in 83% of PCa and > 10ng/ml in 40% (Fisher's p= 0.28). PSA accuracy (> 10ng/ml) was 48%. Levels in Set#II (BCR) were 44±3. ProstaTest-was positive in 48 (96%). Surgical cohort (n= 47): Prostatest accuracy 100% pre-surgery. Resection decreased levels (KW-statistic: 57.4, $p< 0.0001$) from 52±1 to 23.5±2. **Conclusions:** A 27-gene blood signature was developed for PCa that exhibited a diagnostic accuracy of 92%; significantly better than PSA (48%, $p< 0.0001$). Surgical resection significantly ($p< 0.0001$) decreased levels. Biochemical recurrence was accurately detected (96%). A multi-gene prostate cancer liquid biopsy is likely to have clinical utility in both diagnosis and monitoring of PCa. Research Sponsor: None.

5575 Poster Session (Board #156), Fri, 8:00 AM-11:00 AM

Osteonecrosis of the jaw (ONJ) in radium 223 (Ra223)-treated metastatic castration-resistant prostate cancer (mCRPC) patients (pts) with exposure to zoledronic acid and/or denosumab. *First Author: Yen Thi Kim Hong Cao, University of Nevada Las Vegas, Las Vegas, NV*

Background: Bone health agents (BHA) including denosumab, a monoclonal antibody, and Zoledronic acid (ZA), a bisphosphonate, are recommended for men with CRPC and bone metastases to prevent skeletal-related complications. ONJ occurs in about 5% of patients (pts) on BHA. The incidence of ONJ in pts treated with Ra223 and BHA remains unknown, particularly in those who receive sequential treatment of BHAs. Here we describe the rate of ONJ in a real-world setting in mCRPC pts treated with Ra223 in 3 groups: 1) denosumab alone, 2) ZA alone, and 3) sequential ZA /denosumab or vice versa. **Methods:** A retrospective analysis of a cohort of mCRPC pts with bone metastases who received Ra223. Follow-up was until date of death or last data entry. Chart inclusion criteria included patients who received Ra223 between November 2010 to August 2018 with documentations of data points. **Results:** A total of 177 pts received Ra223 between 11/2010 and 8/2018. Median age 73 at 1st Ra223 (range 40-93); Median PSA 15.8- at 1st Ra223 (range 0.1-1952); Demographics-AA-10, C-130, Asian-9, unspecified-28; Median Alk Phos 95 at 1st Ra233 (range 25-1515). 93 % (164/177) received BHA. Of the 164 who received BHA, 45% (73/164) received denosumab only, 37% (61/164) received ZA only, and 18% (30/164) received sequential treatment. ONJ developed in 9.7% (16/164) of all patients on BHA. Denosumab alone caused ONJ in 7 of 73 pts (9.6%). ZA alone caused ONJ in 6 of 61 pts (9.8%). ONJ occurred in 3 of 30 pts (10%) in the sequential group. The median number of doses of BHA before development of ONJ was 10 with denosumab, 20 with ZA, and 19.5 (denosumab) and 22 (ZA) in the sequential group. **Conclusions:** In patients treated with Ra223 and a BHA, the rate of ONJ is 9.7%. The rate of ONJ was similar in groups treated with denosumab alone, ZA alone, and sequential treatment of ZA and denosumab However, ONJ developed more quickly in patients on denosumab. We conclude that the risk of ONJ is increased in patients treated with Ra223 and BHA. ZA or sequential therapy appears to delay time to onset of ONJ compared to denosumab. Clinicians should be mindful of the toxic synergy between Ra223 and BHA. ZA may be the preferred BHA partner with Ra223. Research Sponsor: None.

5576 Poster Session (Board #157), Fri, 8:00 AM-11:00 AM

RESTORE: A single-arm, open-label phase II trial of bipolar androgen therapy (BAT) in men with metastatic castration resistant prostate cancer (mCRPC)—A comparison of post-abiraterone (Abi) versus post-enzalutamide (Enza) patients (Pts). *First Author: Mark Christopher Markowski, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD*

Background: A paradoxical inhibition of cell growth has been observed in both androgen-sensitive and castration resistant prostate cancer cell lines following the addition of high-dose testosterone.We have conducted several clinical trials investigating a mode of supraphysiologic testosterone therapy termed, BAT, in which testosterone levels are rapidly driven to the supraphysiologic range followed by a return to near-castrate levels over 28-day treatment cycles with favorable results. We previously reported the efficacy of BAT in mCRPC pts that were progressing on enza. In this study, we compared the effect of BAT in mCRPC pts whose last therapy was abi vs. enza. In addition, we examined the benefit of abi or enza rechallenge after progression on BAT. **Methods:** 59 mCRPC pts (n = 29 post abi; n = 30 post enza) were enrolled and received at lease one dose of BAT monotherapy, 400mg intramuscularly every 28 days. After clinical or radiographic progression on BAT, pts were rechallenged with the AR targeted therapy to which they were most recently resistant. The co-primary endpoints were a 50% decline in PSA from baseline (PSA50) for BAT and for enza/abi rechallenge. **Results:** 5/29 (17.2%) of post-abi pts compared to 9/30 (30%) in the post enza group achieved a PSA50 response (P = 0.36). Post BAT rechallenge with abi (n = 19) or enza (n = 22) resulted in a PSA50 response rate of 15.8% (n = 3) and 68.2% (n = 15), respectively (P = 0.001). The total duration of benefit (i.e. PFS on BAT + PFS on rechallenge = "PFS2") was significantly longer in the post enza vs. post-abi patients (Median PFS2: 12.75 vs. 8.125 months; P = 0.04. Lastly, AR-V7 negative (n = 42) pts has a significantly longer median PFS2 compared to AR-V7 positive (n = 10) pts. (10.3 vs. 7.1 months, P = 0.005). **Conclusions:** Our data suggest that BAT may be more effective at resensitizing mCRPC to direct AR antagonists (i.e. enza) compared to abi. Detection of AR-V7 portended a worse outcome on BAT/rechallenge. Further clinical study is warranted. Clinical trial information: NCT02090114. Research Sponsor: U.S. National Institutes of Health.

	Post Abi N = 29	Post Enza N = 30	P-value
BAT PSA50 RR	17.2% (N = 5/29)	30.0% (N = 9/30)	0.360
BAT Objective RR	28.6% (N = 2/7)	50.0% (N = 6/12)	0.361
Rechallenge PSA50 RR	15.8% (N = 3/19)	68.2% (N = 15/22)	0.001

5577 Poster Session (Board #158), Fri, 8:00 AM-11:00 AM

Radiographic paradoxical response in patients with metastatic castrate-resistant prostate cancer (mCRPC) undergoing treatment with second-generation hormone therapy (second-HT). *First Author: Jamal Alamiri, Mayo Clinic Rochester, Rochester, MN*

Background: Prostate specific antigen (PSA) has well-recognized limitations as a marker for treatment response and disease progression. A post hoc analysis of the PREVAIL trial reported 24.5% of chemotherapy naïve mCRPC patients on enzalutamide had radiographic progression on conventional imaging with non-rising PSA. In this study, we sought to retrospectively compare PSA levels with C-11 choline positron emission tomography/computed tomography (PET/CT) images in patients with m-CRPC on 2nd-HT with prior use of chemotherapy. **Methods:** We identified 123 patients with mCRPC on 2nd-HT following prior use of docetaxel chemotherapy (Abiraterone, n = 106; Enzalutamide, n = 17). Patients underwent serial PSA testing and C-11 choline PET/ CTs every 3–6 months. Disease progression was defined by the increase in blood pool corrected maximum standardized uptake value (SUVmax) of the index lesion on C-11 choline PET/CT scan. Suspicious lesions were confirmed by biopsy and/or conventional imaging. **Results:** Approximately 43% (n = 53) of patients had radiographic disease progression while on 2nd-HT. At time of radiographic progression, 60.4% of patients showed a parallel rise in PSA (Group-A), while 39.6% showed a paradoxical response; defined as radiographic progression with stable or down-trending PSA (Group-B). Median PSA at time of progression was 3.1 ng/ml for Group-A, and 1.3 ng/ml for Group-B (p-value = 0.0176). Median SUVmax was the same (4.9 Group-A, 4.6 Group-B; p-value = 0.6072). Bone-predominance progression was more significant in Group-B (90%) versus Group-A (65%) (p-value = 0.0309). The median time for radiographic progression was 9.5 months versus 3.9 months for Group-A and Group-B, respectively (Log-Rank = 0.0063). **Conclusions:** Metabolic imaging is a useful tool that should complement PSA in the evaluation of treatment response and disease progression in mCRPC patients on 2nd-HT, especially considering the paradoxical response observed in our data. Research Sponsor: None.

5578 Poster Session (Board #159), Fri, 8:00 AM-11:00 AM

Quality of life (QOL) for the treatment sequence of abiraterone acetate plus prednisone (AAP) followed by enzalutamide (ENZ) versus the opposite sequence for metastatic castration-resistant prostate cancer (mCRPC): Results from a phase II randomized clinical trial. *First Author: Daniel J Khalaf, BC Cancer Agency-Vancouver Centre, Vancouver, BC, Canada*

Background: A randomized cross-over phase II trial (Lancet Oncol 20(12):1730, 2019) showed the sequence of AAP followed by ENZ is associated with a better time to PSA progression compared with the opposite sequence and superior 2nd line activity of ENZ. It is unknown whether one treatment sequence is associated with better QOL than the other. **Methods:** 202 Patients were randomized (1:1) to receive either AAP followed by ENZ at PSA progression (arm A) or the opposite sequence of ENZ followed by AAP (arm B). FACT-P questionnaires were completed at baseline, cross-over and every 4 weeks on treatment. Time to QOL deterioration (TTQOLD) for the treatment sequence was determined from start of 1st line treatment to first questionnaire with a clinically meaningful decrease from baseline and compared between arms using the log-rank test. TTQOLD was also determined for 1st line and 2nd line separately. The proportion of patients with QOL deterioration for total FACT-P score and FACT-P subscores from baseline to week 12 of 1st and 2nd line treatment was compared between arms using X^2 test. **Results:** Median follow-up for 1st and 2nd line and whole sequence were 9.3, 6.6 and 22.0 months (mos) respectively and questionnaire completion rate was 81%. TTQOLD for total FACT-P score for the whole sequence for arm A vs B was 10.5 mo (95% CI 5.0-15.5) vs 10.8 mo (5.5-13.1), p = 0.74. For 1st-line AAP vs ENZ, median TTQOLD was 15.5 mo (5.5-21.2) vs 11.0 (5.5-13.3) respectively (p = 0.23). For 2nd line ENZ vs ABI, median TTQOLD was 3.7 mo (2.0-5.4) vs 5.8 (2.8-12.1), p = 0.13. There was a higher rate of deterioration in physical well-being (PWB) for 1st line ENZ (arm B) and 2nd line ENZ (arm A) (Table). **Conclusions:** There was no difference in TTQOLD between the two treatment sequences of AAP and ENZ. Although treatment with second line ENZ has been associated with greater anti-cancer effects, ENZ was associated worse PWB QOL scores. Clinical trial information: NCT02125357. Research Sponsor: Canadian Cancer Society Research Institute, Other Foundation, Pharmaceutical/Biotech Company.

Clinically significant deterioration at 12 weeks (%).

	1st-line treatment			2nd-line treatment		
FACT-P score	Arm A (1st-line AAP) n = 101	Arm B (1st- line ENZ) n = 101	P	Arm A (2nd-line ENZ) n = 77	Arm B (2nd-line AAP) n = 77	P
Total FACT-P	23	30	0.26	40	34	0.40
Functional well-being	33	43	0.15	49	36	0.10
Physical well-being	26	40	0.036	45	29	0.030
Emotional well-being	24	30	0.34	27	35	0.30
Social well-being	21	25	0.50	18	23	0.43
Prostate cancer score	35	44	0.19	49	35	0.073
Pain score	45	41	0.57	43	34	0.25

5579 Poster Session (Board #160), Fri, 8:00 AM-11:00 AM

Association between BRCA2 status and histologic variants (intraductal [IDC] and cribriform [CRIB] histology) in prostate cancer (PC). *First Author: Elena Castro, Hospitales Virgen de la Victoria y Regional de Málaga, Instituto de Investigación Biomédica de Málaga, Málaga, Spain*

Background: IDC histology in PC has been suggested to associate with germline *BRCA2* mutations *(gBRCA2)* in small series, leading to the potential recommendation of genetic testing for all PC patients with IDC in the primary tumor. **Methods:** We conducted a case-control study in which primary PC from 58 germline *BRCA2* mutation carriers (*gBRCA2*) and 116 from non-carriers (NC) were matched 1:2 by Gleason score and specimen type (core biopsy/prostatectomy). Samples were independently reviewed by two expert pathologists blinded to genetic status who established the presence of IDC and/or CRIB morphology with supportive immunohistochemical stains in a subset of cases. Next-generation sequencing, aCGH and/or FISH were used to assess for somatic mono-/bi-allelic *BRCA2* alterations. PTEN protein loss was determined by IHC, and *TMPRSS2-ERG* was detected by FISH/qRT-PCR. Chi-square tests were used to compare the frequency of IDC and cribriform histology in *gBRCA2* vs NC, as well as to assess the associations with other variables. Logistic regression models were built to identify independent factors associated with IDC and CRIB histology. **Results:** *gBRCA2* cases were younger at diagnosis (median 61.3 vs 64, $p < 0.01$) and had T3-4 disease more often than NC cases (31% vs 10.5%, $p < 0.01$), but the two groups did not differ in any other clinical-pathologic characteristics. After independent histopathological review, 79 cases demonstrated IDC histology and 81 had CRIB histology. No differences in the prevalence of IDC (50% NC vs 36% *gBRCA2*, p = 0.09) or CRIB (43% NC vs 53% *gBRCA2*, p = 0.20) patterns were observed. The probability of IDC was higher in PC with bi-allelic *BRCA2* alterations (OR 5.1, 95%CI 2.1-12.6), PTEN loss (OR 5.1, 95% CI 1.9-13.5) or both (OR 23.0, 95%CI 4.9-107.2) compared to those without these alterations. Bi-allelic *BRCA2* alteration was also associated with higher probability of CRIB histology (OR 7.2, 95%CI 3.1-16.4). *TMPRSS2-ERG* fusions were not associated with IDC or CRIB histology. MVA confirmed the independent association of bi-allelic *BRCA2* alteration ($p < 0.01$) and PTEN loss ($p < 0.01$) with IDC histology. Bi-allelic *BRCA2* alteration ($p < 0.01$) and Gleason >8 ($p < 0.01$) were independent risk factors for CRIB histology. **Conclusions:** Primary PC with bi-allelic *BRCA2* alterations was significantly associated with IDC and CRIB histology, independent of other clinical-pathologic factors (while *gBRCA2* status alone was not). PTEN loss in primary PC was also independently associated with IDC, but not CRIB, histology. Research Sponsor: Prostate Cancer Foundation; Instituto de Salud Carlos III.

5580 Poster Session (Board #161), Fri, 8:00 AM-11:00 AM

Obesity and metabolic syndrome correlate with a higher risk of biochemical recurrence in high risk and intermediate risk prostate cancer patients who underwent robotic-assisted laparoscopic prostatectomy. *First Author: Shifeng Mao, Allegheny Health Network Cancer Institute, Pittsburgh, PA*

Background: Obesity and metabolic syndrome (MS) is prevalent in our society, and have been linked to a higher incidence of prostate cancer (PCa). The relationship of obesity or MS and cancer control has yielded mixed results in previous studies. We examined the correlation between the incidence of biochemical recurrence (BCR) with MS and BMI in a cohort of patients with PCa who underwent robotic-assisted laparoscopic prostatectomy (RALP). **Methods:** A retrospective study of patients who underwent RALP at a single center from 2007 to 2015 was conducted. Parameters including preoperative BMI, fasting glucose, lipid profile, blood pressure, PSA, Gleason score, pathologic stage, time to BCR, and surgical margin status were analyzed. Patients were categorized in high (HR), intermediate (IR), and low-risk (LR) groups based on the National Comprehensive Cancer Network (NCCN) guidelines. WHO classification was used for MS criteria, and BCR was defined as two consecutive postoperative PSA volume of $\geq$ 0.2 ng/mL. Obesity is defined as BMI $\geq$30 kg/m^2. **Results:** A total of 726 patients with 189 in HR, 471 in IR and 66 patients in LR groups were included in this study with the median age of 59 (interquartile range [IQR] 55-64) years old. The median follow-up from surgery was 38 (IQR 22-46) months. More obese patients were found in the HR group compared to IR/LR group (46.5% vs. 33.1%, $p<0.01$). There were also more patients with MS in the HR group compared to IR/LR group (36.5% vs. 12.0%, $p<0.01$). Obese patients had a higher rate of BCR across risk groups in comparison to non-obese patients 32.1% vs. 15.4% ($P<0.001$), specifically 68% vs. 40%($p<0.01$) in HR group and 21.3% vs. 12.7% (p=0.035) in the IR group. Similarly, patients with MS had a higher rate of BCR in HR and IR groups in comparison to the patients without MS, 39.1% vs. 18.7% ($P<0.01$); specifically, 67.7% vs. 42.2% ($p<0.01$) in HR and 29% vs. 11.6% ($p<0.01$) in the IR group. No correlation between MS or obesity and BCR was observed in LR group. There was no statistically significant difference in the positive surgical margin rate between obese and non-obese cohorts in each risk group. **Conclusions:** Among HR and IR-PCa patietns who underwent RALP, both obesity and MS correlate with increased risk of BCR. There were significantly more obesity and MS in HR-PCa patients, suggesting a potential pathophysiologic interplay between obesity or MS and cancer progression. Research Sponsor: the Western Pennsylvania Prostate Cancer Foundation.

5582 Poster Session (Board #163), Fri, 8:00 AM-11:00 AM

Oncological outcomes of 356 patients undergoing salvage focal ablative HIFU or cryotherapy following radiation failure. *First Author: Deepika Reddy, Imperial College London, London, United Kingdom*

Background: Patients that have previously failed radiotherapy for prostate cancer is usually limited to systemic therapy due to morbidity from salvage prostatectomy. We reviewed the outcomes following focal salvage ablative therapy with HIFU or cryotherapy within the UK's HEAT and ICE registries. **Methods:** 356 consecutive patients underwent focal ablative treatment after initial radiation treatment failure (28/1/2004-1/10/2019, 194 (54.5%) underwent HIFU (posterior recurrence) and 162 (45.5%) underwent cryotherapy (mostly anterior or T3b). Primary outcome was failure-free survival (FFS) defined as no systemic therapy, whole-gland treatment, metastases or prostate cancer-specific death. Secondary outcomes were adverse events and overall survival. **Results:** Median (IQR) age was 69years (65-73) and PSA (IQR) was 4.0ng/ml (1-7-7.2). Overall median (IQR) follow-up was 41.3 months (21.4-58.5). Quadrant ablation was performed in 128 (36.0%), hemi-ablation performed in 64 (18.0%), hockey-stick in 5 (1.4%) and 159 (43.8%) had unknown ablative patterns. Due to histological or MRI proven recurrence/residual disease, 31 (8.7%) underwent further focal salvage re-treatment. FFS (95%CI) at 3 and 6 years were 81% (76-87%) and 75% (68-83%) respectively. Median (IQR) time to failure was 15.5 months (19.7). Overall survival (95%CI) at 3 and 6 years were 97% (95-100%) and 88% (81-96%) respectively. Prostate-specific mortality was 2.8%. Overall 3 (0.8%) patients were managed for fistula formation, 16 (4.5%) were treated for UTIs. **Conclusions:** Salvage focal ablative therapy for radio-recurrent prostate cancer is safe and provides good short to medium-term oncological control. The FORECAST study is awaited to further determine oncological outcomes in this cohort. Research Sponsor: None.

5583 Poster Session (Board #164), Fri, 8:00 AM-11:00 AM

Cost-effectiveness of novel antiandrogens (AAs) for treatment of nonmetastatic castrate-resistant prostate cancer (nmCRPC). *First Author: Irbaz Bin Riaz, Mayo Clinic, Rochester, MN*

Background: FDA has approved three novel AAs [Apalutamide(A), Darolutamide(D) and Enzalutamide(E)] in combination with Androgen deprivation therapy (ADT) for treatment of (nmCRPC) patients (pts). We report the cost-effectiveness of these drugs from the US perspective to help facilitate the choice of these agents for clinical practice. **Methods:** A life time Markov state-transition model was constructed with three health states (Metastasis-Free Survival[MFS], Metastatic disease, and Death) to compare cost-effectiveness of AA therapies for treatment of nmCRPC based on US healthcare payer perspective. A network meta-analysis of MFS and OS was conducted due to the lack of head to head trials. An approximation of the original individual-level patient time-to-event data were derived from digitized Kaplan-Meier curves for OS and MFS. Weibull distributions was selected as the best fitted model fitted and extrapolated as per the NICE decision support unit recommendations. Medication costs were based on wholesale acquisition cost. Adverse event (AE) grades 3/4 management costs were incorporated in the model. Discount rate of 3% per year was applied to costs and effects. Life years (LYs) and quality adjusted life years (QALYs) for each treatment as well as the incremental cost effectiveness (ICER) and cost utility (ICUR) ratios were estimated. Base case analyses (BCA) and probabilistic sensitivity analyses (PSA) were estimated. **Results:** The table summarizes the results form BCA analyses. A+ADT offers best gain in LYs (8.37yrs) and QALYs (5.30 yrs) but at higher cost. **Conclusions:** Apalutamide was associated with gains in LYs and QALYs traded off with higher lifetime cost relative to other AA alternatives. ADT was associated with lower gains in LYs and QALYs traded off with lower lifetime cost relative to other alternatives. Based on a $150,000/QALY threshold pay off, A+ADT is likely more cost effective compared to E+ADT or ADT alone; while E+ ADT may be more cost effective compared to D+ ADT. Research Sponsor: None.

Base case analyses for MFSLY and QALY.

Treatment	Cost	LY	QALY
Apalutamide	$512,620	8.37	5.30
Enzalutamide	$458,640	6.99	3.05
Darolutamide	$379,932	7.49	4.68
ADT	$187,264	6.48	3.07
Incremental Cost Effectiveness Ratio (ICER)/Incremental Cost Utility Ratio (ICUR)			
Apalutamide	$39,116	$150,782	$172,146
$23,991	Enzalutamide	$157,416	$532,110
$214,013	$48,287	Darolutamide	$190,760
$145,900	$13,568,800	$119,670	ADT

Blue cells for ICER of LY, Gray Cells for ICUR of QALY

5584 Poster Session (Board #165), Fri, 8:00 AM-11:00 AM

Short-term adjuvant versus neoadjuvant hormone therapy in localized prostate cancer: A pooled individual patient analysis of two phase III trials. *First Author: Daniel Eidelberg Spratt, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: The timing of systemic therapy in relation to radiotherapy (RT) is important in most malignancies. In contrast, androgen deprivation therapy (ADT) has largely been investigated in relation to its duration rather than its sequencing with RT. Herein, we conduct the first combined individual patient analysis of two phase III randomized trials to determine the optimal timing of ADT with RT in localized prostate cancer (PCa). **Methods:** Individual patient data was obtained from the Malone et al trial (JCO 2019), which randomized patients to receive neoadjuvant/concurrent or concurrent/adjuvant ADT for 6 months with prostate only RT. This was combined with the prostate only RT arms of RTOG 9413 that randomized patients to 4 months of neoadjuvant/concurrent or adjuvant ADT. The neoadjuvant/concurrent arms of both trials were combined into the "neoadjuvant" group, and the concurrent/adjuvant (Malone) and adjuvant arm (RTOG 9413) were combined in the "adjuvant" group. The Kaplan-Meier method was used to estimate overall survival (OS) and progression-free survival (PFS). Cumulative incidence of distant metastasis (DM), PCa-specific mortality (PCSM) and biochemical failure (BF) were calculated using the Fine-Gray method with non-PCa deaths as competing events. Late genitourinary (GU) and gastrointestinal (GI) toxicity are also reported. **Results:** The median follow-up was 14.9 years (yrs) and 1065 patients were included (n=531 neoadjuvant, 534 adjuvant). Groups were well balanced for all baseline characteristics. Adjuvant ADT was superior to neoadjuvant ADT in terms of BF (15yr: 33% vs 43%, HR: 1.37 (95%CI: 1.12-1.68), p=0.002), DM (15yr: 12% vs 18%, HR: 1.40 (95%CI: 1.00-1.95), p=0.04), and PFS (15yr: 36% vs 29%, HR: 1.25 (95%CI: 1.07-1.47), p=0.01). Adjuvant ADT yielded lower PCSM (15yr: 15% vs 20%, HR: 1.29 (95%CI: 0.95-1.75), p=0.10), but did not reach statistical significance. This approached statistical significance in high risk PCa (HR 1.39 (95%CI 1.00-1.93), p=0.053). OS was not significantly different between arms (15yr: 39% vs 34%, HR: 1.11 (95%CI: 0.95-1.30), p=0.20). There was no significant difference in either late grade $\geq$3 GI (p=0.21) or GU (p=0.98) toxicity. **Conclusions:** We demonstrate for the first time that sequencing of ADT with RT significantly impacts long-term oncologic outcomes in localized PCa, favoring an adjuvant rather than neoadjuvant approach, without increasing late toxicity. This data has important implications to ongoing and future clinical trial design. Clinical trial information: NCT00769548. Research Sponsor: Prostate Cancer Foundation.

5585 Poster Session (Board #166), Fri, 8:00 AM-11:00 AM

Treatment patterns and outcomes of patients with penile squamous-cell carcinoma (PSCC) undergoing inguinal lymph node dissection (ILND): An analysis of a multicenter contemporary database. *First Author: Marco Bandini, Vita-Salute San Raffaele University, Milan, Italy*

Background: PSCC is a rare tumor and the administration of guidelines-based therapies is still problematic in real-world practice. Survival outcomes remain suboptimal in patients (pts) with ILN involvement. Multinational analyses of real-world patterns are needed. **Methods:** Within an international, multicenter database of 965 PSCC pts who received ILND from 1980-2019, 630 had complete information for the variables of interest, from USA (N=81), Europe (EU, N=355), South America (SA, N=90), and China (Ch, N=104). Descriptive analyses according to geographical and ethnicity/race distribution were made. Comparisons of outcomes were made with Kaplan-Meier analyses and corresponding logrank tests. **Results:** Median age at diagnosis was 59 yrs, with no differences worldwide and according to ethnicity/race. Pts from SA presented with more advanced cT-stage (cT3-4: 26.7% vs. 17.3% USA vs. 7.6% EU) while EU pts presented with more advanced cN-stage (cN3: 14.9% vs. 11% USA vs. 7.8% SA vs. 5.8% Ch) as well as pathological (p)N-stage: pN3 pts were 53% in EU, 33.3% in USA, 20% in SA, and 18.3% in Ch. Perioperative chemotherapy (pCT) was more frequently administered in EU (53.8%) vs. USA (34.6%) SA (5.6%) Ch (7.7%). cT-stage was more frequently advanced in black pts (cT3-4: 33.3% vs. 12% Caucasian, 6.2% Hispanic/latino, 0% Asian) and the same was for cN-stage (cN3: 25% in black, 13% in Caucasian, 6.2% in Hispanic/latino, 6% in Asian). Conversely, pN3 pts were more frequently Caucasian (45.6%) vs. black (25%), Hispanic/latino (19%), and Asian (18%). pCT was more frequently administered in Caucasian pts (45%) vs. black (8.3%), Hispanic/latino (0), and Asian (8%). No significant differences in overall survival (OS) were observed according to geographical region or ethnicity/race, in the total pts and in the subgroups according to cT, cN, pN-stages and pCT. Median OS after pCT and ILND was 95 months. Bilateral ILN involvement was equally observed regardless of geographical region and ethnicity/race. In the total population, pCT significantly prolonged OS in pts with bilateral ILN (p=0.04), but not in pts with pelvic LN. **Conclusions:** Treatment patterns for PSCC undergoing ILND remain heterogeneous worldwide, and adherence to guidelines is seemingly poor. However, long-term outcomes with pCT remain uniformly suboptimal with $<$50% pts alive at 10 yrs. Further collaborative efforts are needed in this orphan disease to harmonize the therapeutic paradigm. Research Sponsor: Fondazione IRCCS Istituto Nazionale dei Tumori.

TPS5586 **Poster Session (Board #167), Fri, 8:00 AM-11:00 AM**

A phase II randomized trial of RAdium-223 dichloride and SABR versus SABR for oligomEtastatic prostate caNcerS (RAVENS). *First Author: Matthew Pierre Deek, Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins Hospital, Baltimore, MD*

Background: Metastasis directed therapy (MDT) is able to prolong progression free survival (PFS) and forestall initiation of androgen deprivation therapy (ADT) in men with hormone-sensitive, oligometastatic prostate cancer (HSOPCa) compared to observation. While MDT appears to be effective in HSOPCa, a large percentage of men will have disease recurrence. Patterns of failure demonstrate patients tend to recur in the bone following MDT, raising the question of subclinically-apparent osseous disease. Radium-223 dichloride is a radiopharmaceutical with structural similarity to calcium, allowing it to be taken up by bone where it emits alpha particles, and therefore might have utility in the treatment of micrometastatic osseous disease. Therefore, the primary goal of the phase II RAVENS trial is to evaluate the efficacy of Stereotactic ablative radiation (SABR) + radium-223 dichloride in prolonging PFS in men with HSOPCa. **Methods:** Patients with HSOPCa and 3 or less metastases with at least 1 bone metastasis (by conventional imaging) will be randomized 1:1 to SABR alone vs. SABR + radium-223 dichloride. Eligibility criteria include PSA doubling time of < 15 months and ECOG performance status of < 2. Patients cannot be on ADT and must have normal testosterone levels at the time of randomization. Patients randomized to the combination arm will receive six doses of Radium-223 dichloride at four week intervals. A sample size using a 1:1 randomization scheme of 30 patients per arm will provide 80% power to detect an increase of median PFS from 10 months to 20 months with type I error = 0.1, using a one-sided log-rank test. To account for 5% early drop out, we will randomize a total of 64 patients (32 per arm). The primary end point is PFS with a primary hypothesis that SABR + radium-223 dichloride will increase median PFS from 10 months in the SABR arm to 20 months in the SABR + radium-223 dichloride arm. Progression is a composite endpoint including PSA progression per Prostate Cancer Working Group 2 (PCWG2), symptomatic progression, radiologic progression per RECIST 1.1 criteria, initiation of ADT, or death due to any cause. Secondary clinical endpoints include toxicity and quality of life assessments, local control at 12 months, locoregional progression, time to distant progression, time to new metastasis, and duration of response. Biological correlates will be evaluated including changes in circulating tumor cells following therapy, deep sequencing of circulating tumor DNA, and T-cell repertoire profiling before and after therapy. Clinical trial information: NCT04037358. Research Sponsor: Bayer.

TPS5587 **Poster Session (Board #168), Fri, 8:00 AM-11:00 AM**

DaroACT: Darolutamide and enzalutamide effects on physical and neurocognitive function and daily activity in patients with castration-resistant prostate cancer (CRPC). *First Author: Tomasz M. Beer, Knight Cancer Institute, Oregon Health & Science University, Portland, OR*

Background: The androgen receptor inhibitors (ARIs) apalutamide and enzalutamide (Enza) are approved for the treatment of men with advanced prostate cancer. These ARIs are associated with adverse events (AEs) including fatigue, neurocognitive dysfunction, and falls. Darolutamide (Daro) is a structurally distinct ARI approved by the FDA to treat nonmetastatic CRPC, based on significantly improved metastasis-free survival vs placebo in the ARAMIS Phase III clinical trial. Daro was not associated with a significant increase in AEs beyond that of concomitant androgen deprivation therapy, compared with placebo. DaroAcT is the first prospective trial to compare the effects of Daro to those of Enza on physical and neurocognitive function, and daily physical activity, in men with CRPC. **Methods:** This randomized, open-label, multicenter, Phase IIb trial (NCT04157088), involving ~20 sites across the US, is open for enrollment. After a lead-in phase of 30 pts treated with Daro alone, approximately 120 pts will be randomized 1:1 to receive Daro (600 mg twice daily) or Enza (160 mg once daily). Eligibility criteria include CRPC (metastatic and non-metastatic); age $\geq$18 years; Karnofsky performance status $\geq$80; no prior abiraterone within 6 months of enrollment, and no prior immunotherapy or apalutamide. All patients will continue luteinizing hormone-releasing hormone agonist or antagonist treatment for the duration of the study. The primary endpoint is the proportion of pts with slowed Timed Up and Go (TUG) time during the 24-week period from baseline. Secondary endpoints include the proportion of pts with worsening in short Physical Performance Battery (sPPB), mean change from baseline in daily physical activity, the proportion of pts with a decline in neurocognitive function or worsening of fatigue, and AEs. This study uses objective measures to assess physical function, including TUG and sPPB, measurements of daily activity levels with an accelerometry device for $\geq$7 days at designated time points, and neurocognitive tests. Fatigue is measured using the Brief Fatigue Inventory. Primary completion is estimated to be December 31, 2022. Clinical trial information: NCT04157088. Research Sponsor: Bayer.

TPS5588 **Poster Session (Board #169), Fri, 8:00 AM-11:00 AM**

A phase III randomized, placebo-controlled, double-blind study of niraparib plus abiraterone acetate and prednisone versus abiraterone acetate and prednisone in patients with metastatic prostate cancer (MAGNITUDE). *First Author: Kim N. Chi, BC Cancer and Vancouver Prostate Centre, Vancouver, BC, Canada*

Background: Preclinical data suggest synergistic antitumor activity when the PARP inhibitor (PARPi) niraparib is combined with the androgen pathway inhibitor abiraterone acetate[1]. The addition of a PARPi to abiraterone acetate plus prednisone (AAP) showed improved radiographic progression-free survival (rPFS) vs AAP alone in patients with mCRPC regardless of DNA repair gene defect (DRD) status[2]. Interim results from a phase I study support safety and tolerability of niraparib 200 mg combined with AAP in patients with mCRPC[3]. The objective of this Phase III study is to compare the efficacy and safety of niraparib plus AAP versus AAP with placebo as first-line therapy for mCRPC. **Methods:** This ongoing multicenter MAGNITUDE study (NCT03748641) will open in approximately 300 sites across 28 countries and will enroll patients with mCRPC who have not received treatment in the metastatic castrate resistant setting other than ongoing androgen deprivation therapy [ADT] and $\leq$4 months of AAP. DRD status will be determined by plasma and tissue assays. The cohort with DRD (n=400) and the cohort without DRD (n=600) will each be randomized 1:1 to niraparib + AAP or placebo + AAP. The first patient was consented in February 2019 and enrollment is ongoing. The primary objective of the study is to compare radiographic progression-free survival (rPFS) as assessed by blinded independent central radiology review in each cohort and treatment group. To test superiority of the combination vs AAP, sample sizes were estimated to provide 92% power to detect HR$\leq$0.65 rPFS in the cohort with DRD and 94% power to detect HR$\leq$0.67 in rPFS in the cohort without DRD, both at a 2-tailed level of significance of 0.05. The secondary objectives are time to symptomatic progression, time to cytotoxic chemotherapy, and overall survival. Safety and pharmacokinetic profiles will be evaluated. [1]Rajendra N, et al. Cancer Res 2019;79(13 Suppl):Abstract nr 2134. [2]Clarke N, et al. Lancet Oncol. 2018;(7):975-986. [3]Saad, et al. Ann Oncol, 2018;29 (suppl 8), mdy284.043, https://doi.org/10.1093/annonc/mdy284.043) Clinical trial information: NCT03748641. Research Sponsor: Janssen Research and Development.

TPS5589 **Poster Session (Board #170), Fri, 8:00 AM-11:00 AM**

Phase I study of AMG 509, a STEAP1 x CD3 T cell-recruiting XmAb 2+1 immune therapy, in patients with metastatic castration-resistant prostate cancer (mCRPC). *First Author: W. Kevin Kelly, Thomas Jefferson University, Philadelphia, PA*

Background: Six transmembrane epithelial antigen of the prostate 1 (STEAP1) is a cell surface antigen that is highly expressed in prostate cancer. AMG 509 is a potent bispecific XmAb 2+1 immune therapy designed to direct T-effector cells to STEAP1-expressing cells. AMG 509 contains two identical humanized anti-STEAP1 Fab domains that bind STEAP1-expressing cells, an anti-CD3 scFv domain that binds T cells, and an Fc domain, engineered to lack effector function, that extends serum half-life. In preclinical studies, AMG 509 induced potent and specific T-cell-mediated lysis of STEAP1-expressing cancer models. **Methods:** This open-label, phase I, first-in-human study will evaluate the safety, tolerability, pharmacokinetics (PK), and efficacy of AMG 509 in patients with relapsed/refractory mCRPC. The dose exploration phase (n=40) will estimate the maximum tolerated dose (MTD) or recommended phase II dose (RP2D) using a Bayesian logistic regression model. The dose expansion phase (n=30) will confirm safety, PK, and pharmacodynamics at the MTD or RP2D and collect further safety, efficacy, and biomarker data. Efficacy will be assessed by prostate-specific antigen response, circulating tumor cell response, and objective tumor response per RECIST 1.1 with Prostate Cancer Working Group 3 modifications. Key inclusion criteria: men $\geq$18 years with histologically/cytologically confirmed mCRPC who are refractory to novel hormonal therapy (e.g., abiraterone and/or enzalutamide) and have failed 1–2 taxane regimens or are medically unsuitable for or have refused taxanes; ongoing castration with total serum testosterone $\leq$50 ng/dL; evidence of progressive disease; ECOG performance status 0–1; life expectancy $\geq$3 months; and adequate hematologic, renal, hepatic, and cardiac function. In the dose exploration phase, novel antiandrogen therapy must have been given in the metastatic setting. Key exclusion criteria: pure small-cell or neuroendocrine carcinoma of the prostate; untreated CNS metastases or leptomeningeal disease; any anticancer therapy or immunotherapy, radiation therapy, or major surgery $<$4 weeks from first dose; history of or current autoimmune disease or any disease requiring immunosuppressive therapy ($\leq$10 mg/d prednisone permitted); prior STEAP1-targeted therapy; infection requiring IV antimicrobials $<$7 days from first dose. The study opened in January 2020 and is recruiting patients. Clinical trial information: NCT04221542. Research Sponsor: Amgen Inc.

TPS5590 **Poster Session (Board #171), Fri, 8:00 AM-11:00 AM**

Phase I study of AMG 160, a half-life extended bispecific T-cell engager (HLE BiTE immune therapy) targeting prostate-specific membrane antigen, in patients with metastatic castration-resistant prostate cancer (mCRPC). *First Author: Ben Tran, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia*

Background: Prostate-specific membrane antigen (PSMA) is a clinically validated therapeutic target for the imaging and treatment of mCRPC. AMG 160 is an HLE BiTE immune therapy designed to redirect T cells to cancer cells by binding to PSMA on cancer cells and CD3 on T cells. BiTE immune therapy leads to direct tumor cell killing, T-cell activation and expansion, and the creation of a pro-inflammatory tumor microenvironment. Combining AMG 160 with a PD-1 inhibitor may enhance antitumor activity by enabling sustained T-cell-dependent killing of tumor cells in the inflamed tumor microenvironment. **Methods:** NCT03792841 is a phase I study of AMG 160 as monotherapy (part 1) and in combination with pembrolizumab (part 2) in men with histologically/cytologically confirmed mCRPC who are refractory to a novel hormonal therapy (abiraterone, enzalutamide, and/or apalutamide) and have failed 1–2 taxane regimens (or are medically unsuitable or have refused taxanes), who have ongoing castration with total serum testosterone $\leq$ 50 ng/dL, and have evidence of progressive disease. Patients who received prior PSMA radionuclide therapy may be eligible. Patients with CNS metastases, leptomeningeal disease, spinal cord compression, or active autoimmune disease will be excluded. Primary objectives are to evaluate safety and tolerability and determine the maximum tolerated dose (MTD) or recommended phase II dose (RP2D) of AMG 160 given as monotherapy or in combination with pembrolizumab. Secondary objectives are to characterize pharmacokinetics and preliminary antitumor activity. Exploratory objectives include evaluation of potential pharmacodynamic and patient selection biomarkers, immunogenicity, and patient-reported pain and functional outcomes. The part 1 dose exploration will determine the MTD/RP2D of AMG 160. The part 1 dose expansion will confirm the safety and tolerability of the MTD/RP2D. The part 2 dose exploration will estimate the MTD/RP2D of AMG 160 in combination with pembrolizumab. Evaluation of preliminary antitumor activity will be based on RECIST 1.1 with Prostate Cancer Working Group 3 modifications, PSA response, CTC response, progression-free survival (radiographic and PSA), and overall survival. PSMA PET/CT and FDG PET/CT imaging will be used for evaluation of exploratory objectives. The study opened in February 2019 and is currently recruiting patients into both part 1 and part 2. Clinical trial information: NCT03792841. Research Sponsor: Amgen Inc.

TPS5591 **Poster Session (Board #172), Fri, 8:00 AM-11:00 AM**

CYCLONE 2: A phase II, randomized, placebo-controlled study of abiraterone acetate plus prednisone with or without abemaciclib in patients with metastatic castration-resistant prostate cancer. *First Author: Matthew Raymond Smith, Massachusetts General Hospital Cancer Center, Boston, MA*

Background: Despite recent advances, nearly all patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) experience disease progression and cancer-specific mortality. Persistent or reactivated androgen receptor (AR) signaling and/or activation of pathways in cross-talk with AR signaling are key drivers of mCRPC progression. Evidence suggests that AR signaling promotes translation of D-type cyclins resulting in cyclin-dependent kinase 4 and 6 (CDK4&6) activation and cell cycle progression. Abemaciclib is an oral selective inhibitor of CDK4&6 dosed on a continuous schedule, that is FDA-approved in combination with endocrine therapy or as monotherapy to treat HR+, HER2- metastatic breast cancer pts. Preclinical studies with prostate cancer cell lines and xenograft models showed that abemaciclib induces cell cycle arrest and tumor growth inhibition. The hypothesis is that addition of abemaciclib to AR targeted therapy may be an effective treatment for mCRPC pts. **Methods:** CYCLONE 2 (NCT03706365) is a phase II, randomized, double-blind, multicenter, placebo-controlled study to assess the safety and efficacy of abemaciclib in combination with abiraterone acetate plus prednisone (AA+P) as first-line treatment of pts with mCRPC. The study is designed in two parts. Part 1 is a 30-patient safety lead-in to determine the recommended phase II dose (RP2D; 150 mg or 200 mg, twice daily) of abemaciclib in combination with AA (1000 mg, once daily) + P (5 mg, twice daily). In part 2, 150 pts are randomized 1:1 to abemaciclib at the RP2D with AA+P or placebo with AA+P. Pts who received prior AA+P, enzalutamide, apalutamide, darolutamide, radiopharmaceuticals, or sipuleucel-T are excluded. Prior docetaxel for metastatic hormone-sensitive prostate cancer, but not for mCRPC, is allowed. Pts must have progressive mCRPC (by PSA and/or imaging) and an accessible metastatic lesion for tumor biopsy. The co-primary objectives are radiographic PFS (per RECIST1.1 for soft tissue and PCWG3 for bone) and time to PSA progression. Secondary objectives include safety, objective response rate, duration of response, OS, time to symptomatic progression, and pharmacokinetics. Assuming hazard ratios of 0.64 (rPFS) and 0.6 (PSA progression), the study is powered to 80% and 85%, respectively, to test the superiority of abemaciclib plus AA+P vs. placebo plus AA+P at one-sided α=0.1 using stratified log-rank tests. Part 1 is completed and part 2 is enrolling in 70 sites worldwide. Clinical trial information: NCT03706365. Research Sponsor: Eli Lilly and Company.

TPS5592 **Poster Session (Board #173), Fri, 8:00 AM-11:00 AM**

A phase I/II study of REGN5678 (Anti-PSMAxCD28, a costimulatory bispecific antibody) with cemiplimab (anti-PD-1) in patients with metastatic castration-resistant prostate cancer. *First Author: Charles G. Drake, Department of Medicine and Division of Hematology/Oncology, Columbia University Medical Center, New York, NY*

Background: Bispecific antibodies (bsAbs) are emerging as a protein-based therapeutic strategy for directing T-cell-mediated cytotoxicity in a tumor antigen-specific manner, typically by binding to both tumor antigen and the CD3 receptor on T cells. REGN5678 is a human IgG4-based, first-in-class costimulatory bsAb designed to target prostate tumors by bridging prostate specific membrane antigen expressing tumor cells with the costimulatory receptor, CD28, on T cells, and providing amplified T-cell receptor-CD3 complex-mediated T-cell activation within the tumor through the activation of CD28 signaling. At the tumor site, REGN5678 may synergize with PD-1 inhibitors. In mouse models, REGN5678 in combination with PD-1 antibody has improved anti-tumor activity compared with either therapy alone (Skokos et al CRI/CICON 2019; oral, session 3). This study evaluates the safety and anti-tumor activity of REGN5678 alone and in combination with cemiplimab in patients with metastatic castration-resistant prostate cancer (mCRPC) who progressed after prior therapy. **Methods:** This is an open label, Phase I/II, first-in-human study evaluating safety, tolerability, pharmacokinetics (PK), and anti-tumor activity of REGN5678 alone and in combination with cemiplimab in treatment-experienced mCRPC (NCT03972657). For inclusion, patients must have received at least two approved therapies for metastatic disease, including a second-generation hormonal agent. REGN5678 is administered weekly and cemiplimab (350 mg) is administered once every 3 weeks. During dose escalation, a 3-week safety lead-in of REGN5678 monotherapy will be administered prior to the addition of cemiplimab. Study therapies are administered until disease progression, intolerable adverse events, withdrawal of consent, or study withdrawal criterion is met. The primary objectives in dose escalation are to evaluate safety, tolerability, and PK of REGN5678 alone and in combination with cemiplimab. Expansion cohort(s) will be enrolled once a REGN5678/cemiplimab recommended Phase II dose is determined. During the expansion phase, the primary trial objective is to assess clinical activity, as measured by objective response rate of REGN5678 in combination with cemiplimab per modified Prostate Cancer Working Group 3 criteria. This study is currently open to enrollment. Clinical trial information: NCT03972657. Research Sponsor: Regeneron Pharmaceuticals Inc.

TPS5593 **Poster Session (Board #174), Fri, 8:00 AM-11:00 AM**

DAROL: DARolutamide ObservationaL study patients in nonmetastatic castration-resistant prostate cancer (nmCRPC) patients. *First Author: Evan Y. Yu, Division of Oncology, Department of Medicine, University of Washington, Seattle, WA*

Background: Patients (pts) with prostate cancer treated with prolonged androgen deprivation therapy (ADT) will eventually develop castration-resistant disease. Treatment of pts with nmCRPC with darolutamide (DARO) delays the development of metastases, which are associated with cancer-related morbidity. DARO is a structurally unique oral androgen receptor inhibitor approved by the FDA for the treatment of nmCRPC, based on prolonged metastasis-free survival (MFS) compared with placebo (median 40.4 months vs.18.4 months, respectively) in the ARAMIS phase III clinical trial. DARO showed a similar incidence of adverse events (AEs) compared to ADT alone and has a low potential for drug-drug interactions. However, phase III clinical trials cannot fully reflect all the facets of real-world pts. Therefore, non-interventional studies in the real-world setting, such as DAROL, are able to provide additional insight into the patterns of use and real-world safety profile of recently approved drugs. **Methods:** (NCT04122976) will enrol participants in the US, Brazil, Japan, and the EU. Eligible pts include men with histologically confirmed nmCRPC aged $\geq$18 yrs, life expectancy $\geq$3 months, and initiated on DARO treatment as per investigators' decision within 3 days prior to enrollment. DAROL opened for enrollment in December 2019 in the US with a projected enrollment of 1000 pts. The primary endpoint of DAROL is safety. Treatment-emergent AEs will be collected during the study. Secondary endpoints to measure clinical effectiveness are MFS, time to symptomatic skeletal event, time to prostate-specific antigen progression, survival rate, and duration of DARO therapy. Other endpoints include pt demographics and characteristics, and prior and subsequent therapy. The estimated primary completion date is December 30, 2024. Clinical trial information: NCT04122976. Research Sponsor: Bayer.

TPS5594 Poster Session (Board #175), Fri, 8:00 AM-11:00 AM

A phase III trial of docetaxel versus docetaxel and radium-223 (Ra-223) in patients with metastatic castration-resistant prostate cancer (mCRPC): DORA. *First Author: Michael J. Morris, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Ra-223, a bone-targeted alpha therapy, prolongs survival in patients (pts) with symptomatic mCRPC to bone. Docetaxel targets microtubule trafficking improving survival in the mCRPC and metastatic hormone-sensitive settings. We hypothesized that simultaneously targeting the tumor and bone compartment yields superior outcomes than targeting either alone. We previously determined the dose and schedule of co-administering Ra-223 + docetaxel in a randomized phase I/IIa trial. The combination appeared to have improved declines in prostate specific antigen (PSA) and bone markers, delayed PSA progression, and was better tolerated (with adjusted dose/schedule) relative to standard docetaxel alone. We are now conducting a phase III study to determine the clinical benefit of the regimen. **Methods:** Randomization (1:1) of 738 men with mCRPC to docetaxel or docetaxel + Ra-223 is planned with a projected hazard ratio for treatment effect (15 vs 20 months median survival) of 0.75. Pts with ≥2 bone lesions and progression by Prostate Cancer Working Group 3 criteria are eligible. Other key inclusion criteria are an Eastern Cooperative Oncology Group performance status of 0-1 and normal organ function. Key exclusion criteria are: use of anticancer therapy ≤4 weeks (wks) before randomization and use of bone-seeking radiopharmaceuticals or chemotherapy in the castration-resistant setting, and bulky visceral metastases (≥3 lung and/or liver or a lesion ≥2 cm in the previous 8 wks). Subjects receive docetaxel 75 mg/m^2 IV q3w for 10 doses or docetaxel 60 mg/m^2 IV q3w for 10 doses + Ra-223 55 kBq/kg IV q6w for 6 doses. The primary endpoint is overall survival. Secondary and exploratory endpoints include: radiographic progression-free survival, symptomatic skeletal event-free survival, safety, markers of bone metabolism, alterations in circulating tumor cells and DNA, detection of androgen-receptor splice variant 7, changes in automated bone scan index (aBSI), and assessment of patient-reported outcome instruments (FACT-P, Brief Pain Inventory, Brief Fatigue Inventory). The study is open at 25 sites in the US and Netherlands, sponsored by Memorial Sloan Kettering Cancer Center, and managed by the Prostate Cancer Clinical Trials Consortium. Clinical trial information: NCT03574571. Research Sponsor: Memorial Sloan Kettering Cancer Center, Other Government Agency, Pharmaceutical/Biotech Company.

TPS5595 Poster Session (Board #176), Fri, 8:00 AM-11:00 AM

Phase III study of pembrolizumab (pembro) plus enzalutamide (enza) and androgen deprivation therapy (ADT) for patients (pts) with metastatic hormone-sensitive prostate cancer (mHSPC): KEYNOTE-991. *First Author: Christian Gratzke, University Medical Center Freiburg, Freiburg, Germany*

Background: Pembro, an anti–PD-1 antibody, has shown antitumor activity as monotherapy and in combination with other agents in metastatic castration-resistant prostate cancer (mCRPC). As the antitumor effects of enza may be pro-immunogenic, we hypothesized that combining pembro and enza could show additive or synergistic antitumor activity. Furthermore, pembro + enza previously showed antitumor activity in pts with mCRPC for whom abiraterone failed (KEYNOTE-365, NCT02861573) and in pts with mCRPC for whom enza monotherapy failed (KEYNOTE 199, NCT02787005). These data warrant further evaluation of the combination of pembro + enza when given at the initiation of ADT. **Methods:** KEYNOTE-991 (NCT04191096) is a phase III trial to evaluate the efficacy and safety of enza + ADT + either pembro or placebo in patients with mHSPC. Approximately 1232 pts will be randomly assigned 1:1 to receive enza 160 mg orally once daily + ADT + pembro 200 mg IV every 3 weeks (Q3W) or enza 160 mg orally once daily + ADT + placebo IV Q3W. ADT is receipt of an LHRH agonist or antagonist during study treatment or bilateral orchiectomy. Treatment will be stratified by prior docetaxel therapy (yes or no) and presence of high-volume disease (yes or no). Pts with mHSPC, with ≥2 bone lesions and/or visceral disease, who are naive to next-generation hormone agents, and who have ECOG PS 0 or 1 are eligible. Pts must provide tissue for biomarker analysis. Responses will be assessed by CT or MRI and radionuclide bone imaging per Prostate Cancer Working Group 3 (PCWG3)–modified RECIST v1.1 by blinded independent central review (BICR) Q12W from the date of randomization. Treatment will continue with pembro for up to 35 cycles, and treatment with enza will proceed continuously from day 1 of cycle 1 until disease progression, unacceptable toxicity, or withdrawal of consent. Dual primary end points are radiographic progression-free survival (PFS) per PCWG3-modified RECIST v1.1 assessed by BICR and overall survival. Secondary end points are time to first subsequent anticancer therapy, time to symptomatic skeletal-related event, PFS2 (progression after next line of therapy or death), prostate-specific antigen (PSA) response rate, time to PSA progression, PSA undetectable rate, objective response rate, duration of response, and time to radiographic soft tissue progression. Other end points are safety and patient-reported outcomes (eg, time to pain progression). Clinical trial information: NCT04191096. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

TPS5596 Poster Session (Board #177), Fri, 8:00 AM-11:00 AM

A multicenter, randomized, controlled phase II study: Efficacy and safety of PSMA-targeted radioligand therapy I-131-1095 (1095) plus enzalutamide (enza) in 18F-DCFPyL PSMA scan avid, metastatic castration-resistant prostate cancer (mCRPC) patients post-abiraterone (abi) progression (ARROW). *First Author: Evan Y. Yu, University of Washington, Seattle, WA*

Background: PSMA is a transmembrane glycoprotein expressed in normal human prostate epithelium at low levels, but highly upregulated in metastatic prostate cancer (PC). ^{18}F-DCFPyL is a novel PSMA-targeted PET imaging agent that has shown highly promising diagnostic performance for detection of metastatic disease, with potential to identify disease amenable to theranostic targeting. 1095 is a novel PSMA-targeted small molecule that binds to the extracellular domain of PSMA selectively with high affinity. The complex is internalized, allowing the beta emitter, I-131, to kill PC cells. **Methods:** ARROW is an open-label, randomized (2:1) trial of enza plus 1095 or enza alone in pts with progressive mCRPC who previously received abi. ~120 pts (80: 1095 + enza; 40: enza alone) will be treated at ~40 sites in the US and Canada. Eligible male pts must be at least 18 yo with metastatic disease documented by bone scan or soft tissue lesions measurable per RECIST 1.1 on CT/MRI, be PSMA-avid as determined by ^{18}F-DCFPyL PET/CT, have evidence of biochemical or radiographic progression on abi, and be ineligible for or refuse to receive chemotherapy. Pts will receive enza (prescribed per approved labeling) with or without 1095 (100 mCi dose, followed by up to 3 additional dose(s) administered at least 8 weeks apart, as determined by dosimetry evaluation and occurrence of dose-limiting events). The primary objective is to determine the efficacy of 1095 plus enza compared to enza alone, based on PSA response (confirmed PSA decline ≥50%) rate according to Prostate Cancer Clinical Trials Working Group 3 (PCWG3) criteria. Additional objectives include objective response rate based on PCWG3-modified RECIST 1.1, progression-free survival (PFS) defined as the first occurrence of radiographic progression (PCWG3-modified RECIST 1.1), unequivocal clinical progression, or death from any cause, duration of response, overall survival, and the safety and tolerability of 1095 radioligand therapy. Clinical trial information: NCT03939689. Research Sponsor: Progenics Pharmaceuticals, Inc.

TPS5597 Poster Session (Board #178), Fri, 8:00 AM-11:00 AM

A phase II study of M6620 in combination with carboplatin compared with docetaxel in combination with carboplatin in metastatic castration-resistant prostate cancer. *First Author: Atish Dipankar Choudhury, Dana-Farber Cancer Institute, Boston, MA*

Background: Alterations in DNA damage repair genes are common in metastatic castration-resistant prostate cancer (mCRPC), and are implicated in responses to carboplatin, PARP inhibitors and immunotherapeutics. The ATR kinase is involved in the DNA damage response, and ATR inhibitors have been demonstrated in preclinical models to have synergistic activity with platinum compounds due to induction of replication stress. **Methods:** This is a randomized open-label Phase 2 study of the ATR inhibitor M6620 + carboplatin vs. docetaxel + carboplatin in mCRPC. Patients (pts) previously treated with at least one secondary hormonal therapy and taxane-based chemotherapy undergo mandatory pre-treatment biopsy and are randomized 1:1 to receive Arm A (docetaxel 60 mg/m2 day 1 + carboplatin AUC 4 day 1) or Arm B (M6620 90 mg/m2 days 2,9 + carboplatin AUC 5 day 1) every 21 days. Pts randomized to Arm A who are not candidates for docetaxel receive carboplatin AUC 5 monotherapy. Stratification factors are 1) prior PARP inhibitor (yes vs. no) and 2) evaluable disease by RECIST 1.1 (yes vs. no). Pts on Arm A crossover to Arm B (M6620+carboplatin) at the earlier of PSA or radiographic progression. For the primary endpoint of overall response rate (ORR; PSA reduction by ≥ 50% or radiographic response by RECIST 1.1), with 65 pts on each arm (total N = 130), there will be 80% power to distinguish ORR of 40% vs. 20% using a chi-square test (one sided $\alpha = 0.05$). 136 pts will be enrolled to account for 5% dropout. Secondary endpoints include time to PSA progression, radiographic PFS, PFS by PCWG3 criteria, safety and adverse events in each arm. Biomarker studies include whole exome sequencing, RAD51 focus formation, and ATM IHC from tumor specimens. Circulating cell-free DNA from pre-treatment and progression plasma specimens will undergo ultra-low pass whole genome sequencing and deep targeted sequencing. The goal of this study is to expand therapeutic options in mCRPC through a novel approach to targeting the DNA damage response, and to identify biomarkers associating with response and resistance to both standard and trial therapy. Enrollment began June 2019 (NCI/ETCTN #10191, NCT03517969). Clinical trial information: NCT03517969. Research Sponsor: U.S. National Institutes of Health.

TPS5598 **Poster Session (Board #179), Fri, 8:00 AM-11:00 AM**

TALAPRO-2: a placebo-controlled phase III study of talazoparib (TALA) plus enzalutamide (ENZA) for patients with first-line metastatic castration-resistant prostate cancer (mCRPC). *First Author: Neeraj Agarwal, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT*

Background: TALA blocks poly(ADP-ribose) polymerase (PARP) activity and traps PARP on single-strand DNA breaks, preventing DNA damage repair (DDR) and causing death of cells with DDR alterations (eg *BRCA1/2*).[a] TALA has been approved in multiple countries as monotherapy for germline *BRCA1/2*-mutated human epidermal growth factor receptor 2-negative advanced breast cancer. ENZA is an androgen receptor (AR) inhibitor and an established therapy for mCRPC. As PARP activity has been shown to support AR function, inhibition of PARP is expected to reduce AR signaling and increase sensitivity to AR-directed therapies. In addition, AR blockade downregulates homologous recombination repair gene transcription which induces '*BRCAness*'. Therefore, combining TALA with ENZA in mCRPC may be efficacious regardless of DDR alterations. TALAPRO-2 (NCT03395197) is a Phase III, 2-part study to evaluate efficacy, safety, pharmacokinetics, and patient-reported outcomes (PROs) of TALA combined with ENZA. **Methods:** Enrollment goal is 1037 patients (19 patients, part 1 dose-finding; 1,018 patients, part 2 placebo-controlled). Key eligibility criteria: age $\geq$18 years; asymptomatic/mildly symptomatic mCRPC; ECOG performance status $\leq$1; metastatic disease (no brain metastases); and no prior life-prolonging systemic therapy for nonmetastatic CRPC or mCRPC. Prior therapies (excluding novel AR inhibitors) in the castration-sensitive (CSPC) setting are allowed. ADT must continue throughout the study. The randomized double-blind portion (part 2) will evaluate safety, efficacy, and PROs of TALA (0.5 mg QD) + ENZA (160 mg QD) vs placebo + ENZA (160 mg QD). Patients are stratified by prior novel hormonal therapy or docetaxel for CSPC (yes or no) and DDR alteration status (deficient vs nondeficient/unknown). The primary endpoint is radiographic progression-free survival (rPFS), defined as time to progression in soft tissue per RECIST v.1.1 or in bone per PCWG3 criteria by independent review or death. The key secondary endpoint is overall survival. Efficacy will be assessed radiographically every 8 weeks up to Week 25 and every 8–12 weeks thereafter. rPFS will be compared between the two arms by a 1-sided stratified log-rank test. Patient recruitment is ongoing in multiple regions including US, Europe/Eastern Europe, Israel, South America, South Africa, and Asia-Pacific region. [a]DDR alterations are defined as known/likely pathogenic variants or homozygous deletions. Funding: Pfizer Inc. Clinical trial information: NCT03395197. Research Sponsor: Pfizer Inc.

TPS5599 **Poster Session (Board #180), Fri, 8:00 AM-11:00 AM**

A phase Ib trial of enzalutamide with venetoclax in metastatic castration-resistant prostate cancer (mCRPC). *First Author: Dharmesh Gopalakrishnan, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: Androgen receptor (AR) signaling plays an important role in prostate cancer (PCa) cell survival and proliferation. Xenograft and PDX models demonstrate that untreated PCa harbors $AR^{-/lo}$ stem cells not critically dependent on androgens for survival.[1] Furthermore, castration and enzalutamide (enza) leads to expansion of both $AR^{-/lo}$ and $AR^{+/hi}$ resistant clones in xenograft tumors, resulting in two distinct CRPC-propagating populations.[2] However, most current CRPC treatments are directed towards $AR^{+/hi}$ cells. RNAseq revealed that BCL-2 is highly up-regulated in $AR^{-/lo}$ tumors post-castration and in $AR^{+/hi}$ CRPC tumors post-enza.[2] Strikingly, BCL-2, but not BCL-X_L and MCL-1, was selectively up-regulated in these xenograft tumors. These results were subsequently validated in patient CRPC datasets.[2,3] Venetoclax (ven), a potent and selective BCL-2 inhibitor, inhibits enza resistance in $AR^{+/hi}$ CRPC and tumor growth in $AR^{-/lo}$ xenograft models.[2] A recent phase I trial of ven combined with tamoxifen showed promising activity in ER^+ and $BCL2^+$ metastatic breast cancer.[4] We hypothesize that co-targeting $AR^{-/lo}$ and $AR^{+/hi}$ PCa clones with ven and enza will prevent the emergence of enza resistance in human mCRPC. **Methods:** This is a phase Ib, single-center, single-arm trial of enza (160mg/d) with ven in patients with mCRPC that has progressed on previous therapies which may include anti-androgens. Three dose-levels of ven (400mg, 600mg and 800mg/d q28d) will be evaluated using a 3+3 study design. Fifteen to 18 patients will be enrolled in this phase to assess dose-limiting toxicities, maximum tolerated dose, and recommended phase II dose. Aims of correlative studies include (1) assessing the pharmacokinetic interaction between enza and ven, (2) identification of potentially predictive blood and tissue biomarkers (including pre- and post-treatment CTC levels, expression of BCL2, AR, ARv7 in pre-and post-treatment biopsies and CTCs), (3) measurement of pre- and post-treatment BCL2 expression in peripheral blood mononuclear cells as a surrogate for ven activity, and (4) the development of 3D organoid models from CTCs and biopsies. The trial is open with 3 patients enrolled to dose-level 1, and 2 patients currently at dose-level 2. Correlative studies are ongoing. References: (1) Qin J, et al. *Cell Stem Cell*. 10(5): 556-69, 2012 (2) Li Q, et al. *Nat Commun*. 9(1): 3600, 2018 (3) Rajan P, et al. *Eur Urol*. 66 (1):32-9, 2014 (4) Lok SW, et al. *Cancer Discov*. 9(3):354-69, 2019. Clinical trial information: NCT03751436. Research Sponsor: AbbVie, U.S. National Institutes of Health.

TPS5600 **Poster Session (Board #181), Fri, 8:00 AM-11:00 AM**

Initial experience of the adjuvant treatments to the local tumor for metastatic prostate cancer: Assessment of novel treatment algorithms, a multicenter, phase II randomized controlled trial (IP2-ATLANTA). *First Author: Martin John Connor, Imperial College London, London, United Kingdom*

Background: Local cytoreductive and metastasis-directed interventions are hypothesised to confer additional survival benefit beyond standard systemic therapy in patients with *de novo* synchronous metastatic prostate cancer. There is accumulating prospective evidence for local cytoreductive therapy. In particular, the phase III study STAMPEDE which demonstrated improved overall survival in a low burden subgroup of men following cytoreductive radiotherapy. Cytoreductive prostatectomy and minimally invasive ablative therapies (MIAT) are now subject to similar trial evaluation. IP2-ATLANTA will evaluate progression-free and overall survival outcomes with the addition of sequential multi-modal local and metastasis-directed treatments in patients with newly diagnosed metastatic prostate cancer compared to standard care alone. **Methods:** Phase II, multicentre, three-arm randomised controlled trial using a positive comparator arm (n=918). An internal pilot (n=80) feasibility phase is incorporated. All men with new histologically diagnosed, hormone sensitive, metastatic prostate cancer, within three months of commencing ADT and of PS 0-2 are eligible. Patients are randomised (1:1:1) to: Control (Standard of Care) OR Intervention 1 (Minimally invasive ablative therapy to the prostate +/- pelvic lymph node dissection [PLND]) OR Intervention 2 (prostate radiotherapy +/- lymph nodes OR Radical prostatectomy +/- PLND). Metastatic burden pre-specified by CHAARTED definition. Men with low-burden disease in intervention arms are eligible for metastasis-directed therapy (stereotactic ablative radiotherapy [SABR] or surgery). Standard systemic therapy given in all arms (incl. docetaxel). Follow-up: min. 2-years; max. 4 years. Primary outcome: progression-free survival (PFS). Secondary outcomes: Overall survival; urinary, sexual & rectal side-effects; patient reported outcome measures. HRA ethical approval (Ref: 19/WA0005). To date, 28/80 (35%) patients have been recruited and randomised across 9 open sites in the internal pilot. Median recruitment rate is 85.7% (IQR 55–86). Internal pilot recruitment expected to be complete by April 2020. IP2-ATLANTA addresses an important research gap in the role of local and metastasis-directed therapy in men with newly diagnosed metastatic prostate cancer. Clinical trial information: NCT03763253. Research Sponsor: Wellcome Trust Charity.

TPS5601 **Poster Session (Board #182), Fri, 8:00 AM-11:00 AM**

RTOG 3506 (STEEL): A study of salvage radiotherapy with or without enzalutamide in recurrent prostate cancer following surgery. *First Author: Edwin Melencio Posadas, Cedars-Sinai Cancer, Los Angeles, CA*

Background: Salvage radiotherapy (SRT) is an important intervention for men with prostate cancer (PCa) who experience biochemical recurrence (BCR) after radical prostatectomy (RP). These patients are in need of cure or else they will develop metastatic disease. NRG/RTOG 9601 (WU Shipley, N Eng J Med 2017) identified a survival benefit from the addition of androgen receptor (AR) inhibition to SRT that was most prominent in men with high-risk features. Enzalutamide (Enza) is a non-steroidal anti-androgen that improves survival in castration-resistant and -sensitive PCa. We hypothesized that enhanced AR suppression with Enza would augment the benefit of SRT + androgen deprivation therapy (ADT) in BCR with high risk features. **Methods:** RTOG 3506 (STEEL, NCT03809000) is a randomized phase II study of SRT in BCR after RP with a serum PSA $\geq$ 0.2 ng/mL active in the USA and Canada. Patients are stratified by number of high-risk features including Gleason score (8-10), locoregional node involvement at RP, seminal vesicle invasion, persistently elevated PSA after RP, and PSA $>$ 0.7 ng/mL. All patients receive SRT with 2 years of ADT. The experimental arm also receives Enza 160 mg daily for 2 years. Patients are followed by PSA every 3 months. SRT can be highly individualized per treating physician beyond the mandatory treatment of the prostatic fossa. Treatment of the pelvis and/or para-aortic nodes, as well as sequential or concurrent boosts to a prostatic fossa mass and/or suspicious lymph nodes, are allowed options. This permits individualization of radiotherapy guided by CT, MRI, PET, and/or biopsy findings. The primary goal of this study is to determine whether SRT enhanced ADT with Enza, will improve progression-free survival (PFS) compared to SRT with standard ADT. PFS defined as the first occurrence of biochemical failure, clinical failure, or initiation of new anticancer treatment. STEEL is designed to demonstrate a 35% reduction in the risk of progression at 5 years. An accrual goal of 242 patients will provide 80% power with a one-sided alpha = 0.10. Secondary endpoints include disease control rates, acute and late physician- and patient-reported toxicity, and quality of life. This study was activated in February 2019. Site recruitment and activation are underway. **Conclusions:** There is an unmet and urgent need for individualized strategies to optimize systemic therapy used with SRT for men with BCR. Outcomes from this study will further clarify the approach to systemic therapy for SRT in high-risk BCR patients. Support: Provided by Pfizer. Clinical trial information: NCT03809000. Research Sponsor: RTOG Foundation.

5602 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

HERO phase III trial: Results comparing relugolix, an oral GnRH receptor antagonist, versus leuprolide acetate for advanced prostate cancer. *First Author: Neal D. Shore, Carolina Urologic Research Center, Myrtle Beach, SC*

Background: LHRH agonists are the mainstay for medical castration in advanced prostate cancer; however, they cause an initial testosterone (T) surge with a delayed onset of castration and require depot injection. Relugolix is the first oral GnRH receptor antagonist, which was previously shown to rapidly suppress T levels. The HERO trial compared the safety and efficacy of relugolix with leuprolide acetate in advanced prostate cancer patients. **Methods:** HERO is a 48-week, global, pivotal phase III trial that randomized 934 patients with androgen-sensitive advanced prostate cancer in a 2:1 ratio to receive relugolix 120 mg orally QD after a single l or leuprolide acetate 3-month depot injection. The primary endpoint was to achieve and maintain serum T suppression to castrate levels (< 50 ng/dL) through 48 weeks. Key secondary endpoints included castration rates at Day 4, profound castration (< 20 ng/dL) rates at Days 4 and 15, PSA response rate at Day 15 and FSH levels at Week 25. Testosterone recovery was evaluated in a subset of 184 patients. Results: A total of 96.7% (95% CI: 94.9%, 97.9%) of men on relugolix achieved and maintained castration through 48 weeks compared to 88.8% on leuprolide. The difference of 7.9% (95% CI: 4.1%, 11.8%) demonstrated non-inferiority (margin -10%) and superiority ($P < 0.0001$) of relugolix to leuprolide. All key secondary efficacy endpoints tested demonstrated superiority over leuprolide ($P < 0.0001$) (Table). In the testosterone recovery subset, median T levels were 270.76 ng/dL in the relugolix compared to 12.26 ng/dL in the leuprolide group 90 days after discontinuation of therapy. In a prespecified analysis, the incidence of major adverse cardiovascular events (MACE) was lower in the relugolix group than in the leuprolide group (2.9% vs. 6.2%, respectively); otherwise the safety and tolerability profiles were generally similar. Conclusion: Relugolix achieved castration as early as Day 4 and demonstrated superiority over leuprolide in sustained T suppression through 48 weeks, faster T recovery after discontinuation and a 50% reduction in MACE. Relugolix has the potential to become a new standard for T suppression for patients with advanced prostate cancer. Clinical trial information: NCT03085095. Research Sponsor: None.

	Endpoint	Relugolix (N= 622)	Leuprolide (N= 308)	P-value
		%	%	
Primary Endpoint	Sustained castration rate from Day 29 to Day 337	96.7	88.8	<0.0001
Key Secondary Endpoints	Testosterone suppression to < 50 ng/dL at Day 4	56.04	0.00	<0.0001
	Testosterone suppression to < 50 ng/dL at Day 15	98.71	12.05	<0.0001
	Confirmed PSA response at Day 15 followed with confirmation at Day 29	79.4	19.8	<0.0001
	Testosterone suppression to <20 ng/dL at Day 15	78.38	0.98	<0.0001
	Mean of FSH level at Week 25 Day 1	1.72	5.95	<0.0001

6000 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Randomized phase III study to evaluate the impact of secondary cytoreductive surgery in recurrent ovarian cancer: Final analysis of AGO DESKTOP III/ENGOT-ov20. *First Author: Andreas Du Bois, AGO & Ev. Kliniken Essen-Mitte, Essen, Germany*

Background: The role of secondary cytoreductive surgery in recurrent ovarian cancer (ROC) has been under debate for decades. A recent trial in unselected patients (pts) failed to show an OS benefit. **Methods:** Pts with ROC and 1st relapse after 6+ months (mos) platinum-free interval (TFIp) were eligible if they presented with a positive AGO-score (PS ECOG 0, ascites ≤500 ml, and complete resection at initial surgery) and were prospectively randomized to second-line chemotherapy alone vs. cytoreductive surgery followed by the same chemotherapy; platinum combination therapy was recommended. OS was primary endpoint in this superiority trial. **Results:** 407pts were randomized 2010-2014. The TFIp exceeded 12 mos in 75% of pts. 206 pts were allocated to the surgery arm of whom finally 187 (91%) were operated. A complete resection was achieved in 75%; almost 90% in both arms received a platinum-containing second-line chemo. Primary endpoint analysis showed median OS of 53.7 mos with and 46.2 mos without surgery (HR 0.76, 95%CI 0.59-0.97, p=0.03); median PFS was 18.4 and 14 mos (HR: 0.66, 95%CI 0.54-0.82, p<0.001), median time to start of first subsequent therapy (TFST) was 17.9 vs. 13.7 mos in favor of the surgery arm (HR 0.65, 95%CI 0.52-0.81, p<0.001). An analysis according to treatment showed an OS benefit exceeding 12 mos for pts with complete resection (CR) compared to pts without surgery (median 60.7 vs. 46.2 mos); pts with surgery and incomplete resection even did worse (median 28.8 mos). 60 d mortality rates were 0 and 0.5% in the surgery and no-surgery arm. Re-laparotomies were performed in 3.7% of operated pts. Further grade 3/4 adverse events did not differ significantly between arms. **Conclusions:** This is the first surgical study demonstrating a meaningful survival benefit in OC: Surgery in pts with first relapse and TFIp of 6+ mos and selected by a positive AGO-Score resulted in a significant increase of OS, PFS and TFST with acceptable morbidity and, therefore, should be offered to suitable pts. The benefit was exclusively seen in pts with CR indicating the importance of both the optimal selection of pts (eg. by AGO score) and of centres with expertise and a high chance of achieving a CR. Clinical trial information: NCT01166737. Research Sponsor: None.

6001 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A randomized phase III trial of secondary cytoreductive surgery in later recurrent ovarian cancer: SOC1/SGOG-OV2. *First Author: Rongyu Zang, Fudan University Zhongshan Hospital, Shanghai, China*

Background: In China, secondary cytoreductive surgery (SCR) has been standard of care in some high volume cancer centers for ovarian cancer (OC) and most pts prefer surgery over the past two decades. Although GOG213 showed no OS benefit, the debate on selected pts and the conflict with certain local clinical care is still open. **Methods:** Pts with 1st relapsed OC after 6m+ platinum-free interval (PFI) were eligible if predicted to be a potential R0 by iMODEL score combined with PET-CT image and were randomized to SCR followed by chemotherapy (surgery arm) vs 2nd line chemotherapy alone (no surgery arm). Co-primary endpoint is PFS and OS. The 2nd endpoint is accumulated treatment-free survival (TFSa), which was defined as the overall survival time minus the time of surgery and chemotherapy after randomization. We report analysis of PFS and interim analysis of TFSa. **Results:** 357 pts were randomized 2012-2019. 6.3% of 175 pts were operated in no surgery arm and cross-over rate was 36.9% in 2nd+ relapsed pts of no surgery arm. 97% and 96% of pts received a platinum-containing 2nd line therapy. Complete resection (R0) rate was 76.7% in overall and 61.1% in pts with iMODEL>4.7. 60 d mortality rates were 0 % in both surgery and no surgery arm. Postoperative 30 d complication rate with ≥ grade 3 was 5.2%. The median follow-up was 36.0 m. Median PFS was 17.4 m and 11.9 m in surgery and no surgery arm, respectively (HR 0.58, 95% CI 0.45-0.74, p < 0.001). Median time to start of first subsequent therapy (TFST) was 18.1 m vs 13.6 m in favor of the surgery arm (HR 0.59, 95%CI 0.46-0.76). 1.1% and 10.1% of pts underwent Bevacizumab and PARPi maintenance in the 2nd line therapy. The OS and TFSa was immatured. The median TFSa was unreached and 39.5 m in R0 subgroup and no surgery arm, respectively (HR0.59, 95%CI 0.38-0.91). TFSa in surgery arm showed a better long-term survival than that in no surgery group (restricted mean survival time from 60 to 72m: 6.2m vs 4.2m). **Conclusions:** SCR in selected pts resulted in a dramatically significant extension of PFS. The interim analysis of TFSa indicate that SCR might contribute to long-term survival. Research Sponsor: Talent Funding from Zhongshan Hospital Fudan University (No. 016).

6002 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Final overall survival (OS) results from SOLO2/ENGOT-ov21: A phase III trial assessing maintenance olaparib in patients (pts) with platinum-sensitive, relapsed ovarian cancer and a BRCA mutation. *First Author: Andres Poveda, Initia Oncology, Hospital Quirónsalud and GEICO, Valencia, Spain*

Background: SOLO2 (ENGOT ov-21; NCT01874353) showed that maintenance therapy with the PARP inhibitor olaparib in pts with platinum-sensitive relapsed ovarian cancer (PSROC) and a BRCA mutation (BRCAm) led to a statistically significant improvement in median progression-free survival (PFS) of 13.6 months vs placebo (hazard ratio [HR] 0.30). Time to second progression or death significantly improved (Pujade-Lauraine *et al Lancet Oncol* 2017) and a quality-adjusted PFS benefit was seen (Friedlander *et al Lancet Oncol* 2018) with maintenance olaparib vs placebo. We report the preplanned final OS analysis for SOLO2. **Methods:** Pts with PSROC and a BRCAm who had received ≥2 lines of treatment and were in response to their most recent platinum-based chemotherapy received maintenance olaparib (300 mg bid tablets) or placebo. Pts were stratified by response to previous chemotherapy (complete vs partial) and length of platinum-free interval (>6–12 months vs >12 months). OS was a secondary endpoint. The only preplanned OS sensitivity analysis was an OS analysis in the Myriad germline BRCAm subset (Myriad BRAC *Analysis* test). **Results:** At final data cut-off (Feb 3, 2020), median follow-up was 65 months in both treatment arms. A long-term treatment benefit was seen with olaparib vs placebo with an OS HR of 0.74 (95% confidence interval [CI] 0.54–1.00) in the full analysis set (FAS; unadjusted for crossover; 38.4% of placebo pts crossed over to a PARP inhibitor) (Table). At 5 years: by Kaplan-Meier estimates, 28.3% of pts in the olaparib arm vs 12.8% of pts in the placebo arm were alive and had still not received subsequent treatment; 42.1% of olaparib pts vs 33.2% of placebo pts were alive. The long-term tolerability profile of olaparib was generally consistent with that reported previously. **Conclusions:** In the final analysis of SOLO2, maintenance olaparib provided an unprecedented improvement of 12.9 months in median OS vs placebo. This is the first study with olaparib tablets, and the first since Study 19 (NCT00753545), to provide long-term follow-up and final OS data in pts with PSROC and a BRCAm. Clinical trial information: NCT01874353. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc, Kenilworth, NJ, USA.

	Olaparib N=196*	Placebo N=99
Cumulative exposure of ≥5 years, n (%)	43 (22.1)	9 (9.1)
OS events, n (%)	116 (59.2)	65 (65.7)
Median OS, months	51.7	38.8
HR (95% CI)	0.74 (0.54–1.00)	
***P* value**	0.0537	
OS events in Myriad germline BRCAm subset, n (%)	111/190 (58.4)	64/96 (66.7)
Median OS, months	52.4	37.4
HR (95% CI)	0.71 (0.52–0.97)	
***P* value**	0.0306	

*Of 196 pts randomized to olaparib (FAS), 195 received treatment

6003 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A phase III study comparing single-agent olaparib or the combination of cediranib and olaparib to standard platinum-based chemotherapy in recurrent platinum-sensitive ovarian cancer. *First Author: Joyce F. Liu, Dana-Farber Cancer Institute, Boston, MA*

Background: Combination cediranib (C) and olaparib (O) improved progression-free survival (PFS) in patients (pts) with relapsed platinum (plat)-sensitive high-grade ovarian cancer (ovca) compared to O alone in a Phase 2 trial (NCT01116648). We conducted this randomized, open-label Phase 3 trial (NCT02446600) to assess whether combination C+O, or O alone, was superior to standard of care (SOC) plat-based therapy in relapsed plat-sensitive ovca. **Methods:** Eligible pts had recurrent plat-sensitive [> 6-month plat-free interval (PFI)] high-grade serous or endometrioid, or BRCA-related, ovca. One prior non-plat therapy and unlimited prior plat-therapies were allowed; prior anti-angiogenics in the recurrent setting or prior PARP inhibitor were exclusions. Pts were randomized 1:1:1 to SOC (carboplatin/paclitaxel; carboplatin/gemcitabine; or carboplatin/liposomal doxorubicin), O (300mg twice daily), or C+O (C 30mg daily + O 200mg twice daily). Randomization was stratified by g*BRCA* status, PFI (6-12 vs > 12 months), and prior anti-angiogenic therapy. Target sample size was 549 pts; primary analysis occurred 2 years after the last pt enrolled. The primary endpoint was PFS. Type 1 error = 0.025 was controlled by a gatekeeping hierarchy that assessed C+O vs SOC, then O alone vs SOC, and finally C+O vs O. All maintenance therapy was prohibited. **Results:** Between 4FEB2016 and 13NOV2017, 565 pts enrolled (187 SOC, 189 O, 189 C+O), and 528 pts initiated treatment (166 SOC, 183 O, 179 C+O). 23.7% of patients had g*BRCA*mut. Median follow-up was 29.1 months. 53 pts on SOC initiated non-protocol therapy (predominantly PARP inhibitor maintenance) before disease progression. The hazard ratio (HR) for PFS was 0.856 (95% CI 0.66-1.11, p = 0.08, 1-tail) between C+O and SOC and 1.20 (95% CI 0.93-1.54) between O and SOC, with median PFS of 10.3, 8.2, and 10.4 months for SOC, O, and C+O, respectively. Response rates were 71.3% (SOC), 52.4% (O), and 69.4% (C+O). In *gBRCA* pts, HR for PFS was 0.55 (95% CI 0.73-1.30) for C+O vs SOC, and 0.63 (95% CI 0.37-1.07) for O vs SOC. In non-g*BRCA* pts, HR for these comparisons was 0.97 (95% CI 0.73-1.30) and 1.41 (1.07-1.86). No OS differences between arms were observed at 44% events. Pts receiving C+O (vs SOC) had more frequent Grade 3 or higher gastrointestinal (30.1% vs 8.4%), hypertension (31.7% vs 1.8%), and fatigue events (17.5% vs 1.8%). **Conclusion:** C+O demonstrated similar activity to SOC in relapsed plat-sensitive ovca but did not meet the primary endpoint of improved PFS. Clinical trial information: NCT02446600. Research Sponsor: U.S. National Institutes of Health.

6004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Mirvetuximab soravtansine, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), in combination with bevacizumab in patients (pts) with platinum-agnostic ovarian cancer. *First Author: Lucy Gilbert, McGill University Health Centre, Royal Victoria Hospital, Montréal, QC, Canada*

Background: Mirvetuximab soravtansine (MIRV) is an ADC comprising a FRα-binding antibody, cleavable linker, and the maytansinoid DM4, a potent tubulin-targeting agent. As part of the Phase 1b FORWARD II trial (NCT02606305), the combination of MIRV with bevacizumab (BEV) was evaluated in pts with FRα-positive (medium/high expression; ≥ 50%/ ≥75% of cells with PS2+ staining intensity), platinum agnostic ovarian cancer, defined as pts with either platinum resistant (PR) (recurrence within 6 months after last platinum dose) or platinum sensitive (PS) responded to the last platinum therapy received before study entry and did not progress within 6 months) disease for whom a non-platinum based doublet would be appropriate. **Methods:** Pts received MIRV (6 mg/kg; adjusted ideal body weight) and BEV (15 mg/kg) on Day 1 of a 21-day cycle. Responses were assessed by investigator according to RECIST 1.1 and adverse events (AEs) evaluated by CTCAE v4.03. **Results:** In total, 60 pts received the combination, with a median age of 60 years, and a median of 2 prior lines of systemic therapy (range 1-4). Platinum status was determined for 56 pts, with 30 (50%) considered PR and 26 (43%) considered PS; platinum status data were incomplete for 4 pts. The most common treatment related AEs (percent all grade/grade 3+) were diarrhea (65/2), blurred vision (62/3), nausea (55/0), and fatigue (55/5). The most common treatment related grade 3+ AEs were hypertension and neutropenia, (10% each); all other grade 3+ events occurred in ≤ 5% of pts. Serious AEs regardless of relationship to study drug were infrequent, with the most common events being small intestinal obstruction in 3 pts, 5% (grade 3) and pneumonitis in 3 pts, 5% (2 grade 1; 1 grade 2). Objective responses were seen in 26 pts for a confirmed overall response rate (ORR) of 43% (95% CI, 31, 57). In a subset analysis of pts with high FRα expressing tumors (n = 33), the confirmed ORR was 61% (95% CI, 42, 77), with an ORR of at least 50% in each of the PR and PS subsets. With a median follow-up of 5.5 months, the duration of response and progression free survival data are immature. **Conclusions:** The combination of MIRV with BEV demonstrates an encouraging ORR with a favorable tolerability profile in pts with recurrent ovarian cancer regardless of platinum sensitivity, particularly in those with tumors that express high levels of FRα. Clinical trial information: NCT02606305. Research Sponsor: ImmunoGen.

6005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Final results from the KEYNOTE-100 trial of pembrolizumab in patients with advanced recurrent ovarian cancer. *First Author: Ursula A. Matulonis, Dana-Farber Cancer Institute, Boston, MA*

Background: Pembrolizumab (pembro) showed modest clinical activity in patients (pts) with recurrent advanced ovarian cancer (AOC) after a median follow-up of 16.9 mo in an interim analysis of KEYNOTE-100 (NCT02674061). We present the protocol-specified final analysis based on a data cutoff of 18-SEP-2019. **Methods:** Key eligibility criteria included epithelial ovarian, fallopian tube, or primary peritoneal cancer, confirmed recurrence following front-line platinum-based therapy, ECOG PS 0-1, and provision of a tumor sample for biomarker analysis. Pts in cohort A received ≤2 prior chemotherapy lines for recurrent AOC and had a platinum-free or treatment-free interval (PFI/TFI) of ≥3 to 12 mo. Pts in cohort B received 3-5 prior chemotherapy lines and had a PFI/TFI of ≥3 mo. Pts received pembro 200 mg Q3W for 2 yr or until progression, death, or unacceptable toxicity. Tumor imaging was performed every 9 wk for 1 yr and every 12 wk thereafter. Primary study endpoint was ORR per RECIST v1.1 by independent central review in both cohorts and by tumor PD-L1 expression using the combined positive score (CPS). Secondary endpoints included DOR, DCR (CR+PR+SD≥24 wk), PFS, OS, and safety. **Results:** 376 pts were enrolled and treated, 285 in cohort A and 91 in cohort B. Median age (range) was 61 (25 to 89) yr, 64.4% had ECOG PS 0, and 75.3% had high grade serous disease. In cohorts A and B, ORR (95% CI) was 8.1% (5.2, 11.9) and 9.9% (4.6, 17.9) in the total population, 6.9% (2.8, 13.8) and 10.2% (3.4, 22.2) in pts with CPS ≥1, and 11.6% (3.9, 25.1) and 18.2% (5.2, 40.3) in pts with CPS ≥10. Median DOR (range) was 8.3 (3.9 to 35.4+) mo in cohort A and 23.6 (3.3+ to 32.8+) mo in cohort B. DCR (95% CI) was 22.1% (17.4, 27.4) and 22.0% (14.0, 31.9). Median PFS was 2.1 mo in both cohorts. In cohorts A and B, median OS was 18.7 mo (17.0, 22.5) and 17.6 mo (13.3, 24.4) in the total population, 20.6 mo (15.2, 23.2) and 20.7 mo (13.6, 27.4) in pts with CPS ≥1, and 21.9 mo (12.9, 26.8) and 24.0 mo (14.5, NR) in pts with CPS ≥10. 73.7% of pts had treatment-related AEs and 20.2% were grades 3-4. There were 2 treatment-related deaths (Stevens-Johnson syndrome and hypoaldosteronism). Immune-mediated AEs occurred in 23.7% of pts. **Conclusions:** Pembro monotherapy was associated with modest antitumor activity in pts with recurrent AOC. There appeared to be a trend toward increased ORR with higher PD-L1 expression in both cohorts. Responses were durable and typically lasted ≥6 months. Median OS was 18.7 months overall, with a trend toward a longer OS with increasing PD-L1 expression in both cohorts. No new safety signals were identified. Clinical trial information: NCT02674061. Research Sponsor: Merck & Co., Inc.

6006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Long-term oncological safety of sentinel lymph node biopsy in early-stage cervical cancer. *First Author: Vincent Balaya, Hopital Européen Georges Pompidou, Paris, France*

Background: The goal of this study was to assess disease-free survival (DFS) and disease-specific survival (DSS) in patients with early-stage cervical cancer who underwent bilateral sentinel lymph node (BSLN) biopsy alone versus bilateral pelvic lymphadenectomy (BPL). **Methods:** An ancillary analysis of two prospective multicentric trials on SLN biopsy for cervical cancer (SENTICOL I and II) was performed. All patients with early stage cervical cancer (IA to IIB FIGO stage), negative SLN after ultrastaging and negative non-SLN after final pathologic examination were included. Risk-factors of recurrency and disease-specific deaths were determined by Cox proportional hazard models. Kaplan-Meier survival curves were compared by applying log-rank test. **Results:** Between January 2005 and July 2012, 259 patients met the inclusion criteria: 85 patients underwent only bilateral SLN biopsy whereas 174 patients underwent BPL. None had positive SLN at ultrastaging or positive non-SLN at final pathologic examination. Between the both groups, there was no differences in histology, final FIGO stage and type of surgical approach. In the BPL group, patients had more frequently tumor size larger than 20 mm (22.9% vs 10.7%, p = 0.02) and postoperative radiochemotherapy (10.7% vs 1.6%, p = 0.01). The median follow-up was 47 months (4-127). During the follow-up, 21 patients (8.1%) experienced reccurencies, including 4 nodal recurrences (1.9%), and 9 patients (3.5%) died of cervical cancer. The 5-year DFS and the DSS were similar between BSLN and BPL groups, 94.1% vs 97.7%, p = 0.14 and 88.2% vs 93.7%, p = 0.14 respectively. After controlling for final FIGO stage and margin status, BSLN compared to BPL was not associated with DFS (HR = 1.76, 95%CI = [0.69 – 4.53], p = 0.24) and DSS (HR = 2.5, 95%CI = [0.64 – 9.83], p = 0.19). Only final FIGO stage was independent predictor of DSS. **Conclusions:** SLN biopsy alone is oncologically safe in early-stage cervical cancer. Full lymphadenectomy could be omitted in case of bilateral negative SLN. Worse prognosis was associated with higher FIGO stage disease. Research Sponsor: None.

6007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Sequential chemoradiation versus radiation alone or concurrent chemoradiation in adjuvant treatment after radical hysterectomy for stage IB1-IIA2 cervical cancer (STARS Study): A randomized, controlled, open-label, phase III trial. *First Author: He Huang, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: There are limited data from previous studies regarding whether the addition of chemotherapy to adjuvant radiation after radical surgery improves outcomes among patients with early-stage cervical cancer and adverse pathological factors. **Methods:** This was a prospective randomized trial including patients with FIGO 2009 stage IB1-IIA2 cervical cancer and squamous-cell, adenocarcinoma, or adenosquamous carcinoma with at least one adverse factor after radical hysterectomy. Patients were randomized 1:1:1 to receive adjuvant radiation alone, concurrent chemoradiation with weekly cisplatin (30-40 mg/m^2), or sequential chemoradiation with cisplatin (60-75 mg/m^2) plus paclitaxel (135-175 mg/m^2) in 21 day cycles, given 2 cycles before and 2 cycles after radiotherapy respectively. The primary outcome was the rate of disease-free survival at 3 years. **Results:** A total of 1,048 patients were included in the study (350, radiation alone; 345, concurrent chemoradiation; and 353, sequential chemoradiation). Overall, the median follow-up was 56 months and the median age of patients was 48 years. Most patients (75%) had stage IB1 or IIA1 disease. The three groups were similar with respect to histologic subtypes, the rate of lymphovascular invasion, parametrial, surgical margin and deep stromal involvement, tumor grade, rate of use of minimally invasive surgery, and neoadjuvant chemotherapy, except for lymph-node involvement that was lowest in radiation alone arm. In the intention-to-treat population, sequential chemoradiation was associated with a higher rate of disease-free survival than radiation alone (3-year rate, 90·0% vs. 82·0%; HR 0·52; 95% CI, 0·35 to 0·76) and concurrent chemoradiation (90·0% vs. 85·0%; HR 0·65; 95% CI, 0·44 to 0·96), differences remained after adjustment for lymph-node involvement. Sequential chemoradiation was also associated with a higher rate of overall survival than radiation alone (5-year rate, 92·0% vs. 88·0%; HR for death from cancer, 0·58; 95% CI, 0·35 to 0·95). However, neither disease-free survival nor cancer death risk was different between patients treated with concurrent chemoradiation or radiation alone. **Conclusions:** In this trial, sequential chemoradiation, rather than concurrent chemoradiation, resulted in a higher disease-free survival and lower risk of cancer death than radiation alone among women with early-stage cervical cancer after radical surgery. Clinical trial information: NCT00806117. Research Sponsor: Sun Yat-sen University Clinical Research 5010 Program.

LBA6008 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Avelumab in patients with gestational trophoblastic tumors resistant to monochemotherapy: Final outcomes of TROPHIMMUN phase II trial, cohort A. *First Author: Benoit You, Institut de Cancérologie des Hospices Civils de Lyon (IC-HCL), CITOHL, EMR UCBL/HCL 3738, Lyon, GINECO & GINEGEPS, Lyon, France*

The full, final text of this abstract will be available at abstracts.asco.org at 5:00 p.m. ET on Thursday, May 28.

6009 **Clinical Science Symposium, Fri, 8:00 AM-9:30 AM**

A phase II trial of the Wee1 inhibitor adavosertib (AZD1775) in recurrent uterine serous carcinoma. *First Author: Joyce F. Liu, Dana-Farber Cancer Institute, Boston, MA*

Background: Uterine serous carcinoma (USC) is an aggressive subtype of endometrial carcinoma characterized by TP53 mutations (> 90%), often concomitantly with oncogenic mutations or amplifications that can increase replication stress. As such, USC may therefore be uniquely sensitive to further interference of cell cycle regulation by Wee1 inhibition. This two-stage single arm Phase 2 study was conducted to assess the activity of the Wee1 inhibitor adavosertib as monotherapy in recurrent USC. **Methods:** Women with recurrent USC (defined as non-carcinosarcoma uterine cancers with any serous component) were eligible. Patients (pts) were required to have had at least one prior platinum-based chemotherapy regimen; those with known MSI-H/MMRd disease were required to have received prior PD1/PDL1 therapy or to be ineligible for such therapy. There was no upper limit on the number of prior lines pts could have received. All pts were required to have RECIST measurable disease. Pts received adavosertib 300mg daily on days 1 through 5 and 8 through 12 of a 21-day cycle. Coprimary endpoints were objective response and progression-free survival at 6 months (PFS6). **Results:** Between OCT-11-2018 and SEP-30-2019, 35 pts enrolled on study. Median follow-up is 4.6 months. The median number of prior lines was 3 (range 1-8). 34 pts were considered evaluable for response. In these pts, 9 confirmed and 1 unconfirmed responses were observed, for an ORR of 29.4% (95% CI 15.1-47.5%). The PFS at 6 months was 58.7% (95% CI: 39.5-73.7%). The median PFS is 6.1 months and the median duration of response is 9.0 months. Frequently observed Grade 3 or higher related adverse events included neutropenia (32.3%), anemia (20.6%), and fatigue (23.5%). Immunohistochemistry and targeted next-generation sequencing were performed to investigate potential biomarkers of response. **Conclusions:** Adavosertib monotherapy demonstrates promising clinical activity in women with USC. The observed monotherapy activity is higher than in other diseases, and additional exploration of the biology of Wee1 inhibition in USC is needed. Further studies of adavosertib in this patient population are planned. Clinical trial information: NCT03668340. Research Sponsor: AstraZeneca.

6010 **Clinical Science Symposium, Fri, 8:00 AM-9:30 AM**

A randomized phase II study of cabozantinib and nivolumab versus nivolumab in recurrent endometrial cancer. *First Author: Stephanie Lheureux, Princess Margaret Hospital, Toronto, ON, Canada*

Background: The efficacy of treatment for recurrent endometrial cancer (EC) remains limited. Vascular endothelial growth factor and inflammatory chemokines are proangiogenic factors and immune modulators involved in immune suppression. Reprogramming the tumor microenvironment by combining antiangiogenic and immunotherapy (IO) could enhance antitumor responses. **Methods:** A 2:1 randomized phase 2 trial compared the combination of cabozantinib and nivolumab (Arm A) versus nivolumab (Arm B) in recurrent EC. Primary endpoint was progression free survival (PFS) assessed by RECIST 1.1 (NCT03367741). Women with recurrent measurable EC were eligible. There were no limits on prior therapy, but at least one prior platinum-based chemotherapy was required. Patients (pts) were stratified according to MSI status and assessed by CT every 8 weeks. Cabozantinib was given at 40 mg daily (Arm A) and nivolumab at 240 mg, on D1 and D15 of a 28-day cycle for 4 cycles, followed by 480 mg every 4 weeks (Arms A & B). Pts with carcinosarcoma or prior IO were enrolled in an exploratory cohort and received combination treatment (Arm C). A baseline biopsy was required for all pts. CyTOF analysis was performed on fresh biopsies. **Results:** 76 evaluable pts were enrolled (Arm A: 36, Arm B: 18, Arm C: 9 carcinosarcoma, and 20 post IO including 7 pts crossed over from Arm B). 55% of pts had received ≥3 prior lines of therapy. Two pts were MSI high in Arm A and none in Arm B. The Kaplan-Meier estimated median PFS was 5.3 (95% CI: 3.5-9.5) months in Arm A and 1.9 (95% CI: 1.6-3.8) months in Arm B, with a log-rank p = 0.07, which met the significance level of 0.1 used for sample size calculation. Objective response rate (ORR) was 25% for Arm A and 16.7% for Arm B; stable disease (SD) was seen in 44.4% *vs* 11.1%, respectively. Clinical benefit (ORR+SD) was significantly higher in arm A *vs* B ($p < 0.001$). In Arm C-carcinosarcoma, one patient had a partial response (11.9 months duration) and four SD. In Arm C-prior IO, six pts responded and eight had SD. The most common related AEs in Arm A were diarrhea (47.2%), elevated liver enzymes (44.4%), fatigue (38.9%), anorexia, hypertension, and nausea (30.6%), mainly grade 1/2. Preliminary CyTOF analysis across treatment arms identified multiple immune subsets for further interrogation including activated CD8+ and CD4+ T cells. **Conclusions:** Cabozantinib plus nivolumab demonstrates improved PFS compared to nivolumab in heavily pre-treated women with recurrent EC. In-depth CyTOF analysis of the tumor microenvironment to identify predictive immune biomarkers of response is ongoing. Clinical trial information: NCT03367741. Research Sponsor: U.S. National Institutes of Health, Conquer Cancer Foundation of the American Society of Clinical Oncology.

6011 **Clinical Science Symposium, Fri, 8:00 AM-9:30 AM**

Impact of chemotherapy alone or in combination with an anti-angiogenic on the immune tumor microenvironment (TME) of ovarian cancer: Data from the randomized CHIVA trial (a GINECO –GINEGEPS study). *First Author: Elisa Yaniz, Gustave Roussy Cancer center, INSERM U981, Villejuif, France*

Background: The neoadjuvant setting is an excellent opportunity to study '*in vivo*' the biological impact of treatment on tumor cells and the immune TME. Both chemotherapy and anti-angiogenics may have immunomodulatory properties which could prime the TME and increase effectiveness of immunotherapeutic agents. We performed comprehensive multiplexed immune biomarker analyses on paired tumor samples at diagnosis and after 3 cycles of neoadjuvant carboplatin+paclitaxel (CP) +/- the anti-angiogenic tyrosine kinase inhibitor nintedanib (N) in the randomized CHIVA trial. **Methods:** Patients were randomized 2:1 to CP + N or placebo for 3 cycles prior to interval debulking, samples were evaluable for immune profiling for 124 pts at diagnosis and 107 at surgery from the CHIVA trial. For 86 patients matched paired samples were available. Multiplexed IF or IHC panels were performed for CD4, CD3, CD8, CK, Granzyme B, FOXP3, CD68, CD163 and DC-Lamp. Wilcoxon tests were used to compare measurements. **Results:** At diagnosis the most abundant cells were CD8+ and CD4+ cells (median=118 and 119cells/mm2, respectively) compared to Foxp3+ TRegs (median=30/mm2). Among the myeloid lineage, the proportion of CD68+ (M1) and CD163+ (M2) macrophages was balanced, while mature dentritic cells (DC) represented <5% of myeloid cells. In the whole population, regardless of arm, neoadjuvant platinum-based treatment significantly increased CD4+ (p=0.03) and CD8+ infiltration (p=0.009), decreased FOXP3+ cells (p=0.01), and these differences pre- and post-treatment remained significant when analysis was restricted to pts with paired samples. Mature DC also increased significantly with neoadjuvant treatment (p=0.0003), there was no significant modification in CD68+ or CD163+ macrophages. Changes in immune parameters did not differ significantly between the CP+B vs CP+placebo arms. **Conclusions:** Neoadjuvant treatment has a profound impact on the immune cell composition of the TME in advanced OC. However this change seems to be mainly mediated by platinum+paclitaxel chemotherapy rather than the anti-angiogenic tyrosine kinase inhibitor nintedanib. Research Sponsor: Maria Pia Award.

6012 Poster Discussion Session; Displayed in Poster Session (Board #183), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Final survival analysis of NSGO-AVANOVA2/ENGOT-OV24: Combination of niraparib and bevacizumab versus niraparib alone as treatment of recurrent platinum-sensitive ovarian cancer—A randomized controlled chemotherapy-free study. *First Author: Mansoor Raza Mirza, The Finsen Centre 5073, Copenhagen, Denmark*

Background: We previously reported significantly improved progression-free survival (PFS) with the chemotherapy-free regimen of niraparib and bevacizumab compared to niraparib alone, in women with platinum-sensitive relapsed ovarian cancer (PSROC), regardless of homologous recombination deficiency (HRD) status (MyChoice HRD), duration of chemotherapy-free interval (CFI) and number of previous lines of therapy (Mirza MR et al, Lancet Oncol 2019). We now present the updated PFS, overall survival (OS) and other efficacy and safety endpoints. **Methods:** In this randomized, open-label, phase 2 study, women with measurable/evaluable, high-grade serous or endometrioid PSROC were randomized to niraparib 300mg once daily or the combination of niraparib 300mg once daily and bevacizumab 15mg/kg IV every 3 weeks until disease progression (1:1 randomization). The primary endpoint was PFS. Stratification was according to HRD status and CFI (6-12months (mo) vs. > 12mo). First-line maintenance bevacizumab was permitted. **Results:** Of 97 enrolled patients, 48 were randomized to niraparib monotherapy and 49 to the chemotherapy-free combination. The combined treatment significantly improved PFS compared to niraparib alone: updated median PFS 12.5 mo vs. 5.5 mo; hazard ratio (HR) adjusted for stratification factors 0.34; 95% confidence interval (CI) [0.21 to 0.55]; P < 0.0001. Preplanned exploratory subgroup analyses: patients with HRD-positive tumors (n = 54) HR 0.41 (CI, 0.23-0.76); HRD-negative disease (n = 43) HR, 0.40 (CI, 0.20-0.79); Time to First Subsequent Therapy (TFST) (n=97) HR, 0.4 (CI, 0.25-0.64); PFS2 (n=97) HR 0.55 (CI, 0.35-0.88); Time to Second Subsequent Therapy (TSST) (n=97) HR, 0.56 (CI, 0.35-0.90); OS (49 events only) HR, 0.77 (CI, 0.42-1.41). There was no difference in treatment-emergent grade 3-4 adverse events except for the rate of hypertension (22.9% vs. 0%) and neutropenia (8.3% vs. 2.0%). Patient-reported outcomes measured using EORTC QLQ-C30 and OV28 were similar for both treatment arms. **Conclusions:** Updated PFS consistently demonstrates that the niraparib-bevacizumab combination had clinically and statistically meaningful activity in PSROC. This phase 2 study was not powered to detect differences in OS or any other efficacy endpoints however TFST, PFS2 & TSST are significantly improved while there is a trend towards OS improvement with niraparib-bevacizumab combination. Clinical trial information: NCT02354131. Research Sponsor: research grant + niraparib from Tesaro Inc for this Invest. Initiated Trial (sponsor Nordic Society of Gynaecological Oncology NSGO).

6013 Poster Discussion Session; Displayed in Poster Session (Board #184), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Olaparib treatment in patients (pts) with platinum-sensitive relapsed (PSR) ovarian cancer (OC) by BRCA mutation (BRCAm) and homologous recombination deficiency (HRD) status: Phase II LIGHT study. *First Author: Karen Anne Cadoo, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: In Study 19 (NCT00753545), olaparib capsules demonstrated improvement in progression-free survival (PFS) vs placebo in the PSR OC maintenance setting, irrespective of BRCAm status (Ledermann *et al. Lancet Oncol* 2014). LIGHT is the first prospective study to evaluate olaparib tablet treatment in PSR OC pts by BRCAm and HRD status. **Methods:** This is an open-label, non-randomized study (NCT02983799) that assessed efficacy and safety of olaparib monotherapy (300 mg BID) in pts with PSR, high-grade serous/endometrioid epithelial OC and ≥1 prior line of platinum chemotherapy. Pts were assigned to one of four cohorts: germline (g) BRCAm; somatic (s) BRCAm; HRD+ve (non-BRCAm); HRD–ve; by Myriad BRACAnalysis CDx and myChoice tests. HRD+ve was a score ≥42. Primary endpoint was objective response rate (ORR). Secondary endpoints included: disease control rate (DCR) and investigator-assessed PFS (RECIST v1.1). Primary analysis was to be ~6 months (mo) after the last pt was enrolled. **Results:** Data cut off was 8/27/19. Of 271 pts treated (median of 31.7 weeks [2.1–96.0]), 270 had measurable disease at baseline and were included in efficacy analyses (Table). The most common treatment-emergent adverse events (AEs) were nausea (66%) and fatigue (62%).Serious AEs and Grade ≥3 AEs were experienced by 25% and 44% of pts, respectively. AEs leading to olaparib dose interruptions, reductions and discontinuations occurred in 33%, 24% and 4% of pts, respectively. **Conclusions:** Olaparib treatment demonstrated activity across all cohorts. As observed in the maintenance setting, similar efficacy was seen in the gBRCAm and sBRCAm cohorts. For non-BRCAm pts, longer median PFS and higher ORR were observed in the HRD+ve cohort. Olaparib treatment was well tolerated with no new safety signals identified and a safety profile consistent with that seen in the PSR and first-line settings. Clinical trial information: NCT02983799. Research Sponsor: AstraZeneca Pharmaceuticals LP.

	gBRCAm (N=75)	sBRCAm (N=25)	HRD+ve (non-BRCAm) (N=68)	HRD–ve (N=89)	Overall population (N=270)*
≥2 prior lines of chemotherapy, n (%)	35 (47)	14 (56)	37 (54)	60 (67)	152 (56)
ORR, n (%)	52 (69)	16 (64)	20 (29)	9 (10)	101 (37)
95% CI	58–80	43–82	19–42	5–18	32–44
DCR, n (%)	72 (96)	25 (100)	54 (79)	67 (75)	230 (85)
95% CI	89–99	86–100	68–88	65–84	80–89
PFS events, n (%)	38 (51)	15 (60)	49 (72)	76 (85)	187 (69)
Median PFS, mo	11.0	10.8	7.2	5.4	7.4
95% CI	8.3–12.2	7.3–NE	5.3–7.6	3.7–5.6	6.4–7.9

*13 pts with a Myriad test result of failed or missing were included in the overall population. CI, confidence interval; NE, not estimable

6014 Poster Discussion Session; Displayed in Poster Session (Board #185), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Concordance between CA-125 and RECIST progression (PD) in patients with germline BRCA-mutated platinum-sensitive, relapsed ovarian cancer treated with a PARP inhibitor (PARPi) as maintenance therapy after response to chemotherapy. *First Author: Angelina Tjokrowidjaja, NHMRC Clinical Trials Centre, Camperdown, NSW, Australia*

Background: There are no data to support CA-125 as a surrogate biomarker for ovarian cancer PD in patients on maintenance therapy with a PARPi. We aimed to assess the concordance of PD by CA-125 with RECIST PD in patients treated with maintenance PARPi. **Methods:** We extracted data on PD as defined by GCIG CA-125 and investigator-assessed RECIST from the SOLO2/ENGOT-Ov21 (NCT01874353) trial. Patients were categorized into: (i) CA-125 and RECIST non-PD concordant; (ii) CA-125 and RECIST PD concordant; and (iii) CA-125 and RECIST discordant. We excluded those with PD other than by RECIST, PD on date of randomization, and no repeat CA-125 beyond baseline. To assess the concordance of CA-125 PD with RECIST PD and CA-125 non-PD with RECIST non-PD, we computed the positive predictive value (PPV), i.e. the probability that patients with CA-125 PD also had RECIST PD, and negative predictive value (NPV), i.e. probability that patients with no CA-125 PD also did not have RECIST PD, respectively. **Results:** Of 295 randomised patients, 275 (184 olaparib, 91 placebo) were included in the primary analysis. 80 (29%) had CA-125 PD and 77 had concordant RECIST PD, resulting in a PPV of 96% (95% CI 90%-99%). Of 195 patients without CA-125 PD, 101 also did not have RECIST PD, resulting in a NPV of 52% (95% CI 45%-59%; Table). Among those with RECIST PD (n = 171), a greater proportion of patients with RECIST-only PD had a normal baseline CA-125 than those with both CA-125 and RECIST PD (94% *vs* 69%; $p< 0.001$). Of 94 patients without CA-125 PD but had RECIST PD, 65 (69%) had CA-125 that remained within normal range, while 27 (29%) had rising and elevated CA-125 that did not meet the criteria for GCIG CA125-PD. Discordance between RECIST PD and CA-125 non-PD was similar in early (≤12 weeks) and late (> 12 weeks) PD (56% *vs* 55%, respectively; $p= 0.96$). **Conclusions:** Almost half the patients with RECIST PD did not have CA-125 PD and most had CA-125 still within the normal range. Regular imaging should be considered as part of surveillance in patients on maintenance olaparib rather than relying on CA-125 alone. Research Sponsor: Astra Zeneca.

Disease status by CA-125 criteria	RECIST-defined disease progression (n = 171)	No RECIST-defined disease progression (n = 104)	Total (n = 275)
Progressive disease, n (%)	77 (96%)	3 (4%)	80
Non-progressive disease, n (%)	94 (48%)	101 (52%)	195

6015 Poster Discussion Session; Displayed in Poster Session (Board #186), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Characterization of patients (pts) with long-term responses to rucaparib in recurrent ovarian cancer (OC). *First Author: Elizabeth M. Swisher, University of Washington, Seattle, WA*

Background: Pts who derive durable benefit from PARP inhibitor treatment may provide insights into improving outcomes. Here we describe long-term responders from Study 10 (NCT01482715) and ARIEL2 (NCT01891344), studies of the PARP inhibitor rucaparib for the treatment of high-grade recurrent OC. **Methods:** This analysis included pts enrolled in Study 10 (Part 2A: *BRCA1* or *BRCA2* [*BRCA*]-mutant OC, platinum sensitive, 2–4 prior chemotherapies; Part 2B: any platinum status, 3–4 prior chemotherapies) and ARIEL2 (Part 1: *BRCA*-mutant or wild-type OC, platinum sensitive; Part 2: any platinum status, 3–4 prior chemotherapies). Final results from Study 10 (n = 54) and ARIEL2 (n = 491) were pooled. Long-term responders were defined as pts with duration of response (DOR) > 1 y, and short-term responders as pts with DOR ≤ 20 weeks; responses were evaluated using RECIST. Targeted next-generation sequencing was used to detect deleterious mutations and loss of heterozygosity (LOH) in tumors. *BRCA1* methylation was quantified by digital droplet PCR. **Results:** Overall, 25% (138/545) of enrolled pts were responders. Of these, 29% (40/138) had long-term responses, including 16/138 (12%) with DOR > 2 y; 21% (29/138) were short-term responders. Both groups received a median of 3 prior anticancer therapies. Among patients with *BRCA* mutations, *BRCA* homozygous deletion or rearrangement was detected in 15% (4/27) of long-term responders vs 0% (0/15) of short-term responders. In an expanded analysis of the 95 pts with *BRCA* mutations and confirmed response, pts with *BRCA* homozygous deletion or rearrangement had significantly longer DOR than pts with other mutation types (median 3.5 vs 0.6 y; HR = 0.30; p = 0.024). There was no apparent difference in *BRCA* gene or mutation location for long- vs short-term responders. Ten of the 13 long-term responders with *BRCA* wild-type OC had high genome-wide LOH (≥16% LOH), a genomic scar indicative of homologous recombination deficiency, including OC associated with *BRCA1* hypermethylation (n = 2) and *RAD51C/D* mutations (n = 2). **Conclusions:** Long-term responders to rucaparib include OC with *BRCA* mutation, particularly homozygous deletion or rearrangements, which would not be susceptible to somatic reversion mutations, as well as *BRCA1* hypermethylation, and *RAD51C/D* mutations. Clinical trial information: NCT01482715; NCT01891344. Research Sponsor: Clovis Oncology, Inc.

6016 Poster Discussion Session; Displayed in Poster Session (Board #187), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A randomized phase II trial of secondary cytoreductive surgery (SCS) +/- carboplatin hyperthermic intraperitoneal chemotherapy (HIPEC) in patients (pts) with recurrent platinum-sensitive ovarian cancer (EOC). *First Author: Oliver Zivanovic, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY*

Background: The role of HIPEC for recurrent EOC is not well defined. The aim of this phase II study was to determine the proportion of pts without evidence of disease progression at 24 months post SCS +/- intraoperative carboplatin HIPEC. **Methods:** After SCS to ≤ 0.5 cm residual visible disease pts were intraoperatively randomized to carboplatin HIPEC (800mg/m^2 for 90 minutes) or no HIPEC. The HIPEC arm received 5 additional and the standard arm received 6 postoperative cycles of IV platinum-based chemotherapy without maintenance treatment. Based on an exact binomial single stage "pick the winner" design, each arm is considered "winner" if ≥ 17/49 pts are without evidence of disease progression at 24 months post SCS. Secondary objectives include postoperative grade ≥ 3 toxicity and complications within 4 weeks post SCS, and pharmacokinetics of carboplatin HIPEC. **Results:** Of 98 pts, 49 (50%) were randomized to the HIPEC arm. The arms were well balanced for age, stage, histology, BRCA mutation status, prior chemotherapy, and disease-free interval. Complete gross SCS was achieved in 94% of the standard and 82% of the HIPEC arm (p = 0.12). Bowel resection was performed more frequently in the standard (65%) compared to the HIPEC arm (37%; p = 0.008). Median operative time was shorter in the standard (296 minutes) compared to the HIPEC arm (475 minutes; p < 0.001). There was no perioperative mortality and no difference in use of ostomies, length of stay or postoperative toxicity. At a median follow-up of 27.7 months (range: 8.8-81.8 months) 70 of 98 pts progressed and 26 died with a median progression free survival (PFS) of 14.3 months (12.1-16 months) and a median overall survival (OS) of 55.2 months (47.7-not reached). At 24 months post SCS 32 pts progressed within 24 months in the standard versus 35 in the HIPEC arm. There was no statistically significant difference in median PFS (15.4 vs 12.3 months, p = 0.173) or median OS (69.2 vs 53.1 months, p = 0.317) between arms. These are preliminary efficacy estimates as 83/98 pts have a minimum of 24 months follow-up. **Conclusions:** The HIPEC arm did not reach the predefined "winner" endpoint; the standard arm is still undetermined as 6 pts did not reach 24 months follow-up. No perioperative mortality, and no increased perioperative morbidity or toxicity was seen with HIPEC. SCS with carboplatin HIPEC followed by 5 cycles of platinum-based chemotherapy was not superior to SCS without HIPEC followed by 6 cycles of platinum-based chemotherapy. Clinical trial information: NCT01767675. Research Sponsor: Gail Baird Foundation, Other Foundation.

6017 Poster Discussion Session; Displayed in Poster Session (Board #188), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Randomized double-blind placebo-controlled trial of primary maintenance vigil immunotherapy (VITAL study) in stage III/IV ovarian cancer: Efficacy assessment in *BRCA1/2*-wt patients. *First Author: Rodney Paul Rocconi, University of South Alabama, Mobile, AL*

Background: Vigil is an autologous tumor cell vaccine constructed from autologous harvested tumor tissue transfected with a DNA plasmid encoding GMCSF and bi-shRNA-furin thereby creating TGFβ expression control. **Methods:** A randomized double-blind placebo-controlled trial of Vigil vs. placebo was performed in advanced stage frontline OC patients. Relapse-free survival (RFS) and safety were endpoints. Patients who achieved complete clinical response were randomized [1:1 to placebo (control group, CG) or Vigil (Vigil group, VG)] after completion of frontline surgery and chemotherapy. All patients received 1 x 10e7 cells/ml of Vigil or placebo intradermally once a month for up to 12 doses. **Results:** Ninety-two patients were randomized with 91 patients in the per-protocol population (PP), (VG n=46; CG n=45). 62 patients were tested for *BRCA1/2* status. VG showed no added overall toxicity compared to CG and no grade 4/5 toxicities were observed. Grade 2/3 toxic events were observed in 18% of CG patients (most common bone pain, fatigue) compared to 8% of VG patients (most common nausea, musculoskeletal pain). From time of randomization median RFS for all 91 patients was favorable in the VG (HR 0.69, one-sided p 0.088).Stratified by BRCA status, an advantage in RFS was seen in the *BRCA1/2*-wt patients in VG (19.4 mo) compared to CG (8 mo) (HR 0.51, 90% CI 0.26 – 1.01, one-sided p 0.050) from time of randomization and HR of 0.49 (90% CI 0.25 – 0.97, one-sided p 0.038) from time of surgery. Median time from surgery to randomization was 208.5 days (6.9 mo) in VG vs. 200 days (6.6 mo) in CG. 37.5% BRCA1/2-wt Vigil treated patients relapsed compared to 71% of placebo at time of data snap for analysis (HR 0.51, one-sided p 0.05), (median follow-up of 34.3 mo for all n=91 subjects). Germline and somatic *BRCA1/2* molecular testing via central third party is underway on all 91 patients under continued blinded conditions to validate activity in *BRCA1/2*-wt. **Conclusions:** Vigil immunotherapy as frontline maintenance in Stage III/IV ovarian cancer is well tolerated and showed RFS clinical benefit, particularly in *BRCA1/2*-wt disease. Clinical trial information: NCT02346747. Research Sponsor: None.

RFS in BRCA1/2-wt population from time of surgery/procurement.

Group	N	Number of events	Median RFS in mo (95% CI)	HR	One-sided p-value
Vigil	24	9/24 (37.5%)	Not reached (14.5 – N/A)	**0.49** (90% CI 0.25 – 0.97)	**0.038**
Placebo	24	17/24 (71%)	14.8 (12 - 21.2)		

6018 Poster Discussion Session; Displayed in Poster Session (Board #189), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Association of chronotype and pain at baseline in ovarian cancer survivors participating in a lifestyle intervention (NRG/GOG 0225). *First Author: Tracy E Crane, University of Arizona Cancer Center, Tucson, AZ*

Background: Chronotype is defined as an individual's propensity to sleep at a specific time in a 24-hour cycle with late chronotype associated with poorer health outcomes including cancer. Chronotype remains relatively undefined in ovarian cancer. The Lifestyle Intervention for oVarian cancer Enhanced Survival (LIVES) study is testing whether 1205 women randomized to a diet and physical activity intervention for 24-months will have longer progression-free survival versus an attention control. Here we determine the association of late and early vs mid chronotypes and patient reported outcomes (PROs), lifestyle behaviors and biomarkers of metabolic health and inflammation in ovarian cancer survivors post-treatment (≤ 6.5 months). **Methods:** Chronotype was determined using self-reported time to bed (early < 9 pm; mid ≥ 9 pm - ≤12 am; late > 12 am) captured through the Pittsburg Sleep Quality Index and PROs were measured using subscales of the Rand-36 questionnaire. Validated questionnaires for diet and physical activity were used and biomarkers were collected at routine clinic visits. A total subsample of 438 ovarian cancer survivors enrolled in NRG/GOG 0225- LIVES study with all available baseline measures were included in analyses. Descriptive statistics, general linear mixed models, and Pearson correlations were performed. **Results:** Reported pain was significantly higher in late chronotypes (P < 0.05) when compared to early and mid-chronotypes. Total sleep duration was significant between the 3 chronotypes (P < 0.05) with late chronotype experiencing less sleep (6.77 ± 1.67 hrs) than mid chronotype (7.04 ± 1.31 hrs) and early chronotype (7.56 ± 1.33 hrs). Higher reported pain was significantly correlated to poorer CRP levels (r = -0.198, P < 0.001) suggesting higher systemic inflammation and poorer blood insulin levels (r = -0.116, P < 0.05) independent of chronotype classification. All other subscales of the RAND 36 and physical activity were not associated with chronotype. Diet quality trended towards significance with a positive association observed in early and an inverse association in late chronotypes (P = 0.06). **Conclusions:** Late chronotypes reported higher levels of pain which was associated with poorer sleep and diet quality and higher levels of inflammation and insulin. More robust data, including actigraphy, are being analyzed and will provide additional insight of the role of circadian rhythm and phenotype on pain and key biomarkers in ovarian cancer survivors. Clinical trial information: NCT00719303. Research Sponsor: U.S. National Institutes of Health.

6019 Poster Discussion Session; Displayed in Poster Session (Board #190), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Beyond Sedlis: A novel, histology-based nomogram for predicting recurrence risk and need for adjuvant radiation in cervical cancer—A NRG/GOG ancillary analysis. *First Author: Kimberly Levinson, The Johns Hopkins School of Medicine, Baltimore, MD*

Background: In GOG 49, factors associated with a 3-year, 30% recurrence risk in squamous cell carcinoma of the cervix (SCC) after surgery alone were defined. These "intermediate" risk factors [tumor size (TS), depth of tumor invasion (DOI), and lymphvascular space invasion (LVSI)] were then studied in GOG 92, which demonstrated the utility of treating patients (pts) with ≥2 intermediate risk factors with adjuvant radiation (RT), Sedlis Criteria. However, pts with < 30% recurrence risk were not eligible and few pts with adenocarcinoma (AC) were included. Our study purpose was 1) to evaluate recurrence risk factors for AC vs SCC, and 2) to define contemporary nomograms for adjuvant treatment in pts with both histologies. **Methods:** We performed an ancillary analysis of GOG 49, 92, and 141, and included Stage I pts who received no neoadjuvant/adjuvant therapy. Multivariable Cox proportional hazards models were created separately for AC and SCC to evaluate independent risk factors for recurrence. Model accuracy was tested with ROC curves. Prognostic nomograms were generated for 2-year recurrence risk for AC and SCC. **Results:** We identified 715 with SCC and 105 pts with AC; 142 with SCC (19.9%) and 18 with AC 17.1%) recurred. For SCC, factors associated independently with recurrence were: LVSI [HR 1.58 (CI 1.12-2.22)], DOI [middle 1/3, HR 4.31 (CI 1.81-10.26); deep 1/3, HR 7.05 (CI 2.99-16.64)] and TS [≥4cm HR 2.67 (CI 1.67-4.29)]. In contrast, for AC, only TS ≥4cm was independently associated with recurrence [HR 4.69 (CI 1.25-17.63)]. At 3 years, ROC curves for these models predicted recurrence with 76% and 75% accuracy for SCC and AC, respectively. Utilizing a nomogram generated from these models, for SCC, DOI had the greatest impact on recurrence, with mid 1/3 conferring an 18% risk and deep 1/3 a 32% risk, while LVSI and TS increased risk by 4-10%, respectively. In contrast, for AC, TS alone had the greatest impact on recurrence risk with TS 2-4cm conferring a 20% risk over 3 years and TS ≥4cm, a 28% risk. **Conclusions:** Our nomogram differs from the Sedlis Criteria in demonstrating that single, as well as a combination of risk factors predict substantial 3-year recurrence rates in Stage I cervical cancer. Furthermore, these factors differ by AC and SCC subtypes, suggesting that distinct, histology-specific nomograms may have greater utility in identifying pts who will most benefit from adjuvant therapy. Research Sponsor: None.

6021 Poster Discussion Session; Displayed in Poster Session (Board #192), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Camrelizumab plus apatinib in patients with advanced cervical cancer: A multicenter, open-label, single-arm, phase II trial. *First Author: Chunyan Lan, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: Camrelizumab is a fully humanized, monoclonal antibody against PD-1. We aimed to assess the efficacy and safety of camrelizumab plus apatinib, a tyrosine kinase inhibitor targeting VEGFR2, in patients with advanced cervical cancer. **Methods:** In this open-label, single-arm, phase 2 study done at four centres in China, eligible patients were aged 18–70 years, had an ECOG performance status of 0 or 1, progressed after at least one line of systemic chemotherapy for metastatic, recurrent or persistent cervical cancer, and had measurable disease. Patients received camrelizumab 200 mg every 2 weeks and apatinib 250 mg once daily. Treatment continued until disease progression, unacceptable toxicity, and withdrawal of consent. The primary endpoint was the objective response rate (ORR) assessed by RECIST version 1.1. An optimal Simon two-stage design was employed to test the null hypothesis of a 17% ORR versus 35% alternative (1-sided alpha 0.10, 80% power), if >3 responses out of the first 16 patients were observed, then the study would continue to enroll a total of 44 patients. **Results:** Between Jan 21st, 2019, and Aug 1st, 2019, 45 patients were enrolled and received study treatment (safety population). The median age was 51 (range, 33–67) years. Median previous treatment lines were 2 (range, 1–4). As of Jan 22, 2020, median follow-up was 9.2 months (range, 2.4–12.2). 25 (59.5%; 95%: CI 44.7–74.4) of 42 patients who had at least one post-baseline tumor assessment (efficacy evaluable population) achieved an objective response, including two (4.8%) complete response, and 23 (54.8%) partial response. Median duration of response was not reached. The disease control rate was 88.1% (37/42). Median progression-free survival (PFS) was 7.6 months (95% CI: 5.8–not reached). 31 (68.9%) patients had grade ≥ 3 treatment-related adverse events (TRAEs). Grade ≥ 3 TRAEs occurring in $\geq 5\%$ of patients were hypertension (24.4%), anemia (20.0%), fatigue (15.6%), γ-glutamyltransferase increased (13.3%), neutropenia (6.7%), and thrombocytopenia (6.7%). In post-hoc analyses, objective response was noted in 20 (69%) of 29 patients with PD-L1-positive tumors, and in 5 (50.0%) of 10 patients with PD-L1-negative tumors (Chi-square test, P = 0.281). PFS was longer in patients with PD-L1-positive tumors than patients with PD-L1-negative tumors (median PFS: 9.6 versus 5.3 months; log-rank test, P = 0.017). **Conclusions:** Camrelizumab plus apatinib showed promising antitumor activity and tolerable toxicities in patients with advanced cervical cancer. Clinical trial information: NCT03816553. Research Sponsor: Jiangsu Hengrui Medicine Co. Ltd., National Natural Science Foundation of China

6022 Poster Discussion Session; Displayed in Poster Session (Board #193), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A Big Ten Cancer Research Consortium phase II trial of pembrolizumab with carboplatin and paclitaxel for advanced or recurrent endometrial cancer. *First Author: Mario Javier Pineda, Ironwood Cancer and Research Centers, Gilbert, AZ*

Background: There are limited chemotherapeutic options for patients (pts) with advanced or recurrent endometrial cancer (EC). Reported objective response rates (ORR) for first-line doxorubicin/cisplatin/ paclitaxel combination therapy was 57%; with a median progression-free survival (PFS) of 8.3 months. The goal of this phase II study was to assess the efficacy and safety of pembrolizumab in combination with standard carboplatin/paclitaxel in pts with measurable advanced or recurrent EC. **Methods:** This was a single-arm, open-label, multicenter phase II study for pts with RECIST measurable advanced or recurrent EC coordinated by the Big Ten Cancer Research Consortium. Patients may have had received 1 prior platinum-based regimen, with a platinum free interval $>$ 6 months, $<$ one non-platinum chemotherapy, or prior hormonal therapy. Pts received carboplatin AUC 6, paclitaxel 175mg/m^2 (CT) and pembrolizumab 200mg IV every 3 weeks for up to 6 cycles; with dose reduced for prior radiation. The primary endpoint was ORR per immune-related RECIST. Planned sample size of 46 subjects provided 77% power to detect 15% ORR improvement compared to historical controls, with one-tailed test and 10% type I error rate. **Results:** 46 pts were enrolled. Median age was 67 (range: 43-86). 32 pts had recurrent and 14 had primary metastatic EC. Histological types were: 26 endometrioid, 11 serous, 3 clear cell, 6 other. 19 patients had received prior carboplatin/paclitaxel, 23 pelvic EBRT, 14 brachytherapy, 1 adriamycin and 1 hormonal therapy. Grade 3-4 adverse events (AEs) included: laboratory abnormalities (20), hematological (8), metabolism (6), nervous system (4), gastrointestinal (2), and others (6). There were 15 grade 3-4 SAEs occurring in 7 pts: vomiting (1), anaphylaxis (3), fever (2), dehydration (1), syncope (2), vascular (2), fatigue (1), neurological (2), thrombocytopenia (1), and no grade 5 SAEs. 36 patients were evaluable for response at the time of abstract submission. ORR was 77.8% (28/36) and median PFS was 10.55 months. **Conclusions:** The addition of pembrolizumab to standard of care CT chemotherapy for advanced or recurrent EC induced a clinically significant improvement in ORR compared to historical outcomes and toxicity did not exceed anticipated toxicity with standard treatment, supporting further testing in a phase III trial. Clinical trial information: NCT02549209. Research Sponsor: Merck.

6023 Poster Discussion Session; Displayed in Poster Session (Board #194), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Effect of high-dose chemotherapy with autologous stem cell rescue (HDC-aSCR) on outcome in ovarian small-cell carcinoma, hypercalcemic type (SCCOHT): Prospective series from the French Rare Gynecologic Malignant Tumors Network (TMRG). *First Author: Felix Blanc, Institut Gustave Roussy, Villejuif, France*

Background: Small cell carcinoma of the ovary, hypercalcemic type (SCCOHT), is a rare and rapidly lethal disease affecting young women with over half dying within 2 years of diagnosis. We previously reported improved outcomes with cytoreductive surgery followed by HDC-aSCR in a prospective study, but these encouraging results needed to be confirmed in an independent and larger cohort. **Methods:** Between 2008 and 2019, out of 44 patients (pts) diagnosed with centrally confirmed SCCOHT in 16 referent centers of the TMRG network, 38 were treated prospectively according to the French recommendations of the network with complete surgery (primary or after neoadjuvant chemotherapy), 4 to 6 cycles of PAVEP chemotherapy (cisplatin, doxorubicin, vepeside, and cyclophosphamide), and for pts with complete response (CR), HDC-aSCR, followed by pelvic radiotherapy. The 6 patients who could not receive PAVEP (unfit or diagnostic delay) relapsed and died rapidly. The primary endpoint was the event-free survival (EFS) in the intention-to-treat cohort. **Results:** Median age at diagnosis was 33 years (14-76). 13 pts presented with FIGO stage I, 17 stage III and 6 stage IV, 2 unknown. Median follow-up was 55.5 months. 34 patients achieved CR with CT + surgery and 30 received HDC-aSCR (40%, 47% and 10% with stages I, III and IV diseases respectively) and 21 received also pelvic radiotherapy. Median overall and event-free survival was 36.4 and 15.9 months respectively, and 2-years event-free survival rate was 40% (CI95% 25-56). Median OS was respectively not reached, 18 and 9.6 months for FIGO I, III and IV patients. Among the pts (N = 14) who did not receive HDC-aSCR (rapid progression during or after PAVEP), the 2-yr EFS was 0% compared to 50.5% for the 30 patients receiving HDC. In multivariate analysis, HDC was significantly correlated with better outcomes ($p < 0.001$). For the 21 patients receiving also pelvic radiotherapy, 57% (12/21) are free of recurrence at 4 years. Grades 3/4 adverse events were frequent (78%) but, in most cases, manageable, although one toxic death (3%) occurred during HDC (fungal septic shock). **Conclusions:** Treatment of SCCOHT, with intensive multimodal therapy, is associated with a 40% 2-yr event-free survival. However, this protocol is associated with significant toxicity and should be restricted to good performance status patient and expert centers. Research Sponsor: None.

6025 Poster Session (Board #196), Fri, 8:00 AM-11:00 AM

Phase II trial of guadecitabine priming and pembrolizumab in platinum resistant recurrent ovarian cancer. *First Author: Daniela Matei, Northwestern University Feinberg School of Medicine, Chicago, IL*

Background: Platinum resistant ovarian cancer (PROC) remains a disease of high need. Immune checkpoint inhibitors (ICI) have modest activity. We hypothesized that priming with a hypomethylating agent (HMA) guadecitabine (G) will improve the anti-tumor activity of ICI in PROC by enhancing tumor cell recognition by CD8+ T cells. **Methods:** This open-label phase II study used a Simon's two-stage design. Eligible patients (pts) had recurrent PROC; ECOG PS of 0-1; normal end organ function; and measurable disease. Up to 5 prior cytotoxic regimens were allowed. Treatment consisted of G 30mg/m2 sq D1-4 and pembrolizumab (P) 200mg iv D5. Each cycle was 21 days. The primary endpoint was response rate (RR). Secondary endpoints were progression-free survival (PFS), clinical benefit rate (CBR), and toxicity assessment. Translational endpoints were LINE1 methylation in PBMCs, global tumor methylation, and immune endpoints. Tumor biopsies were obtained at baseline and after 2 cycles. If 2 patients experienced clinical benefit in stage I [n = 16], enrollment proceeded to stage II. The null hypothesis was rejected for ≥ 6 responses in 35 evaluable patients. **Results:** 48 pts were enrolled, 43 were treated, and 33 were evaluable for response. Histology was serous (35), endometrioid (2), clear cell (3) and other (3). Median age was 63 (range 40-88) and median number of prior regimens was 4 [range 1-8]. Two PRs were recorded in the first stage, allowing second stage of enrollment. Overall, there were 2 PRs (RR = 6.6%) and 16 pts had stable disease (SD) [48%]. The clinical benefit rate (PR + SD $>$ 3 months) was 27%. One patient continued treatment for $>$ 2 yrs. Grade 3-4 related toxicities were neutropenia [20], lymphopenia, (9), anemia (2), neutropenic fever (1), rash (1), and others (8). There were 13 grade 3-4 SAEs and 4 grade 5 SAEs, assessed as being unrelated to treatment. LINE1 was hypomethylated in PBMCs D5 vs. D1 (n = 21, p = 0.001). Epic arrays measured global tumor methylation, with 39579 CpG sites (0.05%) being differentially methylated (C2D5 vs. C1D1, n = 11, paired t-test; $p < 0.01$). Main pathways affected included *endosomal transport, K+ transport, cathecolamine secretion, etc.* PDL1 staining in archival tissue showed tumor staining > 0 in 16 of 35 and tumor/stroma interface staining > 0 in 20 of 35 specimens. Antigen-specific cytotoxic T cell activity was increased in CD8+ cells from ascites (C2D5 vs. C1D1). **Conclusions:** G+P has modest anti-tumor activity in patients with PROC, but some patients experienced prolonged disease stabilization. Biomarkers of response are being investigated. Clinical trial information: NCT02901899. Research Sponsor: Department of Defense, Pharmaceutical/ Biotech Company.

6027 Poster Session (Board #198), Fri, 8:00 AM-11:00 AM

A randomized phase II/III trial of conventional paclitaxel and carboplatin with/without bevacizumab versus dose-dense paclitaxel and carboplatin with/without bevacizumab, in stage IVB, recurrent, or persistent cervical carcinoma (JCOG1311): Results of the phase II part. *First Author: Mitsuya Ishikawa, Department of Gynecology, National Cancer Center Hospital, Tokyo, Japan*

Background: A randomized controlled trial was conducted to assess the efficacy and safety of dose-dense, weekly paclitaxel plus carboplatin (ddTC) with or without bevacizumab (Bmab) compared to conventional, tri-weekly paclitaxel plus carboplatin (cTC) with or without Bmab, in metastatic or recurrent cervical carcinoma not amenable to curative treatments with local therapy. **Methods:** Patients were randomly assigned to either a cTC or a ddTC regimen. After Bmab was approved in Japan (in May 2016) the protocol was amended, and patients on both arms received Bmab if not contraindicated. The cTC was paclitaxel 175 mg/m^2 intravenously (IV) for 3 h on day 1 followed by carboplatin at an area under the curve of five IV for 1 h on day 1. The ddTC was paclitaxel 80 mg/m^2 IV for 1 h on day 1 followed by carboplatin at an area under the curve of five IV for 1 h on day 1 and paclitaxel 80 mg/m^2 IV for 1 h on day 8 and day 15. Both cTC and ddTC treatments were repeated every three weeks, for up to nine cycles. Bmab 15 mg/kg IV was repeated until progression or unacceptable toxicity. The primary endpoint of phase II was the response rate (RR) in patients with measurable lesion, who had received Bmab. If the RR of the ddTC + Bmab arm was greater than that of the cTC + Bmab arm for more than 5%, the study would proceed to phase III, which had overall survival (OS) as its primary endpoint. The planned sample size in the phase II part was 56 to select the ddTC arm with a probability of at least 75% if the difference of RR was 15% or more (45% vs. 60%). **Results:** Patient accrual started in October 2015. It was suspended in May 2019 because the number of Bmab-treated patients with measurable lesions reached 56. In total, 122 patients were enrolled and randomly assigned to either the cTC arm (cTC: 29 patients; cTC + Bmab: 32 patients) or the ddTC arm (ddTC: 30 patients; ddTC + Bmab: 31 patients). The primary analysis of the phase II part was conducted in November 2019. The RRs of each regimen were 67.9% [95% CI, 47.7-84.1] (19/28, cTC + Bmab), 60.7% [40.6-78.5] (17/28, ddTC + Bmab), 55.2% [35.7-73.6] (16/29, cTC), and 50.0% [29.9-70.1] (13/26, ddTC). **Conclusions:** The study did not meet the primary endpoint of phase II. Dose-dense, weekly paclitaxel plus carboplatin is not promising for metastatic or recurrent cervical carcinoma. Clinical trial information: jRCTs031180007. Research Sponsor: Japan Agency for Medical Research and Development, National Cancer Center Research and Development Fund of Japan.

6028 Poster Session (Board #199), Fri, 8:00 AM-11:00 AM

Histopathologic validation of the sentinel node technique in early-stage cervical cancer patients. *First Author: Patrice Mathevet, University Hospital of Lausanne, Lausanne, Switzerland*

Background: Sentinel lymph node biopsy (SLN) could be an alternative to systematic lymphadenectomy in early cervical cancer. SLN is less morbid and had shown a high sensitivity for metastasis detection. However, sensitivity of the SLN technique could be over evaluated because SLN are examined with ultrastaging and non sentinel nodes are only examined with routine techniques. The aim of this study was to validate the negative predictive value (NPV) of the SLN technique, with ultrastaging of SLN and non sentinel nodes (NSLN). **Methods:** We used the SENTICOL 1 study data, published in 2011. All nodes, SLN and NSLN have been secondarily subjected to ultrastaging. The ultrastaging consisted in sectioning every 200 μm and immunohistochemistry. A central reviewing of the positive slides and 10% of the negative slides was undertaken. **Results:** One hundred thirty-nine patients were included. SLNs were detected in 136 (97.8%) of the 139 patients. SLNs were found bilaterally in 104 (76.5%) of the 136 patients. 2056 NSLNs were identified (median = 13 NSLNs per patient [range 1-54]). Of 136 patients with SLNs detection, 23 had positive SLNs, after serial sectioning and IHC. NSLNs were metastatic in 8 patients. However, in case of bilateral SLN detection, the FN rate was 1/99 (1%) with detection of ITC in one NSLN from 99 bilateral negative SLNs. The NPV was 99% (0,99 [IC 95% = 0,97-1,00]). **Conclusions:** The pelvic SLN technic is a safe and trustfully technic to determine the nodal status in patients with early-stage cervical cancer. In case of optimal mapping with bilateral detection, NPV is 99% (IC 95% = 0,97-1,00). Research Sponsor: the National French Cancer Institute (PHRC 2004).

6029 Poster Session (Board #200), Fri, 8:00 AM-11:00 AM

Survival differences by race after minimally invasive versus open radical hysterectomy. *First Author: Rebekah Summey, University of Texas at Austin, Austin, TX*

Background: Black patients with cervical cancer have historically experienced worse survival compared with white women, as well as decreased rates of minimally invasive surgery (MIS) including radical hysterectomy. The goal of our study is to evaluate if this disparity in survival outcomes reverses in light of new findings favoring an open approach for patients with stage IA2 and IB1 cervical cancer compared to MIS. **Methods:** The National Cancer Database was queried, and all black and white women with stages IA2 and IB1 cervical cancer who underwent radical hysterectomy from 2010 to 2015 were included. Patients without survival data or documented surgical approach were excluded. Demographic factors were compared using student t-tests and Z-test of proportions as appropriate. Hazard ratios (HR) for the event of mortality were calculated by race and by route of surgery. Kaplan-Meier plots were created to compare survival between groups, and the Cox proportional hazards model was used to adjust for covariates. **Results:** 4915 patients were identified for inclusion, 12.1% black and 87.9% white. 43.0% of patients underwent open surgery (84.9% white and 15.1% black) and 57.0% underwent MIS (90.1% white and 9.9% black). Average follow up time between groups was 39.5 months for black patients and 40.6 months for white patients. Black patients who underwent open surgery had a hazard ratio (HR) for mortality of 1.44 (95% CI: 1.03-2.00), and those who underwent MIS had a HR of 1.48 (95% CI: 1.03-2.12), when compared to white patients. Mortality rates for black patients undergoing open radical hysterectomy remained higher than those for white patients who underwent MIS. When adjusted for age, insurance status, neighborhood income and educational level, tumor type, Hispanic ethnicity, node positivity and tumor size, these hazard ratios were no longer significant. **Conclusions:** Following discoveries of improved outcomes following abdominal radical hysterectomy as compared with MIS, we have identified that the discrepancy in ability to undergo MIS did not resolve previously identified disparities in the outcome of death for black women. Research Sponsor: None.

6030 Poster Session (Board #201), Fri, 8:00 AM-11:00 AM

Gastric-type adenocarcinoma of the cervix: Genomic drivers and clinical outcomes. *First Author: Dib Sassine, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Cervical Gastric-type adenocarcinoma (CGA) is a non-HPV-associated adenocarcinoma, comprising 10% of all cervical adenocarcinomas (Park et al, 2019). The optimal management approach is unclear, given that most data in advanced cervical cancer is driven by HPV-positive disease. We summarize our experience with this rare tumor type at a large cancer center. **Methods:** A retrospective review was performed for all women diagnosed with CGA 6/1/2002- 7/1/2019. Patients who did not follow up after a single visit were excluded. Kaplan-Meier survival analysis was performed to determine progression-free survival (PFS) and overall survival (OS) from date of diagnosis. Tumors from a subset of patients were subjected to MSK-IMPACT targeted sequencing and analysis (Zehir et al, 2017). **Results:** A total of 68 women were identified; 47 met inclusion criteria. The median age at diagnosis was 52 years (range 27-83). The majority of patients were white (70%), an additional 19% were Asian. The majority of patients (60%, n=28) presented with advanced disease (FIGO 2018, stage II-IV), while 40% (n=19) were Stage I. Of note, 26% (n=12) had positive pelvic lymph nodes and 13% (n=6) had ovarian metastases at time of surgical resection. For upfront treatment: 13% (n=6) had surgery alone of whom 83% had stage 1 disease, 36% (n=17) had surgery followed by adjuvant therapy, 30% (n =14) received definitive chemoradiation (CRT). All patients with stage IV disease 15% (n=7) received chemotherapy alone. At completion of primary treatment, 19% (n=9) of patients had persistent disease. In patients who received CCRT, 65% (n=22) recurred, the majority (64%) within 12 months of completion of upfront therapy. Pelvic recurrence was the most common site (n=14, 64%). With a median follow up time of 30 months (range 1-159), the median PFS for Stage I was 34.4 months, compared to 17.5 months in patients with Stage II-IV disease (p= 0.29). Of the 24 patients that had MSK-IMPACT, the most common mutation was TP53 (n=16, 64%) followed by mutations in the RAS pathway (n=8, 33%), PIK3CA (n=3, 12.5%), STK11 (n=3, 12.5%), and ERBB2 alterations (n=2, 8.3 %). 2 (8.3%) women enrolled on a clinical trial based on their NGS results, one targeting ERBB2 and one targeting PIK3CA. **Conclusions:** Consistent with prior published literature, CGA is an aggressive form of cervical cancer with poor median OS in the advanced setting. With universal HPV vaccination, HPV negative cervical cancer will represent a larger percentage of newly diagnosed cancers and further research is needed to identify the optimal management approach. Research Sponsor: None.

6031 Poster Session (Board #202), Fri, 8:00 AM-11:00 AM

Adjuvant chemotherapy after concurrent chemoradiation therapy for locally advanced cervical cancer. *First Author: Lingna Kou, Department of Oncology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China*

Background: Standard treatment nowadays for locally advanced cervical cancer (LACC) is concurrent chemoradiation therapy (CCRT). However, due to distant metastasis, survival outcomes are still not optimistic. We tried to evaluate the clinical efficacy and safety of adjuvant chemotherapy for patients with LACC after treated with concurrent chemoradiation therapy (CCRT). **Methods:** Patients diagnosed between May, 2013 to May, 2018 with stage IIA-IIIB LACC were retrospectively analyzed. All the patients received platinum-based radical concurrent chemoradiotherapy and were divided into two groups: adjuvant chemotherapy after CCRT (CCRT+ACT group) and observation after CCRT (CCRT group). Overall survival (OS), progression free survival (PFS) and adverse effects were recorded and analyzed. Kaplan–Meier method and log-rank test were used to calculate and compare differences between survival outcomes. Toxicities were analyzed using chi-square test. **Results:** In total, 375 patients were included in this study, and 262 patients accepted ACT after CCRT while the remaining 113 patients chose to observe. With a median follow-up of 40 months (range 5-73 months), no significant differences were found in both overall survival (OS) and progression free survival (PFS) between two groups referring as 88.5% vs. 90.3% (P= 0.904) and 83.2% vs. 87.6% (P= 0.374). OS rates for patients in CCRT+ACT and CCRT groups at 1 year and 3 years were 97.3% vs. 94.7% (P= 0.195) and 90.2% vs. 88.4% (P= 0.694), respectively. Meanwhile, PFS rates at 1 year and 3 years were 92% vs. 94.7% (P= 0.371) and 87.5% vs. 85.5% (P= 0.761) for two arms separately. 3-4 grades acute adverse events happened more frequently in CCRT+ACT group than in CCRT group, with significant differences in neutropenia and anemia (P< 0.05). **Conclusions:** In this study, adjuvant chemotherapy after concomitant chemoradiotherapy did not show benefit of survival but do induce adverse effects. We do not suggest it unless further large scale randomized controlled trials are executed to verify it. Research Sponsor: None.

6032 Poster Session (Board #203), Fri, 8:00 AM-11:00 AM

Gls-010, a novel anti-PD-1 mAb in Chinese patients with recurrent or metastatic cervical cancer: Results from a multicenter, open-label and single-arm phase II trial. *First Author: Xiaohua Wu, Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Shanghai, China*

Background: GLS-010 is a novel fully human anti-PD-1 mAb. Previous Phase I study exhibited favorable result of tolerance, preliminary efficacy and 240mg fixed dose q2w was selected as Recommended Phase II Dose (RP2D). This Phase II clinical trial is aimed to further evaluate the safety and anti-tumor activity of GLS-010 in patients with recurrent or metastatic cervical cancer. **Methods:** PD-L1 positive (combined positive score (CPS) ≥1) patients with recurrent or metastatic cervical cancer who had received one or more lines of chemotherapy were enrolled and received GLS-010 240mg every 2 weeks. Primary endpoint was the objective response rate (ORR) per RECIST 1.1, secondary endpoints included duration of response (DoR) and safety. **Results:** From May 16th 2019 to December 24th 2019, 44 pts were enrolled and treated in the study. As of December 24th 2019,the median line of prior systemic chemotherapy was 2(range: 1~4) , and 59% (26/44) of pts had received ≥2 previous lines of chemotherapy. The median number of GLS-010 doses was 1.5(range: 1~4). 25 pts received response evaluation per investigator review. With a median follow-up of 2.9 months, 7 of 25 evaluable pts achieved a partial response (PR). The ORR was 28% (95% CI, 12.07-49.39), with 7 pts achieving a PR (3 of 7 confirmed), 3 pts achieving stable disease (SD) and 15 pts with progressive disease (PD), 1 of which was assessed as dissociated response with treatment ongoing. Median duration of response had not been reached yet. 33 of 44 patients (75%) experienced one or more treatment-related adverse events (TRAEs) per NCI CTCAE v4.03, most of which were grade 1 or 2. The most common TRAEs were Anaemia (15/44), and 73.3% of them were grade 1 or 2. The most common ≥grade 3 TRAE included Anaemia (4/44). As data cut off, only 1 pt discontinued treatment due to adverse event. **Conclusions:** GLS-010 showed impressive therapeutic activity and manageable safety profile in Chinese recurrent or metastatic cervical cancer patients. Current evidence support further development of GLS-010 in this and more indications. This trial is still ongoing, and we are looking forward to further results. Clinical trial information: NCT03972722. Research Sponsor: Guangzhou Gloria Biosciences Co., Ltd.

6033 Poster Session (Board #204), Fri, 8:00 AM-11:00 AM

Genome-wide association analysis in host genetic characteristics of progression to high-grade cervical intraepithelial neoplasia or higher for women with human papillomavirus infection and normal cytology. *First Author: Chyong-Huey Lai, Department of OB/GYN, Chang Gung Memorial Hospital, Taoyuan, Taiwan*

Background: Human papillomavirus (HPV) testing is widely used for cervical cancer screening. The hazard ratio of developing cervical intraepithelial neoplasia grade 2 or higher (CIN2+) in HPV-positive/ normal cytology women is 20–34 fold as compared to those with HPV-negative/normal cytology. HPV-positivity would cause substantial anxiety. Apart from viral factors such as high-risk (hr) types, it is important to identify host characteristics for predicting outcome. **Methods:** An initial genome-wide association study (GWAS) of single nucleotide polymorphisms (SNPs) by Affymetrix Axiom™ Genome-Wide Human Arrays was conducted on 505 cases with histological diagnosis of CIN2+ (group D1) versus 920 female controls. An additional set of 2315 female controls from the Taiwan Biobank genotype array were added in the discovery stage. The identified 29 CIN2+ -associated SNPs from GWAS ($p < 5 \times 10^{-6}$) were verified in an independent cohort (group D2 [n = 306] versus group N [n = 600]). Group N were HPV-negative/normal cytology women from a population-based cervical cytology and HPV co-test study. A cohort with HPV-positive/normal cytology (group P, n = 755) underwent follow-up and was served as the prediction set. The predictive validity was analyzed by logistic regression and receiver operating characteristic (ROC) curve analysis. **Results:** Thirty-three individuals of the group P progressed to CIN2+ (median follow-up: 23.7 months, range 4.0–122.1). A risk-predictive panel of 8 SNPs rs3097662, rs35979982, rs7763822, rs4282438, rs3128927, rs7759943, rs213194, rs17835649 which were significant in the replication ($p < 0.05$) was used to train models for disease risk prediction using the combination of GWAS and verification sets. Two prediction models were finalized and determined using 7 SNPs for hr- and low-risk (lr) HPV groups respectively (sensitivity 0.72 and 0.75, specificity 0.651 and 0.884, area under the ROC curve 0.703 and 0.701). Among group P with hr-HPV, those carried < 6 risk-alleles had significantly decreased hazard (log-rank $p < 0{\cdot}001$) of progression to CIN2+ than those with ≧6 risk-alleles, while among group P with lr-HPV, those with predictive probability of ≥ 0·095 had a cumulative risk of progression of 10% at 3 years. **Conclusions:** Two risk-predictive SNP panels including 7 SNPs with hr- or lr-HPV groups can assist risk stratification among HPV-positive/ normal cytology women. These panels could be further tested in other ethnic populations. Research Sponsor: Supported by grants from Chang Gung Medical Foundation (OMRPG3B0041, CMRPG371151-3, CMRPG380731, CMRPG391451, and CRRPG3D0021/2/3), and the Ministry of Health and Welfare-Taiwan (DOHW105-TDU-B-212-113003, MOHW106-TDU-B-212-113005, and MOHW107-TDU-B-212-11.

6034 Poster Session (Board #205), Fri, 8:00 AM-11:00 AM

Anlotinib in patients with recurrent advanced cervical cancer: A prospective single-arm, open-label, phase II trial. *First Author: Xiaohua Wu, Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Shanghai, China*

Background: Anlotinib is a novel multi-target tyrosine kinase inhibitor that has previously shown clinical antitumor activity in various cancers, including the phase I study on female genital tumors. This phase II study (ChiCTR1800020116) aims to further evaluate the safety and efficacy of anlotinib, in those patients with recurrent advanced cervical cancer. **Methods:** Eligible patients were advanced cervical cancer who had received at least two previous lines of chemotherapy. Patients were given anlotinib (12 mg/day) from day 1 to day 14 in a 21-day cycle until disease progression or had unacceptable toxic effects. The primary endpoint of this study was objective response rate (ORR) and the secondary endpoints were progression-free survival (PFS), overall survival (OS) and safety. **Results:** Between 2018 December and 2019 October, 41 patients (female) were enrolled. As of January 15, 2020, median follow-up duration, from randomization to data cutoff, was 2.6 months (range, 0.7-10.3). Therapeutic evaluation showed the ORR was 32.1% (95%CI, 13.7%-50.6%) and the median PFS was 3.9 months (95% CI, 1.3%-6.5%). The most frequently reported adverse events were lymphocyte count decreased, anemia, hand-foot syndrome, blood uric acid increased, blood creatinine increased, blood thyroid stimulating hormone increased. All frequently occurring AEs were grade 1 or 2. High grade AE was only observed in 1 patient with white blood cells urine positive of grade 3. Neither unexpected safety signals nor treatment related death occurred. **Conclusions:** Anlotinib showed a promising activity with an acceptable safety profile for patients with recurrent advanced cervical cancer. Clinical trial information: ChiCTR1800020116. Research Sponsor: Chia-Tai Tianqing Pharmaceutical Group Co Ltd.

6035 Poster Session (Board #206), Fri, 8:00 AM-11:00 AM

Photodynamic therapy for preinvasive cervical cancer. *First Author: Viktoria A. Ivanova, Rostov Research Institute of Oncology, Rostov-on-Don, Russian Federation*

Background: Photodynamic therapy (PDT) is an effective treatment for various cancers ensuring maximum preservation of the viability of healthy tissues surrounding the tumor. The purpose of the study was to reveal the effectiveness of PDT in treatment for preinvasive cervical cancer. **Methods:** The study included 45 patients aged 22-53 years with preinvasive cervical cancer. The patients were divided into two groups depending on the type of the transformation area and the tumor site: group 1–on the exocervix (type I-II), n=24; group 2–on the endocervix (type III), n=21. Infection with high-risk genotypes of HPV (16, 18, 31, 33, 35, 45, 56) was detected with PCR in 37 (82%) women. All patients received PDT with the semiconductor Latus laser up to 3 W, a single-use diffusing fiber for the exocervix irradiation and a single-use cylindrical diffusing fiber for tumors in the cervical canal. Photoditazine and photolon were used as photosensitizers. Effectiveness criteria included the normalization of the colposcopic picture, the absence of atypical cells, and the pathogen elimination confirmed by PCR. **Results:** A normal cytogram profile was observed after PDT in 84% of group 1 and in 88% of group 2. PCR 3 months after PDT showed a positive HPV reaction in 9.1%. Neither group of patients had negative changes in cytogram after 6 and 12 months. Repeated HPV DNA tests detected HPV DNAs in 2.8% in group 1 and 3.2% in group 2. The effectiveness of PDT did not depend on the photosensitizer. The maximum follow-up period has lasted for 4.5 years, with no recurrences registered. During this period, three young women successfully gave birth to healthy children. **Conclusions:** PDT is an alternative treatment for pre-tumor and initial tumor pathology of the cervix with preservation of the anatomical and functional integrity of the organ, which is important for the female reproductive function. The results support the use of PDT in treatment for preinvasive cervical cancer. Research Sponsor: None.

6036 Poster Session (Board #207), Fri, 8:00 AM-11:00 AM

Gut microbiome diversity as an independent predictor of survival in cervical cancer patients receiving chemoradiation. *First Author: Travis T. Sims, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Diversity of the gut microbiome is associated with response rates for patients receiving immunotherapy. Studies investigating the gut microbiome and outcomes in cancer patients often do not adjust for confounding patient and tumor characteristics. We sought to identify independent gut microbial risk factors in cervical cancer (CC) patients receiving chemoradiation (CRT) and to evaluate their impact on survival. **Methods:** We analyzed baseline 16S rDNA fecal microbiomes of CC patients receiving standard CRT. Patient and tumor characteristics were analyzed by univariate and multivariate Cox regression models for Recurrence-free survival (RFS) and Overall survival (OS) based on univariate p-value>0.2. Characteristics included age, body mass index (BMI), race, stage, grade, histology, nodal status, and max tumor size. Alpha (within sample) diversity was evaluated using Shannon diversity index (SDI). Kaplan-Meier curves were generated for patients with normal BMI and overweight/obese BMI based on Cox analysis. **Results:** 55 CC patients were included. Univariate analysis identified older age (Hazard Ratio (HR) of 0.93 (95% CI = 0.87-0.98, p = 0.0096)), SDI (HR of 0.51 (95% CI = 0.23-1.1, p = 0.087)) and BMI (HR of 0.92 (95% CI = 0.84-1, p = 0.096)) as risk factors for RFS. Multivariate survival analyses identified BMI and SDI as independent prognostic factors for RFS with a HR of 0.87 (95% CI = 0.77-0.98, p = 0.02) and 0.36 (95% CI = 0.15-0.84, p = 0.018) respectively. For OS, multivariate survival analyses again identified BMI and SDI as independent prognostic factors with a HR of 0.78 (95% CI = 0.623-0.97, p = 0.025) and 0.19 (95% CI = 0.043-0.83, p = 0.028) respectively. **Conclusions:** Gut diversity is a significant factor for predicting OS in CC patients undergoing CRT when BMI is accounted for, and may help explain the "obesity paradox" in cancer response. Studies exploring the relationship between gut diversity, CRT, and treatment efficacy are needed to further understand the role of the gut microbiome in treatment outcomes. Research Sponsor: U.S. National Institutes of Health, The University of Texas MD Anderson Cancer Center HPV-related Cancers Moonshot.

Univariate and multivariate analysis for RFS and OS.

Characteristics	Uni-variate HR (95% CI)	Model *P*value	Multivariate HR (95% CI)	Model *P*value
Age				
RFS	0.93* (0.87-0.98)	0.0096‡	—	—
OS	0.95 (0.87-1)	0.23	—	—
BMI				
RFS	0.92 (0.84-1)	0.096	0.87* (0.77-0.98)	0.02‡
OS	0.83 (0.69-1)	0.055	0.78* (0.623-0.97)	0.025‡
Shannon diversity index (SDI)				
RFS	0.51 (0.23-1.1)	0.087	0.36* (0.15-0.84)	0.018‡
OS	0.34 (0.1-1.1)	0.08	0.19* (0.043-0.83)	0.028‡

CI, Confidence interval; *HR*, hazard ratio; *Significant *HR*; ‡Significant *P* value

6037 Poster Session (Board #208), Fri, 8:00 AM-11:00 AM

Delayed adjuvant radiotherapy in early-stage cervical cancer with intermediate-risk features has a detrimental effect on survival that cannot be corrected by adjuvant chemotherapy. *First Author: Joyson Kodiyan, NewYork-Presbyterian Brooklyn Methodist Hospital, Brooklyn, NY*

Background: GOG-0263 is currently investigating the role of adjuvant chemotherapy (CT) concurrently with radiotherapy (RT) in patients with early stage cervical cancer that underwent radical hysterectomy and pelvic lymphadenectomy harboring intermediate risk features. We used a retrospective database to investigate whether adjuvant chemotherapy significantly influenced overall survival (OS), and whether its effectiveness is influenced by delays in radiotherapy. **Methods:** All data was obtained from the NCDB (National Cancer Database) and initially contained 115,747 cases of cervical cancer diagnosed between 2004 and 2015. Analyzed patients had early stage disease, received radical hysterectomy with pathologic stage I to IIA, and had intermediate risk features including size greater than 4 cm or lymphovascular invasion. All patients received adjuvant RT with or without CT. Cases with positive margin or nodes, with parametrial extension, or metastasis were excluded. Cases were weighted by inverse probability of treatment (CT) using clinical and socioeconomic variables, and analyzed for OS using multivariate models. Predictors of receiving CT were determined using multivariate logistic regression. **Results:** The final cohort was 557 patients with median follow-up of 43 months (range, 1.54-143.7). Median survival without CT (n = 244) versus with CT (n = 313) was 42.2 versus 43.9 months (HR 0.81, 95%CI 0.661-0.995, p = 0.045). Median time from diagnosis to RT was 91 days (range, 21-691), and predicted for inferior OS (p = 0.007). No significant interaction existed between RT delay and receipt of CT (p = 0.997). Cases with squamous histology were less likely to receive CT than adenocarcinoma histology (OR 0.345, 95% CI 0.159-0.725, p = 0.006). **Conclusions:** Poor survival outcomes are observed in patients with early stage cervical cancer harboring intermediate risk features when adjuvant radiotherapy is delayed. This outcome was not corrected by addition of chemotherapy. Research Sponsor: None.

6038 Poster Session (Board #209), Fri, 8:00 AM-11:00 AM

Prexasertib, a cell cycle checkpoint kinase 1 inhibitor, in *BRCA* mutant recurrent high-grade serous ovarian cancer (HGSOC): A proof-of-concept single arm phase II study. *First Author: Erika Joelle Lampert, Women's Malignancies Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD*

Background: Preclinical data suggest cell cycle checkpoint inhibition induces greater cell death in *BRCA* mutant HGSOC by causing replication stress and dysregulation of DNA damage responses. We hypothesized that prexasertib, a cell cycle checkpoint kinase 1 (CHK1) inhibitor, would be active in *BRCA* mutated HGSOC patients. **Methods:** We conducted a single center, two-stage phase II study of prexasertib (105mg/m^2 IV every 2 weeks) in HGSOC patients with known germline or somatic *BRCA* mutations. The primary endpoint was RECIST response rate (RR). Progression-free survival (PFS) and safety (CTCAE v4) were secondary endpoints. Baseline research biopsies and blood samples were collected for exploratory biomarker endpoints. **Results:** Between February 2015 and July 2019, 22 heavily pretreated (median 5 prior systemic therapies [1-12]) women with *BRCA* mutant HGSOC (median age 58.7 [44-74.8]) received at least one dose of prexasertib. 13 (59%) patients were secondary platinum-resistant (median 8 [3-12] prior therapies) and 9 (41%) maintained platinum-sensitivity (median 4 [1-5] prior therapies). All but one received prior PARP inhibitor (PARPi) either in combination (10 [48%]) or as monotherapy (11 [52%]), with a median 5 month [mo; 1-29] PARPi-free interval prior to study entry. There was one complete response (41+mo, platinum-sensitive, no prior PARPi) and one partial response (9+mo, platinum-sensitive, 13.5mo PARPi-free interval) yielding an 11% RR (2/18 evaluable). No response was seen in platinum-resistant patients with prior PARPi. Median duration on study treatment was 4mo [1-9] among 21 patients with prior PARPi and 4mo [1.5-9] among 17 evaluable patients with prior PARPi. Common (>10%) grade 3/4 adverse events were neutropenia (82%), leukopenia (64%), and thrombocytopenia (14%); only one patient had grade 3 febrile neutropenia. 16 of 18 (89%) patients with grade 3/4 neutropenia received prophylactic growth factors for subsequent treatments. **Conclusions:** Prexasertib is tolerable and has modest activity in heavily pretreated *BRCA* mutant HGSOC patients. Further evaluation of predictive biomarkers for exceptional responders is ongoing. Clinical trial information: NCT02203513. Research Sponsor: U.S. National Institutes of Health, Stand Up To Cancer – Ovarian Cancer Research Fund Alliance – National Ovarian Cancer Coalition Dream Team Translational Research Grant.

6039 Poster Session (Board #210), Fri, 8:00 AM-11:00 AM

Maintenance olaparib plus bevacizumab (bev) after platinum-based chemotherapy plus bev in patients (pts) with newly diagnosed advanced high-grade ovarian cancer (HGOC): Efficacy by BRCA1 or BRCA2 mutation in the phase III PAOLA-1 trial. *First Author: Domenica Lorusso, Fondazione IRCCS Istituto Nazionale Tumori and Multicenter Italian Trials in Ovarian Cancer and Gynecologic Malignancies (MITO), Milan, Italy*

Background: In PAOLA-1/ENGOT-ov25 (NCT02477644), adding the PARP inhibitor olaparib to maintenance bev after first-line platinum-based chemotherapy plus bev led to a statistically significant progression-free survival (PFS) benefit in pts with advanced HGOC (HR 0.59; 95% CI 0.49–0.72) (Ray-Coquard *et al.* 2019). Retrospective subgroup analysis in GOG-0218 (Norquist *et al.* 2018) suggested BRCA mutation (BRCAm) status did not significantly impact the PFS benefit provided by bev. We explored the efficacy of olaparib plus bev by *BRCA1* mutation (*BRCA1*m) or *BRCA2* mutation (*BRCA2*m) in PAOLA-1. **Methods:** PAOLA-1 is a randomized, double-blind, Phase III trial in pts with newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid OC, fallopian tube or primary peritoneal cancer receiving platinum-based chemotherapy plus bev then maintenance bev. Pts unrestricted by surgical outcome or BRCAm status and in response to first-line therapy were randomized to maintenance olaparib tablets (300 mg bid for up to 24 months) plus bev (15 mg/kg q3w for up to 15 months in total) or placebo plus bev, stratified by first-line treatment outcome and tumor BRCAm status. Investigator-assessed PFS (modified RECIST v1.1) by BRCAm was a predefined analysis. **Results:** Of 806 randomized pts, 160 (20%) had tumor *BRCA1*m, 76 (9%) had tumor *BRCA2*m and 1 (<1%) had both. Median PFS follow-up was 24.1 and 27.4 months in *BRCA1*m and *BRCA2*m pts, respectively. At primary data cutoff, PFS was prolonged with olaparib plus bev versus placebo plus bev in *BRCA1*m pts and *BRCA2*m pts (Table). The percentage of *BRCA1*m pts who received olaparib plus bev and were progression-free at 1 and 2 years was 95% and 73% (vs. 70% and 29% for placebo plus bev) and for *BRCA2*m pts was 89% and 84% (vs. 84% and 53%) (Kaplan-Meier estimates). **Conclusions:** In PAOLA-1, maintenance olaparib plus bev provided a significant PFS benefit versus placebo plus bev in all pts analysed, regardless of whether they had *BRCA1*m or *BRCA2*m. The median PFS in the control arm suggests a role for bev in this subgroup and the hazard ratio versus an active control arm shows the value of adding maintenance olaparib to bev. Clinical trial information: NCT02477644. Research Sponsor: Funded by AstraZeneca, Merck Sharp & Dohme Corp, and F. Hoffmann La Roche, ARCAGY Research.

	No. of pts with events/total no. of pts	Median PFS, months	HR (95% CI)
***BRCA1*m**	33/111	37.2*	0.29
Olaparib + bev	32/49	19.4	(0.176, 0.470)
Placebo + bev			
***BRCA2*m**	7/45	NR	0.23
Olaparib + bev	17/31	24.0	(0.090, 0.541)
Placebo + bev			

*Median unstable due to lack of events. CI, confidence interval; HR, hazard ratio; NR, not reached

6040 Poster Session (Board #211), Fri, 8:00 AM-11:00 AM

A randomized multicenter phase II trial to evaluate the safety and efficacy of vaccination with folate receptor alpha (FRα) peptides admixed with GM-CSF as an adjuvant versus GM-CSF alone in patients with platinum-sensitive ovarian cancer (EOC). *First Author: Roisin Eilish O'Cearbhaill, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY*

Background: FRα is overexpressed on > 90% of high-grade EOC. We conducted a randomized double-blind multicenter phase II clinical trial to evaluate the safety and efficacy of TPIV200 (a multi-epitope FRα peptide vaccine admixed with GM-CSF adjuvant) versus GM-CSF alone as a control in patients with stage III-IV high-grade platinum-sensitive epithelial ovarian, fallopian tube, or primary peritoneal carcinoma in first complete or partial remission, irrespective of baseline level of FRα expression. **Methods:** Patients with stage III-IV high-grade serous, high-grade endometrioid, carcinosarcoma or poorly differentiated EOC who had previously completed standard upfront therapy without evidence of disease progression and who were within a year of last platinum were randomized 1:1 to intradermal vaccination of TPIV200 versus intradermal GM-CSF alone. The vaccination period included 6 administrations of the study drug at 4-week intervals. Up to 6 booster vaccinations at 12-week intervals were permitted for patients who did not have disease progression. AEs were assessed using CTCAE. Tumor response was assessed via RECIST every 12 weeks. The primary endpoint, progression free survival (PFS), was calculated from date of first vaccination to the date of progression, death or study termination. **Results:** Of 120 patients randomized, 63 (53%) were treated on the TPIV200 arm. The median age at study entry was 63 years (range 37-88). AEs were generally mild. Injection site reaction was more frequent in the TPIV200 (63%) versus GM-CSF arm (39%). The other most common AEs, abdominal pain (25%) and fatigue (23%), were comparable in both arms. At study termination with a median follow-up of 15.2 months (range: 1.2-28.3 months), 68 of 119 intention-to-treat patients had progressed (55% in the TPIV200 arm and 59% in the GM-CSF arm). The median PFS was 11.1 months (95% CI: 8.3-16.6 months) and there was no statistically significant difference in median PFS between the arms (10.9 months with TPIV200 versus 11.1 months with GM-CSF, HR = 0.85 [upper 90% CI = 1.17]). **Conclusions:** Although TPIV200 had a manageable safety profile, the study was terminated for futility after the planned interim analysis. Future development of FRα-targeted therapy will likely focus on the careful selection of patients whose cancers show high FRα expression. Clinical trial information: NCT02978222. Research Sponsor: Marker Therapeutics, Inc.

6041 Poster Session (Board #212), Fri, 8:00 AM-11:00 AM

Low rates of *BRCA1* and *BRCA2* testing for patients with ovarian cancer in ASCO's CancerLinQ, a real-world database. *First Author: Summer Dewdney, Rush University Medical Center, Chicago, IL*

Background: Ovarian cancer is the deadliest gynecological cancer and has limited screening options for early stage diagnosis. Genetic mutations in genes such as *BRCA1* and *BRCA2* increase the risk of ovarian cancer, and if identified, patients can undergo risk-reducing surgery. It is recommended and well accepted to test any new ovarian cancer patient for genetic mutations, particulary *BRCA1* and *BRCA2*. If a *BRCA1/2* mutation is found in a patient (somatic or germ line), this information can be used to guide therapy. We sought to analyze the characteristics of genetic testing in a real-world database, ASCO's CancerLinQ. **Methods:** We performed a retrospective cohort study using the CancerLinQ Discovery database. Women with ovarian, fallopian tube, or primary peritoneal cancer were identified using ICD9 and ICD10 codes. We included patients diagnosed between 1/1/11 to 12/31/18 and age >18. We included all epithelial histologies including carcinosarcomas and excluded patients without a known histology. **Results:** Of the 2654 patients meeting inclusion criteria, 600 had been tested for a *BRCA1/2* mutation (22.6%). Of those tested, 63% were stage III/IV, 14% stage I/II, and 21.8% an unknown stage. The majority of the histologies were serous (76%), followed by undifferentiated (21.2%). The majority of patients tested were white (69.9%), with 18.8% unknown, and 9.9% black. The rate of a positive *BRCA1* or *BRCA2* mutation in this population was 17.2%. Of the patients with a *BRCA1/2* mutation, the majority had serous histology (87%), followed by 18.5% undifferentiated, and 3.9% transitional cell. The majority of the patients found to have a *BRCA1/2* mutation were age >50 (57.3%). **Conclusions:** Since 2008 evidence-based guidelines have recommended that all ovarian cancer patients be tested for *BRCA1* and *BRCA2* mutations, but in this real-world database only 22.6% have a recorded test. Of those tested, we found a *BRCA1* or *BRCA2* mutation rate of 17.2%. Our data is limited by what is recorded in the database and may not represent the true number of patients tested because of data missing from the EHR; however, these percentages appear similar to previous studies. Not only is testing important for cancer prevention for family members of patients, it now impacts the type of treatments for which these patients are eligible. Since genetic testing remains low at only 22.6% in this population, significant opportunities exist to impact cancer prevention and treatment. Research Sponsor: None.

6042 Poster Session (Board #213), Fri, 8:00 AM-11:00 AM

Low expression of gamma-glutamyl transpeptidase 1 is an independent poor prognostic factor in ovarian clear cell carcinoma, in relation to up-regulation of immune suppressive genes and EMT-related genes. *First Author: Hiroshi Asano, Department of Obstetrics and Gynecology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan*

Background: Ovarian clear cell carcinoma (OCCC) is a distinct entity from other epithelial ovarian cancers such as the most prevalent high-grade serous cancer (HGSC), and often exhibit less sensitivity to platinum-based chemotherapy. Several studies using cell lines have reported that glutathione (GSH) metabolism plays an important role in chemo-resistance of OCCC. Here, we aimed to correlate the prognosis of OCCC and the expression of gamma-glutamyltransferase 1 (GGT1), one of the key enzymes in GSH metabolism. **Methods:** We prepared a FFPE-tissue microarray, and analyzed 56 OCCC patients with the follow-up periods over 3 years. Expression level of GGT1 was evaluated by immunohistochemistry (IHC) using H-score (0-300), and was correlated with clinical outcomes. The prognostic significance was assessed by multivariate analysis using Cox regression model. To investigate the possible related pathways, we performed transcriptome analysis using Ion AmpliSeq Transcriptome Human Gene Expression Kit (Thermo Fisher Scientific) from the frozen tissue specimens collected from 33 ovarian cancer patients including 15 OCCC patients and 18 HGSC patients. **Results:** The OCCC patients were divided into two populations in the histogram of H-score in IHC staining, and the cut-off value was 90; 44 cases showed GGT1-high, and remaining 12 cases were GGT1-low. Follow-up periods, FIGO stage, and optimal surgery rate were not significantly different between two groups. However, platinum-resistant recurrent rate was significantly higher (42% vs. 14%, p=0.027), and overall survival (OS) was significantly shorter (5-year OS; 42% vs. 72%, p=0.0226) in GGT1-low OCCC. Multivariate analysis revealed that low expression of GGT1 was one of the independent poor prognostic factors as well as platinum-drug resistance. In enrichment analysis, the genes related to GSH metabolism, such as SLC3A1, GGT1, CSE, and GPX3 were up-regulated and positively correlated with HNF1B expression in OCCC. The expression level of GGT1 was inversely correlated with that of immune suppressive genes (TGF-b, IFNG, IL10, FOXP3, PD-L1, CTLA4) and epithelial-mesenchymal transition (EMT)-related genes (CDH2, VIM, TWIST1, ZEB1, ZEB2) in OCCC samples. **Conclusions:** Low expression of GGT1 is an independent poor prognostic factor probably in part due to suppression of tumor immunity and induction of EMT in OCCC. Research Sponsor: None.

6043 Poster Session (Board #214), Fri, 8:00 AM-11:00 AM

A phase I trial a FR alpha targeted thymidylate synthase inhibitor CT900 exploring four schedules of treatment in expansion cohorts of patients with high-grade serous ovarian cancer. *First Author: Susana N. Banerjee, The Royal Marsden and The Institute of Cancer Research, London, United Kingdom*

Background: CT900 (BTG945/ONX-0801) is a novel small molecule that binds to folate receptor alpha (FRα), is internalized and causes cytotoxicity by thymidylate synthase inhibition. **Methods:** The aims of the expansion cohorts were to determine toxicity, response rates and correlation of the response to FRα expression in patients with HGSOC (NCT02360345). Four expansion cohorts were studied which included: schedule A (6 mg/m^2/q every 2 weeks), schedule B (12 mg/m^2/q every 2 weeks), schedule C (12 mg/m^2/q every 2 weeks with 12 mg dexamethasone IV and 8 mg of dexamethasone for 2 days) and schedule D (12 mg/m^2/q every 3 weeks). Response rates were assessed by RECIST V1.1 and GCIG CA125 response criteria. Patients who were withdrawn for reasons other than toxicity within 8 weeks (cohorts A, B, C) and 12 weeks (cohort D) were not assessable for efficacy. FRα expression was quantified using immunohistochemistry. **Results:** A total of 67 patients were treated in the 4 cohorts (14, 25, 15 and 13 for cohorts A, B, C and D). The median age was 62 (IQR 57 - 68) and the median lines of previous treatment was 5 (range 1 to 13). A majority of patients were platinum resistant. The most common toxicities across all expansion cohorts were: fatigue (51%), nausea (36%), anemia (27%), fever (25%), AST elevation (21%), most of which were grade 1 - 2. Toxicity of special interest included radiological changes of pneumonitis and was 15% in all cohorts (7%, 16%, 27% and 8% in cohorts A, B, C and D, respectively). These changes were grade 1 - 2 in all but one case. RECIST response rates in evaluable patients across the different cohorts were: A 1/8 (13%), B 6/21 (29%), C 5/12 (42%) and D 2/12 (17%). FRα expression in archival tumor tissue was measured in 59/67 patients. Expression was found to be high/medium in 43/59 (73%), low in 7/59 (12%) and negative/very low in 9/59 (15%). In patients with high/medium FRα expression, the RECIST response rates in different cohorts were: A 0/9 (0%), B 6/16 (38%), C 4/12 (33%) and D 1/6 (17%). The CA125 response rate in all patients within cohort B was 13/25 (52%) and 10/16 (63%) in patients with high/medium FRα expression. **Conclusions:** CT900 has shown clinical activity in patients with heavily pre-treated platinum-resistant, high/medium FRα expressing HGSOC. Based on toxicity and efficacy, the schedule of 12 mg/m^2/q2 weekly (schedule B) is the recommended phase II dose for further evaluation in patients with relapsed high/medium FRα expressing HGSOC. Clinical trial information: NCT02360345. Research Sponsor: Carrick Therapeutics;BTG; Onyx.

6044 Poster Session (Board #215), Fri, 8:00 AM-11:00 AM

APOLLO: A phase I study of adaptive memory natural killer (NK) cells in recurrent ovarian cancer. *First Author: Melissa Ann Geller, University of Minnesota, Minneapolis, MN*

Background: Human cytomegalovirus (CMV) infection induces a subset of long-lived CD57$^+$NKG2C$^+$ adaptive NK cells that exhibit enhanced antibody-dependent cellular cytotoxicity and resistance to tumor-suppressive mechanisms. We developed a 7-day culture process using a GSK3 inhibitor and IL-15 to manufacture modulated adaptive NK cells (FATE-NK100) from CMV$^+$ haploidentical donors for adoptive transfer. The phase I Apollo trial tests the maximum tolerated dose/maximum feasible dose (MTD/MFD) of FATE-NK100 administered intraperitoneally (IP) to treat platinum-sensitive or -resistant recurrent ovarian, fallopian tube, and primary peritoneal cancer. **Methods:** FATE-NK100 via IP port was tested using 3 dose cohorts ([DC]; 1×10^7 cells/kg; $>1 \times 10^7$ cells/kg to $\leq 3 \times 10^7$ cells/kg; or $>3 \times 10^7$ to $\leq 10 \times 10^7$ cells/kg) after lympho-conditioning with fludarabine 25 mg/m^2 IV and cyclophosphamide 300 mg/m^2 IV on days -6 and -5. After FATE-NK100 infusion on day 0, rhIL-2 at 6 million IU was given IP 3 times a week for 6 doses for in vivo NK activation. IP fluid and peripheral blood were collected regularly until response assessment (day 28). Patients with stable disease or better were eligible for retreatment. Pre- and post-treatment tumor biopsies were collected. **Results:** Nine patients were treated with no dose-limiting toxicities (DLTs) to date. Retreatment based on clinical benefit was performed on 3 patients (33%), 2 following stable disease (DC 2) and 1 with partial remission (48% tumor reduction, DC 3). IP samples were collected for PK and functional analysis. FATE-NK100 product was detected by flow cytometry in 5 of 6 patients with evaluable samples (range 4.8%–91.2% donor NK cells at day +5-7). Retreatment samples were available in 1 patient, where FATE-NK100 persisted to day +21, demonstrating that repeated IP dosing did not accelerate clearance of the donor NK cells. In that same patient, measurement of NK cell CD107a degranulation or IFNg production in response to K562 targets demonstrated sustained enhanced in vivo function of FATE-NK100 compared to endogenous patient NK cells (e.g. at Day +12 CD107a$^+$ NK were 39.0% vs. 22.5% cycle 1, and 40.3% vs. 18.2% retreatment cycle 2, and IFNg$^+$ NK were 12.3% vs. 5.9% cycle 1, and 2.4% vs. 0.2% retreatment cycle 2). **Conclusions:** IP delivery of FATE-NK100 is safe, with clinical benefit in 3/9 patients treated. The allogeneic product cells persist and have enhanced function compared to patient NK cells for up to 21 days, even after retreatment. This phase I study in recurrent/refractory ovarian cancer shows promise for IP NK cell delivery. Clinical trial information: NCT00652899. Research Sponsor: Fate Therapeutics.

6045 Poster Session (Board #216), Fri, 8:00 AM-11:00 AM

A clinical study of tremelimumab alone or in combination with olaparib in patients with advanced epithelial ovarian cancer. *First Author: Stephanie Gaillard, Johns Hopkins School of Medicine, Baltimore, MD*

Background: Single agent immunotherapy (IO) has shown only modest clinical activity for the treatment of ovarian cancer. The combination of anti-programmed death-1 and PARP inhibitors showed promising activity in early trials. Here, we report the results of an open-label, parallel arm, dose escalation study of tremelimumab (T) alone or in combination with olaparib (O) in patients (pts) with advanced epithelial ovarian cancer (EOC). **Methods:** Pts with recurrent/persistent EOC who had progression $<$ 12 months from last platinum exposure were enrolled. Prior therapy with IO (except anti-CTLA-4) or PARP inhibitor was allowed. Pts were randomized to either T 10mg/kg every 4 weeks (wks) x 7 then every 12 wks (Arm A) or T with O twice daily at three planned dose levels (Arm B). The primary objectives were safety, pharmacodynamic (PD) change in CD4$^+$ICOS^{hi} peripheral T cells by flow cytometry, and identification of the optimal dose combination of T with O. Secondary objectives included 6-month progression-free survival (PFS6) and objective response rate (ORR). **Results:** A total of 24 pts were treated, 12 on Arm A, and 12 on two Arm B dose levels. Pts had a median age of 60 years (range 44-81). Histologic subtypes included high-grade serous EOC (20 pts, 83%), clear cell (3 pts, 13%), and moderately-differentiated adenocarcinoma (1 pt, 4%). BRCA1 mutation (mt) was present in 2 cases, BRCA2 mt in 1. Median number of prior regimens was 3.5 (range 1-9). Most adverse events (AEs) were attributable to T, the most common grade 3 toxicities were rash (13%), immune-mediated hepatitis (8%), and colitis (8%). No grade $\geq$4 toxicities were identified. Immune-mediated AEs also included acute kidney injury, hypophysitis, and hypothyroidism. No dose limiting toxicities were identified on Arm B. Two pts in Arm B had $>$PFS6. Of 20 pts evaluable for response, there was 1 partial response (Arm B), and 9 pts had stable disease (6 on Arm A, 3 on Arm B). Mean percentage of CD4+ICOS^{hi} T cells was significantly increased on Days 15 and 22 compared to Day 1 at both T dose levels (Table).T at 3 mg/kg with O at 150mg is the optimal dose of those tested. **Conclusions:** T and T with O was tolerable, with modest clinical activity in this pt population. AEs were as expected, and peripheral CD4$^+$ICOS^{hi} T cells increased on therapy. Clinical trial information: 02485990. Research Sponsor: AstraZeneca.

	Percent CD4$^+$ICOS^{hi}		
	Day 1	Day 15	Day 22
All Pts	17.9 ± 8.8	40.7 ± 12.1***	39.2 ± 11.8***
T 3mg/kg	18.5 ± 5.6	28.3 ± 6.9***	32.4 ± 12.0***
T 10mg/kg	17.5 ± 8.2	41.2 ± 10.8***	40.0 ± 10.8***

*** $p < 0.0001$ when compared to Day 1

6046 Poster Session (Board #217), Fri, 8:00 AM-11:00 AM

Long-term survival outcomes of intravenous versus intraperitoneal chemotherapy in the treatment of advanced ovarian cancer. *First Author: Rachel Soyoun Kim, University of Toronto, Toronto, ON, Canada*

Background: The role of intraperitoneal (IP) chemotherapy in the management of advanced ovarian cancer has been questioned given emerging evidence showing lack of survival benefits. The objective of this study was to compare the long-term survival associated with IP chemotherapy at a tertiary cancer center. **Methods:** We reviewed the long-term survival records of 271 women with stage IIIC or IV high-grade serous ovarian cancer treated with primary cytoreductive surgery (PCS) followed by IP or intravenous (IV) chemotherapy between 2001-2015 with a minimum follow-up of 4 years. 5-year progression free (PFS) and overall survival (OS) rates were compared using Kaplan-Meier survival analysis and covariates were evaluated using Cox regression analysis. **Results:** Women who received IP chemotherapy after PCS (n = 91) were more likely to have undergone aggressive surgery ($p < 0.001$), longer surgery ($p < 0.001$), and had no residual disease ($p < 0.001$) compared to the IV arm (n = 180). Median follow-up was 51.6 months. Five-year PFS was 19% vs. 18% (p = 0.63) and OS was 73% vs. 44% (p = 0.00016) in the IP vs. IV arms, respectively. After controlling for covariates in a multivariable model, the use of IP was no longer a significant predictor of OS in the entire cohort (p = 0.12). In patients with 0mm residual disease, PFS was 28% vs. 26% (p = 0.67) and OS was 81% vs. 60% (p = 0.059) in IP (n = 61) vs. IV (n = 69), respectively. In patients with residual of 1-9mm, PFS was 30% vs. 48% (p = 0.076) and OS was 60% vs. 43% (p = 0.74) in IP (n = 29) vs. IV (n = 31), respectively. **Conclusions:** IP chemotherapy showed a trend towards improved survival over conventional IV chemotherapy, especially in patients with no residual disease. Given the retrospective nature and small numbers in this study, prospective non-randomized cohort studies are warranted to evaluate the role of IP chemotherapy in advanced ovarian cancer. Research Sponsor: None.

6047 Poster Session (Board #218), Fri, 8:00 AM-11:00 AM

Phase I study to assess the safety, tolerability, pharmacokinetics/ pharmacodynamics and preliminary efficacy of SC10914 in patients with advanced solid tumors. *First Author: Jifang Gong, Gastrointestinal Medical Oncology, Beijing Cancer Hospital, Beijing, China*

Background: SC10914 is a highly selective inhibitor of PARP enzymes, including PARP1 and PARP2. SC10914 has a similar structure with olaparib. We conducted a phase I study to assess the safety, tolerability, PK/PD and preliminary efficacy of SC10914 in patients with advanced solid tumors. **Methods:** This is a phase I dose-escalation study with 3+3 design, we enrolled patients at 4 sites in China. Eligible patients were diagnosed with advanced solid malignancies who are refractory to standard therapies or for which no standard therapy exists; had measurable disease; had adequate organ function. Patients received SC10914 daily at ten escalating doses from 30 mg QD to 500 mg TID in a 28-day cycle. We obtained blood for PK and CA125 assessments. Toxic effects were assessed by CTCAE 4.03 criteria and tumour responses ascribed by RECIST 1.1 and CA125 was assessed by GCIG criteria. **Results:** As of January 2020, 52 patients were enrolled, of which 14 were males and 38 were females. Ten doses were escalated to 500mg TID, and no DLT was observed, and MTD was not obtained. The incidence of grade 3/4 AEs and SAEs that were related to SC10914 were 34.6% (18/52) and 13.5% (7/52). Grade 3/4 adverse reaction happened in at least two patients were anaemia/reduced hemoglobin (10/52, 19.2%), decreased WBC count (5/52, 9.6%), neutropenia (3/52, 5.8%), thrombocytopenia (2/52, 3.8%), and decreased lymphocyte count (2/52, 3.8%). A total of 17 gBRCAm evaluable ovarian cancer patients were enrolled, 6 of them had PR, the ORR was 35.3% (6/17). 10 gBRCAm ovarian cancer patients were enrolled in TID groups (including 2 patients who received BID doses at the beginning and changed to 300 mg TID dose after several cycles of treatment), 5 of them had PR, the ORR was 50% (5/10). The ORR of 400 mg TID group was 66.7%(4/6). PK data showed that the exposure of SC10914 was increased with dose increasing at the dose of 30 mg to 250 mg. The half-life of SC10914 was about 2-5 hours. **Conclusions:** SC10914 was safe in patients with advanced solid tumors. The main toxicity was blood-related adverse reactions. SC10914 was effective in gBRCAm ovarian cancer patients. 400 mg TID might be RP2D. Clinical trial information: NCT02940132. Research Sponsor: Jiangxi Qingfeng Pharmaceutical Co., Ltd, Other Government Agency.

6048 Poster Session (Board #219), Fri, 8:00 AM-11:00 AM

Quality of life, vascular endothelial growth factor inhibition, and survival outcomes with combination oral metronomic therapy in platinum refractory epithelial ovarian carcinoma: Results from a randomized study. *First Author: Aparna Sharma, Dr. B.R. A. IRCH, All India Institute of Medical Sciences, Delhi, India*

Background: Patients with recurrent and refractory epithelial ovarian cancer (EOC) have dismal outcomes. We evaluated a combination of oral metronomic therapy in platinum refractory EOC vis-à-vis angiogenic marker expression and its impact on patient reported outcomes. **Methods:** Between October 2017 and September 2019, 75 patients were randomized to receive etoposide (VP-16) (50 mg daily for 14 days) cyclophosphamide (50 mg daily for 28 days) (Arm A, n = 38) or etoposide (VP-16) (50 mg daily for 14 days) cyclophosphamide (50 mg daily for 28 days) and pazopanib (400 mg daily 28 days) every 28 days (Arm B, n = 37). Eligibility criteria included histopathological diagnosis of EOC, platinum refractory disease and ECOG performance status 0-2. Primary endpoint was serological progression free survival (PFS) as defined by Rustin criteria. Quality of Life (QoL) (evaluated using the EORTC QLQC30 and OV 28 questionnaires) and serum vascular endothelial growth factor (VEGF) were ascertained at baseline and after 3rd and 6th cycle. Intention to treat analysis was done. **Results:** Baseline characteristics were well matched in 2 arms. At a median follow up 14.4 months (95% CI 13.2-15.7), the median serological PFS is better for patients in Arm B 5.1 months (95%CI 3.13-10.33) compared to 3.4 months (95%CI 3-6.53) in arm A (P= 0.045). Median overall survival (OS) is not reached in arm B versus 11.2 months (95%CI 5.66-NR) in arm A (P= 0.032). Disease progression was seen in 42.1% (n = 16) in Arm A versus 40.5 %(n = 15) in arm B (P= 0.40). Sixteen patients are maintaining response. Mucositis (29.7% n = 11) and fatigue (13.5%, n = 5) were more in the pazopanib-containing arm (P= 0.36). Serum VEGF demonstrated significant decline with subsequent cycles of therapy {median values (range): Arm A, baseline; 466.0 pg/mL(123.9-1930) vs. 6 cycles; 92.05pg/ mL(42.34-279.5) P< 0.0001; Arm B, baseline; 382.0 pg/mL(49.44-2054.0) vs 6 cycles; 119.7 pg/mL(18.20-367.5) P= 0.013} without any difference between the two arms (P= 0.18). QoL symptom scales in both QLQC 30 and OV 28 questionnaires indicated small but significant improvement in pazopanib arm (P= 0.02) without differences in global (p = 0.96) and physical functioning scales. (P= 0.68). **Conclusions:** Addition of pazopanib to etoposide and cyclophosphamide resulted in improvement in serological PFS and OS with a well-tolerated toxicity profile and modest improvement in QoL.Serum VEGF expression requires validation in a larger cohort. Clinical trial information: CTRI/ 2017/10/010219. Research Sponsor: Department of Health resources (DHR) Grant in Aid scheme, Government of India (Project number R.11012/04/2018).

6049 Poster Session (Board #220), Fri, 8:00 AM-11:00 AM

Phase I/II trial assessing hydroxychloroquine and itraconazole in women with advanced platinum-resistant epithelial ovarian cancer (EOC) (HYDRA-01). *First Author: Ainhoa Madariaga, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada*

Background: Autophagy is a mechanism of resistance to platinum chemotherapy. Itraconazole (Itr), an antifungal agent, can alter cholesterol-trafficking, leading to accumulation of cholesterol in endosomes/lysosomes and resulting in cancer cell death. Itr is also involved in regulation of angiogenesis, mTOR and Hedgehog pathways. In preclinical studies the Itr effect can be enhanced by combining it with the autophagy inhibitor hydroxychloroquine (H). Drug repurposing studies with Itr have shown a signal of activity in prostate, lung and basal cell carcinoma. **Methods:** A rolling-6 phase I design was used to enroll patients (pts) with platinum-resistant/refractory EOC. Pts received Itr 300mg twice daily (BID) with H as per dose escalation schedule (range 200mg BID- 600mg BID), continuously in a 28-day cycle. Primary objective was establishment of MTD; secondary objective was objective response rate, progression free survival (PFS). Pre- and on-treatment biopsies were mandatory to evaluate exploratory objectives assessing effect on apoptosis/proliferation, angiogenesis, cholesterol metabolism and mechanism of cytotoxicity. RNAseq and IHC was performed in the sequential biopsies. **Results:** 11 pts were enrolled, 9 evaluable for efficacy. Histology was high 91% and low-grade serous 9%. Median lines of prior therapy was 7. RP2D was Itr 300mg BID and H 600mg BID. 1 DLT was seen in dose-level 2 was grade 3 hypertension. Other grade ≥3 related toxicity were grade 3 hypokalemia and grade 4 QTc prolongation (1 pt, dose-level 3). No objective responses were observed and 1 pt had stable disease. Median PFS was 1.6 months (1-1.7). Pre- and on-treatment biopsy was available for 10 pts. Increase in autophagy related protein, LC3, P62 and lysosomal marker, LAMP1, expression by IHC was identified in 3 pts. RNAseq revealed no differences between pre and on treatment samples in cholesterol homeostasis, angiogenesis, lysosomal-autophagy, PI3K-mTOR pathways. **Conclusions:** The combination of Itr and H was feasible but did not show antitumour activity in this heavily pre-treated platinum resistant EOC population. Increase of IHC expression in autophagy related proteins was detected in 30% of pts but did not correlate with patient benefit. Clinical trial information: NCT03081702. Research Sponsor: OICR Ovarian TRI grant.

Related AEs seen in >10% of pts.

AE term	Grade 1-2 %	Grade 3-4 %
Nausea	36	0
Diarrhea	27	0
Dry skin	27	0
Fatigue	27	0
Vomiting	27	0
ALT increase	18	0
Anemia	18	0
Anorexia	18	0
AST increase	18	0
Constipation	18	0
QT corrected interval prolonged	9	9
Neutropenia	18	0
Pruritus	18	0
White blood cell decrease	18	0

6050 Poster Session (Board #221), Fri, 8:00 AM-11:00 AM

Evaluation of an individualized starting-dose of niraparib in the PRIMA/ ENGOT-OV26/GOG-3012 study. *First Author: Mansoor Raza Mirza, Nordic Society of Gynecologic Oncology (NSGO) and Rigshospitalet–Copenhagen University Hospital, Copenhagen, Denmark*

Background: Niraparib is approved at a fixed starting dose (FSD) of 300 mg QD for maintenance treatment of patients (pts) with recurrent ovarian cancer (OC) achieving a complete or partial response to platinum-based chemotherapy based in the ENGOT-OV16/NOVA study. A post-hoc analysis of NOVA showed baseline bodyweight (BW) and platelet count (PC) were predictive for hematologic toxicities and dose reductions. Following this analysis, the PRIMA/ENGOT-OV26/GOG-3012 study was amended to prospectively evaluate the safety and efficacy of an individualized starting dose (ISD) regimen. **Methods:** This double-blind, placebo-controlled, phase III study randomized 733 pts with newly diagnosed advanced OC with a complete or partial response to first-line (1L) platinum-based chemotherapy. The protocol was amended to change the dose from 300 mg FSD for all patients to an ISD regimen: 200 mg QD in pts with BW <77 kg and/or PC <150,000/μL or 300 mg QD in pts with BW ≥77 kg and PC ≥150,000/μL. Exposure, efficacy, and safety data were compared between patients treated with FSD vs ISD. **Results:** Efficacy in the ISD subgroup was comparable to the FSD subgroup relative to placebo (Table). An interaction test showed no treatment difference between ISD and FSD at the pre-specified 0.10 significance level (p=0.30). Medians for dose intensity and relative dose intensity in pts who received niraparib were similar. The overall safety profile among pts in the niraparib arm (n=484), including grade ≥3 hematologic toxicities, improved with the ISD. **Conclusions:** The ISD in the 1L maintenance setting provides comparable efficacy to the FSD while reducing the risk of hematologic toxicities. No new safety signals were identified. Clinical trial information: NCT02655016. Research Sponsor: GlaxoSmithKline.

Parameter	Fixed Starting Dose (300 mg)		Individualized Starting Dose (200 or 300 mg)	
PFS	**N=475**		**N=258**	
Hazard ratio	0.59		0.69	
95% CI	0.46–0.76		0.48–0.98	
Dose intensity[a]	**n=315**		**n=169**	
Median, mg/day	181.8		178.6	
Median, relative, %	60.6		66.4	
Grade ≥3 hematologic toxicities,[b] n (%)	Niraparib n=315	Placebo n=158	Niraparib n=169	Placebo n=86
Thrombocytopenia event	152 (48)	0	36 (21)	1 (1)
Anemia event	112 (36)	3 (2)	38 (22)	1 (1)
Neutropenia event	75 (24)	2 (1)	25 (15)	1 (1)

[a]Dose intensity is only in pts receiving niraparib.
[b]Combined clinical and laboratory events.

6051 Poster Session (Board #222), Fri, 8:00 AM-11:00 AM

Niraparib exposure-response relationship in patients (pts) with newly diagnosed advanced ovarian cancer (AOC). *First Author: Bradley J. Monk, Arizona Oncology (US Oncology Network), University of Arizona College of Medicine, Phoenix, AZ*

Background: Niraparib improves progression-free survival (PFS) in pts with newly diagnosed AOC after complete or partial response to first-line, platinum-based chemotherapy. In the PRIMA/ENGOT-OV26/GOG-3012 (PRIMA) trial, pts were treated with a fixed starting dose (FSD) of 300 mg QD until a protocol amendment introduced the individualized starting dose (ISD) regimen: 200 mg QD for pts with baseline bodyweight (BW) $<$ 77 kg and/or platelet count (PC) $<$ 150,000/μL, or 300 mg QD for pts with baseline BW $\geq$77 kg and PC $\geq$150,000/μL. Here, we developed a population pharmacokinetic (PopPK) model for niraparib and evaluated exposure-response relationships for pts receiving niraparib using safety and efficacy data from PRIMA. **Methods:** The PopPK model for niraparib was developed based on 7418 plasma samples from 1442 pts from 4 studies: PN001, NOVA, QUADRA, and PRIMA. PRIMA PK samples were collected on cycle 1, day 1 (C1D1), C2D1 pre-dose and 2 h post-dose, C4D1, and C8D1 pre-dose (or EOT if patient discontinued before C8D1). The relationship between PopPK model-based prospective exposure (average concentration [C_{ave}] until progression/death) and efficacy (PFS) were evaluated in pts receiving niraparib in both the homologous-recombination deficient (HRd) and overall population. The relationship between model-predicted exposure metrics and incidence of clinically relevant adverse events (AEs) was analyzed using univariate logistic regression in pts receiving niraparib. **Results:** Of 484 pts receiving niraparib in PRIMA, 480 had PK data and were included in the efficacy and safety analysis. The safety exposure-response showed significant associations ($p \leq 0.0128$) between increasing niraparib exposure and increasing probability of experiencing any-grade and grade $\geq$3 AEs, except grade $\geq$3 hypertension. The incidence of AEs, including thrombocytopenia, was lower in pts who received a 200-mg ISD. Efficacy was not compromised in these pts. **Conclusions:** Niraparib exposure was associated with increased risk of select AEs. However, the ISD regimen decreased AE risk without compromising efficacy. Clinical trial information: NCT02655016. Research Sponsor: GlaxoSmithKline.

6052 Poster Session (Board #223), Fri, 8:00 AM-11:00 AM

Population-adjusted indirect treatment comparison (PAITC) of maintenance PARP inhibitor (PARPi) with or without bevacizumab versus bevacizumab in women with newly diagnosed ovarian cancer (OC). *First Author: Robert Hettle, AstraZeneca, Cambridge, United Kingdom*

Background: In patients (pts) with newly diagnosed OC, bevacizumab (B), PARPi, and PARPi + B have shown benefit as maintenance treatment options after platinum chemotherapy response. Phase III trials have demonstrated longer median progression-free survival (PFS) with PARPi + B (PAOLA-1, olaparib [O]; NCT02477644) vs placebo (P) + B and with PARPi alone (PRIMA, niraparib [N]; NCT02655016) vs P. As there are no randomized head-to-head trials comparing PARPi + B vs PARPi, or PARPi vs B, we performed indirect treatment comparison across these regimens. **Methods:** Unanchored PAITC was performed with individual pt data (IPD) from a PAOLA-1 subset comprising pts with stage IV disease, stage III with residual disease after primary surgery, inoperable stage III disease, or any patient who received neoadjuvant chemotherapy. Propensity weights were used to match the baseline (BL) characteristics of the PRIMA population. PRIMA dataset was reconstructed using published PFS curves. Both datasets were pooled; treatment efficacy was assessed by weighted Cox regression and Kaplan–Meier methods. PAITC was performed in all pts (biomarker unselected) and the homologous recombination repair deficiency positive (HRD+; cut-off 42) subgroup. **Results:** 595/806 (266/387 HRD+) PAOLA-1 pts were included. After matching, the effective sample size (ESS) for PAOLA-1 was 532 (242 HRD+; weights 0.241–2.37). Weighted BL data were balanced across cohorts. **Conclusions:** In biomarker-unselected and HRD+ pts, PAITC suggests that adding O to B significantly improved PFS vs. N or B alone. In biomarker-unselected pts, PAITC results show no significant difference in PFS between N and B. In HRD+, improved efficacy with N appears to translate into improved PFS vs. B alone, although follow-up was $<$2 years (14 vs 22 months, respectively). Results are hypothesis generating and could guide randomized trial design. Clinical trial information: NCT02477644 and NCT02655016. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc, Kenilworth, NJ, USA.

PAITC results.

	Treatment	PFS 12 months (%)	PFS 24 months (%)	PFS HR vs P (95% CI)	PFS HR vs B (95% CI)	PFS HR vs N (95% CI)
All pts	O + B, ESS=358*	78	40	0.33 (0.27–0.41)	0.60 (0.49–0.75)	0.57 (0.47–0.69)
	N, n=487†	54	32	0.59 (0.48–0.72)	1.07 (0.86–1.32)	–
	B, ESS=174*	63	23	0.55 (0.44–0.69)	–	–
	P, n=246†	35	23	–	–	–
HRD+	O + B, ESS=163*	88	58	0.23 (0.16–0.33)	0.40 (0.28–0.57)	0.57 (0.41–0.80)
	N, n=247†	71	47	0.41 (0.30–0.56)	0.70 (0.50–0.98)	–
	B, ESS=79*	73	26	0.58 (0.41–0.82)	–	–
	P, n=126†	42	26	–	–	–

*Results from IPD after matching to PRIMA BL data; †Results from estimated IPD. CI, confidence interval; HR, hazard ratio

6053 Poster Session (Board #224), Fri, 8:00 AM-11:00 AM

Hypersensitivity to platinum salts according to BRCA status in ovarian cancer: Retrospective analysis of clinical outcomes. *First Author: Gaia Giannone, Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Italy*

Background: Hypersensitivity reactions (HSRs) to platinum salts are an important issue in the treatment of ovarian cancer (OC) patients (pts). Few data suggest that, along with number of previous cycles, germline BRCA mutations could be a risk factor. We aimed at evaluating the incidence and severity of HSRs to platinum salts in a large group of OC pts with known BRCA status and correlated them with drug exposure time. **Methods:** Between March 2003 and September 2019, 432 pts with a diagnosis of OC and a known BRCA status, were recorded in our 5 Institutions and retrospectively analyzed. The following data were collected: histology, BRCA status, type of surgery and first line therapy, number of total lines and cycles received, line and cycle of HSR onset, symptoms, history of other allergies and if desensitization was attempted. We graded the severity of HSRs according to CTCAE v5.0. We calculated the total duration of exposure to platinum salts, summing up the duration of all platinum lines received by the pts. **Results:** Four hundred nine of 432 (94.7%) pts were treated with at least one platinum-based line of therapy and were eligible for the analysis. Among them, 314 pts were BRCA wild type (BRCAwt) (76.8%) and 95 were BRCA mutated (BRCAmut) (23.2%). There was no statistical difference in number of prior lines of therapy [median 1 (2-6) for BRCA wt and 2 (1-6) for BRCAmut pts (p = 0.194)] and duration of exposure to platinum [median 126 (42 – 893) and 197 (42 – 896) days for BRCAwt and BRCAmut pts, respectively (p = 0.145)]. Incidence of any grade HSRs was 29 / 314 (9.2%) among BRCAwt pts vs. 17/ 95 (17.9%) among BRCAmut pts (Odds ratio [OR] 0.47, 95% CI 0.24 – 0.89, p= 0.019). All recorded HSRs to platinum salts were related to carboplatin. We observed a numerically higher incidence of Grade 3-4 HSRs in BRCAmut pts (5.1% in BRCAwt vs. 10.5% in BRCAmut cohort, OR 0.46, 95% CI 0.20 – 1.04, p = 0.057). The risk to develop HSRs increases with duration of exposure to platinum, particularly in BRCAmut pts. The cumulative incidence of any grade HSRs was 20.6% vs. 23.3% after 12 months and 38.4% vs. 59.7% after 18 months in BRCAwt and BRCAmut pts, respectively (Hazard Ratio [HR] 1.72, 95% CI 0.94 – 3.12, p = 0.073). The cumulative incidence of severe HSRs was 10.9% vs. 15.7% after 12 months and 26.5% vs. 41.0% after 18 months in BRCAwt and BRCAmut pts, respectively (HR 1.88, 95% CI 0.85 – 4.16, p = 0.11). **Conclusions:** In BRCAmut OC pts, there is a significantly higher incidence of HSRs to carboplatin, that seems not justified by longer drug exposure only. Research Sponsor: None.

6054 Poster Session (Board #225), Fri, 8:00 AM-11:00 AM

Pharmacokinetics and safety following a single oral dose of niraparib in patients with moderate hepatic impairment. *First Author: Mehmet Akce, Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: Niraparib is approved for the maintenance treatment of adult patients (pts) with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy, or with similar cancers but advanced, associated with homologous recombination deficiency (HRD) and have been treated with ^{3}3 prior chemotherapy regimens. Niraparib is extensively metabolized in the liver and eliminated via both hepatobiliary and renal routes. Objectives of this study included characterization of niraparib pharmacokinetics (PK) and safety in pts with normal hepatic function vs. pts with moderate hepatic impairment. **Methods:** This phase I, open-label, parallel-group, single-dose study enrolled pts with advanced solid tumors into 2 groups: normal hepatic function and moderately impaired hepatic function, defined as bilirubin $>$1.5 to 3 times the upper limit of normal and any aspartate aminotransferase elevation. Pts received a single 300-mg dose and underwent PK sampling for 7 days. Exposure parameters included maximum concentration (C_{max}), area under the concentration-time curve calculated to last measured concentration (AUC_{last}), and extrapolated to infinity (AUC_{inf}). PK parameters were determined using a non-compartmental analysis in WinNonlin. **Results:** Seventeen pts were enrolled; 9 with normal hepatic function and 8 with hepatic impairment. Niraparib C_{max} was 7% lower in pts with moderate hepatic impairment compared with pts with normal hepatic function (Table). Overall exposure was increased in pts with moderate hepatic impairment, with niraparib AUC_{last} and AUC_{inf} increased 45% and 60%, respectively. Safety data during the PK phase of the study is consistent with the known profile for niraparib. **Conclusions:** Pts with moderate hepatic impairment experienced increased niraparib exposure which did not noticeably alter the toxicity profile in this population. Clinical trial information: NCT03359850. Research Sponsor: GlaxoSmithKline.

	NHF GLSM	MHI GLSM	NHF/MHI Ratio, %	90% CI
C_{max} (ng/mL)	594.0	552.7	93.0	63.9–135.6
AUC_{last} (ng·h/mL)	18478.9	26694.3	144.5	101.5–205.6
AUC_{inf} (ng·h/mL)	19707.5	31447.9	159.6	111.4–228.6

GLSM, geometric least squares mean; MHI, moderate hepatic impairment; NHF, normal hepatic function.

6055 Poster Session (Board #226), Fri, 8:00 AM-11:00 AM

Laboratory cross-comparison of tumor BRCA1/2 analysis in a multicenter epithelial ovarian cancer series: The BORNEO GEICO60-0 study. *First Author: Ignacio Romero, Instituto Valenciano de Oncología, Valencia, Spain*

Background: Epithelial ovarian cancer (EOC) identification of *BRCA1* and *BRCA2* mutations is usually carried out in germline, representing around 17% in high grade serous ovarian cancer (HGSOC) and further 5-7% are only identified in the tumor (somatic). The aim of this study was to identify in EOC tumor BRCA mutation frequency and inter-laboratory reproducibility using different Next-generation Sequencing (NGS) approaches. **Methods:** In an ambispective study design, a population of unselected consecutive non mucinous EOC was clinically annotated and Formalin-Fixed Paraffin-Embedded (FFPE) tumor *BRCA1/2* mutation analysis was undertaken in two laboratories (Lab-1 and Lab-2) simultaneously. Both laboratories used their own validated NGS panels; variant allele frequency threshold was 5% for single nucleotide polymorphism and 10% for indels. Each laboratory classified variants into three categories based on ACMG criteria: non-mutated (class 1-2), Variants of Uncertain Significance (VUS: class 3) and likely pathogenic/pathogenic (class 4-5). Germline *BRCA* analysis was available according to local clinical practice or centralized in Lab-1 if histology was low grade. **Results:** Ninety FFPE samples were received, 8 had insufficient material to be analyzed in both laboratories and 6 cases were discarded due to tumor cellularity below 20% leaving 76 cases to be sequenced. The population had a median age of 58 (25-84) years, 87% (66/76) of HGSOC histology and 70% of advanced stages (III-IVB: 53) and 14.5% (11) germline *BRCA* mutations (3 with not available results). Lab-1 identified 17 class 4-5 mutations, 11 correspond to germline, 4 (5.3%) are just somatic and 2 have germline results not available yet. Lab-2 had one not valuable analysis and identified 16 class 4-5 mutations, 10 corresponding to germline and 4 somatic variants. Percentage of concordance between both laboratories was 96% (kappa coefficient 0.883; p value < 0.0001). Three discordant out of 18 class 4-5 mutations included 2 undetected (VAF of 14.9% and 60.3% respectively) and one class 4 in Lab-2 classified as VUS in Lab-1 due to different interpretation criteria. **Conclusions:** The global *BRCA* mutation frequency in our series was 22.3% for Lab-1 and 21.0% for Lab-2. Concordance between tumor *BRCA* mutation analysis was high (96%). Nevertheless, further effort is required on harmonizing the technical and analytical aspects in tumor mutational analysis. Research Sponsor: Astra Zeneca.

6056 Poster Session (Board #227), Fri, 8:00 AM-11:00 AM

Cediranib in combination with olaparib in patients without a germline BRCA1/2 mutation with recurrent platinum-resistant ovarian cancer: Phase IIb CONCERTO trial. *First Author: Jung-min Lee, National Cancer Institute, Bethesda, MD*

Background: A Phase I trial (NCT01116648) of cediranib (cedi) in combination with olaparib (ola) (cedi + ola) demonstrated an overall response rate of 44% in patients (pts) with recurrent ovarian cancer (OC), including pts without a deleterious or suspected deleterious gBRCAm (non-gBRCAm; Liu *et al. Eur J Cancer* 2013). The subsequent Phase II trial (NCT01116648) showed significant improvement in progression-free survival (PFS) with cedi + ola versus ola monotherapy in recurrent platinum-sensitive OC pts, notably in non-gBRCAm pts (Liu *et al. Lancet Oncol* 2014). We report data from the Phase IIb, single-arm, open-label CONCERTO study investigating cedi + ola in non-gBRCAm pts with recurrent platinum-resistant OC who had received ≥3 previous lines of therapy for advanced OC (NCT02889900). **Methods:** Pts with disease progression <6 months from the last receipt of platinum-based chemotherapy received cedi tablets (30 mg once daily) plus ola tablets (200 mg twice daily) until progression or unacceptable toxicity. gBRCAm pts were ineligible. Primary endpoint: objective response rate (ORR) by independent central review (ICR; RECIST 1.1). Key secondary endpoints: PFS and safety. **Results:** 60 pts from the USA were included (median age: 64.5 years; median number of previous systemic treatment regimens: 4 [range: 2–9]; previous bevacizumab: 53). All pts had high-grade OC (90% serous; 3.3% clear cell; 3.3% endometrioid; 3.3% other). 7% of pts had tumor *BRCA2* (confirmed somatic) mutations, 80% of pts had no tumor BRCA mutation (non-tBRCAm) and 13% of pts were not evaluable for tBRCAm. Five (8%) pts who were non-tBRCAm carried somatic homologous recombination repair gene mutations (FoundationOne Clinical Trial Assay, Foundation Medicine, Inc). The Table shows results of key endpoints. Most common grade ≥3 adverse events (AEs) that occurred in pts were hypertension (30%), fatigue (22%) and diarrhea (13%). 37% of pts reported serious AEs, of which nausea (7%) was most common. Dose interruptions, reductions and discontinuations were caused by AEs in 55%, 18% and 18% of pts, respectively, who received cedi + ola. **Conclusions:** Cedi + ola showed evidence of antitumor activity in heavily pretreated non-gBRCAm pts with recurrent platinum-resistant OC. Toxicity was manageable with dose modifications. Clinical trial information: NCT02889900. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc, Kenilworth, NJ, USA.

Endpoint	Cedi + ola (n=60)	95% CI
Confirmed ORR,*† %	15.3	7.2–27.0
Median PFS,* months	5.1	3.5–5.5
Median duration of response,*‡ months	8.3	5.6–10.3
Median overall survival, months	13.2	9.4–16.4

*By ICR; †n=59; ‡n=9

6057 Poster Session (Board #228), Fri, 8:00 AM-11:00 AM

Olaparib maintenance monotherapy for non-germline BRCA1/2-mutated (non-gBRCAm) platinum-sensitive relapsed ovarian cancer (PSR OC) patients (pts): Phase IIIb OPINION interim analysis. *First Author: Andres Poveda, Initia Oncology, Hospital Quirónsalud, Valencia, Spain*

Background: In the Phase II Study 19 trial (NCT00753545; Ledermann *et al. Lancet Oncol* 2014), maintenance olaparib improved progression-free survival (PFS) vs placebo in PSR OC pts, including those in the non-BRCAm subgroup. A significant PFS benefit was also seen with maintenance olaparib vs placebo in gBRCAm PSR OC pts in the Phase III SOLO2 trial (NCT01874353; Pujade-Lauraine *et al. Lancet Oncol* 2017). To investigate olaparib maintenance monotherapy in non-gBRCAm PSR OC pts who had received ≥2 previous lines of platinum-based chemotherapy, we performed the Phase IIIb, single-arm, OPINION study (NCT03402841). **Methods:** Pts had high-grade serous or endometrioid OC and had responded to platinum-based chemotherapy. Pts initiated maintenance olaparib tablets (300 mg bid) until disease progression or unacceptable toxicity. Primary endpoint was investigator-assessed PFS (modified RECIST 1.1). Secondary endpoints included PFS by homologous recombination repair deficiency (HRD; assessed with the Myriad myChoice HRD plus test; HRD+ve: score ≥42) and somatic BRCA mutation (sBRCAm) status. An interim analysis was planned after ~135 PFS events. **Results:** 279 pts were enrolled from 17 countries (mean age: 64 yrs); 94.3% were confirmed non-gBRCAm by local testing. At data cut-off (Nov 15, 2019), the median PFS was 9.2 months (95% confidence interval [CI]: 7.6–10.9 months), with 152 PFS events (54.5% maturity). The Table presents PFS outcomes by key subgroups. The median exposure to olaparib was 8.1 months. Grade ≥3 adverse events (AEs) occurred in 72 (26%) pts. 19% of pts reported serious AEs. No deaths related to AEs were reported. AEs led to dose interruption, dose reduction and treatment discontinuation in 39%, 15% and 7% of pts, respectively. **Conclusions:** Maintenance olaparib demonstrated activity in non-gBRCAm PSR OC pts. There were no new safety signals. Clinical trial information: NCT03402841. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

PFS outcomes by key subgroups.

	Subgroup	Events, n (%)	Median PFS, months (95% CI)
HRD/BRCAm status	HRD+ve including sBRCAm, n=128	63 (49)	10.9 (9.1–14.5)
	HRD+ve excluding sBRCAm, n=94	51 (54)	9.7 (8.1–11.1)
	sBRCAm, n=34	12 (35)	14.5 (9.2–NE)
	HRD-ve, n=115	72 (63)	7.3 (5.5–9.1)
Prior platinum regimens	2, n=172	97 (56)	9.2 (7.4–10.9)
	>2, n=107	55 (51)	9.0 (7.2–NE)
Response to last platinum therapy	CR/NED, n=96	45 (47)	10.8 (9.2–13.8)
	PR, n=179	104 (58)	7.4 (7.2–10.8)

CR, complete response; NE, not evaluable; NED, no evidence of disease; PR, partial response

6058 Poster Session (Board #229), Fri, 8:00 AM-11:00 AM

The safety and efficacy of weekly paclitaxel and cisplatin chemotherapy for patients with ovarian cancer who developed carboplatin hypersensitivity reaction in previous chemotherapy. *First Author: Kyoko Nishikimi, Departments of Reproductive Medicine, Graduate School of Medicine, Chiba University, Chiba, Japan*

Background: Carboplatin (CBDCA) hypersensitivity reactions (HSR) often occur in patients with ovarian cancer. Once CBACA HSR occurs, it is difficult to use platinum even though the patients had platinum-sensitive disease and consequently the survival of the patients cannot be prolonged. We had administered weekly paclitaxel and cisplatin (CDDP) chemotherapy (wTP) for patients with ovarian cancer who developed CBDCA HSR in previous chemotherapy. We investigated the safety and efficacy of wTP. **Methods:** We investigated 86 patients with ovarian, fallopian tube, and peritoneal carcinoma who developed CBDCA HSR in previous chemotherapy (paclitaxel/CBDCA) at our institution between 2011 and 2019. After premedication was administered, paclitaxel and sequentially CDDP were administered as one hour infusion, respectively (paclitaxel 80 mg/m^2, CDDP 25 mg/m^2; 1, 8, 15 day/4 weeks). **Results:** The median cycle of the previous chemotherapy of CBDCA was 8 (interquartile range [IQR], 6–11). The grade of CBDCA HSR was 1 in 57 (66%), 2 in 26 (30%), and, 3 in 1 (1%) patient(s). WTP was administered for the first line in 21 (24%), second line in 35 (41%) and third or more line in 30 patients (34%). The median cycles of wTP administration was 4 (IQR, 3–7). We observed that severe CDDP HSR did not occur in any patients and 15 patients (17.4%, grade 1, 10 patients; grade 2, 5) developed CDDP HSR. All CDDP HSR were successfully managed with infusion interruption and Hydrocortisone Sodium Phosphate administration. There was no relation between the grade of CBDCA HSR in the previous chemotherapy and the rate of CDDP HSR ($p = 0.363$). Progression-free survival and overall survival after administration of wTP were 10.9 months (95% CI: 7.7–17.7) and 25.9 months (95%Ci: 19.0–50.2), respectively. **Conclusions:** 71 patients (82%) who developed CBDCA HSR in previous chemotherapy were able to continue administration of wTP without CDDP HSR. WTP was safe and effective for the patients who developed CBDCA HSR. Research Sponsor: None.

Patient characteristics.

No. of Cycles in previous CBDCA	n (%)	Grade of previous CBDCA HSR	n (%)	Line of cisplatin	n (%)
2–6	28 33%	1	57 66%	First	21 24%
7–12	42 49%	2	26 30%	Second	35 41%
≥13	16 19%	3	1 1%	Third or more	30 35%
		unknown	1 1%		

6059 Poster Session (Board #230), Fri, 8:00 AM-11:00 AM

Phase I/II study of weekly topotecan and gefitinib in patients with platinum-resistant ovarian, peritoneal, or fallopian tube cancer. *First Author: Anca Chelariu- Raicu, MD Anderson, Houston, TX*

Background: The epidermal growth factor receptor (EGFR) is expressed in many types of cancer. Fifty to 70% of epithelial ovarian can overexpress EGFR, and its expression has been correlated with poor prognosis features in many cases. While these tumors are chemosensitive to platinum-based therapy, chemoresistance often develops. We conducted a phase I/II trial to examine the efficacy, safety, and toxicity of gefitinib, a tyrosine kinase inhibitor, combined with topotecan in women with recurrent ovarian cancer with EGFR receptor positivity (1+ or greater). **Methods:** Patients with measurable, recurrent or persistent cancer after treatment with a platinum and paclitaxel-containing regimen were eligible for this study (n = 19). We first used "run-in" dose escalation, in which a conventional 3+3 algorithm was used. Initial treatment was gefitinib 250 mg oral dose daily and topotecan at a dose of 2.0 mg/m^2 on days 1, 8, and 15, with cycles repeated every 28 days. Dose escalations were planned for topotecan (Dose Levels 1–3: 2, 3, 4 mg/m^2) until the MTD was reached. Next, an additional 10 patients with refractory or progressive ovarian cancer were enrolled in the phase II study. **Results:** 19 patients received a total of 61 cycles. Median age was 60 years. Histological types of treated patients included 73% serous (n = 14), 12.5% mixed (n = 2), 12.5% transitional (n = 2) and 6.3% clear cell (n = 1). There were 3 patients treated at dose level 1, 3 patients at dose level 2, and 3 patients treated at dose level 3. The maximum tolerated dose was topotecan 4.0mg/m^2 IV days 1, 8 and 15, and gefitinib 250mg p.o. QD x28 days. Therefore, dose level 3 was used for the Phase II portion of the trial. Of the 19 patients included in the phase I/II, 3 patients were inevaluable for response to therapy due to toxicity, missed therapy or decline in performance status. Of the 16 patients, 81% patients (n = 13) had progressive disease, 12.5% stable disease (n = 2), and 6% partial response (n = 1). We assessed all 19 patients for adverse events; 60% had treatment-related grade 3 events, primarily blood disorders such as anemia (n = 3, 16%), neutrophil count decrease (n = 4, 21%). **Conclusions:** This prospective phase I/II clinical trial failed to show sufficient clinical activity of topotecan in combination with gefitinib in patients with EGFR-positive recurrent ovarian, fallopian tube, or peritoneal cancers. The drug combination was relatively well-tolerated in this cohort. As such, the study did not proceed to the next accrual goal secondary to the lack of response. Clinical trial information: NCT00317772. Research Sponsor: MD Anderson.

6060 Poster Session (Board #231), Fri, 8:00 AM-11:00 AM

Whole transcriptome changes correlate to exceptional ovarian cancer responders: A sub-analysis of a HIPEC Phase I trial. *First Author: Thanh Hue Dellinger, City of Hope Natl Comp Cancer Ctr, Duarte, CA*

Background: Advanced stage ovarian cancer patients benefit from hyperthermic intraperitoneal chemotherapy (HIPEC), prolonging overall survival by nearly 12 months. However, molecular changes triggered by HIPEC are not well characterized, and no molecular signatures of response are known. We analyzed early gene expression changes after HIPEC treatment in ovarian tumors. **Methods:** This is an interval subgroup analysis of a single institution Phase I trial using HIPEC with cisplatin 75 mg/m^2 at time of optimal cytoreduction. Snap-frozen biopsies from tumor and normal peritoneum from 20 patients with ovarian cancer before and after HIPEC underwent whole-transcriptome sequencing using Illumina's NovaSeq 6000 for paired 100 base-pair reads. Differential expression analysis comparing post and pre-samples was done to identify significantly changed genes, and pathway analysis was conducted using GSEA. **Results:** Sixty-three genes were differentially expressed ($P < 0.05$, fold change ≥ 2) between pre- and post-HIPEC tumors. Hierarchical clustering analysis of these genes confirmed that all tumors and normal tissues clustered based on pre-HIPEC versus post-HIPEC status, and not based on their patient source. Gene set enrichment analysis using a collection of 50 "hallmark" gene sets revealed that post-HIPEC tumors demonstrate significant upregulation in immune pathways (TNFA signaling via NFKB, coagulation, complement), followed by epithelial-mesenchymal transition, inflammation, apoptosis, hypoxia, angiogenesis, KRAS signaling and JAK/STAT3 signaling. In contrast, post-HIPEC normal tissues exhibited upregulation in cell cycle pathways (Myc targets V2, G2M checkpoint). As expected, both post-HIPEC tumor and normal samples shared upregulation of genes related to inflammatory response. Lastly, post-HIPEC normal samples revealed downregulation of growth and metabolism pathways; in contrast, cell cycle or DNA repair pathways were downregulated in post-HIPEC tumors. Two exceptional-responders with recurrent platinum-sensitive disease (ongoing PFS 47 and 12+ months) demonstrated the most substantial changes in gene expression. **Conclusions:** Exceptional ovarian cancer responders to HIPEC are characterized by extensive gene expression changes; specifically, early HIPEC-induced molecular changes are strongly associated with immune pathways changes, implicating a role for immunotherapy after HIPEC in ovarian cancer. Clinical trial information: NCT01970722. Research Sponsor: None.

6061 Poster Session (Board #232), Fri, 8:00 AM-11:00 AM

Anlotinib in patients with recurrent platinum-resistant or refractory ovarian carcinoma: A prospective, single-arm, single-center, phase II clinical study. *First Author: Boer Shan, Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China*

Background: Recurrent platinum-resistant or refractory ovarian carcinoma is difficult to treat, and how to improve the treatment effect of these patients is still an urgent problem to solve. Anlotinib is a new multi-target tyrosine kinase inhibitor and its anti-tumor vascular targets include VEGFR, PDGFR and FGFR. Previous researches have shown clinical antitumor activity of anlotinib in various cancers, including the phase I study on gynecologic tumor. This phase II study (ChiCTR2000029654) aims to further evaluate the safety and efficacy of anlotinib in patients with recurrent or refractory ovarian carcinoma. **Methods:** Patients who have previously received second-line or more chemotherapy, with histopathologically confirmed ovarian high-grade serous gonadal carcinoma (including salpingocarcinoma and peritoneal carcinoma), ECOG 0-2 were considered eligible for enrollment. Anlotinib was administered orally (12 mg qd, d1-14; 21 days per cycle) till disease progression, death or intolerant toxicity. Therapeutic effects are evaluated every 6 weeks. The primary endpoint was objective response rate (ORR) and the secondary endpoints included disease control rate (DCR), progression-free survival (PFS), overall survival (OS), safety and quality of life (QOL). **Results:** Between 2019 March to 2020 January, 15 patients (female) with FIGO histopathological stage IA(6.7%), IIIA (73.3%), IIIC (6.7%) and IV (13.3%) were enrolled and 14 patients were evaluable with a median age of 59 years (range: 47-69). The mean follow-up period is 3.5 months (95% CI: 2.1-4.8). Therapeutic evaluation showed the incidence of partial response, stable disease and progression disease was 14.3%, 57.1% and 28.6% respectively, yielding the ORR of 14.3% (2/14; 95% CI: 1.8%-42.8%) and the DCR of 71.4% (10/14; 95% CI: 41.9%-91.6%). The median PFS was not reached. Most of the occurring AEs were grade 1, including hypertention (57.1%), fatigue (50.0%), hand-foot syndrome (35.7%), hoarseness (14.3%), diarrhea (7.1%), gum-pain (7.1%), decrease in leukocyte count (6.7%) and urine protein (7.1%). Only cancer pain (7.1%) was grade 2. No high grade AE was observed in these 14 patients. Neither unexpected safety signals nor treatment related death occurred. **Conclusions:** Anlotinib showed a promising efficacy with a favourable toxicity profile for patients with recurrent platinum-resistant or refractory ovarian carcinoma. And we will report more results ahout anlotinib in the future. Clinical trial information: ChiCTR2000029654. Research Sponsor: Chia-Tai Tianqing Pharmaceutical Group Co Ltd.

6062 Poster Session (Board #233), Fri, 8:00 AM-11:00 AM

Risk stratified multidisciplinary ambulatory management of malignant bowel obstruction (MAMBO) program for women with gynecological cancers: Preliminary results from a prospective single-center study. *First Author: Shiru Lucy Liu, Princess Margaret Cancer Centre-University Health Network, Toronto, ON, Canada*

Background: Malignant Bowel Obstruction (MBO) is one of the most common and devastating complications in women with gynecological cancer (GC). There is currently no consensus guideline to improve patient (pt) care in this setting. MAMBO (NCT03260647) is an ongoing prospective study evaluating the clinical implementation of a novel management algorithm for multidisciplinary management of MBO in GC pts. We report preliminary patient outcomes. **Methods:** All GC pts at Princess Margaret Cancer Centre with a confirmed diagnosis of or are at risk of MBO are eligible for enrollment. Participants follow a low fiber diet titrated by severity of symptom and their monthly weight and albumin levels are recorded, along with standardized patient-reported outcome measures (PROMs) at different time points. For pts who develop MBO, inpatient and ambulatory management algorithms are applied using a multidisciplinary and interprofessional care model consisting of nurses, surgeons, oncologists, radiologists, nutritionists, total parenteral nutrition team, social work, and palliative care. Decisions regarding most optimal management strategies are made by this team with regular MAMBO rounds. A retrospective analysis of pts hospitalized with MBO between 2012 and 2017 was performed in order to have a historical comparison for outcome and survival analysis using Kaplan Meier methods. **Results:** Since August 2017, 70 pts have been enrolled in MAMBO. Most had high-grade serous ovarian carcinoma (75%), of whom 68% are platinum-resistant. So far, 36 (51%) developed MBO, 6 of whom had multiple sequential episodes. Mean number of days in hospital with MBO was 10 days (median 7, range 0-45), compared to 18 days (median 9, range 0-134) for historical control ($p = 0.009$). There was no significant loss in weight 6 months from MBO diagnosis but a significant reduction in albumin level by 2.75 g/L after 3 months ($p = 0.005$). PROMs suggest fatigue and general lack of wellbeing were the symptoms with highest distress. Most patients (78%) received chemotherapy following MBO and most received weekly paclitaxel (36%). Median time from first MBO to death was 219 days (95% CI: 101-not reached) for all-comers in MAMBO and 174 days (95% CI: 98-363) for MBO requiring hospitalization, compared to 108 days (95% CI: 79-160) for historical controls ($p = 0.007$ and $p = 0.062$, respectively). **Conclusions:** Patient care and outcomes from MBO seem to be improved in GC pts enrolled in MAMBO compared to historical controls. Clinical trial information: NCT03260647. Research Sponsor: Clinical Cancer Research Unit, Princess Margaret Cancer Centre.

6063 Poster Session (Board #234), Fri, 8:00 AM-11:00 AM

Are symptoms distinguishable in ovarian cancer? A nested case control study of insurance claims. *First Author: Denise Manon Langabeer, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Over 60% of ovarian cancer cases are diagnosed with Stage III and IV disease. The US healthcare system does not support a standard screening method for ovarian cancer. Our goal was to determine whether certain symptoms based on ICD-9 categories are distinguishable among women diagnosed with ovarian cancer and women without ovarian cancer. **Methods:** Women diagnosed with ovarian cancer were randomly matched 1:1 to women without cancer to support a nested case-control analysis of health insurance claims between 2008 through 2013 from a commercial payer. The following eligibility criteria were applied: 1) 24 years of age or older; 2) continuously enrolled in healthcare plan for a minimum period of 6 months; 3) experienced more than 1 symptom over the observation period; and 4) an observation period of a minimum of 6 months. Symptoms were based on 47 ICD-9 diagnosis codes and categorized specific to pain, abdominal and pelvic, digestive, and bladder. The analysis was based on 1,578 women (789 cases; 789 controls). **Results:** Overall, 90% (n = 1,421) of the women experienced abdominal and pelvic symptoms, and 92% (n = 725) of the women with ovarian cancer visited their physician for this complaint 6-70 months prior to diagnosis, OR 1.66 (CI 1.14 to 2.41; p = .008). Pain was reported as a complaint by cases at nearly 60% (n = 464) and controls at 48% (n = 376); OR 1.75 (CI 1.39 to 2.19; $p < .001$). Symptoms for bladder and digestive combined represented 68% of complaints for both cases (n = 507) and controls (n = 555), p = .024 and p = .298, respectively. Of the 1,578 women, 77% (cases = 621; controls = 595) experienced more than one category of symptoms. Both cases (n = 206) and controls (n = 153) complained of abdomen and pelvic symptoms along with pain; OR 1.54 (CI 1.19 to 1.99; p = .001). A second combination included abdomen and pelvic symptoms with pain and digestive symptoms in 14% of women (cases n = 99; controls n = 67); OR 1.58 (CI 1.13 to 2.22; p = .008). Sixty percent (n = 473) of women with ovarian cancer experienced the majority of associated prediagnosed symptoms analyzed for the study. **Conclusions:** Certain recurring symptoms associated with abdomen and pelvic as well as pain appear to indicate an association with ovarian cancer, signifying that symptom awareness remains relevant to this disease that is diagnosed at a late stage and currently does not have routine screening methods to support early detection. Research Sponsor: None.

6064 Poster Session (Board #235), Fri, 8:00 AM-11:00 AM

Juvenile granulosa cell tumor: An interim report from the international ovarian and testicular stromal tumor (OTST) registry. *First Author: Anne Harris, Children's Hospitals and Clinics of Minnesota, Minneapolis, MN*

Background: Juvenile granulosa cell tumors (JGCT) are rare sex cord-stromal tumors which occur primarily in children and adolescents. **Methods:** All individuals or proxy caregivers provided informed consent/assent for participation in the International OTST Registry. Clinical data was collected. When available, pathology was centrally reviewed. Staging was evaluated using the International Federation of Gynecology and Obstetrics (FIGO) classification. Kaplan-Meier survival analyses and exact permutation tests were performed. **Results:** Forty-two individuals with ovarian JGCT were enrolled. Median age at diagnosis was 9 years (range 0-27). Most individuals had Stage I disease (Stage Ia=16; Stage Ib=1; Stage Ic=16). Seven individuals presented with higher stage (Stage II=2; Stage III=5). Stage was unknown for 2 individuals. Three-year overall survival (OS) was 88% (CI 77%, 100%) and event-free survival (EFS) was 69% (CI 54%, 88%). At median follow-up time of 25 months (range 0-416), 9 patients (Stage Ia=1, Stage Ic=5, Stage III=3) had recurrent disease. Use of post-operative adjuvant chemotherapy varied by stage and timing of rupture. Of those with Stage Ic JGCT, 2/7 with preoperative rupture and 3/9 with intraoperative rupture recurred. Among individuals with recurrence, median time to recurrence was 11.5 months (range 3-19). Four of 9 individuals with recurrence survived (no evidence of disease n=2; alive with disease n=2). All individuals who died presented with extrapelvic recurrence. Median time from recurrence to death was 10 months (range 2-53). In individuals with recurrence, advanced stage at diagnosis (HR 5.1; p-value 0.087) and recurrence outside the tumor bed (HR Infinity; p-value 0.048) were associated with inferior OS. Three-year OS for individuals with recurrence was 57% (CI 30%, 100%). **Conclusions:** Low stage JGCT is associated with a favorable prognosis, however, recurrence is associated with lower survival rate. Within this series, recurrences presented within 2 years of diagnosis. Novel strategies are needed to address recurrent and extrapelvic disease. Research Sponsor: Pine Tree Apple Tennis Classic Foundation.

6066 Poster Session (Board #237), Fri, 8:00 AM-11:00 AM

ctDNA from ascites as an alternative to tumor sampling for HRD (homologous recombination deficiency) testing in ovarian cancer (OC). *First Author: Alexandra Leary, Gustave Roussy Cancer Center, Villejuif, France*

Background: Knowledge regarding HRD status is becoming crucial to guide maintenance strategies for patients with newly diagnosed OC. Unfortunately, for patients (pts) treated with neoadjuvant chemotherapy (NACT), HRD testing on small biopsies from diagnostic laparoscopies (Dx Lap) or interval debulking has a high failure rate. At relapse, biopsies may not be feasible. Aim: Evaluate the feasibility and usefulness of HRD testing on cfDNA from ascites **Methods:** Pts enrolled in a prospective biological study (OvBIOMark) consented to analysis of biological samples obtained as part of routine diagnosis. cfDNA was extracted from 1-2ml of double-centrifuged fresh ascites and subjected to 1) targeted NGS including the most common somatic mutations in high grade ovarian cancer (*TP53*) to confirm presence of tumor cfDNA and 2) SNParray for copy number (CN) analyses to calculate a genomic instability score (GIS) for HRD. **Results:** Thirty four ascites samples were collected from 25 pts with suspected or confirmed OC. For 15/25 pts samples were obtained at Dx Lap, and for 10 pts samples were obtained at relapse. Seven pts underwent repeat ascitic drains during treatment or at relapse. 97% (33/34) of ascitic samples had detectable cfDNA (median = 980ng, range:80-5730ng) even when obtained during chemotherapy. A deleterious mutation was identified in 87% (29/33) of samples with high allelic frequencies (median allelic frequency, AF = 60%; 3.3-87%), confirming that most of detected cfDNA was tumoral. The most common mutation was a *TP53m (*86%; 25/29). We have performed CN analysis on cfDNA from ascites on 17 of these patients to evaluate their HRD status. Ten pts had a high GIS (HRD+), and 7 pts a low GIS (HRD-). The 4 pts with confirmed *BRCA*m included in this study had a high GIS on ascites. When available from the same patient, the CN profiles derived from ascites cfDNA and tumor sampling were superimposable. **Conclusions:** Ascites yields large amounts of cfDNA, which can be confirmed as tumoral based on *TP53* mutation detection. CN analysis on ascitic cfDNA is feasible and can be used to detect the same HRD scar as tumor testing. Ascites is frequent at diagnosis, especially in pts with inoperable disease planned for NACT and could provide a useful alternative to tumor for HRD and *BRCA* testing. Research Sponsor: Institut National du Cancer TransCAN european grant.

6067 Poster Session (Board #238), Fri, 8:00 AM-11:00 AM

Laparoscopy compared with laparotomy for comprehensive surgical staging of early ovarian cancer: Results of a retrospective multicenter case-control study. *First Author: Julia Caroline Radosa, Department of Obstetrics and Gynecology, Homburg, Germany*

Background: The objective of this study was to compare laparoscopy and laparotomy for comprehensive surgical staging of early ovarian cancer in terms of efficacy and oncologic safety. **Methods:** Patients who had laparoscopic staging for early stage (I/II) ovarian cancer between 01/2000 and 10/2018 at the participating sites (Gynecologic comprehensive cancer centers with respective expertise in minimal invasive surgery) were included in this retrospective case-control study. The control group consisted of all patients treated via laparotomy during the study period. Clinical data were abstracted from medical record and recent follow up information were obtained. Comparisons were made between patients regarding surgical parameters and oncologic outcome and multivariate models were used to identify factors independently associated with disease recurrence. **Results:** Among 313 patients, staging was performed via laparoscopy in 208 (66 %) patients and via laparotomy in 105 (34 %) patients. Patients staged laparoscopically were younger (median 52 (15-86) vs. 59 (17-92) vears, $p \leq 0.01$) and had a lower BMI (24.4 (16.5-46.8) vs. 26 (15.5-53.8), $p \leq 0.01$). Regarding surgical parameters, duration of surgery was longer (291 (159-778) vs. 277 (159-690) minutes, $p \leq 0.01$), postoperative hospitalization was shorter (7 (0-27) vs. 9 (0-92) days, $p \leq 0.01$) and postoperative complications were lower in the laparoscopy group. On univariate analysis there were no differences in rates of tumor stage according to FIGO, intraoperative rupture of ovarian cysts (14 % vs. 13 %, p=0.87), number of lymph nodes removed (24 (0-89) vs. 22 (0-96), p=0.81) or any recurrence of disease (14 % vs. 16 %, p=0.52). At a median follow-up of 46 months (0-227), there were no differences in DFS and OS by surgical technique (5yr DFS 82 % (SE 0.04) vs. 83 % (SE 0.05), p=0.43; OS 91 % (SE 0.03) vs. 87 % (SE 0.04), p=0.87). On multivariate analysis route of surgery was not associated with an increased risk of recurrence. **Conclusions:** According to this preliminary analysis, laparoscopic surgical staging in patients with early ovarian cancer seems to be adequate and safe, but a longer follow-up and prospective data are needed to enhance evidence on oncologic outcomes. Research Sponsor: None.

6068 Poster Session (Board #239), Fri, 8:00 AM-11:00 AM

Efficacy and safety of olaparib according to age in BRCA-1/2 mutated patients with recurrent platinum-sensitive ovarian cancer: Analysis of the phase III SOLO2 (AGO-OVAR 2.23/ENGOT-Ov21) study. *First Author: Fabian Trillsch, AGO and Department of Obstetrics and Gynecology, University Hospital, LMU Munich, Munich, Germany*

Background: Adding olaparib as maintenance treatment to BRCA-1/2 mutated patients (pts) with recurrent platinum-sensitive ovarian cancer (PSOC) has significantly improved progression-free survival (PFS) as well as patient-centered endpoints. As BRCA mutated pts tend to be younger, specific information on efficacy and safety of olaparib for elderly pts is of special interest. **Methods:** 295 pts from the SOLO2 trial that randomly assigned to olaparib or placebo were categorized according to age cutoff at 65 years. The efficacy and tolerability of olaparib relative to placebo within in each age group was assessed based on PFS and toxicity outcomes. Quality of life (QoL) was assessed using EQ-5D-5L descriptive system score and FACT Trial Outcome Index (TOI) and evaluated using generalized estimating equations (GEE) and time without significant symptoms of toxicity (TWiST) analysis. **Results:** Baseline characteristics were similar in pts ≥65 years (N=62; 21%) compared to pts <65 years (N=233; 79%), except for more BRCA2 mutations in elderly pts (39% vs. 23%). There was no significant difference in the magnitude of PFS benefit from olaparib in elderly as compared with younger pts (interaction P=0.33). The PFS adjusted hazard ratio (HR) of olaparib vs. placebo arms were respectively $HR_{\geq 65}$ 0.43 (95%-confidence interval [CI] 0.24-0.81) and $HR_{<65}$ 0.31 (95%-CI 0.22-0.43). Elderly and younger pts also had comparable safety profiles with no significant differences in median time on olaparib treatment (≥65: 27 vs. <65: 33 months), percentage of pts experiencing at least one grade >2 adverse event with olaparib (≥65: 73% vs. <65: 79%), or requiring at least one dose interruption or dose reduction (≥65: 77.5 vs. <65: 77.6%). No differences were found with regards to QoL scores. Quality adjusted TWiST analysis showed only non-significant differences in duration of good QoL under olaparib (≥65: 8.02 vs. <65: 9.24 months, P=0.48). **Conclusions:** In this large cohort of BRCA mutated PSOC pts treated with a PARP inhibitor within a phase III trial, no significant differences were detected in terms of efficacy, safety, and QoL with olaparib treatment for pts ≥65 years compared to younger pts. This information supports the use of PARP inhibitors as maintenance therapy for PSOC pts irrespective of age. Clinical trial information: NCT01874353. Research Sponsor: AstraZeneca.

6069 Poster Session (Board #240), Fri, 8:00 AM-11:00 AM

Ovarian cancer clinical trials: Study the studies to terminate the terminations. *First Author: Daniel Spinosa, Division of Gynecologic Oncology, Duke Cancer Institute, Duke University Medical Center, Durham, NC*

Background: Clinical trials safely expand the arsenal of treatments available to future patients while providing hope to current patients, particularly ovarian cancer patients who often have poor prognoses. Trial termination for lack of efficacy or unacceptable toxicity are consistent with the aim of protecting patients in the pursuit of knowledge, but those are not the only reasons trials terminate early. Understanding why some clinical trials do not achieve their stated goals may aid in the design of future trials. **Methods:** Data were gathered from clinical trials registered to ClinicalTrials.gov. Included trials were interventional (as opposed to observational), were closed between 2004 and 2019, enrolled ovarian cancer patients, had submitted results, and were open at one or more domestic sites. For each trial, data were captured regarding study completion, reason for non-completion (if applicable), sites, phase, sponsor (defined as the study initiator, not necessarily the funder), and intervention type. **Results:** A total of 313 trials were examined, of which 262 met inclusion criteria. Of the 262 evaluable trials, 189 (72%) were completed and 72 (27%) terminated early. The most common reasons for early termination were low accrual (27 trials, 38%), lack of efficacy (15 trials, 21%), or insufficient funding (9 trials, 13%). Five trials (7%) were terminated early due to toxicity. Early phase trials are less likely to complete enrollment, with 11 out of 16 (65%) phase 1 trials, 135 out of 180 (75%) phase 2 trials, and 15 out of 16 (94%) phase 3 trials completed. Trials initiated by an academic center were twice as likely to be terminated early (41/103, 40%) as those initiated by industry (16/80, 20%), with remaining trials initiated by consortia, NCI, or non-academic oncology practices. Terminated trials were open at an average of 11 sites (range 1-317), while completed trials were open at an average of 27 sites (range 1-632). Trials that had multiple types of interventions, for instance a drug and a procedure, had a 34% early termination rate which was higher than the rate for trials with any single type of intervention. **Conclusions:** More than one in four ovarian cancer clinical trials are terminated early, rarely due to treatment efficacy or tolerability. Trials terminated for reasons other than patient outcomes represent a misallocation of resources or a missed opportunity for innovation. Further research is needed to understand the circumstances that allow for clinical trial completion such that available resources maximize patient benefit. Research Sponsor: None.

6070 Poster Session (Board #241), Fri, 8:00 AM-11:00 AM

Patterns of progression and subsequent management of patients with *BRCA1/2* mutated platinum-sensitive recurrent epithelial ovarian cancer (EOC) progressing on olaparib versus placebo: the SOLO2/ENGOT Ov-21 trial (NCT01874353). *First Author: Jean-Sebastien Frenel, GINECO & Institut de Cancerologie de l'Ouest, Centre René Gauducheau, Saint-Herblain, France*

Background: Olaparib maintenance is a standard treatment of *BRCA1/2* mutated platinum-sensitive recurrent EOC. Despite improvement in PFS, olaparib (O) resistance often occurs and the optimal management of post-olaparib progression remains undefined. **Methods:** Data of patients who participated in the SOLO-2 trial and progressed were analyzed. Primary objective was to depict the patterns of progression of patients treated with O compared to placebo (P). Secondary objectives include description of post-progression treatments. **Results:** 106/195 (54%) and 80/99 (81%) patients had a RECIST progression in the O and P arms respectively. As permitted in the protocol, 37 (35%) pts continued O despite a RECIST progression and 10 remained on treatment at the date of data base cut-off of the primary endpoint. Median duration of O post progression was 3.2 months (range: 1 to 19.4). In the placebo arm, only 20% of the patients with progressive disease continued placebo during a median of 1.6 months (range:1.1 to 16.1). Patterns of sites of progressive disease were similar in the O and P arms respectively in terms of liver (21% vs 18%), lung (4% vs 3%), lymph node (20% vs 16%) peritoneal (48% vs 32%) or brain metastases (0% vs 2%). Number of sites of relapsing disease were similar in the O and P arm respectively (1 (68% vs 64), ≥2 (32% vs 36%). A total of 54 (51%) patients in the O arm and 42 (53%) in the P arm received subsequent platinum-based therapy. In both arms, 8% received bevacizumab and 6% received no further treatment. Median PFS with first post-study platinum-based and non platinum-based therapy were 7.1 months and 5.6 months respectively. In the P arm, 18 (23) patients received PARP inhibitors following the first subsequent chemotherapy. **Conclusions:** Patterns of disease progression and subsequent chemotherapy were similar in patients receiving O or P in the SOLO2 trial. Instead of switching to chemotherapy, continuing O at the time of RECIST progression was an option for 35% of the patients. Clinical trial information: NCT01874353. Research Sponsor: ASTRA ZENECA.

6071 Poster Session (Board #242), Fri, 8:00 AM-11:00 AM

Combined regimen of inhalable STING agonist plus chemoimmunotherapy in platinum-resistant or platinum-refratory ovarian cancer: A randomized, open-label, phase II trial. *First Author: Yan Zhang, Chinese PLA General Hospital, Beijing, China*

Background: Approximately 70% patients with advanced ovarian cancer have a relapse and ultimately succumb to their disease. Treatment options are limited in this context with an unacceptable low response (less than 20%). Immunotherapy with checkpoint inhibitors presented to date are not very convincing with 10-15% response because of inadequate immunity. We previously discovered the critical role of manganese in innate immune sensing of tumors by activating STING signaling. This ongoing, randomized, phase II study is to assess STING agonist plus nPP chemotherapy and anti-PD-1 antibody sintilimab in platinum-resistant/refractory ovarian cancer. **Methods:** Enrolled patients were 2:1 randomizedly assigned to receive nab-paclitaxel (180-220mg/m^2), cisplatin (60-80mg/m^2) and sintilimab 200mg per 3 weeks with (cohort 1) or without (cohort 2) inhalable $MnCl_2$ (0.4mg/kg) daily. Safety was assessed by CTCAE v5.0, and clinical response by MRI or CT every 2 cycles referred to RECIST version 1.1. The primary endpoints were objective response rate (ORR) and safety. Key secondary end points were disease control rate (DCR), progression-free survival (PFS) and overall survival (OS). **Results:** 27 patients were enrolled, and 21 were included in efficacy population by the end of Jan. 2020. All enrolled patients were with heavily treated history, median 4 lines of prior therapy, median 19 cycles of multiagent regimens. The addition of $MnCl_2$ to the combined chemo-immunotherapy did not appear to exacerbate treatment-related adverse events (AEs). The most common AEs are hematological toxicity (87%), nausea (56%) and vomiting (47%) in both two cohorts. All 14 evaluable patients (14/19) from cohort 1 had an effective control (11 PR [78.6%], 3 SD [21.4%]) . Ten patients (71.4%) achieved PR at the first tumor scan assessment. For 8 cases from cohort 2, 7 were assessable and all showed SD, 4 of whom exhibited SD with enlarged lesions and disease progression after 4-cycle treatment. **Conclusions:** $MnCl_2$ administration induced encouraging objective clinical responses (78.6%) and disease control (100%) in relapsed/refractory ovarian cancer. The combined regimen showed accepted and manageable safety profile. Clinical trial information: NCT03989336. Research Sponsor: the National Key Research and Development Program of China (No.2016YFC1303501 and 2016YFC1303504 to WDH).

6072 Poster Session (Board #243), Fri, 8:00 AM-11:00 AM

Methylated DNA markers for plasma detection of ovarian cancer: Discovery, validation, and clinical feasibility. *First Author: Jamie Nadine Bakkum-Gamez, Mayo Clinic, Rochester, MN*

Background: Effective screening tests for ovarian cancer (OC) are lacking; most cases present at advanced stage and portend poor prognosis. DNA methylation is an early event in carcinogenesis and can be detected in blood plasma samples from cancer patients. In DNA extracted from tissues, we first discovered, then validated discriminant methylated DNA marker (MDM) candidates for OC and subsequently tested independent plasma from women with and without OC. **Methods:** For discovery, DNA from 67 frozen tissues (18 high grade serous (HGS), 18 endometrioid, 15 clear cell (CC), 6 mucinous OCs; 10 benign fallopian tube epithelium (FT); and 19 buffy coats from cancer-free women underwent reduced representation bisulfite sequencing (RRBS) to identify MDMs associated with OC. Candidate MDM selection was based on receiver operating characteristic (ROC) discrimination, methylation fold change, and low background methylation among controls. Blinded biological validation was performed using methylated specific PCR on DNA extracted from independent FFPE tissues from OCs (36 HGS, 22 endometrioid, 21 CC, and 14 mucinous) and 29 FT. Top performing MDMs in tissue were tested using long-probe quantitative amplified signal assays in independent pre-treatment plasma samples from women newly-diagnosed with OC and population-sampled healthy women. A random forest modeling analysis was performed to generate predictive probability of disease; results were 500-fold in silico cross-validated. **Results:** After RRBS discovery and biological validation, 33 MDMs showed marked methylation fold changes (10 to > 1000) across all OC histologies vs FT. The top 11 MDMs (*GPRIN1, CDO1, SRC, SIM2, AGRN, FAIM2, CELF2, DSCR6, GYPC, CAPN2, BCAT1*) were tested on plasma from 91 women with OC (76 (84%) HGS) and 91 without OC; the cross-validated 11-MDM panel highly discriminated OC from controls (96% (95%CI 89-99%) specificity; 79% (69-87%) sensitivity, and AUC 0.91 (0.86 - 0.96)). Among HGS, the panel correctly identified 83%, including 5/6 stage I/II, and the majority of other subtypes (Table). **Conclusions:** Whole methylome sequencing, stringent filtering criteria, and biological validation yielded outstanding candidate MDMs for OC that performed with promisingly high sensitivity and specificity in plasma. Larger plasma-based OC MDM testing studies, with larger numbers of non-HGS histologies are warranted. Research Sponsor: Mayo Clinic Transform the Practice Grant, Other Foundation, Pharmaceutical/Biotech Company, U.S. National Institutes of Health.

OC histology	Serous	Clear cell	Endometrioid	Mucinous	Mixed
N	76	4	8	2	1
Sensitivity at 95% specificity % (95% CI)	83% (73 - 90%)	75% (19 - 99%)	50% (16 - 84%)	50% (13 - 99%)	100% (3 - 100%)

6073 Poster Session (Board #244), Fri, 8:00 AM-11:00 AM

Risk of venous thromboembolism in patients receiving neoadjuvant chemotherapy for ovarian cancer. *First Author: Derman Basaran, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: To identify the incidence of newly occurring venous thromboembolism (VTE) in patients with ovarian cancer receiving neoadjuvant chemotherapy (NACT). **Methods:** Using our prospectively maintained ovarian cancer database, we identified all ovarian cancer patients who received NACT at our institution from 4/15-9/18. VTE events included clinically diagnosed deep venous thrombosis (DVT) or pulmonary embolism (PE). Patients who presented with VTE prior to induction of NACT or patients on anticoagulation therapy prior to diagnosis were excluded. The incidence of newly occurring thrombotic events were categorized according to treatment phases, defined as 1) NACT prior to interval debulking surgery (IDS); 2) intraoperative and 30-day post-IDS; and 3) adjuvant chemotherapy. **Results:** 290 patients underwent NACT during the study period. Thirty-eight patients (13%) who presented with VTE, 12 (4%) on anticoagulation at presentation, and 4 (1.4%) seeking only a second opinion were excluded from analysis. Of the 236 evaluable patients, the overall rate of VTE during all treatment phases was 15% (35/236). In treatment phase I, 11% (27/236) of patients experienced VTE during NACT. In phase II, an additional 2.5% (6/236) developed VTE in the intraoperative and 30-day postoperative period. In phase III, an additional 0.8% (2/236) experienced a thrombotic event >30 days postoperatively. Sevety-seven percent (27/35) of VTE events occured during phase I. **Conclusions:** Patients receiving NACT for advanced ovarian cancer are at high risk for the development of clinically detectable thromboembolic events. The highest rate of new VTE events was seen during induction of NACT, a phase of treatment traditionally without any prophylactic anticoagulation. Further research regarding the timing of thromboprophylaxis for this patient population is warranted. Research Sponsor: None.

Demographics and clinical features of all patients underwent neo-adjuvant chemotherapy (N=290).

	All patients (N=290)	
Age, years [Median (range)]	61.6	(31-92.6)
Stage		
IIIA	1	(0.3)
IIIB	4	(1.4)
IIIC	89	(29.7)
IV	197	(67.9)
Histology		
Serous	236	(81.4)
Mullerian	39	(13.4)
Clear Cell	4	(1.4)
Carcinosarcoma	4	(1.4)
Low grade serous	2	(0.7)
Endometrioid	1	(0.3)
Mixed	1	(0.3)
Other	3	(1.0)
Genetic testing		
Not Tested	75	(25.9)
Negative	170	(58.6)
Positive	38	(13.1)
BRCA1	22	(7.6)
BRCA2	16	(5.5)
VUS	7	(2.4)
NACT Indications		
Unresectable disease	233	(80.3)
Comorbidity	40	(13.8)
VTE	12	(4.1)
Other	5	(1.7)

Data are expressed as n (%) unless otherwise specified *NACT* neo-adjuvant chemotherapy *VUS*variant of uncertain significance

6074 Poster Session (Board #245), Fri, 8:00 AM-11:00 AM

Computerized features of spatial arrangement of tumor-infiltrating lymphocytes from H&E images predicts survival and response to checkpoint inhibitors in gynecologic cancers. *First Author: Sepideh Azarianpour Esfahani, Case Western Reserve University, Cleveland Heights, OH*

Background: Immune checkpoint inhibitors (ICI) have demonstrated success in solid tumors. In gynecologic cancers (GC), the response rate is still low (~10-15%) except in MSI-H endometrial cancer (~ 50%). Current biomarkers (e.g. PDL1 expression) have limited utility in identifying benefit from ICI in GC. In this work we evaluated the ability of computational measurements of spatial arrangement of tumor infiltrating lymphocytes (TIL) from H&E slide images in predicting overall survival (OS) and response to ICI in ovarian, cervical and endometrial cancers. **Methods:** The study included 151 patients, including 102 ovarian carcinomas treated with surgery and chemotherapy (D1) and another set (D2) of n=49 patients (n=14 ovarian, n=27 endometrial and n=8 cervical), treated with different ICI agents (Pembrolizumab, Nivolumab, Ipilimumab, Avelumab) in the second line setting. Progressors and non-progressors in D2 were classified according to clinical improvement and radiologic assessment by RECIST. A machine learning approach was employed to identify tumor regions on the diagnostic slides from D1 and D2 and then used to automatically identify TILs within the tumor regions. Subsequently machine learning was used to define TIL clusters based on TIL proximity, and graph network theory was used to capture measurements relating to spatial arrangement of TIL clusters. The multivariable Cox regression model (MCRM) was trained on n=51 patients from D1 to predict OS and then independently evaluated in predicting (1) OS on the hold-out n=51 patients in D1 and (2) response and progression-free survival (PFS) in D2. **Results:** Statistical analysis identified 7 prognostic features relating to interaction of TIL clusters with cancer nuclei. MCRM was prognostic of OS on the n=51 hold out patients in D1 (hazard ratio (HR)=2.06, 95% confidence interval [1.04- 4.07], p=0.008) and predictive of PFS in D2 (HR=2.24, CI=[1.13-4.44], p=0.03). The AUC for MCRM in predicting progression in D2 was 82%. **Conclusions:** Computerized features of spatial arrangement of TILs on H&E images were prognostic of OS and PFS and predicted response to ICI in three gynecological cancers. These findings need to be validated in larger, multi-site validation sets. Research Sponsor: U.S. National Institutes of Health.

	Multivariable analysis	
	HR	p
SpaTIL	2.24 [1.13-4.44]	0.03
Age (>65 vs. <65)	0.97 [0.48-1.96]	0.93
BMI (>30 vs. <30)	1.09 [0.52-2.28]	0.82
Grade (1,2 vs. 3)	1.20 [0.50-2.85]	0.68
Stage at initial diagnosis (1, 2 vs. others)	0.96 [0.43-2.11]	0.91

6075 Poster Session (Board #246), Fri, 8:00 AM-11:00 AM

Infiltration of tumor by T cells following treatment with DPX-Survivac and intermittent low dose cyclophosphamide (CPA) leads to clinical responses in advanced recurrent ovarian cancer (OvCa). *First Author: Oliver Dorigo, Stanford Cancer Institute, Stanford, CA*

Background: DPX-Survivac is a novel T-cell activating therapy designed to elicit an effective immune response against survivin expressing tumors. Its unique mechanism of action (MOA) facilitates active and sustained uptake of target peptides by APC at the injection site. APCs subsequently present the antigen in local lymph nodes generating survivin-specific T cells that traffic to distant tumor sites and elicit effective tumor cell death. DPX-Survivac is used in combination with intermittent low dose CPA which acts as an immunomodulator of T-cell responses. **Methods:** The study enrolled 22 patients with recurrent, advanced platinum-sensitive and -resistant ovarian cancer. Patients received 2 subcutaneous injections of DPX-Survivac 3 weeks apart and every 8 weeks thereafter, and intermittent low dose CPA for up to 1 year. Paired tumor biopsies were performed prior to treatment and on treatment. Primary endpoints were ORR, DCR and safety. Secondary endpoints include cell mediated immunity, immune cell infiltration in paired biopsy samples, DOR, TTP, OS and biomarker analyses. **Results:** Twenty-two patients were enrolled in the study. Three patients were discontinued prematurely due to early progression leaving 19 patients for response evaluation. The population is heavily pre-treated with a median of 3 lines of prior treatment [range 1 to 8]; 77.3% of patients are platinum-resistant. At the time of data cut-off, 3/19 patients (15.8%) achieved PR and one additional patient met PR on target lesions but had a newly detected lesion; 10/19 patients (52.6%) showed tumor regression on target lesions at > 1 scan. The median time on study (N=19) is 131 days [63 to ˚295]. Six patients are still on trial. The clinical responses and benefits observed with treatment are associated with an increase in systemic survivin-specific T cells and tumor immune-infiltration. Moreover, RNAseq analysis on paired tumor tissue revealed an enrichment in cytolytic T-cell signature. The most common AEs were grade 1-2 injection site reactions; 4 treatment-related SAEs were reported. **Conclusions:** DPX-Survivac and intermittent low dose CPA shows promising clinical activity in heavily pre-treated patients with recurrent OvCa. The preliminary results, supported by strong translational data, link the observed clinical benefits with the unique MOA of DPX-Survivac. These clinical results suggest that DPX-Survivac/CPA is an active regimen in OvCa and warrant testing in an expanded cohort of patients. Clinical trial information: NCT02785250. Research Sponsor: IMV Inc.

6076 Poster Session (Board #247), Fri, 8:00 AM-11:00 AM

Influence of BRCA pathogenic variants in the benefit of secondary cytoreductive surgery. *First Author: Felipe Leonardo Estati, AC Camargo Cancer Center, São Paulo, Brazil*

Background: Germline BRCA pathogenic variants are present in 15% to 25% of ovarian carcinoma patients. These tumors are more sensitive to platinum and PARP inhibitor therapy and have a better prognosis. Two retrospective studies with limited number of patients have shown conflicting results regarding the benefit of secondary cytoreductive surgery (SCS) in patients with BRCA mutations. Our aim was to evaluate the impact of SCS in recurrent ovarian cancer according to BRCA status. **Methods:** All patients with ovarian carcinoma with recurrent disease and who were tested for BRCA pathogenic variants treated at a tertiary Cancer Center in Brazil were included. Patients characteristics were compared between patients treated with SCS and not treated with SCS. Cox regression analysis was used to evaluate the impact of SCS on progression free survival (PFS) and the influence of BRCA pathogenic variants on the effect of SCS. **Results:** One hundred and forty patients were included, 49.6% were treated with SCS and chemotherapy and 50.4% treated with chemotherapy only. Patients treated with SCS were younger, presented better performance status, lower CA 125 and longer platinum free interval. After adjusting for relevant covariables SCS was associated with longer PFS (HR 0.53, 95%CI 0.29-0.97, p = 0.039). Germline BRCA pathogenic variants were found in 37 patients (26.4%). No patient was treated with PARP inhibitors. Among non-carriers of pathogenic variants in BRCA, SCS lead to a longer PFS (HR 0.48, 95%CI 0.28-0.81, p = 0.006) but among carriers there was no benefit of SCS (HR 0.84, 95%CI 0.30-2.34, p = 0.735). Test for interaction was not statistically significant (p = 0.359). **Conclusions:** Our study is the second to demonstrate no benefit of SCS among patients with BRCA pathogenic variants and not treated with PARP inhibitor. The only other study to show a benefit of SCS in this group of patients included a limited number of patients and all of them were treated with PARP inhibitors. BRCA germline status might influence the efficacy of SCS, and should be evaluated as a potential biomarker to be assessed together with clinical factors to better select patients for SCS. Research Sponsor: None.

6077 Poster Session (Board #248), Fri, 8:00 AM-11:00 AM

PFS by blinded independent central review (BICR) in the VELIA trial of veliparib (V) plus carboplatin/paclitaxel (CP) and as monotherapy in newly diagnosed patients (pts) with high-grade serous ovarian cancer (HGSC). *First Author: Carol Aghajanian, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: The phase III VELIA trial (NCT02470585) demonstrated statistically significant improvement in PFS per investigator (INV) for V added to CP and continued as maintenance (CPV-V) vs. CP alone in pts with newly diagnosed HGSC in the *BRCA* mutated (*BRCA*m), homologous recombination deficient (HRD), and whole populations. Here we present pre-specified analyses of PFS per BICR. **Methods:** Pts with Stage III-IV HGSC received V or Placebo (PL) with CP (6 cycles) and as maintenance (30 additional cycles). Primary analysis of PFS by INV compared CPV-V to CP alone in the *BRCA*m, HRD, and whole populations. Exploratory analyses of PFS in *BRCA* wildtype (wt) and non-HRD HGSC were performed. Radiologic tumor assessments were also prospectively submitted to an independent central reviewer for blinded assessment per RECIST v 1.1. PFS per BICR and rates of concordance between INV and BICR for determination of disease progression were analyzed. Safety data from the primary analysis were previously reported. **Results:** 1140 total pts were enrolled (CPV-V 382; CP 375). In the whole population, 26% of HGSCs were *BRCA*m and 55% were HRD. Concordance rates between INV and BICR were 68-85% by arm for each population. Analyses of PFS per BICR and per INV were consistent (Table). PFS was prolonged in the CPV-V vs. CP arm in all primary and exploratory populations assessed. **Conclusions:** Analyses of PFS per BICR supported the primary analysis of PFS per INV in the *BRCA*m, HRD, and whole populations, as well as exploratory *BRCA*wt and non-HRD populations. Median PFS per BICR was longer compared to PFS per INV assessments in all populations and in both arms. These findings support the reliability of PFS by INV in ovarian cancer trials. Alternate strategies like audits may be appropriate to support PFS by INV with less time and expense than full BICR. Clinical trial information: NCT02470585. Research Sponsor: AbbVie.

Median PFS per INV and BICR.

	mPFS INV (mo)		mPFS BICR (mo)	
	CPV-V	CP	CPV-V	CP
***BRCA*m**	34.7	22.0	Not reached	28.8
	0.44 [0.28, 0.68] <0.001*		0.44 [0.26, 0.73]	
HRD	31.9	20.5	34.7	22.7
	0.57 [0.43, 0.76] < 0.001		0.60 [0.43, 0.83]	
Whole	23.5	17.3	29.3	19.2
	0.68 [0.56, 0.83] < 0.001		0.64 [0.50, 0.81]	
***BRCA*wt (incl HRD and Non-HRD)**	18.2	15.1	23.6	17.1
	0.80 [0.64, 1.00]		0.73 [0.56, 0.96]	
Non-HRD	15.0	11.5	21.1	13.1
	0.81 [0.60, 1.09]		0.65 [0.45, 0.94]	

*HR [95% CI] and P values by log rank test.
Analyses stratified by residual disease and stage of disease for *BRCA*m, HRD & whole; unstratified for *BRCA*wt & Non-HRD. Whole population stratification incl *BRCA* status, paclitaxel schedule.

6078 Poster Session (Board #249), Fri, 8:00 AM-11:00 AM

Elucidating resistance mechanism to PARP inhibitors for the development of novel therapeutic approaches in high-grade serous ovarian cancer. *First Author: Hagen Kulbe, Charité Medizinische Universität Berlin, Berlin, Germany*

Background: PARP inhibitors (PARPi) have been established as a targeted therapeutic approach not only in patients with high-grade serous ovarian cancer (HGSOC) that have genetic loss of function of BRCA1/2-associated DNA repair. However, treatment efficacy varies and neither BRCA mutation, nor homolog recombination deficiency (HRD) status seem to be optimal predictors. Moreover, mechanisms of treatment resistance are poorly understood and novel approaches are urgently required. **Methods:** Here we created gene expression data of HGSOC patients (n = 52) before PARPi treatment to elucidate key signaling pathways of resistance to increase their efficacy in combinatorial therapeutic strategies. We performed a comprehensive bioinformatics analysis of the differentially expressed genes between the 25% extreme responders (n = 26; 13 each group), including gene set enrichment analysis (GSEA) and causal inference analysis with the CARNIVAL pipeline to elucidate the underlying molecular and regulatory mechanisms governing treatment efficacy and resistance. **Results:** In accordance with recent publications, we found higher levels of MYC activity in non-responders and deregulation of the Wnt/ß-catenin signaling pathway resulting in PARPi treatment resistance. The pathway enrichment analysis also revealed specific pathways especially PDGFR, FGFR, PI3K/mTOR and MAPK signaling pathway associated with resistant phenotype. Furthermore, we have identified key kinases, particularly JAK1/2 and SRC that might mediate resistance to PARP inhibition. In addition, differential gene expression analysis revealed folate receptor 1 (FOLR1) to be significantly higher expressed in non-responders (logFC = 2.66; $p < 0.0026$) with the potential as a serum-based biomarker not only for ovarian cancer, as it correlates closely with CA125, but also PARPi treatment efficacy. **Conclusions:** In conclusion, these findings define a network of pathways, that are crucial to mediate mechanism of PARPi resistance and identified key signaling kinases as therapeutic targets in ovarian cancer. Research Sponsor: Institutional research funds, Pharmaceutical/Biotech Company.

6079 Poster Session (Board #250), Fri, 8:00 AM-11:00 AM

Financial toxicity and patient-reported outcomes over time: A longitudinal study of women with recurrent ovarian cancer. *First Author: Larissa Meyer, The University of Texas - MD Anderson Cancer Center, Houston, TX*

Background: The chronic nature of treatment for ovarian cancer (OC) can place women at increased risk of financial toxicity (FT) from ongoing direct and indirect costs coupled with potential loss of income. We explored FT and its association with anxiety, depression, and quality of life over time in women with recurrent OC. **Methods:** Women with recurrent OC enrolled in a longitudinal study were given the following validated instruments at baseline and every 3 months: FACIT Comprehensive Score for Financial Toxicity (COST), GAD-7 (anxiety), CES-D (depression) and FACT-Ovary. Mixed models were performed on longitudinal data over 12 months of follow-up. Multivariable analysis of demographic data was performed. **Results:** 225 patients were divided into low FT (top 2 terciles, n = 152) and high FT (bottom tercile, n = 73,) by baseline COST scores. The median age was 59 (range 22.9-78.9). There were no significant differences between the groups in regards to marital status, number of people in household or education level. There were significant differences between the low and high financial toxicity groups in terms of median age (low FT = 61 yrs vs. high FT = 54 yrs, $p < 0.0001$); race (5.4% black in low FT vs. 15.1% in high FT, p = 0.04), number of children < 18 years in the home ((p = 0.02), employment status p(< 0.0001) and annual income p(< 0.0001). On multivariable analysis, only income and age remained significantly associated with FT. The mean baseline COST score in the low FT group was 34 vs. 16 in the high FT group. Interestingly, pts with low baseline FT had significant worsening of FT over the 12 month time period while those with high FT had slight improvement over time. Consistently, the high FT group had higher scores on screening measures for anxiety and depression, as well as lower overall quality of life which persisted over time. **Conclusions:** Financial toxicity is a measurable and clinically relevant patient reported outcome. The cohort of women with high FT demonstrated higher mean scores on screening measures for depression and anxiety as well as persistently lower quality of life. Targeted interventions to decrease financial toxicity may provide more global improvements in mental health and quality of life. Research Sponsor: AstraZeneca, U.S. National Institutes of Health.

6080 Poster Session (Board #251), Fri, 8:00 AM-11:00 AM

Effect on response to neoadjuvant chemotherapy in high-grade serous ovarian cancer by inhibiting the GAS6/AXL pathway and inducing homologous recombination deficiency. *First Author: Mary M Mullen, Washington University in St. Louis School of Medicine, St. Louis, MO*

Background: Less than 10% of patients with high grade serous ovarian cancer (HGSC) have a complete pathologic response to neoadjuvant chemotherapy. We aimed to identify a biomarker predictive of response to neoadjuvant chemotherapy and to determine if GAS6/AXL inhibition with AVB500 (AVB) could increase platinum response. **Methods:** AVB was supplied by Aravive Biologics. HGSC tumor samples were obtained pre- and post-neoadjuvant chemotherapy. GAS6 expression was measured by tissue immunohistochemistry (IHC) and serum ELISA. Four HGSC cell lines were used for all experiments. Immunofluorescent (IF) assays targeting γH2AX for DNA damage, RAD51, BRCA1, and BRCA2 for homologous recombination (HR) and 53BP1 for non-homologous end joining (NHEJ) were performed. Flow cytometry was used to evaluate RPA binding. DNA fiber assays were performed. In vitro clonogenic assays were done on chemoresistant ovarian tumor cells treated with carboplatin (carbo) +/- AVB and olaparib +/- AVB. Synergy assays were analyzed using Combenefit software. Mouse models were used to evaluate the combination of carboplatin + AVB and olaparib + AVB on tumor burden. **Results:** Patients with high pretreatment tumor GAS6 IHC expression ($>$ 85%) or serum GAS6 concentrations ($>$ 25ng/mL) were more likely to have a poor response to neoadjuvant chemotherapy than those with low GAS6 (P = 0.002). Additionally, high GAS6 concentration was associated with decreased overall survival (24.4 months versus undefined, P = 0.009). Carbo + AVB resulted in decreased clonogenic colonies compared to carbo alone ($p < 0.05$). In vivo tumor mouse models treated with chemotherapy + AVB had significantly less tumor burden than those treated with chemotherapy alone (50mg vs 357mg, P = 0.003). We identified an induction in HR deficiency by a decrease in RAD51, BRCA1, and BRCA2 foci and RPA binding in cells treated with carbo + AVB compared to carbo ($P < 0.05$). There was increase in γH2AX and 53BP1 foci as well as replication fork slowing in tumor cells treated with carboplatin + AVB ($P < 0.01$). We also AVB and carboplatin were synergistic. Olaparib + AVB resulted in decreased clonogenic colonies ($P < 0.05$) and decreased tumor burden in mouse models (76mg vs 171mg, P = 0.03) compared to olaparib alone. **Conclusions:** GAS6 is a potential biomarker predictive of poor response to neoadjuvant chemotherapy in HGSC. Inhibition of this GAS6/AXL pathway with AVB improves sensitivity to traditional neoadjuvant chemotherapy by inducing a homologous recombination deficiency. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

6081 Poster Session (Board #252), Fri, 8:00 AM-11:00 AM

Sacituzumab govitecan (SG) in patients (pts) with previously treated metastatic endometrial cancer (mEC): results from a phase I/II study. *First Author: Alessandro Santin, Yale University School of Medicine, New Haven, CT*

Background: Unselected pts with EC who progressed on prior chemotherapy have a poor prognosis with limited treatment options. SG is a novel antibody-drug conjugate that targets Trop-2, a cell surface glycoprotein highly expressed in many epithelial tumors. It is conjugated to deliver SN-38, the active metabolite of irinotecan, via a proprietary hydrolyzable linker. Preclinical studies show SG has activity against chemotherapy-resistant EC and significant bystander effect against EC with heterogenous Trop-2 expression (Perrone E. *Mol Oncol.* 2019). **Methods:** The phase I/II basket study (NCT01631552) evaluated pts unselected for Trop-2 with advanced solid tumors who received intravenous SG (days 1 and 8 of 21-day cycles), until progression or unacceptable toxicity. CT/MRI scans were obtained at 8-week intervals for response assessment by RECIST 1.1. We report results for mEC pts who progressed after $\geq$1 prior systemic therapy and were treated with SG 10 mg/kg. Endpoints include safety, objective response rate (ORR), clinical benefit rate (CBR), duration of response (DOR), progression-free survival (PFS), and overall survival (OS). **Results:** 18 mEC pts (all women; 17 white and 1 black; median age 69 years [range, 41–76]) had a median 3.5 (range 2–6) prior lines of therapy. All pts received prior treatment with platinum therapies. At a median follow-up of 12.7 months, the ORR (95% CI) was 22.2% (6.4–47.6), with 4 partial responses. CBR (95% CI) was 44.4% (21.5–69.2), with 8 of 18 pts having either an objective response or stable disease $\geq$6 months. The DOR of responders ranged from 9.1 to 26.6 months, with 2 of 4 responders having a duration of $\geq$18 months. Median PFS (95% CI) was 3.2 months (1.9–9.4), and median OS (95% CI) was 11.9 months (4.7–not calculable). Key grade $\geq$3 TRAEs in the overall basket study safety population (n=495) included neutropenia (28%), neutrophil count decrease (14%), anemia (10%), diarrhea (8%), fatigue (6%), and febrile neutropenia (5%). A similar safety profile was seen in the mEC cohort. **Conclusions:** Median OS in unselected pts with mEC who progressed on prior platinum therapy is ~10 months with an ORR of ~10%. SG monotherapy showed clinical activity in pts with relapsed/refractory mEC, consistent with previous preclinical findings, and support further clinical investigation (NCT04251416). The phase II TROPiCS-03 (NCT03964727) study in pts with metastatic solid tumors selected based on elevated Trop-2 expression by a validated IHC assay will also provide further insights. Clinical trial information: NCT01631552. Research Sponsor: Immunomedics, Inc.

6082 Poster Session (Board #253), Fri, 8:00 AM-11:00 AM

Mutation in homologous recombination to predict a better prognosis in endometrial cancer. *First Author: Luyang Zhao, Department of Gynecology and Obstetrics,Peking University People's Hospital, Beijing, China*

Background: Endometrial cancers have been categorized into four genomic classes by The Cancer Genome Atlas Research Network (TCGA) with comprehensive genomic analysis. However, TCGA molecular subtypes are hard to utilize in clinic as the expensive cost and a simply version of POLE, TP53 genes cannot fully differentiate the four subtypes. Therefore, more convenient and reliable biomarkers need to be identified for clinical practice. **Methods:** Whole-exome sequencing and RNA sequencing data for 515 patients with endometrial carcinomas were downloaded from TCGA. Mutations in 48 genes of homologous recombination repair (HR) signaling were defined as HR mutation. Associations between HR mutation and survival and RNA expression were analyzed.Gene set enrichment analysis (GSEA) were used to invesgate the gene signaling. **Results:** HR mutation was associated with a prolonged disease specific survival (DSS) (HR, 0.39; 95% CI, 0.22-0.71; P = 0.002), progression-free survival (PFS) (HR, 0.46; 95% CI, 0.31-0.68; $P < 0.001$) and overall survival (OS) (HR, 0.45; 95% CI, 0.28-0.72; P = 0.001) in endometrial cancers. HR mutation was related with clinical characteristics including histological types ($P < 0.05$). In the multivariable cox proportional hazards regression model including FIGO 2008, histology types, tumor grade and TCGA subtypes, TP53 mutation, POLE mutation, the association between HR mutation and PFS was still significant (HR, 0.48; 95% CI, 0.27-0.86; $P < 0.05$), which indicating the HR mutation is an independent prognostic factor for PFS. HR mutations were associated with a higher tumor mutation burden. GSEA suggested that HR mutation was involved with the increase of genes related to activated T cells, immune cytolytic activity, and IFN-γ release. In MSS endometrial cancers, *HR* mutation still showed a longer PFS (HR, 0.57; 95% CI, 0.34-0.98; P = 0.04), suggested HR mutation may help predict the effect of immunotherapy in MSS endometrial carcinoma. **Conclusions:** HR mutation was related with a favorable prognosis through increasing T cells signature. Identification of HR mutation by genomic profiling provides a potentially novel and convenient approach for endometrial cancer patients to predict the prognosis independent of TCGA four subtype classifications and provides an inspiration for screening patients who may benefit from ICBs in endometrial cancer in the future. Research Sponsor: None.

6083 Poster Session (Board #254), Fri, 8:00 AM-11:00 AM

Lenvatinib (LEN) plus pembrolizumab (PEMBRO) for early-line treatment of advanced/recurrent endometrial cancer (EC). *First Author: Vicky Makker, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: As part of an ongoing phase Ib/II study (NCT02501096) in patients (pts) with selected solid tumors, LEN (20 mg PO QD) + PEMBRO (200 mg IV Q3W) displayed substantial and durable antitumor activity in advanced EC. In previously treated EC that was not microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR; n=94 pts), the objective response rate (ORR) by independent imaging review (IIR) per RECIST 1.1 was 38.3% (95% CI 28.5–48.9). In this post hoc analysis, we assessed 2 subgroups of pts with previously treated, advanced, non MSI-H or dMMR EC who received LEN + PEMBRO in an early-treatment setting. **Methods:** Pts were examined in 2 subgroups: (1) Pts with only 1 prior line of cytotoxic therapy regardless of surgical stage or setting (adjuvant treatment for local-regional disease or treatment for metastatic disease); and (2) pts from subgroup 1 with local-regional disease at diagnosis who received only adjuvant cytotoxic therapy. There were no restrictions on prior hormonal or chemoradiation therapies in either subgroup. Tumor responses were assessed by IIR per RECIST 1.1. **Results:** Subgroup 1 included 63 pts and subgroup 2 had 21 pts. ORR (95% CI) was 41.3% (29.0–54.4) for subgroup 1 and 57.1% (34.0–78.2) for subgroup 2. Additional efficacy outcomes are summarized in the table. In subgroup 1, treatment-related adverse events (TRAEs) occurred in 62 (98%) pts (42 [67%] $\geq$ grade 3). TRAEs led to study-drug interruption of one or both drugs in 43 (68%) pts and dose reductions of LEN in 42 (67%) pts; 12 (19%) pts discontinued one or both drugs due to a TRAE. Serious TRAEs occurred in 18 (29%) pts and 2 (3%) pts died from a TRAE. The safety profile for subgroup 2 was generally similar to the profile for subgroup 1. **Conclusions:** The efficacy of LEN + PEMBRO for early-line treatment of advanced non MSI-H or dMMR EC appears promising. No new safety signals have emerged. A phase III study of LEN + PEMBRO vs paclitaxel + carboplatin for first-line treatment in advanced or recurrent EC is underway. Clinical trial information: NCT02501096. Research Sponsor: Eisai Inc., Woodcliff Lake, NJ, USA and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	Subgroup 1 (n=63)	Subgroup 2 (n=21)
ORR, n (%)	26 (41.3)	12 (57.1)
(95% CI)	29.0–54.4	34.0–78.2
Complete response	8 (12.7)	5 (23.8)
Partial response	18 (28.6)	7 (33.3)
Median duration of response, months (95% CI)	NE (6.2–NE)	NE (2.9–NE)
Median progression-free survival, months (95% CI)	7.5 (4.4–8.9)	8.3 (4.4–NE)
Median overall survival, months (95% CI)	18.3 (15.0–NE)	NE (13.2–NE)

NE, not estimable.

6084 Poster Session (Board #255), Fri, 8:00 AM-11:00 AM

Human epidermal growth factor 2 (HER2) in early stage uterine serous carcinoma: A multi-institutional cohort. *First Author: Britt Kristina Erickson, University of Minnesota, Minneapolis, MN*

Background: Uterine serous carcinoma (USC) is a rare and aggressive malignancy, accounting for 40% of all endometrial cancer deaths. Human Epidermal Growth Factor Receptor 2 (HER2) has emerged as an important prognostic and therapeutic target in USC. Given recent randomized trial results, HER2-directed therapy is now recommended in advanced-stage or recurrent, HER2-positive disease. The significance of tumoral HER2 expression in early-stage disease has not yet been established. **Methods:** In this IRB-approved, retrospective, multi-institutional cohort, women diagnosed with stage I USC from 2000-2018 were identified. Patient demographic, treatment, and survival data were collected. Immunohistochemistry (IHC) was performed for HER2 and scored 0-3+. Equivocal IHC results (2+) were further tested with in-situ hybridization (ISH) per the 2007 ASCO-CAP HER2 breast cancer guidelines. HER2 overexpression ("positive") was defined as 3+ IHC or ISH positive. Kaplan-Meier analyses and Cox-proportional hazards were used to compare survival between the cohorts. **Results:** In total, 173 patients with stage I USC were tested for HER2; 25% were HER2-positive, 77.4% had stage IA and 22.6% had stage IB disease. Adequate clinical follow up was available for 168 patients. There were no significant differences in age, race/ethnicity, body mass index, surgical management, sub-stage, tumor size, adjuvant therapy, or follow-up duration between the HER2-positive and negative cohorts. On univarite analysis, presence of lymph-vascular space invasion was correlated with HER2-positive tumors (p=0.003). After a median follow-up of 50 months, there were 41 (24.4%) recurrences. Significantly more recurrences were observed in the HER2-positive cohort (47.6% vs. 16.7%, $p<0.001$). HER2 overexpression was also associated with poorer progression-free (PFS) and overall survival (OS) ($p<0.001$ and p=0.012). After adjusting for prognostic factors including sub-stage and adjuvant treatment, those with HER2-positive tumors experienced inferior PFS (aHR 3.67, 95%CI 1.92-6.98; $p<0.001$) and OS (aHR 2.03, 95%CI 1.03-4.01; p=0.042) compared to HER2-negative tumors. **Conclusions:** Uterine serous carcinoma is a poor prognostic tumor, even in patients with early-stage disease. Given its significant association with worse survival outcomes, tumoral HER2 overexpression appears to be a prognostic biomarker in women with stage I disease. These data provide rationale for clinical trials with HER2-directed therapy in early-stage uterine serous carcinoma. Research Sponsor: U.S. National Institutes of Health.

6085 Poster Session (Board #256), Fri, 8:00 AM-11:00 AM

An open-label, multicenter, phase Ib/II study of rebastinib in combination with paclitaxel in a dose-expansion cohort to assess safety and preliminary efficacy in patients with advanced or metastatic endometrial cancer. *First Author: Filip Janku, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, MD Anderson Cancer Center, Houston, TX*

Background: Rebastinib is a switch control inhibitor targeting tunica interna endothelial cell kinase (TIE2). TIE2 is primarily expressed in endothelial cells playing a role in angiogenesis. TIE2 is also expressed in a subset of macrophages with pro-metastatic and immunosuppressive properties and linked to chemoresistance. This study is a 2-part open-label, phase Ib/II, multicenter study of rebastinib orally administered, in combination with paclitaxel. In Part 1, we observed encouraging antitumor activity of rebastinib with 5 PRs in 24 patients (pts) at 50 mg BID and 3 PRs in 19 pts at 100 mg BID from a heavily pretreated heterogeneous patient population. Here we summarize preliminary results from the endometrial cancer (EC) cohort of Part 2. **Methods:** Part 2 of this study has four disease-specific cohorts (TNBC, inflammatory breast cancer, ovarian cancer and EC). Pts were evaluated for safety (CTCAE v5.0) and efficacy (RECIST v1.1). According to the Simon 2-stage design of this study, for each cohort, 15 additional pts will be enrolled if more than 4 PRs are observed. **Results:** As of Jan 21, 2020, 19 EC pts were enrolled with a median age of 66 years. All pts received at least one prior line of paclitaxel and 12 (63%) pts received >3 prior anti-cancer therapies. Sixteen pts were treated with rebastinib starting dose 100 mg BID (reduced to 50 mg BID due to a higher frequency of muscular weakness) and 3 pts with 50 mg BID, in combination with 80 mg/m^2 weekly paclitaxel with a median duration of treatment 85 days (6, 225). In 15 evaluable pts, there were 5 PRs (4 confirmed) and 6 $SD_{8\ weeks}$ for an ORR of 33% and clinical benefit rate of 73%. Treatment-emergent AEs (>20%) were mostly ≤ grade 2: constipation, fatigue (each n=9); alopecia, peripheral edema (each n=8); dysgeusia, peripheral sensory neuropathy, arthralgia (each n=6); diarrhea, hypomagnesaemia, vomiting, dry mouth (each n=5); anemia, decreased appetite, dyspnea, nausea, and muscular weakness (each n=4). Serious AEs possibly related or related to rebastinib included muscular weakness (n=2, at 100 mg BID), head discomfort (n=1) and increase troponin (n=1) which resolved after dose interruption. **Conclusions:** Preliminary activity of rebastinib in combination with paclitaxel was encouraging in heavily pretreated EC pts, all of whom received prior paclitaxel. The safety profile of rebastinib at 50 mg BID was generally well tolerated. The EC cohort is enrolling at 50 mg BID in stage 2 of the study. Clinical trial information: NCT03601897. Research Sponsor: Deciphera Pharmaceuticals, Inc.

6086 Poster Session (Board #257), Fri, 8:00 AM-11:00 AM

Clinical outcomes of MSI-high (MSI-H) versus stable (MSS) endometrial carcinoma (EC) after front-line platinum chemotherapy and subsequent matched therapy. *First Author: Natalie Ngoi, Department of Haematology-Oncology, National University Cancer Institute, Singapore, Singapore*

Background: Precision oncology approaches in EC patients (pts) are evolving with emerging targeted therapy. We reviewed the effect of genomic findings on treatment choice and outcome in an Asian EC cohort. **Methods:** Recurrent or metastatic ECs were prospectively profiled with next-generation sequencing (NGS) and relevant immunohistochemistry. Clinical data were collected to assess outcomes. **Results:** Between 12/2014 to 12/2019, 51 Asian EC pts of endometrioid (26/51), serous (7/51), carcinosarcoma (4/51), clear cell (4/51) and mixed (10/51) histology were enrolled. 35/51(69%) of tumors were high grade. The median age at diagnosis was 56 (range 37-77), and the median lines of treatment received was 3 (range 1-8). 45/51(88%) of pts had successful NGS profiling, 31/45(69%) using FoundationOne CDx, and 14/45 (31%) on an in-house platform. Frequent mutations (>20%) occurred in *PTEN* (60%), *PIK3CA* (49%),*TP53* (46%), *ARID1A* (27%), *CTNNB1* (24%) and *KRAS* (22%). There were 12/51(24%) MSI-H, 25/51(49%) MSS, and 14/51(27%) MSI-unknown tumors. The 6 mth progression free survival (PFS) rate for MSS versus MSI-H pts treated with front-line carboplatin+paclitaxel (CP) was 83% versus 50% (RR 1.67, fisher's exact 2-sided p=0.09), with a shorter median PFS after 1st line CP for MSI-H versus MSS pts (median 5.2 mth vs. 8.3 mth, not sig). Upon progression, 29/51(57%) of pts were matched to therapy based on tumor profiles. Of these, 7/29(24%), 13/29(45%) and 9/29(31%) matched to anti-PD1/PD-L1, endocrine therapy and other targeted therapy, respectively. Among 7 MSI-H pts matched to anti-PD1/PD-L1 therapy, median PFS was 14.6 mth (95% CI 0.4-29), and objective response rate was 57%(4/7). In subsequent-line, matching to endocrine therapy (HR 4.3 95% CI 0.95-19.0, p=0.06) or other targeted therapy (HR 5.1, 95% CI 1.1-24.5, p=0.04) was associated with worse PFS compared to anti-PD1/PD-L1 therapy. Despite a short median PFS after front-line CP, median overall survival (OS) was not reached for MSI-H pts, compared to 38 mth (95% CI 30.7-46.0) for MSS and MSI-unknown pts. **Conclusions:** MSI-H EC pts appear to have shorter PFS to front-line CP chemotherapy compared with MSS pts, but may derive durable responses from immunotherapy in subsequent-line therapy. Early use of immunotherapy in advanced MSI-H EC pts should be considered. Further optimisation of therapy is urgently needed in advanced MSS EC. Research Sponsor: National Medical Research Council Singapore, NMRC/CSA-INV-0016/2017.

6087 Poster Session (Board #258), Fri, 8:00 AM-11:00 AM

Randomized phase II study of sapanisertib (SAP) + paclitaxel (PAC) versus PAC alone in patients (pts) with advanced, recurrent, or persistent endometrial cancer. *First Author: Giovanni Scambia, Fondazione Policlinico Universitario A. Gemelli IRCCS Roma, Università Cattolica del Sacro Cuore, Rome, Italy*

Background: SAP (TAK-228, MLN0128) is a selective dual inhibitor of mammalian target of rapamycin complexes 1 and 2. In endometrial tumor xenograft models, SAP+PAC exhibited stronger antitumor efficacy than PAC alone. **Methods:** Female pts with histologic/cytologic diagnosis of endometrial cancer were randomized to receive SAP 4 mg by mouth (days [d] 2–4, 9–11, 16–18, 23–25) plus PAC 80 mg/m^2 intravenously (d 1, 8, 15), or PAC alone, in 28-day cycles until unacceptable toxicity or disease progression. Randomization was stratified by histologic subtype, lines of prior chemotherapy (1 vs. 2), and prior taxane therapy. The primary endpoint was progression-free survival (PFS); secondary endpoints included overall survival (OS), overall response rate (ORR), clinical benefit rate (CBR; ORR + stable disease), and safety. Additional treatment arms of SAP alone (weekly dosing) and SAP+TAK-117 were closed after futility analyses. **Results:** 180 pts were randomized to SAP+PAC (n=90) or PAC (n=90); 86 and 87 pts received SAP+PAC and PAC, respectively; 3 pts from each arm were ongoing on treatment at data cut (30 July 2019). Baseline characteristics were balanced between arms. After a median follow-up of 17.2 vs. 14.4 mos with SAP+PAC vs. PAC, median PFS was 5.6 mos vs. 3.7 mos (hazard ratio [HR] 0.82; 95% CI 0.58–1.15). In pts with endometrioid histology (n=116), median PFS was 5.7 mos with SAP+PAC vs 3.3 mos with PAC (HR 0.66; 95% CI 0.43–1.03). In pts with nonendometrioid histology (n=64), median PFS was 3.6 mos with SAP+PAC vs. 5.4 mos with PAC (HR 1.09; 95% CI 0.62–1.90). Median OS was 13.7 mos with SAP+PAC vs. 14.6 mos with PAC (HR 1.01; 95% CI 0.67–1.53). Confirmed ORR was 24% with SAP+PAC vs. 18% with PAC (endometrioid, 23% vs. 16%; nonendometrioid, 28% vs. 22%); CBR was 80% vs. 58% (endometrioid, 84% vs. 55%; nonendometrioid, 72% vs. 63%). Median number of cycles received was 5 (range 1–23) with SAP+PAC and 4 (range 1–37) with PAC. Rates of grade ≥3 treatment-emergent adverse events (TEAEs) were 90% with SAP+PAC vs. 54% with PAC; the most common included anemia (21% vs.12%), neutropenia (12% vs. 3%), fatigue (12% vs. 5%), hypophosphatemia (12% vs. 1%), and pulmonary embolism (11% vs. 3%). **Conclusions:** Median PFS was longer with SAP+PAC vs. PAC in pts with endometrial cancer but did not reach statistical significance. PFS was particularly longer in the endometrioid subtype but again was not significant, and further studies are warranted. Incidence of grade ≥3 TEAEs was higher with SAP+PAC vs. PAC, but SAP+PAC toxicity was manageable, with no new safety signals. Clinical trial information: NCT02725268. Research Sponsor: Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

6088 Poster Session (Board #259), Fri, 8:00 AM-11:00 AM

Preoperative chemotherapy for advanced endometrial cancer-registry analysis of outcomes. *First Author: Samer Salamekh, The University of Texas Southwestern Medical Center, Dallas, TX*

Background: Hysterectomy followed by risk-adjusted adjuvant treatment is the standard of care for staging and treatment of locally advanced endometrial cancer. Up-front surgery is difficult in some locally advanced cases with extensive local invasion since negative margins may not be achievable. Preoperative systemic treatment may be used to shrink the tumor and facilitate resection, echoing the experience from ovarian cancer. There is limited data for this paradigm in endometrial cancer. **Methods:** The National Cancer Database (NCDB) was queried for cases with FIGO stage III/IV endometrial cancer (serous, clear cell, or endometrial histology) who underwent surgery and had known chemotherapy/radiation sequencing. Those who received pre-operative chemotherapy +/- post-operative chemotherapy (PreCT) were compared to those who received post-operative chemotherapy alone (PostCT). PreCT cases were considered to be initially borderline resectable or unresectable. Downstaging was determined by comparing clinical and pathologic T-stage. Univariable (UV) and multivariable (MV) analyses were performed, with statistically significant values reported. **Results:** 12,310 cases in PostCT and 1,059 cases in PreCT were included in the analysis. Pre-CT cases were more likely to have higher AJCC T-stage, clinically positive nodes, serous histology, higher grade, and positive surgical margins (28% compared to 16%). Overall survival (OS) was lower for PreCT compared to PostCT (HR = 2.18 UV; HR = 1.87 MV). 20% of patients who received PreCT were down-staged compared to 2% in PostCT group. Patients who were downstaged with PreCT were more likely to achieve negative margins (OR 0.36 UV) and had improved OS compared to those whose stage did not change (HR = 0.61 UV; HR = 0.37 MV). Positive margins portended worse OS for both PreCT (HR = 1.93 UV) and PostCT (HR = 2.63 UV). Negative margins in PreCT had improved OS compared to positive margins in PostCT (HR = 1.2 UV; 2.67 MV). Post-operative radiation benefited both PreCT (HR = 0.45 UV; HR = 0.34 MV) and PostCT groups (HR = 0.48 UV; HR 0.64 MV). **Conclusions:** Preoperative chemotherapy increased the number of patients who were downstaged and those who were downstaged were more likely to achieve a negative margin. Patients who achieved negative margins in PreCT had improved OS compared to those with positive margins in PostCT. Adjuvant radiation further improved OS in both cohorts. Pre-operative chemotherapy can be considered for patients with unresectable/borderline resectable locally advanced endometrial cancer. Research Sponsor: None.

6089 Poster Session (Board #260), Fri, 8:00 AM-11:00 AM

Uterine cancer histology and stage at presentation in black and white women: A cohort study of 488,000 patients. *First Author: Mary Kathryn Abel, UCSF School of Medicine and Department of Surgery, San Francisco, CA*

Background: Although mortality among black women diagnosed with uterine cancer is higher than in white women, the reason for this difference is not completely understood. We proposed to investigate the differences in the incidence and presentation of uterine cancer histology among black women compared to white women. **Methods:** Data were obtained from the United States Cancer Statistics (USCS) and the National Cancer Database (NCDB) between 2004 and 2016. Chi-squared tests were used for statistical analyses. **Results:** Of 488,811 patients with uterine cancer, 411,904 (84.3%) were white and 51,093 (10.5%) were black. Based on USCS data, the incidence of endometrioid carcinoma in white women was 19.63 (per 100,000 per year) compared to 12.53 in black women. However, the incidence of high-risk histologies was higher in black women, particularly for serous tumors (3.32 vs. 1.29), clear cell tumors (0.59 vs. 0.31), carcinosarcoma (2.88 vs. 1.05), and leiomyosarcoma (1.02 vs. 0.48). Using the NCDB database, we evaluated the proportion of these histologies based on race. Compared to white women, black women have a higher proportion of serous (14.2% vs. 5.6%), clear cell (2.4% vs. 1.3%), carcinosarcoma (12.3% vs. 4.5%), and leiomyosarcoma (4.3% vs. 1.7%). black women were less likely to have endometrioid (52.7% vs. 75.9%) and mucinous (0.4% vs. 0.8%) tumors. In addition, black women were more likely to have stage III or IV disease at presentation when all histological subtypes were combined (22.8% vs. 17.7%). However, of those with endometrioid and grade 1 tumors, black women did not have more advanced stage at presentation compared to white women (3.8% vs. 4.7%). **Conclusions:** Compared to white women, black women are more likely to be diagnosed with serous, clear cell, carcinosarcoma, and leiomyosarcomas at a more advanced stage upon presentation, but they are less likely to have endometrioid tumors. More research is needed to understand why this disparity exists. Research Sponsor: None.

6090 Poster Session (Board #261), Fri, 8:00 AM-11:00 AM

Evaluation of treatment patterns and prognosis in correlation with age in patients with vulvar cancer: A subset analysis of the AGO-CaRE-1 study. *First Author: Katharina Prieske, Department of Gynecology and Gynecologic Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*

Background: Despite an increasing incidence with simultaneous decreasing age of onset, the impact of age on prognosis and treatment patterns in primary squamous cell vulvar cancer (VSCC) has not extensively been studied yet. **Methods:** This is a subgroup analysis of the AGO-CaRE-1 study. Patients (pts) with VSCC (FIGO stage ≥1B), treated at 29 cancer centers in Germany from 1998-2008, were included in a centralized database (n = 1618). In this subgroup analysis pts were analyzed according to age (< 50yrs (n = 220), 50–69yrs (n = 506), ≥70yrs (n = 521)) with regard to treatment patterns and prognosis. Only pts with documented age, surgical groin staging and known nodal status were included (n = 1247). Median follow-up was 27.5 months. **Results:** At first diagnosis, women ≥70yrs presented with more advanced tumor stages (< 0.001), larger tumor diameter (< 0.001), poorer ECOG status (< 0.001), higher tumor grading (0.048), as well as a higher rate of nodal involvement (< 0.001). Older women ≥70yrs showed more commonly HPV negative tumors compared to the other age groups (54% vs. 36.5% in < 50yrs vs. 47.9% in 50-69yrs, p = 0.03). Disease recurrence occurred significantly more often in elderly women (48% vs. 21% in < 50yrs vs. 37.4% in 50-69yrs, p = 0.001). Particularly isolated vulvar recurrence was more frequent in the elderly in comparison to the younger groups (18.2% vs. 15.2% in 50-69yrs vs. 12.7% in < 50yrs, p = 0.001). Age was an independent prognostic factor for disease-free survival (DFS) (HR: 1.7, 95%CI: 1.24-2.46, p = 0.001) with 2-year DFS being 81.1% (< 50yrs), 65.8% (50–69yrs), and 59.3% (≥70yrs), respectively. Elderly women (age group ≥70) had a 221% higher risk for death or recurrence, compared to the youngest group (HR: 3.21, p < 0.001). In a multivariate analysis ECOG, tumor stage, grading, and receipt of (chemo)radiation were further independent prognostic factors for recurrence. **Conclusions:** Older women with VSCC present with advanced tumor stages at first diagnosis and have an increased risk of recurrence as well as a decreased 2-year PFS in comparison to younger pts groups. Potential reasons for delayed time of diagnosis could be self-awareness and/or more aggressive tumor biology due to HPV negative disease. Research Sponsor: None.

6091 Poster Session (Board #262), Fri, 8:00 AM-11:00 AM

Combination immunotherapy with ipilimumab and nivolumab in patients with rare gynaecological malignancies. *First Author: Oliver Klein, Medical Oncology Unit, Austin Health, Heidelberg, Australia*

Background: Up to 50% of gynecological cancers are considered rare. The outcome of these patients (pts) is poor given a lack of scientific and clinical knowledge. Immunotherapy using single agent anti- PD-1/PD-L1 treatment (tx) has shown only modest activity in patients with common gynecological malignancies, such as high grade serous ovarian cancer (ca) and microsatellite stable endometrial ca. Combined CTLA-4/PD-1 blockade using ipilimumab (ipi) and nivolumab (nivo) has demonstrated superior efficacy compared to single agent anti-PD-1 therapy in pts with advanced melanoma and renal cell ca. To date, no trials have been undertaken with ipi/nivo in patients with rare gynecological malignancies. **Methods:** 41 pts with advanced rare gynecological malignancies were enrolled into the CA209-538 trial. Pts received nivo 3mg/kg and ipi 1mg/kg q 3 weekly for four doses, followed by nivo 3mg/kg q 2 weekly. Tx continued for up to 96 weeks, or until disease progression or the development of unacceptable toxicity. Response (RECIST 1.1) was assessed every 12 weeks. The primary endpoint was clinical benefit rate (CBR = CR + PR + SD). Exploratory endpoints include correlation of efficacy with biomarkers (incl PD-L1/TMB). **Results:** Pts with 10 rare tumor types were enrolled (Table). 39/41 pts have received prior therapy (1-7 lines). Objective responses were observed in 11 pts (27%) including pts with vaginal SCC, ovarian clear cell and low grade serous ca, ovarian and uterine carcinosarcoma, uterine clear cell, uterine serous ca and leiomyosarcoma. A further 9 pts had SD as their best radiological response resulting in a CBR of 49%. The median duration of response had not been reached (range 3.5 – 25+ months) with seven responses being ongoing. 63% of pts experienced an immune related adverse event (irAEs) with 4 pts developing Grade 3/4 irAEs. **Conclusions:** Ipi/Nivo tx demonstrates efficacy in a range of different rare gynecological cancers with a significant number of durable responses being observed. Tumor agnostic biomarkers are required to assist with better patient selection. Clinical trial information: NCT02923934. Research Sponsor: Australian Federal Department of Health.

Ovarian carcinosarcoma	5
Low grade serous ovarian ca	4
Ovarian clear cell ca	5
Ovarian granulosa cell tumour	2
Ovarian Sertoli-Leydig cell tumour	2
Uterine serous ca	8
Uterine clear cell	2
Uterine carcinosarcoma	4
Uterine leiomyosarcoma	4
Vulva/Vaginal SCC	5

6092 Poster Session (Board #263), Fri, 8:00 AM-11:00 AM

Efficacy and safety of laterally extended endopelvic resection for the pelvic side wall gynecologic tumors: A four-year prospective cohort study with historical comparison. *First Author: Haerin Paik, Seoul National University Hospital, Seoul, South Korea*

Background: Although laterally extended endopelvic resection (LEER) has been introduced to control the pelvic sidewall tumors, there is a lack of evidence about its efficacy and safety despite high skillful procedure, compared with the other treatments. Thus, we performed a prospective cohort study with historical comparison for four years. **Methods:** One gynecologic oncologist performed LEER consecutively for patients with the pelvic sidewall tumors between March 2014 and July 2018. We compared clinicopathologic characteristics and survival between patients who received primary LEER and with those treated with other treatments. **Results:** We enrolled 37 patients treated with LEER. Among them, 22 (59.5%) and 15 (40.5%) had recurrent and primary disease. Among perioperative outcomes, there was more estimated blood loss, and hospitalization was longer in recurrent disease and previous surgery ($p < 0.05$). In recurrent disease, previous progression-free survival < 8 months was related to poor recurrence-free survival after LEER (median, 5.4 vs. 10.2 months; $p < 0.05$). When LEER was applied for the first recurrence of cervical cancer, recurrence-free survival and overall survival after treatment seemed to be longer in LEER (n = 9) than in palliative chemotherapy (n = 27) without statistical significance (median, 12.2 vs. 4.7 months and 23.2 vs. 12.4 months; $p = 0.13$ and $p = 0.63$). In 15 patients with primary locally advanced cervical cancer, LEER after partial response to neoadjuvant chemotherapy showed longer progression-free survival than LEER after stable or progressive disease to neoadjuvant chemotherapy and primary radiotherapy ($p = 0.012$). After LEER, grade 3 and 4 complications developed in 15 (23.1%) and 2 (3.1%) patients. **Conclusions:** Compared with palliative chemotherapy, LEER followed by palliative chemotherapy may improve progression-free survival in patients with recurrent cervical cancer located in the pelvic sidewall. If possible, it is more effective to apply LEER without preceding palliative chemotherapy for recurrent cervical cancer located in the pelvic sidewall. Research Sponsor: None.

6093 Poster Session (Board #264), Fri, 8:00 AM-11:00 AM

Genomic and transcriptomic profiles of gynecologic neuroendocrine carcinoma are distinct from pulmonary neuroendocrine small cell carcinoma. *First Author: Haider Mahdi, Cleveland Clinic, Cleveland, OH*

Background: High-grade neuroendocrine carcinoma (NEC) of the cervix and other gynecologic origins are rare and aggressive cancers that unfortunately affect young women with high mortality. Treatment recommendations are often extrapolated from their counterpart, small cell carcinoma of the lung (SCLC). In the present study, we have performed comprehensive genomic and transcriptomic analyses in a cohort of patients with NEC of the cervix and other gynecologic origins and compared them to SCLC. **Methods:** We have identified 27 patients diagnosed with NEC of gynecologic origin from 1998-2019. Of them, we were able to obtain archival tissue from 14 patients (17 samples), including seven cervical NEC, three ovarian NEC, and two endometrial NEC. Two ovarian and one cervical patient have recurrent tumors. Whole exome sequencing (WES) and RNA-seq were successfully performed in 14 and 13 samples, respectively. BWA-MEM was used for mapping (hg38), and GATK Haplotype Caller was used for WES analysis. Ensemble-VEP was used for variant annotation, and SIFT and PolyPhen-2 were used for pathogenic prediction of missense mutations. Stranded pair-end RNA-seq data were analyzed using STAR and DESeq2. SCLC data from cBioPortal and EBI (accession number EGAS00001000334) were used to compare mutation and transcriptomic profiles. **Results:** We found that TP53 is not mutated in our cohort, and RB1 is mutated only in 1 (7%) tumor. TP53 and RB1 are the most frequently mutated genes in small cell lung carcinoma. However, LRP1B, the third most mutated gene in SCLC was also mutated in 4 (29%) tumors. We observed that WNT, RTK-RAS, NOTCH, and MYC are among the top mutated pathways in our cohort. Among the top 20 mutated genes, only four genes, MUC4, KMT2C, MAP3K1, and HLA-A, were common in cervical, ovarian, and endometrial tumors suggesting a high diversity within the NEC of gynecologic origin. Our RNA-seq analysis revealed a distinct transcriptional signature when compared to SCLC, especially the expression pattern of SCLC molecular subtypes defining ASCL1, NEUROD1, POU3F2, and YAP1 genes. Surprisingly, we observed a high expression of the YAP1 gene in all of the 13 tumors. However, the YAP1+ subtype represents a minority in SCLC and known to predict chemotherapy resistance and lower survival. **Conclusions:** Our results suggest a unique mutational profile and transcriptional signature that are distinct compared to SCLC tumors. Therefore, there is an urgent need to re-evaluate the therapeutic options and targets for NEC of gynecologic origin. Research Sponsor: None.

TPS6094 Poster Session (Board #265), Fri, 8:00 AM-11:00 AM

A randomized phase III trial of adjuvant chemotherapy versus concurrent chemoradiotherapy (CCRT) for postoperative cervical cancer: Japanese Gynecologic Oncology Group study (JGOG1082). *First Author: Akiko Furusawa, Department of Gynecology, Tokyo Metropolitan Cancer and Infectious Disease Center Komagome Hospital, Tokyo, Japan*

Background: Cervical cancer is one of the common gynecologic cancer and the incidence of invasive cervical cancer has increased over the past few decades, particularly in younger women. The standard treatment for stage IB to IIB cervical cancer is a radical hysterectomy. In Japan, more than 80% of institutions, radical hysterectomy is chosen as the primary treatment for patients with stage IB1 and IIA1 cervical cancer. Patients with high-risk factors would be recommend adjuvant concurrent chemoradiotherapy (CCRT). However, adjuvant CCRT might not reduce distant metastasis and might cause of severe gastrointestinal and urinal toxicity. To avoid those adverse events of adjuvant CCRT, many Japanese gynecologic oncologists perform chemotherapy as adjuvant therapy. In the first multi-institutional phase II trial conducted in stage IB-IIA cervical cancer with pelvic lymph node metastasis (JGOG1067), we found a 5-years disease free-survival rate of 86.5%, suggesting the adjuvant chemotherapy had promising efficacy and would be feasible for a long time. No prospective study reported that adjuvant chemotherapy would improve overall survival in patients with the high-risk cervical cancer. **Methods:** High risk stage IB-IIB cervical cancer patients who underwent radical hysterectomy are eligible for the study. Patients with high risk are defined as those with pelvic lymph-node metastasis and/or parametrial invasion. Patents with SCC, adenocarcinoma, adenosquamous cell carcinoma are eligible for the study. After providing informed consent, patients are randomized on a 1:1 basis to receive CCRT or chemotherapy. Randomization is stratified by the faculty, FIGO stage, and pathological subtype (SCC or non-SCC). Treatment have to be started within 6 weeks after surgery. CCRT group is given whole pelvis irradiation 50.4Gy and cisplatin ($40mg/m^2$/week). Chemotherapy group is given paclitaxel ($175mg/m^2$) plus cisplatin ($50mg/m^2$) or paclitaxel ($175mg/m^2$) plus carboplatin(AUC of 6). The primary endpoint is overall survival (OS). Secondary endpoints are disease free survival (DFS), adverse events and QOL. This study began in November 2019 and a total of 290 patients will be accrued within 5 years. The study is coordinated by of the JGOG cervical cancer committee. Clinical trial information: 041190042. Research Sponsor: None.

TPS6095 Poster Session (Board #266), Fri, 8:00 AM-11:00 AM

Phase Ib/II trial of tisotumab vedotin (TV) ± bevacizumab (BEV), pembrolizumab (PEM), or carboplatin (CBP) in recurrent or metastatic cervical cancer (innovaTV 205/ENGOT-cx8/GOG-3024). *First Author: Ignace Vergote, Belgium and Luxembourg Gynaecological Oncology Group, University of Leuven, Leuven Cancer Institute, Leuven, Belgium*

Background: Patients (pts) with recurrent/metastatic cervical cancer (r/mCC) receive paclitaxel/platinum or paclitaxel/topotecan ± BEV as first-line standard-of-care therapy. Tissue factor (TF) expression has been associated with poor prognosis in solid tumors, and TF is highly expressed in r/mCC. TV is an investigational antibody-drug conjugate composed of a fully human, TF-directed monoclonal antibody covalently attached to the microtubule-disrupting agent monomethyl auristatin E (MMAE) via a protease-cleavable linker. Upon internalization, MMAE is released resulting in cell cycle arrest and apoptotic cell death. In pts with previously treated r/mCC, TV monotherapy (IV 2.0 mg/kg Q3W) demonstrated a manageable safety profile and encouraging antitumor activity (investigator-assessed confirmed ORR, 24%; median DOR, 4.2 mo) [Hong DS et al. *Clin Cancer Res.* 2019. doi: 10.1158/1078-0432.CCR-19-2962]. The preliminary safety and efficacy data for TV monotherapy suggest a positive benefit/risk profile and warrant further investigation of TV in combination with therapies commonly administered to pts with r/mCC. The global, open-label, phase Ib/II trial innovaTV 205/ENGOT-cx8/GOG-3024 (NCT03786081) evaluates the safety and antitumor activity of TV monotherapy and TV in combination with BEV, PEM, or CBP in pts with untreated or previously treated r/mCC. This abstract presents the new TV monotherapy weekly dosing schedule. Results from this study will inform the further clinical development of TV in the treatment of r/mCC. **Methods:** Approximately 170 adult pts with recurrent or stage IVB squamous, adenosquamous, or adenocarcinoma of the cervix; measurable disease; and ECOG PS 0-1 will be enrolled. The phase I part of the study will consist of 3 dose-escalation arms for identification of the recommended phase II dose (RP2D) of TV administered Q3W with BEV, PEM, or CBP. In this part, previously treated pts will receive escalating doses of TV (IV Q3W) in combination with escalating doses of BEV (IV Q3W), a fixed dose of PEM (IV Q3W), or a fixed dose of CBP (IV Q3W). The phase II part will include 4 expansion arms. In this phase, pts who have not received prior systemic therapy for r/mCC will receive 1) TV RP2D + PEM or 2) TV RP2D + CBP; pts who received 1-2 prior treatments for r/mCC will receive 3) TV RP2D + PEM or 4) TV monotherapy with weekly dosing (IV 3Q4W). The primary endpoint of phase II is ORR by RECIST v1.1. Secondary endpoints include DOR, time to response, PFS, OS, and safety. Clinical trial information: NCT03786081. Research Sponsor: Genmab A/S.

TPS6096 **Poster Session (Board #267), Fri, 8:00 AM-11:00 AM**

ENGOT-cx11/KEYNOTE-A18: A phase III, randomized, double-blind study of pembrolizumab with chemoradiotherapy in patients with high-risk locally advanced cervical cancer. *First Author: Domenica Lorusso, Fondazione IRCCS, Foundation Policlinico Universitario Agostino Gemelli IRCCS, Istituto Nazionale dei Tumori, Milan, Italy*

Background: High-risk locally advanced cervical cancer has a poor prognosis, and more than half of patients recur in 2 y. External beam radiotherapy (EBRT) with concurrent chemotherapy followed by brachytherapy is the standard of care for locally advanced cervical cancer. The immunostimulatory activity of the PD-1 inhibitor pembrolizumab (pembro) may be enhanced by concurrent chemoradiotherapy (CRT). After the KEYNOTE-158 study, in which pembro showed durable antitumor activity, pembro monotherapy was approved for patients with PD-L1–positive recurrent or metastatic cervical cancer who progressed during or after chemotherapy. ENGOT-cx11/KEYNOTE-A18 (NCT04221945) is a phase III, randomized, placebo-controlled study evaluating pembro with concurrent CRT for the treatment of locally advanced cervical cancer. **Methods:** Approximately 980 patients with high-risk (FIGO 2014 stage IB2-IIB with node-positive disease or stage III-IVA), locally advanced, histologically confirmed cervical cancer who have not received systemic therapy, immunotherapy, definitive surgery, or radiation will be randomized 1:1 to receive either 5 cycles of pembro 200 mg every 3 wk (Q3W) + CRT followed by 15 cycles of pembro 400 mg Q6W or 5 cycles of placebo Q3W + CRT followed by 15 cycles of placebo Q6W. The CRT regimen includes 5 cycles (with optional 6th dose) of cisplatin 40 mg/m^2 Q1W + EBRT followed by brachytherapy. Randomization is stratified by planned EBRT type (intensity-modulated radiotherapy [IMRT] or volumetric-modulated arc therapy [VMAT] vs non-IMRT or non-VMAT), cancer stage at screening (stage IB2-IIB vs III-IVA), and planned total radiotherapy dose. Treatment will continue until the patient has received 20 cycles of pembro (5 cycles 200 mg Q3W, 15 cycles 400 mg Q6W) vs placebo (~2 y) or until disease progression, unacceptable toxicity, or withdrawal. Primary endpoints are PFS per RECIST v1.1 by blinded independent central review and OS. Secondary endpoints are PFS at 2 y, OS at 3 y, complete response at 12 wk, ORR, PFS and OS in PD-L1–positive patients, EORTC QLQ-C30 and QLQ-CX24, and safety. Enrollment is ongoing. Clinical trial information: NCT04221945. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

TPS6097 **Poster Session (Board #268), Fri, 8:00 AM-11:00 AM**

Clinical trial in progress: Pivotal study of VB-111 combined with paclitaxel versus paclitaxel for treatment of platinum-resistant ovarian cancer (OVAL, VB-111-701/GOG-3018). *First Author: Rebecca Christian Arend, University of Alabama at Birmingham, Birmingham, AL*

Background: Ofranergene obadenovec (VB-111) is a targeted anti-cancer gene therapy with a dual mechanism: a broad antiangiogenic effect and induction of a tumor directed viral immune response. In a phase II trial in platinum resistant ovarian cancer VB-111 in combination with weekly paclitaxel showed a CA-125 response rate (RR) of 58% and median overall survival (OS) of 498 days compared to 172.5 days in the sub-therapeutic dose ($p = 0.028$). The combination treatment was well tolerated. Favorable outcomes were associated with induction of an immunotherapeutic effect of tumor infiltration with CD-8 T cells. Based on these observations, a phase III randomized controlled trial, VB-111-701/GOG-3018 (OVAL) was initiated in collaboration with the GOG Foundation, Inc. **Methods:** The OVAL study, NCT03398655, is an international, randomized, double-blind, placebo-controlled, phase III study. Patients with recurrent platinum-resistant epithelial ovarian cancer, who have measurable disease (RECIST 1.1) and were previously treated with up to 5 lines are randomized 1:1 to receive VB-111 ($1x10^{13}$ VPs) with weekly paclitaxel (80mg/m^2), or weekly paclitaxel with placebo. Randomization is stratified by number of prior treatment lines, prior antiangiogenic therapy and platinum refractory disease status. Treatment beyond asymptomatic RECIST progression may continue until progression is confirmed by follow up imaging. The primary endpoints are OS, safety and tolerability. Secondary endpoints include progression free survival, and objective RR by CA-125 (per GCIG criteria) and RECIST 1.1. The sample size calculation of 400 patients (event driven) provides 92% power to detect a difference in survival at the two-sided 5% significance level using the logrank test. A pre-planned interim analysis will take place in Q1 2020 to assess whether the CA-125 RR per GCIG criteria in the treatment arm is sufficiently larger than in the control arm and is comparable to the positive results of the phase II study. Study enrolment is ongoing and over 80 patients were enrolled in the US and Israel. Enrollment expansion to Europe is planned in 2020. Clinical trial information: NCT03398655. Research Sponsor: VBL Therapeutics.

TPS6098 **Poster Session (Board #269), Fri, 8:00 AM-11:00 AM**

Basket study of the oral progesterone antagonist onapristone ER in women with progesterone receptor positive (PR+) recurrent granulosa cell tumor (GCT), low-grade serous ovarian cancer (LGSOC), or endometrioid endometrial cancer (EEC). *First Author: Rachel N. Grisham, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY*

Background: Onapristone extended release (ER) is a type I full progesterone antagonist that inhibits progesterone mediated PR activation and stabilizes PR association with corepressors. Onapristone has shown activity across multiple preclinical models of hormonally driven cancer. A phase I dose escalation study of onapristone ER in PR+ breast, endometrial and ovarian cancer patients found all doses tested to be well tolerated, with 50mg PO BID determined to be the recommended phase 2 dose (RP2D). GCT (98% of cases PR+), LGSOC (58% of cases PR+) and EEC (67% of cases PR+) are hormonally driven cancers which generally have poor responses to chemotherapy and limited treatment options in the recurrent setting. **Methods:** This is an open-label, investigator-initiated basket study of onapristone ER in patients with PR+ recurrent GCT, LGSOC, or EEC currently enrolling patients at Memorial Sloan Kettering Cancer Center in NY, USA (NCT03909152). The primary objective is to evaluate the efficacy, in terms of response rate by RECIST 1.1 criteria, within 36 weeks of treatment. Eligible patients must have received at least 1 prior line of chemotherapy, have measurable disease by RECIST 1.1 criteria, and have tumor tissue collected within 3 years prior to enrollment with PR expression $\geq$ 1% by IHC. Patients are allowed to have unlimited additional prior lines of chemotherapy, biologic therapy, immunotherapy or hormonal therapy. Enrolled patients are treated with onapristone ER 50mg PO BID until time of progression or intolerable toxicity. The 3 disease cohorts are currently enrolling to Stage I in parallel with expansion from stage I to stage II planned when the prespecified response criteria are met for each cohort as described in the table below. Clinical trial information: NCT03909152. Research Sponsor: Context.

Histology	Stage I	Stage II (expansion)	Response rate to be deemed worthy of further study
PR+ Granulosa Cell Tumor	Enroll 14 patients, if $\geq$ 1 response(s) expand to stage II	Expand to a total of 23 patients	$\geq$ 3/23
PR+ Low Grade Serous Ovarian Cancer	Enroll 16 patients, if $\geq$ 2 responses expand to stage II	Expand to a total of 25 patients	$\geq$ 5/25
PR+ Endometrioid Endometrial Cancer	Enroll 19 patients, if $\geq$ 4 responses expand to Stage II	Expand to a total of 36 patients	$\geq$ 11/36

TPS6099 **Poster Session (Board #270), Fri, 8:00 AM-11:00 AM**

A phase Ib/II, multicenter, open-label study of DSP-7888 dosing emulsion in combination with immune checkpoint inhibitors (CPI) nivolumab or pembrolizumab in adult patients (pts) with advanced solid tumors, including platinum-resistant ovarian cancer (PROC). *First Author: Makoto Origuchi, Boston Biomedical, Inc., Cambridge, MA*

Background: DSP-7888 is a therapeutic cancer vaccine composed of two synthetic peptides derived from Wilms' tumor 1 (WT1) to promote both cytotoxic and helper T-lymphocyte-mediated immune responses against *WT1*-expressing tumors. *WT1* is overexpressed in various solid tumors, including ovarian cancer. Combining cancer vaccines like DSP-7888 with a CPI may reduce resistance to immunomodulators and improve clinical benefit. A phase Ib/II study is being conducted to evaluate DSP-7888 in combination with a CPI in pts with advanced solid tumors, including PROC (NCT03311334). **Methods:** This phase Ib/II, open-label, multicenter, two-part dose-search/dose-expansion study investigates DSP-7888 + nivolumab or pembrolizumab in pts with advanced solid tumors (phase Ib), including PROC (phase II). The phase Ib primary objectives are safety, tolerability, and identification of the recommended phase II dose (RP2D). The phase II primary objective is evaluation of objective response rate (ORR); secondary objectives are clinical activity, safety, and tolerability. Pts aged $\geq$18 years with unresectable, metastatic cancer approved for treatment with nivolumab (phase Ib, Arm 1, n=6–12, 7 enrolled) or pembrolizumab (phase Ib, Arm 2, n=6–12, 6 enrolled), or with PROC (phase II) are eligible. Phase II will enroll ~40 pts into two groups based on programmed death-ligand 1 status (combined positive score of $\geq$10 [Group 1] or $<$10 [Group 2]). Clinical activity will be assessed continuously using Bayesian analysis and actual enrollment may increase by ~20 pts/group based on this analysis. Pts in phase II will receive DSP-7888 intradermally (RP2D from phase Ib) once a week (wk) for 6 wks in the induction phase then every 3 wks in the maintenance phase. Beginning Day 1, pembrolizumab will be administered intravenously every 3 wks. In phase II, objective disease will be assessed every 6 wks for 24 wks, then every 12 wks until progression. Endpoints include ORR (per RECIST v1.1) (primary), duration of response, disease control rate (DCR), progression-free survival (PFS), 6-month PFS rate (per RECIST v1.1), and overall survival, immune (i)ORR, iDCR, and iPFS (per iRECIST) (secondary). Exploratory endpoints include blood and tumor tissue biomarkers. Safety and tolerability, assessed by adverse events, will be evaluated throughout the duration of the study and follow-up. This study is currently recruiting patients. Clinical trial information: NCT03311334. Research Sponsor: Boston Biomedical, Inc.

TPS6100 Poster Session (Board #271), Fri, 8:00 AM-11:00 AM

Primary cytoreductive surgery with or without Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for FIGO stage III epithelial ovarian cancer: The OVHIPEC-2 trial in progress. *First Author: Ruby M. van Stein, The Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: The addition of Hyperthermic Intraperitoneal Chemotherapy (HIPEC) to interval cytoreductive surgery improves recurrence-free and overall survival in patients with FIGO stage III ovarian cancer who are ineligible for primary cytoreductive surgery due to extensive intraperitoneal disease. The effect of HIPEC remains undetermined in patients who are eligible for primary cytoreductive surgery. We hypothesize that the addition of HIPEC to a complete or near-complete (residual disease $\leq$2.5 mm) primary cytoreductive surgery improves overall survival in patients with FIGO stage III ovarian cancer. **Methods:** This international, randomized, open-label, phase III trial enrolls patients with newly diagnosed, histological proven FIGO stage III epithelial ovarian, fallopian tube, or primary peritoneal cancer. Patients with resectable umbilical, spleen or local bowel lesions may be included. Following complete or near-complete primary cytoreduction, patients are intra-operatively randomized (1:1) to receive HIPEC or no HIPEC. Patients in both study arms will receive six courses of adjuvant carboplatin-paclitaxel and maintenance PARP-inhibitor or bevacizumab according to current guidelines. The primary endpoint is overall survival. To detect a Hazard Ratio of 0.67 in favor of HIPEC, 200 overall survival events are required. Assuming that accrual will be completed in 60 months, and 12 months additional follow-up, 538 patients need to be randomized. All randomized patients will be included in the analysis for overall survival according to the intention to treat principle. Pre-specified subgroup analyses will be performed based on stratification factors (peritoneal cancer index at start of surgery, completeness of surgery), histologic subtype (high-grade serous versus other), and BRCA mutation (BRCA1/2 mutation versus wildtype). Secondary endpoints are recurrence-free survival, time to first subsequent anticancer treatment, and treatment related complications and toxicity. Exploratory endpoints are time to second subsequent anticancer treatment, health-related quality of life, and cost-effectiveness. The Institutional Review Board of the Netherlands Cancer Institute approved the trial, which is actively enrolling patients since January 2020. Clinical trial information: NCT03772028. Research Sponsor: Dutch Cancer Society (DCS), Other Foundation, Other Government Agency, French PHRC (programme hospitalier de recherche Clinique) program for participation of French centers.

TPS6101 Poster Session (Board #272), Fri, 8:00 AM-11:00 AM

ENGOT-OV44/FIRST study: a randomized, double-blind, adaptive, phase III study of standard of care (SOC) platinum-based therapy $\pm$ dostarlimab followed by niraparib $\pm$ dostarlimab maintenance as first-line (1L) treatment of stage 3 or 4 ovarian cancer (OC). *First Author: Anne-Claire Hardy-Bessard, Medical Oncology Department, CARIO-HPCA and Cooperative Gynecological Cancer Research Group (GINECO), Plerin, France*

Background: Despite surgery and CT (paclitaxel + carboplatin $\pm$ bevacizumab [bev]), 5-year survival rates remain low for patients (pts) with FIGO stage 3 or 4 OC. Niraparib is a poly (ADP-ribose) polymerase (PARP) inhibitor that has recently demonstrated efficacy in 1L therapy. Dostarlimab (TSR-042) is an anti-programmed death (PD)-1 humanized monoclonal antibody that has shown clinical activity as monotherapy in early phase trials. The currently enrolling ENGOT-OV44/FIRST study will compare efficacy and safety of CT + dostarlimab + niraparib $\pm$ bev (Arm 3) vs CT + niraparib $\pm$ bev (Arm 2). **Methods:** Eligible pts are $\geq$18 years of age, with FIGO stage 3 or 4 non-mucinous epithelial OC, ECOG performance status $<$ 2, and tumor tissue available for PD-1 ligand (PD-L1) testing. After cycle 1 of CT, pts are stratified by concurrent bev use, *BRCA* mutation/homologous recombination repair status, and disease burden, then randomized 1:2 into trial Arms 2 and 3 (Table). Dostarlimab is administered at 500 mg IV Q3W during the CT period, then 1000 mg IV Q6W during the maintenance period. Niraparib dosing is 200 mg PO QD for pts with baseline bodyweight (BW) $<$ 77 kg and/or platelet count (PC) $<$ 150,000/μL, or 300 mg QD for pts with baseline BW $\geq$77 kg and PC $\geq$150,000/μL. The dual primary endpoints are PFS, based on investigator assessment per RECIST v1.1, in both PD-L1+ and all patients. Initially the study enrolled pts to Arm 1. This arm was discontinued following positive results from the PRIMA/ENGOT-OV26/GOG-3012 and PAOLA-1/ENGOT-OV25 studies. This allows investigators to offer the current standard of care to all patients. Clinical trial information: NCT03602859, EUDRACT 2018-000413-20. Research Sponsor: GlaxoSmithKline.

	Randomization Scheme 0:1:2		
Treatment period	**Arm 1 (discontinued)**	**Arm 2**	**Arm 3**
CT*	CT + IV placebo	CT + IV placebo	CT + IV dostarlimab
Maintenance up to 3 years*	Oral placebo + IV placebo	Oral niraparib + IV placebo	Oral niraparib + IV dostarlimab

*Bev is optional in all arms.

TPS6102 Poster Session (Board #273), Fri, 8:00 AM-11:00 AM

NOGGO Ov-42/MAMOC: Rucaparib maintenance after bevacizumab maintenance following carboplatin-based first line-chemotherapy in ovarian cancer patients. *First Author: Elena Ioana Braicu, Department of Gynecology, Charité Medical University, Berlin, Germany*

Background: Ovarian cancer (OC) is associated with the highest mortality rates among gynecological malignancies, with most patients being diagnosed in advanced stages. The most common histological subtype is high grade serous OC, which is characterized by deficiency in homologous recombination. Debulking surgery, followed by platinum based chemotherapy and bevacizumab (bev), followed by maintenance therapy with bev, is the standard therapy for advanced BRCA wild type (BRCAwt) OC patients in Germany. BRCA mutant patients will receive maintenance with olaparib, according to SOLO1 data. The anticancer effects of PARP inhibitors (PARPi) seem to be increased by the addition of antiangiogenic drugs. Preclinical data showed increased HRD in tumors pretreated with bev, and clinical trials showed a benefit of the combination of antiangiogenic drugs and PARPi vs. PARPi alone. NOGGO Ov-42/MAMOC trial (NCT04227522) is a phase III, randomized, placebo-controlled study evaluating rucaparib maintenance following bevacizumab maintenance for the treatment of advanced primary high grade BRCAwt OC. **Methods:** 190 patients with histologically confirmed advanced (FIGO stage IIIA- IV of the 2014 FIGO classification) high grade serous or high grade endometrioid (based on local histopathological findings) OC, fallopian tube cancer, primary peritoneal cancer or clear cell carcinoma of the ovary will be randomized 2:1 to receive either rucaparib 600mg BID or placebo as maintenance therapy following first line chemotherapy with 6 cycles of Carboplatin/Paclitaxel and at least 12 cycles of bev, given together with chemotherapy and as maintenance. Only BRCAwt patients will be included in the trial. Randomization is stratified by surgery planned timepoint (neoadjuvant vs. adjuvant), surgical outcome (no residual tumor mass vs. residual tumor mass), response to chemotherapy followed by bev (CR/NED vs. PR/SD) and study center. Treatment will continue for 24 months or until disease progression, unacceptable toxicity, or withdrawal. Primary endpoint is PFS in BRCAwt patients per RECIST v1.1. Secondary endpoints are PFS2, quality of life (EORTC QLQ-C30/OV28, FSI, SF-12, PROC-CTCAE, every day memory questionnaire), daily activity, time to next medical intervention, time to next subsequent therapy, safety assessments and OS. Clinical trial information: NCT04227522. Research Sponsor: CLOVIS.

TPS6103 Poster Session (Board #274), Fri, 8:00 AM-11:00 AM

MIRASOL (GOG 3045/ENGOT OV-55): A randomized, open-label, phase III study of mirvetuximab soravtansine versus investigator's choice of chemotherapy in advanced high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate-alpha (FRα) expression. *First Author: Kathleen N. Moore, University of Oklahoma Medical Center, Oklahoma City, OK*

Background: Elevated FRα expression is a characteristic of several solid tumors, including epithelial ovarian cancer (EOC), thereby providing an attractive candidate for targeted therapeutic approaches. Mirvetuximab soravtansine is an antibody-drug conjugate (ADC) comprising a FRα-binding antibody, cleavable linker, and the maytansinoid DM4, a potent tubulin-targeting agent that has shown consistent and meaningful single agent clinical activity, along with favorable tolerability, in patients with high FRα expressing tumors. **Methods:** MIRASOL is a randomized phase III study designed to evaluate the efficacy of mirvetuximab soravtansine compared with that of standard-of-care chemotherapy in adult patients with platinum-resistant EOC, primary peritoneal cancer, or fallopian tube cancer. Confirmation of high FRα positivity by immunohistochemistry (high expression; $\geq$ 75% of cells with PS2+ staining intensity) and $\leq$ 3 prior lines of therapy are required for inclusion. MIRASOL is designed to randomize 430 patients, 1:1 to Arm 1 (intravenous mirvetuximab soravtansine at a dose of 6 mg/kg, calculated using adjusted ideal body weight, on Day 1 of a 21-day cycle) or Arm 2 (investigators' choice chemotherapy: paclitaxel, pegylated liposomal doxorubicin, or topotecan). The primary efficacy endpoint is progression-free survival (PFS; by investigator) and secondary endpoints include objective response rate, quality of life, overall survival, and safety and tolerability. MIRASOL opened for enrollment in December 2019. Clinical trial information: NCT04209855. Research Sponsor: ImmunoGen.

TPS6104 **Poster Session (Board #275), Fri, 8:00 AM-11:00 AM**

DUETTE: A randomized phase II study to assess a second maintenance treatment with olaparib (ola) or ola+ceralasertib (cer), in patients (pts) with platinum-sensitive relapsed (PSR) epithelial ovarian cancer who have previously received PARP inhibitor maintenance treatment (NCT04239014). *First Author: Amit M. Oza, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Ovarian cancer is the leading cause of death from gynecological cancers in the USA, and the fifth most common cause of cancer death in women. Ola is a PARPi approved for first-line maintenance treatment of *BRCA*-mutated advanced ovarian cancer in women who achieve a complete or partial response to platinum-based chemotherapy. Ola is also efficacious in combination with bevacizumab in the same population, independent of BRCA mutation status. Cer is a potent, oral, selective inhibitor of ATR. ATR is a critical DDR kinase that is activated in response to replication stress and stalled replication forks. There is no second maintenance standard of care for patients with PSR ovarian cancer who have previously received a PARPi in the maintenance setting. Pre-clinical models have shown that several mechanisms of PARPi resistance may be overcome by ATR inhibition, such as BRCA reversion, replication fork protection and DDR rewiring. DUETTE will select pts with tumor response or stable disease after second or third-line platinum-based treatment, with the expectation to enrich for non-BRCA reversion PARPi resistance mechanisms. The study will address the role of a second maintenance treatment following prior 1L or 2L maintenance, an emerging population of unmet need, and includes translational studies that aim to further our knowledge of clinical PARPi resistance mechanisms and predictors of treatment response. **Methods:** DUETTE is a global, multi-center, phase II study. 192 pts with PSR epithelial ovarian cancer who have previously received PARPi maintenance treatment, will be retreated with platinum and those who have not progressed after $\geq$ 4 cycles will be randomized (1:1:1) to 3 treatment arms: Arm 1, open-label: cer 160 mg once daily (qd) days 1 to 7 plus ola 300 mg twice daily (bd); Arm 2, blinded: ola monotherapy 300 mg bd and Arm 3, blinded: ola-placebo. Treatment is administered in 28-day cycles. All pts will be stratified by BRCA status (mutation or wildtype) and response to most recent line of platinum-based chemotherapy (CR/PR or SD). The primary endpoint is to assess the efficacy of maintenance ola monotherapy and cer+ola combination therapy compared with placebo by PFS using blinded, independent central review. Secondary endpoints are overall survival, PFS2, ORR, DoR, safety and tolerability. Enrolment is planned to start in April 2020. Research Sponsor: Astra Zeneca.

TPS6105 **Poster Session (Board #276), Fri, 8:00 AM-11:00 AM**

SIENDO/ENGOT-EN5: A randomized phase III trial of maintenance with selinexor/placebo after combination chemotherapy in patients with advanced or recurrent endometrial cancer. *First Author: Ignace Vergote, BGOG and University Hospitals Leuven, Leuven Cancer Institute, Leuven, Belgium*

Background: Endometrial cancer is one of the most common gynecologic malignancies with increasing incidence and mortality. Patients with advanced disease that has relapsed or received prior platinum-based therapy or radiotherapy have limited options and the prognosis remains poor. Selinexor is a novel, oral selective inhibitor of nuclear export (SINE) which forces nuclear retention and activation of tumor suppressor proteins. Selinexor in combination with low dose dexamethasone was recently approved for patients with multiple myeloma. In addition, single agent selinexor has demonstrated broad activity in other hematologic malignancies and solid tumors. In a phase II study, 50 mg/m^2 (~80 mg) selinexor administered twice weekly demonstrated a disease control rate of 35% with 2 confirmed partial responses among 23 patients with heavily pretreated endometrial cancer (Vergote I et al. Gynecol Oncol 2020). In the absence of approved maintenance therapies, we conducted this study to evaluate the efficacy of selinexor compared with placebo as maintenance therapy in patients with advanced or recurrent endometrial cancer. **Methods:** This is a multicenter, double-blind, placebo-controlled, randomized phase III study in patients in partial or complete remission after completing at least 12 weeks of taxane-platinum combination therapy for primary Stage IV disease and recurrent disease (i.e., relapse after primary therapy for early stage disease including surgery and/or adjuvant therapy). A total of 192 patients will be enrolled at 80 sites in Europe, North America, and Israel. Patients will be randomized in a 2:1 ratio to either maintenance therapy with 80 mg oral selinexor once weekly or placebo. Stratification factors include primary Stage IV versus first recurrent disease at the time of taxane-platinum therapy and disease status after chemotherapy (partial versus complete response). Treatment will continue until disease progression. The primary endpoint is progression free survival (PFS) per RECIST v1.1. Secondary endpoints include disease-specific survival, overall survival, time to first subsequent therapy, time to second subsequent therapy, PFS on subsequent therapy and safety and tolerability. The study is currently open and enrolling patients. Clinical trial information: NCT03555422. Research Sponsor: Karyopharm Therapeutics Inc.

TPS6106 **Poster Session (Board #277), Fri, 8:00 AM-11:00 AM**

ENGOT-en9/LEAP-001: A phase III study of first-line pembrolizumab plus lenvatinib versus chemotherapy in advanced or recurrent endometrial cancer. *First Author: Christian Marth, Department of Gynecology and Obstetrics, Medical University of Innsbruck, Innsbruck, Austria*

Background: The prognosis for endometrial cancer (EC) can be favorable when diagnosed in early stages, but prognosis and overall survival are poor in patients with advanced or recurrent EC. First-line standard of care for patients with advanced or recurrent EC is paclitaxel and carboplatin chemotherapy; however, there is a need for more effective and tolerable therapies. In the phase Ib/II trial KEYNOTE-146, which assessed the PD-1 inhibitor pembrolizumab (pembro) in combination with the multikinase inhibitor lenvatinib, an objective response rate (ORR) of 38% was observed (N=108) in patients with previously treated advanced EC. ENGOT-en9/LEAP-001 (NCT03884101) is a randomized, open-label, active-controlled, phase III study investigating pembro + lenvatinib vs chemotherapy in patients with newly diagnosed advanced or recurrent EC. **Methods:** Patients with newly diagnosed advanced (stage III-IV) or recurrent EC not previously treated with antiangiogenic agents; systemic chemotherapy (unless within a chemoradiation regimen); PD-1, PD-L1, or PD-L2 inhibitors; or other T-cell receptor–targeted therapies will be eligible. Patients will be randomized 1:1 to receive pembro 200 mg every 3 wk (Q3W) + lenvatinib 20 mg daily or paclitaxel 175 mg/m^2 Q3W + carboplatin AUC 6 Q3W. Randomization will be stratified on the basis of proficient vs deficient mismatch repair (pMMR vs dMMR) status. The pMMR population will be further stratified by prior chemoradiation (yes vs no), measurable disease (yes vs no), and ECOG performance status (0 vs. 1). Patients will continue on treatment for up to 35 cycles of pembro vs 7 cycles of chemotherapy or until initiation of a new anticancer treatment, unacceptable adverse events, or withdrawal of consent. Primary study endpoints are progression-free survival (per RECIST v1.1 by blinded independent central review) and overall survival. Secondary study endpoints are ORR, health-related quality of life, safety and tolerability, and lenvatinib pharmacokinetics. Exploratory endpoints will include disease control rate, clinical benefit rate, and duration of response. Enrollment is ongoing. Clinical trial information: NCT03884101. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA and Eisai Inc., Woodcliff Lake, NJ, USA.

TPS6107 **Poster Session (Board #278), Fri, 8:00 AM-11:00 AM**

ENGOT-EN6/NSGO-RUBY: A phase III, randomized, double-blind, multicenter study of dostarlimab + carboplatin-paclitaxel versus placebo + carboplatin-paclitaxel in recurrent or primary advanced endometrial cancer (EC). *First Author: Mansoor Raza Mirza, Nordic Society of Gynecologic Oncology (NSGO) and Rigshospitalet–Copenhagen University Hospital, Copenhagen, Denmark*

Background: Carboplatin-paclitaxel is considered standard systemic anticancer therapy for recurrent or advanced EC for which surgery and/or radiation are not curative. Dostarlimab (TSR-042) is an anti-programmed cell death (PD)-1 humanized monoclonal antibody that has demonstrated antitumor activity and an acceptable safety profile in patients (pts) with recurrent or advanced EC in the GARNET trial. The RUBY trial was designed to evaluate the efficacy and safety of dostarlimab in combination with carboplatin-paclitaxel in recurrent or primary advanced EC compared with carboplatin-paclitaxel alone. **Methods:** This is a global, randomized, double-blind, multicenter, placebo-controlled study. Eligible pts must have first recurrent or primary stage III or stage IV EC with a low potential for cure by radiation therapy or surgery alone or in combination. Pts with carcinosarcoma are eligible for enrollment. 470 pts will be enrolled from approximately 160 sites in the ENGOT countries, United States, and Canada. Stratification factors are microsatellite instability (MSI) status (MSI-high [MSI-H] or microsatellite stable [MSS]), prior external pelvic radiotherapy (yes or no), and disease status (recurrent, primary stage III, or primary stage IV). Pts will be randomized 1:1 to receive combination dostarlimab 500 mg or placebo + carboplatin AUC 5 + paclitaxel 175 mg/m^2 every 3 weeks for 6 cycles followed by dostarlimab 1000 mg or placebo monotherapy every 6 weeks for up to 3 years in the absence of progressive disease, death, unacceptable toxicity, or patient/physician decision to withdraw from the study. The primary endpoint is progression-free survival (PFS) as assessed by the investigator in the all-comers population and the MSI-H population per RECIST version 1.1. Secondary efficacy endpoints are PFS assessed by blinded independent central review per RECIST version 1.1, overall survival, objective response rate, duration of response, disease control rate, safety and tolerability, and patient-reported outcomes. Clinical trial information: NCT03981796. Research Sponsor: GlaxoSmithKline.

TPS6108 Poster Session (Board #279), Fri, 8:00 AM-11:00 AM

DUO-E/GOG-3041/ENGOT-EN10: a randomized phase III trial of first-line carboplatin (carb) and paclitaxel (pac) in combination with durvalumab (durva), followed by maintenance durva with or without olaparib (ola), in patients (pts) with newly diagnosed (nd) advanced or recurrent endometrial cancer (EC). *First Author: Shannon Neville Westin, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: There is a high unmet need for advances in EC treatment that provide progression-free survival (PFS) and overall survival (OS) benefits. EC tumors are sensitive to carb/pac (Pectasides *et al. Gynecol Oncol* 2008). Maintenance therapy with the poly(ADP-ribose) polymerase inhibitor (PARPi) ola (with or without bevacizumab) led to significant PFS benefits in advanced ovarian cancer pts with either nd (SOLO1, Moore *et al. NEJM* 2018; PAOLA-1, Ray-Coquard *et al. NEJM* 2019) or recurrent (SOLO2, Pujade-Lauraine *et al. Lancet Oncol* 2017; Study 19, Friedlander *et al. Br J Cancer* 2018) platinum-sensitive disease, regardless of BRCA mutation status (PAOLA-1; Study 19), and in BRCA-mutated metastatic pancreatic cancer pts (POLO, Golan *et al. NEJM* 2019). Molecular features of EC could predict sensitivity to PARPi (de Jonge *et al. Clin Cancer Res* 2019; Auguste *et al. Mod Pathol* 2018). PARPi has been shown to prime the immune microenvironment in a preclinical *BRCA1* mutant ovarian model (Higuchi *et al. Cancer Immunol Res* 2015). Clinical trials have demonstrated antitumor activity of the anti-programmed cell death ligand-1 (anti-PD-L1) blocker durva (Antill *et al. J Clin Oncol* 2019) and anti-programmed cell death-1 (anti-PD-1) antibody therapies (Makker *et al. ESMO* 2019; Oaknin *et al. SGO* 2019) in EC pts. The DUO-E trial (EUDRACT 2019-004112-60, D9311C00001, NCT04269200) will investigate whether the addition of durva to carb/pac, followed by durva (with or without ola) maintenance treatment, improves PFS in pts with nd advanced or recurrent EC. **Methods:** Eligible pts for this multicenter, double-blind, Phase III trial must have nd Stage III/IV or recurrent EC and be naïve to first-line chemotherapy. Pts will be randomized (1:1:1; n=~233 per arm) to: arm A) carb/pac + placebo (pbo) (q3w for six cycles) followed by pbo maintenance treatment; arm B) carb/pac + durva (1120 mg; q3w for six cycles) followed by maintenance treatment with durva (1500 mg q4w) + pbo (tablets bid); or arm C) carb/pac + durva (1120 mg; q3w for six cycles) followed by maintenance treatment with durva (1500 mg q4w) + ola (300 mg bid tablets). Pts received maintenance treatment until disease progression. Primary endpoint: investigator-assessed PFS (RECIST 1.1) of arm B vs. arm A. Key secondary endpoints: PFS of arm C vs. arm A; OS of arm B vs. arm A, and of arm C vs. arm A. Enrollment began in Q1 2020. Clinical trial information: 2019-004112-60. Research Sponsor: AstraZeneca.

TPS6109 Poster Session (Board #280), Fri, 8:00 AM-11:00 AM

Multicentre randomized phase II trial of olaparib as maintenance therapy in platinum-sensitive advanced endometrial carcinoma: The GINECO-UTOLA study. *First Author: Florence Joly, Department of Medical Oncology, Centre François Baclesse, Caen, France*

Background: Advanced endometrial cancer (EC) patients relapse despite treatment with combination chemotherapy and have a short progression-free survival (PFS). Data from the TGCA suggest opportunities to targeting DNA repair in women with EC. Particularly type 4 (High copy number or serous like, with frequent TP53 mutations) and type 2 (microsatellite instability hyper-mutated) EC can be associated with defects in double strand break DNA repair by homologous recombination (HR) and could potentially be targeted by olaparib. We propose a placebo-controlled, multicenter, two-arm, phase II trial comparing olaparib versus placebo in maintenance therapy after chemotherapy in patients with advanced/metastatic EC. **Methods:** The primary objective of this trial is to evaluate the efficacy of maintenance olaparib in comparison to placebo after platinum based chemotherapy, defined by PFS according to Recist. Key eligibility criteria include: advanced/metastatic histologically confirmed EC (excepted carcino-sarcoma, small cells& neuroendocrine); prior surgery, adjuvant chemotherapy, radiation and hormonal therapy are permitted; objective or stable response after first-line chemotherapy is mandatory. 147 patients are randomized (2:1) after chemotherapy to receive Olaparib 300mg twice daily or placebo in maintenance after at least 4 cycles of platinum based chemotherapy. Olaparib/placebo is continued until disease progression, unacceptable toxicity, or withdrawal. Stratification is on IHC P53 and MMR status. Primary hypothesis is a 66.7% relative increase in the median PFS rate in the olaparib arm (from 4.5 to 7.5 months), corresponding to a 0.60 Hazard Ratio. Secondary endpoints include PFS according to P53, MMR and NGS HRD status, PFS2, disease specific survival, time to subsequent therapy, overall survival, objective response, disease control rate, patient reported outcomes (assessed via EORTC QLQ-C30 and EORTC QLQ-EN24, EORTC-FA, EQ5D) and safety. Trial is recruiting in France (in February n= 40 randomization). **Conclusion:** this will be the first study that evaluate the efficacy of olaparib in maintenace after chemotherapy in advanced/metastastic EC, stratified on molecular profil. Clinical trial information: NCT03745950. Research Sponsor: Astrazeneca.

6500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Transoral robotic surgical resection followed by randomization to low- or standard-dose IMRT in resectable p16+ locally advanced oropharynx cancer: A trial of the ECOG-ACRIN Cancer Research Group (E3311). *First Author: Robert L. Ferris, University of Pittsburgh Medical Center and University of Pittsburgh Cancer Institute, Pittsburgh, PA*

Background: ECOG-ACRIN 3311 examines reduced postoperative therapy in patients with "intermediate risk" p16+ oropharynx cancer (OPC) undergoing primary transoral surgical management. We report the primary endpoint of 2-year progression free survival (PFS) for patients randomized to 50Gy vs 60Gy without chemotherapy. **Methods:** Between December 2013 and July 2017, 82 credentialed surgeons performed transoral resection (TOS) for 519 OPC patients (cT1-2 stage III/IV AJCC7 without matted neck nodes); post-operative management was determined by pathologically assessed risk. Among 353 eligible and treated patients, Arm A enrolled 10% (N=37) for clear margins, 0-1 nodes, no extranodal extension (ENE)), Arms B (50Gy, N=102) or C (60Gy, N=104) randomized 58%, for clear/close margins, 2-4 + nodes, or ENE ≤1mm, while Arm D (N=110, 60-66Gy plus weekly cisplatin, 40 mg/m2, positive margin with any T stage, >4 + nodes, or >1mm ENE) enrolled 31%. Arm D assignment was based on >1mm ENE (76%), > 4 nodes (27%), and/or positive margins (11%). Intermediate-risk patients were stratified by smoking history (>10 pk-yr). Of the 80 pts (15%) deemed ineligible, 28 had scans/labs not done per protocol, however treatment arm distribution for all patients mirrored that for the 353 pts eligible and treated. **Results:** Median follow-up was 31.8 months. 2 yr PFS for Arms A, B and C were 93.9% (90% CI=87.3%, 100%), 95.0% (90% CI=91.4%, 98.6%) and 95.9% (90% CI=92.6%, 99.3%) respectively, while Arm D was 90.5% (90% CI=85.9%, 95.3%). The regimen of TOS + low-dose radiation is considered worthy of further study, since the primary endpoint of the upper bound of the 90% CI (in the intermediate risk group) exceeding 85% was met. Of 17 progression events, 7 were locoregional. There were 10 distant recurrences: Arm A=1, Arm B=2, Arm C=4, Arm D=3. Grade III/IV treatment-related AE rates were 15%/2% during surgery, 13%/2% for Arm B and 25%/0% for Arm C. There were 2 treatment-related deaths (one surgical and one Arm D). **Conclusions:** Transoral resection of p16+ OPC is safe and results in good oncologic outcome, presenting a promising deintensification approach. For patients with low-risk disease, 2-yr PFS is favorable without post-operative therapy. For those with uninvolved surgical margins, <5 involved nodes, and minimal (<1mm) ENE, reduced dose post-operative RT without chemotherapy appears sufficient. Transoral surgery plus 50Gy should be compared to optimal non-surgical therapy in a phase III trial. Clinical trial information: NCT01898494. Research Sponsor: Eastern Cooperative Oncology Group, U.S. National Institutes of Health.

6501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Equivalence randomized trial comparing treatment based on sentinel node biopsy versus neck dissection in operable T1-T2N0 oral and oropharyngeal cancer. *First Author: Renaud Garrel, Head Neck Departement CHU Montpellier, Montpellier, France*

Background: Although sentinel node (SN) biopsy is known to be accurate in operable oral and oropharyngeal cT1-T2N0 squamous cell carcinomas (OC), the oncological equivalence of a treatment based on SN compared to that based on neck dissection (ND) has to be evaluated. **Methods:** A prospective multicenter randomized medico economic study included patients with OC operated of primary tumor and systematic neck dissection in ND-arm (standard treatment) versus patients operated of primary tumor and SN biopsy only if negative or ND if SN biopsy positive (SN-arm, experimental treatment). Primary endpoint was neck-relapse-free survival at 2 years and 5 years. Hypothesis of equivalence was tested with a delta of 10%. Functional outcomes were assessed by comparing the length of the hospital stay, the number of physiotherapy prescriptions and dysfunctions in neck and shoulder scales during the 2 post-operative years. **Results:** Out of 307 included patients in 10 hospital centers, 279 evaluable cases showed a neck-relapse-free survival at 2 years and 5 years respectively of 89,6% (95%CI: 0.827; 0.938) and 89,6 %, (95%CI: 0.827; 0.938) in the ND-arm (14 neck relapses out of 139 patients) and of 90,7% (95%CI: 0.842; 0.946) and 89,4% (95%CI: 0.823; 0.938) in the SN-arm (13 neck relapses out of 140 patients). The survival difference between the two arms was less than the 10% expected interval, confirming the equivalence with p = 0.008. The median length of hospital stay was 7 days (ext. 3-30) in SN-arm and 8 days (ext. 2-94) in ND-arm (Wilcoxon's test, p = 0.001). The other functional outcomes were statistically worse in the ND-arm at the 2nd, 4th and 6th postoperative months. There was no more difference at 12 months and later. **Conclusions:** This study demonstrated the oncological equivalence of the SN approach compared to the ND approach in a multicenter study with a lower morbidity and care consumption in the SN approach during the 6 first post-operative months. Treatment based on sentinel node biopsy is established as a standard of care in OC. Clinical trial information: NCT02855723. Research Sponsor: French National Institute of Cancer.

6502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase II/III trial of post-operative chemoradiotherapy comparing 3-weekly cisplatin with weekly cisplatin in high-risk patients with squamous cell carcinoma of head and neck (JCOG1008). *First Author: Naomi Kiyota, Medical Oncology and Hematology, Cancer Center, Kobe University Hospital, Kobe, Japan*

Background: The standard treatment for post-operative high-risk patients (pts) with locally advanced squamous cell carcinoma of the head and neck (LA-SCCHN) is chemoradiotherapy with 3-weekly cisplatin (CDDP) (100 mg/m^2, q3wk, 66 Gy/33Fr; 3-weekly CDDP+RT). However, one concern with 3-weekly CDDP+RT is insufficient CDDP compliance due to high-dose-related toxicities. Weekly CDDP+RT (40 mg/m^2, qwk, 66 Gy/33Fr; weekly CDDP+RT) is an alternative regimen with better compliance. Here, we conducted a phase II/III trial of weekly CDDP+RT in post-operative high-risk LA-SCCHN. **Methods:** This is a multi-institutional randomized phase II/III trial to confirm the non-inferiority of weekly CDDP+RT (Arm B) compared with 3-weekly CDDP+RT (Arm A). The trial enrolled pts aged 20-75 years with post-operative high-risk features (microscopically positive margin and/or extranodal extension) and ECOG-PS 0-1. Pts were randomized in a 1:1 ratio to Arm A or Arm B. Primary endpoint of phase II was the proportion of treatment completion and that of phase III was overall survival (OS). A non-inferiority margin of hazard ratio (HR) was set at 1.32. **Results:** Between Oct 2012 and Dec 2018, 261 pts were enrolled (Arm A 132 pts, Arm B 129 pts). At the planned second interim analysis in phase III with 76/161 events, the Data and Safety Monitoring Committee recommended terminating the trial and publishing the results because the statistical boundary for OS non-inferiority had met the pre-specified stop criteria. With a median follow-up of 2.2 years in all randomized pts, 3-year OS was 59.1% in Arm A and 71.6% in Arm B with a HR of 0.69 (99.1% CI, 0.374-1.273 [< 1.32], one-sided p for non-inferiority = 0.00272 < 0.00433). 3-year RFS was 53.0% in Arm A and 64.5% in Arm B with a HR of 0.71 (95% CI, 0.48-1.06). Regarding acute adverse events, neutropenia (≥ grade 3), increased creatinine (≥ grade 2), hearing impairment (≥ grade 2) and mucositis (≥ grade 2) occurred in 48.8%, 8.5%, 7.8% and 55.0% in Arm A and 35.3%, 5.7%, 2.5% and 59.0% in Arm B, respectively. For compliance, median total dose of CDDP was 280 mg/m^2 (IQR, 250-299) in Arm A and 239 mg/m^2 (IQR, 199-277) in Arm B. Total radiation dose was 66 Gy (IQR, 66-66) in both arms. Proportion of treatment completion was 93.2% in Arm A and 86.8% in Arm B. **Conclusions:** Weekly CDDP+RT is non-inferior to 3-weekly CDDP+RT for post-operative high-risk LA-SCCHN pts and has a favorable toxicity profile. Weekly CDDP+RT should be considered the new standard treatment option for these pts. Clinical trial information: 000009125. Research Sponsor: National Cancer Center Research and Development Fund, Japan Agency for Medical Research and Develpmet Fund.

6503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Randomized phase II study of axitinib versus observation in patients with recurred or metastatic adenoid cystic carcinoma. *First Author: Bhumsuk Keam, Seoul National University Hospital, Seoul, South Korea*

Background: Adenoid cystic carcinoma (ACC) does not respond to cytotoxic chemotherapy. Several anti-angiogenic agents were evaluated in single arm phase II trials. However, the role of chemotherapy is still controversial, because of natural stable disease course without chemotherapy and lack of randomized trial. We firstly conducted a randomized trial to evaluate the efficacy of axitinib compared to observation. **Methods:** In this multicenter, prospective phase II trial, we enrolled recurred, metastatic ACC patients who progressed within 9 months. Patients were randomly assigned either axitinib (5mg twice daily) or observation arm with 1:1 ratio. Crossover to the axitinib arm was permitted for patients in the observation arm who had disease progression. The primary endpoint was 6-month progression-free survival (PFS) rate. The secondary endpoints included objective response rate (ORR), overall survival (OS), PFS, duration of response and adverse events. **Results:** A total of 60 patients randomly allocated to axitinib (N=30) and observation arm (N=30) and response evaluation was conducted in 57 patients. With a median follow-up of 25.4 months, the 6-month PFS rate was 73.2% (95% confidence interval [CI], 54.8 to 88.1%) in the axitinib arm and 23.2% (95% CI, 9.3 to 41.1%) in the observation arm (hazard ratio, 0.19; 95% CI, 0.08 to 0.45; $P < 0.001$). Median PFS was 10.8 months in axitinib arm and 2.8 months in observation arm ($P < 0.001$). The ORR was 3.3% (95% CI, 0.1 to 17.2%) in the axitinib arm, and 0% (95% CI, 0 to 12.8%) in the observation arm. The disease control rate was 100% (95% CI, 88.4 to 100%) in the axitinib arm and 51.9% (95% CI, 32.0 to 71.3%) in the observation arm. After crossover, ORR of axitinib in the observation arm was 11.1% (95% CI, 2.4 to 29.2%). Median OS was not reached in axitinib arm, 28.5 months in observation arm ($P = 0.688$). The most frequently reported adverse events of axitinib were grade 1 or 2 oral mucositis and fatigue. Detailed data of adverse events and mutational profile data will be presented. **Conclusions:** In this first randomized trial in patients with recurred or metastatic ACC, axitinib significantly increased 6-month PFS rate compared to observation. Clinical trial information: NCT02859012. Research Sponsor: Adenoid cystic carcinoma research foundation.

6504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Preliminary activity of tipifarnib in tumors of the head and neck, salivary gland and urothelial tract with HRAS mutations. *First Author: Alan Loh Ho, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: HRAS is a proto-oncogene overexpressed and mutated in some human carcinomas. Tipifarnib is a potent and highly selective inhibitor of farnesyltransferase, a critical enzyme for proper HRAS function. **Methods:** We report data from two phase 2 clinical trials investigating the activity of tipifarnib in HRAS mutant (HRASm) solid tumors: KO-TIP-001 (NCT02383927: Squamous carcinomas [SCC], thyroid and salivary gland tumors, among others) and IST-01 (NCT02535650: Urothelial carcinomas, UC).Primary endpoints were overall response rate (ORR, KO-TIP-001) and progression free survival (PFS) rate at 6 months (IST-01). All pts had RECIST v1.1. measurable disease at study entry. Pts receive a starting dose of tipifarnib of either 600 or 900 mg administered orally twice daily on days 1-7 and 15-21 of 28-day treatment cycles until progression of disease (PD) or unacceptable toxicity. **Results:** Proof of concept was achieved in studies KO-TIP-001 and IST-01. Based on preliminary efficacy results (Ho, et. al, ESMO 2018), KO-TIP-001 was amended to continue enrolling only in Head & Neck SCC (HNSCC) pts (Cohort 2) and other SCC pts (Cohort 3) with tumors carrying high HRASm variant allele frequency (VAF) >20%. As of 17 October 2019, 21 HNSCC pts meeting the high HRASm VAF criteria had been treated with tipifarnib of whom 18 were efficacy evaluable at data cut off. Pts had received a median of 2 prior systemic regimens. Ten objective responses were observed in 18 evaluable pts for an ORR of 56%. No responses were observed on last therapy prior to study entry. PFS on tipifarnib and on prior last therapy were, respectively, 6.1 and 2.8 months. In addition, 13 pts with recurrent/metastatic salivary gland tumors (SGT) were treated in KO-TIP-001 or in extended access programs. One objective response was observed in 12 (8%) evaluable pts and an additional 7 (58%) had stable disease as best response. Median PFS in SGT pts was 7 months. In IST-01, 224 UC pts were screened of whom 16 (7%) carried HRAS mutations and 15 of those were enrolled into the study. Five responses were observed in 12 evaluable UC pts (42%) and 3 additional pts had tumor size reduction. Median PFS was 5.1 months. **Conclusions:** Encouraging activity of tipifarnib was observed in HRASm solid tumors. Clinical trial information: NCT02383927, NCT02535650. Research Sponsor: Kura Oncology.

6505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

KEYNOTE-048: Progression after the next line of therapy following pembrolizumab (P) or P plus chemotherapy (P+C) vs EXTREME (E) as first-line (1L) therapy for recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). *First Author: Kevin Joseph Harrington, The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust National Institute of Health Research Biomedical Research Centre, London, United Kingdom*

Background: 1L P vs E improved OS in PD-L1 CPS ≥20 and CPS ≥1 populations, and led to noninferior OS in the total population, with favorable safety; 1L P+C vs E had superior OS in CPS ≥20, CPS ≥1, and total populations with comparable safety in the phase 3 KEYNOTE-048 study (NCT02358031) in patients with R/M HNSCC. Neither P vs E nor P+C vs E improved PFS in the PD-L1 CPS ≥20, CPS ≥1, or total populations. Here, we present the progression after the next line of therapy (PFS2) to assess the effect of 1L P or P+C and subsequent anticancer therapy on patient outcomes. **Methods:** Patients with locally incurable R/M HNSCC and no prior systemic therapy in the R/M setting were randomly assigned 1:1:1 to P, P+C, or E. PFS2 was defined as time from randomization to objective tumor progression on next-line therapy or death from any cause. PFS2 was estimated using the Kaplan-Meier method as an exploratory outcome confined to those receiving subsequent therapy after 1L P. HR and 95% CIs were based on a Cox regression model with Efron's method of tie handling with treatment as a covariate (stratified by ECOG performance status [PS], HPV status, and PD-L1 for CPS ≥1 and total populations; by ECOG PS and HPV status for CPS ≥20 population). Data cutoff: Feb 25, 2019. **Results:** Of 882 (301 [P]; 281 [P+C]; 300 [E]) treated patients,422 (P: 148 [49.2%]; P+C: 115 [40.9%]; E: 159 [53.0%]) received subsequent anticancer therapy after 1L P, most commonly C (P: 135 [44.9%]; P+C: 88 [31.3%]; E: 102 [34.0%]); EGFR inhibitor (P: 59 [19.6%]; P+C: 37 [13.2%]; E: 19 [6.3%]); and immune checkpoint inhibitor (P: 6 [2.0%]; P+C: 12 [4.3%]; E: 50 [16.7%]); patients may have received more than one type of subsequent therapy. Median PFS2 is reported in Table. **Conclusions:** In patients with R/M HNSCC, longer median PFS2 was observed in the CPS ≥20 and CPS ≥1 populations for P vs E, and in the CPS ≥20, CPS ≥1, and total populations for P+C vs E. These data further support use of 1L P or P+C in patients with R/M HNSCC. Clinical trial information: NCT02358031. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Population	Treatment	Median PFS2, month	HR (95% CI)	24-mo PFS2 rate, %
CPS ≥20	P (n=133) vs E (n=122)	11.7 vs 9.4	0.64 (0.48-0.84)	27.0 vs 12.5
CPS ≥1	P (n=257) vs E (n=255)	9.4 vs 8.8	0.80 (0.66-0.96)	22.0 vs 9.9
Total	P (n=301) vs E (n=300)	9.0 vs 9.0	0.90 (0.75-1.07)	19.7 vs 11.4
CPS ≥20	P+C (n=126) vs E (n=110)	11.3 vs. 9.7	0.63 (0.47-0.84)	28.9 vs 12.0
CPS ≥1	P+C (n=242) vs E (n=235)	10.3 vs 8.9	0.66 (0.54-0.80)	23.7 vs 9.0
Total	P+C (n=281) vs E (n=278)	10.3 vs 9.0	0.74 (0.62-0.88)	21.4 vs 10.5

6506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Low-cost oral metronomic versus intravenous chemotherapy in recurrent, inoperable and metastatic head and neck cancer: Phase III Metro-CIS study. *First Author: Nandini Sharrel Menon, Tata Memorial Hospital, Mumbai, India*

Background: The NCCN preferred regimens for palliation in head and neck cancer, either EXTREME or KEYNOTE-048 are the only two regimens which have improved outcomes over chemotherapy, but they have limited applicability (1-3%) in low and middle-income countries due to the cost. Oral metronomic chemotherapy (OMC) has shown better outcomes than intravenous cisplatin; these results were obtained with a low incidence of adverse events and the cost of 1/100th of NCCN-preferred regimens in a Phase II study. **Methods:** This was a randomized Phase III non-inferiority open-label study. Adult patients with relapsed-recurrent or metastatic upfront palliatively treated squamous cell carcinoma of head and neck and ECOG PS 0-1 were eligible. Patients were randomized 1:1 between OMC (oral methotrexate 15 mg/m^2 weekly with celecoxib 200 mg once daily or intravenous cisplatin (IVC) 75 mg/m^2, 3-weekly for 6 cycles. CTCAE version 4.0 was used for adverse event recording. Response assessment (RECIST version 1.1) was performed every 2 months. EORTC QLQ-C 30 and EORTC QLQ -H&N 35 questionnaires were self-administered at baseline and 2-monthly thereafter. The primary endpoint was overall survival (OS) and was measured from the date of randomization to death. Assuming a 6-month OS in IVC arm of 40%, the non-inferiority margin of 13%, type 1 error of 5% (2-sided), type 2 error of 20% and lost-to-follow up rate of 20%, a total sample size of 422 subjects was required. Kaplan Meier method was used for the estimation of OS and progression-free survival (PFS). To determine non-inferiority the upper limit of 95% CI of difference between 6 months OS of the 2 arms had to be below 13%. **Results:** In the intention to treat analysis, the 6-months OS was 50.89% (95% CI, 43.3-57.97) and 62.26% (95% CI, 54.72-68.9) in the IVC and OMC arm respectively. The difference in 6-months OS between the 2 arms was - 11.37% (95% CI, -20.77 to -0.97). The median OS was 6.1 (95% CI, 5.33-6.93) versus 7.5 (95% CI, 6.5-8.8) months in IVC arm and OMC arm respectively (P= .026). The unadjusted hazard ratio for death was 0.773 (95% CI, 0.615-0.97, P= .026). The median PFS was 1.67 (95% CI, 1.47-2.03) versus 3.23 (95% CI, 2.57-4.13) months in IVC and OMC arms respectively (P< 0.001). Any grade 3 or above adverse events were seen in 61 (30.2%) versus 37 (18.9%) patients in IVC and OMC arm respectively (P= .01). **Conclusions:** OMC improves outcomes in palliatively treated head and neck cancer and is a new standard of care in this setting, in addition to the EXTREME and KEYNOTE-048 regimen. Clinical trial information: CTRI/2015/11/006388. Research Sponsor: Tata Memorial Center Research Administration Council.

6507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

TPExtreme randomized trial: Quality of Life (QoL) and survival according to second-line treatments in patients with recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC). *First Author: Joel Guigay, Centre Antoine Lacassagne, FHU OncoAge, Université Côte d'Azur, Nice, France*

Background: TPExtreme trial comparing EXTREME regimen to the taxane-based TPEx confirmed the encouraging survival results of the TPEx regimen, despite lack of significant overall survival (OS) increase, with a significantly lower toxicity than the EXTREME regimen. Herein, the QoL and exploratory analyses of survival according to 2nd line treatments focusing on immunotherapy (IO) are presented. **Methods:** Randomized (1:1), open-label trial. Main inclusion criteria were R/M HNSCC not suitable for loco-regional treatment, age 18-70 years, PS < 2, creatinin clearance > 60ml/min, prior cisplatin < 300 mg/m^2. 539 pts were enrolled over a period of 37 months (mo). QoL was evaluated with QLQ-C30 questionnaire at baseline, week(W)12, W18, W26 and analyzed by linear mixed model. The primary QoL endpoint was the Global Health Status score. 2nd line treatments were collected for 501 (93%) patients (pts), 256 in the EXTREME arm and 245 in the TPEx arm. **Results:** The percentage of QLQ-C30 questionnaires filled at baseline, W12, W18 and W26 were similar in the 2 arms, 89%, 52%, 43%, and 39% in the EXTREME arm and 91%, 59%, 40%, and 37% in the TPEx arm, respectively.. Higher scores of Global Health Status (p = 0.02), physical functioning (p = 0.009) and role functioning (p = 0.013) and lower scores of appetite loss (p = 0.041) were observed in the TPEx arm than in the EXTREME arm. No significant difference was observed for the other scores. In 2nd line treatment, 120 (47%) pts in the EXTREME arm and 109 (44%) in the TPEx arm received chemotherapy +/- cetuximab (CT); 41 (16%) pts in the EXTREME arm and 41 (17%) in the TPEx arm received IO, mainly anti-PD-1/PD-L1. 79% and 85% of these 2nd line treatments were given after progression in EXTREME and TPEx arms respectively. Median OS (95%CI) since randomization was 17.6 (15.2 – 19.5) mo with CT and 19.4 (13.4 – 22.3) mo with IO in the EXTREME arm vs 14.9 (13.0 – 16.3) and 21.9 (15.9 – 35.0) mo in the TPEx arm (interaction test p = 0.077) respectively. Median OS since start of 2nd line was 9.3 mo with CT and 8.3 mo with IO in the EXTREME arm, and 7.1 and 11.6 mo respectively in the TPEx arm. **Conclusions:** An improvement in the QoL of patients was observed in the TPEx arm compared to that of the EXTREME arm. Exploratory analysis showed that the taxane-based TPEx regimen followed by IO in 2nd line could provide interesting median OS for pts who need CT in 1st line, with less toxicity than EXTREME. This sequential treatment deserves to be compared to a strategy that starts with Platinum+5FU+pembrolizumab. Clinical trial information: NCT02268695. Research Sponsor: Merck SERONO, GORTEC.

6508 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Results of a randomized phase III study of dysphagia-optimized intensity modulated radiotherapy (Do-IMRT) versus standard IMRT (S-IMRT) in head and neck cancer. *First Author: Christopher Nutting, Royal Marsden NHS Foundation Trust, London, United Kingdom*

Background: Most newly diagnosed oro- & hypopharngeal cancers (OPC, HPC) are treated with (chemo)RT with curative intent but at the consequence of adverse effects on quality of life. CRUK/14/014 investigated if using Do-IMRT to reduce RT dose to the dysphagia/aspiration related structures (DARS) improved swallowing function compared to S-IMRT. **Methods:** Patients with T1-4, N0-3, M0 OPC/HPC were randomised 1:1 to S-IMRT (65 Gray (Gy)/30 fractions (f) to primary & nodal tumour; 54Gy/30f to remaining pharyngeal subsite & nodal areas at risk of microscopic disease) or Do-IMRT. The volume of the superior & middle pharyngeal constrictor muscle (PCM) (OPC) or inferior PCM (HPC) lying outside the high-dose target volume was set a mandatory mean dose constraint in Do-IMRT. Treatment allocation was by minimisation balanced by centre, use of induction/concomitant chemotherapy, tumour site & AJCC stage. Primary endpoint was mean MD Anderson Dysphagia Inventory (MDADI) composite score 12 months after RT with 102 patients needed to detect a 10 point improvement (assuming S-IMRT score of 72, standard deviation (SD) 13.8; 90% power, 2-sided 5% alpha). Patients were blind to treatment allocation. Secondary endpoints included local control. **Results:** 112 patients (56 S-IMRT, 56 Do-IMRT) were randomised from 22 UK centres from 06/2016 to 04/2018. Mean age was 57 years; 80% were male; 97% had OPC; 90% had AJCC stage 3&4 disease; 86% had concomitant chemotherapy only, 4% induction & concomitant and 10% no chemotherapy. 111/112 had RT doses as prescribed (1 patient died before RT). Median of the mean inferior PCM dose was S-IMRT 49.8Gy (IQR 47.1-52.4) vs. Do-IMRT 28.4Gy (21.3–37.4), $p < 0.0001$; superior & middle PCM dose was S-IMRT 57.2Gy (56.3–58.3) vs. Do-IMRT 49.7Gy (49.4–49.9), $p < 0.0001$. Do-IMRT had significantly higher MDADI scores: S-IMRT 70.3 (SD 17.3) vs. Do-IMRT 77.7 (16.1), $p = 0.016$. 3 local recurrences (1 S-IMRT, 2 Do-IMRT) have been reported. **Conclusions:** Do-IMRT reduced RT dose to the DARS and improved patient reported swallowing function compared with S-IMRT. This is the first randomised study to demonstrate functional benefit of swallow-sparing IMRT in OPC. Clinical trial information: 25458988. Research Sponsor: Cancer Research UK and the National Institute for Health Research.

6509 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Evaluation of the correlation between antibiotic use and survival in patients with recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC) treated with immune checkpoint inhibitors (ICIs). *First Author: Paz J. Vellanki, US Food and Drug Administration, Silver Spring, MD*

Background: Recent evidence suggests that treatment with systemic antibiotics (Abx) disrupts the intestinal microbiome and may be associated with decreased survival for patients receiving treatment with ICIs for advanced cancers, including R/M HNSCC. However, a potential confounder is that Abx use identifies a subgroup of patients with a worse prognosis. The FDA examined the association between Abx use and survival for ICIs and other drugs used for the treatment of patients with R/M HNSCC. **Methods:** Data submitted to the FDA from three randomized controlled trials with ICI as a single agent or with chemotherapy (ICI group) compared to chemotherapy and/or cetuximab (Control group) were pooled. The association between systemic Abx use within 30 days of initiating anticancer therapy and survival for the ICI and Control groups was evaluated using Kaplan-Meier (KM) estimates and compared using Cox proportional hazards regression models, controlling for ECOG performance status, line of therapy, HPV status, PD-L1 expression, and other important prognostic factors. **Results:** In the ICI and Control groups, 36% and 46% of patients received Abx, respectively. For the ICI group, the difference in KM-estimated median overall survival (OS) was 5.6 months based on receipt of Abx (hazard ratio [HR] 1.70). Abx had no impact on OS for the Control group. Similar trends were observed for progression-free survival (PFS). **Conclusions:** In this exploratory analysis, systemic Abx within 30 days of initiating treatment for R/M HNSCC was associated with decreased survival for patients treated with ICIs compared with patients who did not receive Abx. Use of Abx had no apparent difference in survival in the control group. Further examination of the association between Abx use and clinical outcomes for patients with R/M HNSCC treated with ICIs is needed. Research Sponsor: None.

	ICI +Abx N = 372	ICI -Abx N = 666	Control +Abx N = 300	Control -Abx N = 349
Median OS, mo. (95% CI)	6.7 (5.6, 8.1)	12.3 (11.2, 13.6)	8.6 (7.2, 9.1)	8.8 (7.9, 9.7)
HR (95% CI)	1.70 (1.40, 2.00)		0.99 (0.70, 1.40)	
Median PFS, mo. (95% CI)	2.1 (2.1, 2.2)	3.5 (3.3, 3.6)	3.6 (3.5, 4.0)	4.5 (3.6, 4.9)
HR (95% CI)	1.48 (1.30, 1.70)		1.04 (0.73, 1.46)	

6511 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Plasma-based tumor mutational burden (bTMB) as predictor for survival in phase III EAGLE study: Durvalumab (D) ± tremelimumab (T) versus chemotherapy (CT) in recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) after platinum failure. *First Author: Weimin Li, AstraZeneca, Cambridge, MD*

Background: In NSCLC, bTMB assessed from circulating tumor DNA shows promise as a predictive survival biomarker for immunotherapy, but its value in R/M HNSCC is uncertain. We evaluated bTMB as a predictor of survival in R/M HNSCC. **Methods:** EAGLE (NCT02369874) was a randomized, open-label, phase 3 trial evaluating D (anti-PD-L1), or D+T (anti-CTLA-4), vs CT in R/M HNSCC. Patients (pts) with disease progression after platinum-based CT were randomized (1:1:1) to D (10 mg/kg intravenous [IV] every 2 weeks [Q2W]), D (20 mg/kg IV Q4W) + T (1 mg/kg IV Q4W for up to 4 doses, followed by D at 10 mg/kg Q2W) or CT. bTMB was assessed in pretreatment plasma samples using the Guardant Health OMNI platform. Association of somatic loss of function mutations with OS was assessed. **Results:** 736 intent-to-treat pts were randomized; 247 were evaluable for bTMB (BEP). bTMB expression was not linked to HPV status, PD-L1 status, age, gender, tumor location, or ECOG PS. Smoking and progression within 6 months on multi-modality CT in localized disease trended with higher bTMB. OS and PFS HRs were significantly improved for D or D+T vs CT in pts with high bTMB (≥16 mut/Mb) vs low (<16 mut/Mb; Table). The benefit of D or D+T vs CT in pts with high bTMB generally improved with increasing cutoff. 74 pts (27 D, 20 D+T, 27 CT pts) were bTMB high. 18-month OS rates were higher for D+T (22%; 95% CI 7%–42%) and D (33%; 95% CI 17%–51%) vs CT (0%; 95% CI 0%–0%) in pts with high bTMB. Pts with mutations in *KMT2D*, a HNSCC tumor suppressor gene, showed improved OS for D+T vs CT (HR 0.39; 95% CI 0.18–0.85). A trend of improved OS for D+T vs CT (HR 0.19; 95% CI 0.03–1.03) was also seen in pts with *ATM* mutations. **Conclusions:** This is the first retrospective analysis of a phase 3 trial to show bTMB may be predictive of outcomes for checkpoint inhibitors in R/M HNSCC. In pts with high bTMB, D or D+T improved OS hazards by at least 60%, vs CT at cutoffs ≥16 mut/Mb. Validation of bTMB as a predictive biomarker is ongoing. Clinical trial information: NCT02369874. Research Sponsor: AstraZeneca.

OS HRs (95% CI) for high versus low bTMB.

bTMB cutoff (mut/Mb)	D vs CT		D+T vs CT	
	High	Low	High	Low
≥8	0.63 (0.42–0.94)	1.04 (0.54–2.03)	0.68 (0.46–0.98)	1.34 (0.61–2.92)
≥12	0.65 (0.41–1.05)	0.75 (0.46–1.23)	0.61 (0.39–0.97)	0.98 (0.60–1.61)
≥16	0.39 (0.20–0.75)	0.91 (0.61–1.37)	0.40 (0.20–0.81)	0.92 (0.62–1.36)
≥20	0.40 (0.18–0.88)	0.81 (0.55–1.18)	0.41 (0.17–1.00)	0.84 (0.58–1.22)
≥24	0.26 (0.08–0.81)	0.82 (0.57–1.18)	0.29 (0.09–0.99)	0.83 (0.58–1.17)

6512 Poster Discussion Session; Displayed in Poster Session (Board #173), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Lenvatinib plus pembrolizumab combination therapy in patients with radioiodine-refractory (RAIR), progressive differentiated thyroid cancer (DTC): Results of a multicenter phase II international thyroid oncology group trial. *First Author: Bryan Haugen, University of Colorado, Aurora, CO*

Background: Lenvatinib is an approved therapy for patients with RAIR DTC. While the overall response rate (ORR) is high, few patients achieve a complete response (CR) and most patients eventually have progressive disease (PD). Combination lenvatinib and pembrolizumab is being explored in many different cancers, and this combination has been approved for advanced endometrial carcinoma. **Methods:** Patients with RAIR DTC with Response Evaluation Criteria in Solid Tumor (RECIST v1.1) measurable PD (<14 months (mo) prior to registration) were enrolled in this single-arm multicenter phase II study. Patients were excluded if they had received previous VEGFR-directed multikinase therapy. The lenvatinib starting dose was 20 mg/day orally and pembrolizumab was 200mg IV every 3 weeks. The primary endpoint was CR. ORR, progression-free survival (PFS) and safety graded by Common Terminology Criteria for Adverse Events v4.0 were secondary endpoints. **Results:** Thirty patients were enrolled. The median age was 62.5 years, and 53% of the patients were women. Seventy percent of patients had grade 3 adverse events (AEs) and 10 percent had grade 4 AEs. There were no treatment-related deaths. The most common > grade 3 AEs were hypertension (47%), weight loss (13%), maculopapular rash (13%), leukopenia (7%), diarrhea (7%) and oral mucositis (7%). Twenty-one patients (70%) required lenvatinib dose reduction. Of 29 evaluable patients, 18 (62%) had a partial response (PR) and 10 (35%) had stable disease (SD). The clinical benefit rate (ORR +SD) was 97%. Median time to tumor nadir was 7.4 mo (1.6-17.8 mo). Median PFS was not yet reached. The PFS at 12 months was 74%. Median time on therapy was 9.9 mo (3.2-18.9 mo). Fourteen patients are continuing therapy (7.6-18.9 mo). Six of these patients (43%) have not yet reached tumor size nadir. Three patients (10%) had > 80% target tumor shrinkage. **Conclusions:** Lenvatinib plus pembrolizumab is reasonably tolerated in patients with RAIR DTC. To date, there have been no documented complete responses. Combination lenvatinib plus pembrolizumab therapy has a high ORR in patients with RAIR DTC. Continuation of this study will help determine the depth and length of the responses. Clinical trial information: NCT02973997. Research Sponsor: Merck and Eisai, International Thyroid Oncology Group.

6513 Poster Discussion Session; Displayed in Poster Session (Board #174), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase II study of nivolumab (N) plus ipilimumab (I) in radioidine refractory differentiated thyroid cancer (RAIR DTC) with exploratory cohorts in anaplastic (ATC) and medullary thyroid cancer (MTC). *First Author: Jochen H. Lorch, Dana-Farber Cancer Institute, Boston, MA*

Background: Treatment options for aggressive TC are limited. Pre-clinical data suggests efficacy of CTLA-4 plus PD-1 blockade in aggressive RAIR TC. **Methods:** This investigator initiated phase II study tested N (3mg/kg every 2 weeks) plus I (1mg/kg every 6 weeks) until disease progression or completion of 24 mo of treatment in RAIR differentiated TC including poorly differentiated TC (PDTC) with exploratory cohorts in anaplastic (ATC) and medullary TC (MTC). Radiographic response rate by RECIST v1.1 (CR+PR) was primary endpoint. At least 6 pts with disease response among n=32 DTC provided 84% power to distinguish between a 10% and a 25% RR (one-sided 9% binomial test). **Results:** Accrual is complete with n=32 patients with DTC, 10 with ATC and 7 with MTC enrolled between October 2017 and May 2019. Thirty-two DTC included: n=17 papillary, n=7 Hurthle, n=4 follicular TC, n=4 PDTC. Among n=49, median (range) age was 65 (30-88), 51% (25/49) were female. To date, in DTC, 3/32 achieved a PR (n=2 Hurthle and n=1 PDTC), 9.4% RR (.95CI:2%-25%). One near complete response has been observed. Among pts w ATC, 3/ 10 profound PR by RECIST occurred (30% RR, .95CI: 7%-65%). Among them, two remain without clear evidence of disease at 26 and 13 mo after treatment start. No PR's were observed in MTC. Most frequent grade 3-4 TRAEs were as expected and included increased lipase (n=8), increased serum amylase (n=4). There was an unexpected number of treatment related adrenal insufficiency (AI) (n=4) which was associated with long PFS (range 10.1—16.4+mo). **Conclusions:** N+I appears to have considerable activity in ATC. In unselected RAIR DTC, activity was low but responses were seen in PDTC and Hurthle cell TC. Exceptional responses with prolonged remissions were observed. Clinical trial information: NCT03246958. Research Sponsor: Bristol-Myers-Squibb.

6514 Poster Discussion Session; Displayed in Poster Session (Board #175), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Atezolizumab combinations with targeted therapy for anaplastic thyroid carcinoma (ATC). *First Author: Maria E. Cabanillas, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: ATC is a rare/aggressive cancer with dismal outcome. Dabrafenib/trametinib is approved for BRAF-mutated ATC but pts eventually develop resistance. There are no approved drugs for pts with BRAF-wild type ATC. Better treatments (tx) are needed. **Methods:** ATC pts with PS $<$ 3 enrolled on a prospective trial at a single center, and tx was assigned by driver mutation: BRAF (cohort 1), RAS, NF1, or NF2 (cohort 2), or none of these (cohort 3). Cohort 4 with paclitaxel was exploratory for pts who did not qualify for 1-3. All pts received atezolizumab (A) IV + targeted therapy. Cohort 1 had run-in with vemurafenib (V) 960mg BID/cobimetinib (C) 60mg QD po for 28 days, followed by A 840mg Q2 weeks, at which time V dose was decreased to 720mg BID. Cohort 2: A + C (same doses as cohort 1); cohort 3: A 1200 mg Q3 weeks + bevacizumab 15 mg/kg q3 weeks. Pts unable to swallow used alternative drug preparation (ADP; crushed vemurafenib, suspension cobimetinib). Primary objective is to determine whether the tx in cohorts 1-3 leads to improved overall survival (OS). The trial was designed to enroll 36 pts but we are reporting early due to positive findings. Response rate (RR) was measured by RECISTv1.1. Median OS was estimated by Kaplan-Meier method. cfDNA and biopsy were obtained at baseline, course 2 and progression. Pts were allowed to undergo surgery and radiation while on trial. **Results:** From August 2017-January 2020, 34 ATC pts were enrolled in cohorts 1-3 and 9 in cohort 4. Cohort 3 closed early for futility. 3 pts had ADP. Median follow-up time was 7.51 mos (range: 0.43 – 27.37). Median OS in cohorts 1-3 was 18.23 mos (CI 10.45-NE) and 1-year OS was 67% (95%CI: 45%, 82%). See table. Response rate (RR) in cohort 1 was 71%: CR 1/17 (6%), PR 11/17 (65%), SD 4/17 (23%), 1 never restaged; in cohort 2 RR was 7%: PR 1/14 (7%), SD 7/14 (50%), PD 4/14 (29%), 2 died early. 8 (24% of cohort 1-3) pts had complete tumor resection after tx with VCA (n = 7) or CA (n = 1); all but 1 of these pts are alive. AEs as expected. cfDNA data will be reported at meeting. **Conclusions:** Atezolizumab + vemurafenib/cobimetinib for BRAF-mutated or + cobimetinib for NF1/2 or RAS-mutated ATC is effective, as evidenced by the long OS in these pts (13 mos $>$ historical control). A significant number of patients, particularly in cohort 1, were able to undergo complete tumor resection due to a favorable response to tx. Clinical trial information: NCT03181100. Research Sponsor: Genentech.

Female [N (%)]	17 (50%)	
Age, in yrs [median (range)]	66 (44-74)	
	N	Median OS in mos (95%CI)
Cohort 1	17	Not reached
Cohort 2	14	18.23 (4.47-NE)
Cohort 3	3	6.21 (4.11-11.99)
Cohort 4	9	4.44 (1.12-NE)
Cohort 1-3	34	18.23 (10.45, NE)

6515 Poster Discussion Session; Displayed in Poster Session (Board #176), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Concurrent cetuximab (CTX) and nivolumab (NIVO) in patients with recurrent and/or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): Results of phase II study. *First Author: Christine H. Chung, Moffit Cancer Center, Tampa, FL*

Background: While anti-Programmed Death-1 (anti-PD-1) inhibitors have efficacy, only some patients (pts) with R/M HNSCC achieve clinically significant benefits. We designed the study to determine the 1-year overall survival (OS) rate of concurrent CTX and NIVO in patients who had progressed on at least one prior treatment for their R/M HNSCC. **Methods:** Pts were treated with CTX 500 mg/m2 IV on Day (D) -14 as a lead-in followed by CTX 500 mg/m2 IV and NIVO 240 mg/m2 IV on D1 and D15 every 28-D cycle (C). Pts with CTX infusion reaction or who did not receive C1D1 for any reason were non-evaluable and replaced. NIVO dose reduction was not allowed but withheld/discontinued based on adverse event (AE) severity. **Results:** Total 47 pts are enrolled. 2 pts are non-evaluable. 45 evaluable pts are analyzed. Median age is 64 (24-77). ECOG performance status at baseline is 0 (9, 20%), 1 (33, 73%), and 2 (3, 7%). Primary sites are oral cavity 10 (22%), oropharynx 24 (53%), hypopharynx 3 (7%), larynx 6 (13%), and unknown primary 2 (4%). p16 status is available in 33 (73%). Prior treatments before the study enrollment are: chemotherapy (CT) 42 (93%), no CT 3 (7%), radiotherapy (RT) 38 (84%), no RT 7 (16%), checkpoint inhibitors (CPI) 23 (51%), and no CPI 22 (49%). PD-L1 combined positive scores (CPS) is available in 30 (67%). Median follow up time for overall survival (OS) is 12.6 months. The most common grade 3 treatment-related AE (TRAE) occurring $\geq$2 are fatigue 6 (13%) and rash-acneiform 2 (4.4%). The only grade 4 TRAE is CTX infusion reaction in 1 (2.2%). The most common grade 3 immune-related AE (IRAE) occurring $\geq$2 is fatigue 3 (6.7%). No grade 4 IRAE is observed. The median progression-free survival (PFS) and median OS are summarized in Table. Pts with no prior exposure to CPI have favorable PFS and OS relative to pts with prior CPI (PFS: HR 0.49, 95% CI 0.25-0.97, p=0.04 and OS: HR 0.5, 95% CI 0.22-1.14, p=0.09). **Conclusions:** Our data suggest the combination of CTX and NIVO is active in pts without prior CPI exposure and overall well tolerated in all pts. These preliminary results support further evaluation of the combination in CPI naïve pts. Clinical trial information: NCT03370276. Research Sponsor: Eli Lilly, Bristol Myers-Squibb, James and Esther King Biomedical Research Program.

Survival analyses.

	Total (N=45)	Prior CPI (N=23, 51%)	No prior CPI (N=22, 49%)	PD-L1 CPS <20 (N=11, 24%)	PD-L1 CPS ≥20 (N=19, 42%)	PD-L1 CPS unknown (N=15, 33%)	p16+ (N=22, 49%)	p16- (N=11, 24%)	p16 unknown (N=12, 27%)
Median PFS (months)	3.4	3.1	6.0	2.1	5.2	3.6	3.1	3.1	7.9
1-yr PFS	19%	9%	32%	0%	29%	17%	11%	9%	48%
Median OS (months)	11.5	9.7	13.3	13.3	11.5	8.6	9.7	12.6	11.5
1-yr OS	44%	29%	60%	69%	40%	36%	37%	55%	47%

6516 Poster Discussion Session; Displayed in Poster Session (Board #177), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Combination of monalizumab and cetuximab in recurrent or metastatic head and neck cancer patients previously treated with platinum-based chemotherapy and PD-(L)1 inhibitors. *First Author: Roger B. Cohen, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA*

Background: Monalizumab is a first-in-class immune checkpoint inhibitor targeting Natural Killer Group 2A (NKG2A), which is expressed on subsets of Natural Killer (NK), gd T and tumor-infiltrating $CD8^+$T cells. NKG2A blockade promotes innate anti-tumor immunity mediated by NK and $CD8^+$T cells and enhances NK cell antibody-dependent cell-mediated cytotoxicity induced by cetuximab. In a Phase I study, the combination of monalizumab and cetuximab was well tolerated. In an initial expansion cohort 1 of 40 patients (pts) who had progressed after platinum-based therapy, we reported an overall response rate (ORR) of 27.5%, a 4.5 month median PFS and an 8.5 month median OS. In a subset of patients (n=18) previously treated with PD-(L)1 inhibitors (IO), corresponding results were 17%, 5.1, and 14.1 months, respectively (ESMO 2019). Here we present data from a second expansion cohort 2 (n=40) conducted specifically in the post-IO setting to independently confirm the cohort 1 results. **Methods:** Eligible patients had R/M SCCHN previously treated with platinum and a PD-(L)1 inhibitor. Pts received monalizumab 750 mg q2weeks and cetuximab according to the label until progression or toxicity. Cohort 2 was designed as a confirmatory multicenter single arm phase II study, with a pre-planned total of 40 patients. The primary endpoint was ORR assessed per RECIST 1.1. **Results:** As of January 31, 2020, 40 pts have been treated in cohort 2. Median follow-up is 7.3 months (range, 1.9-13.6+). Eight (8) pts have a confirmed partial response (PR); ORR is 20% [95% confidence interval: 11-35]. Median time to response is 1.6 months [1.6-5.3]. At the time of data analysis, 3 pts were still in PR and 3 pts had stable disease continue on treatment. PFS and OS are still immature. **Conclusions:** In pts previously treated with platinum and PD-(L)1 inhibitors, the combination of monalizumab and cetuximab demonstrated promising activity. The second extension cohort confirmed prospectively the ORR reported in cohort 1. A randomized phase III trial of monalizumab and cetuximab is planned in this platinum and IO-pretreated SCCHN population. Clinical trial information: NCT02643550. Research Sponsor: INNATE PHARMA, Pharmaceutical/Biotech Company.

6517 Poster Discussion Session; Displayed in Poster Session (Board #178), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Updated analysis of the inducible T-cell co-stimulatory receptor (ICOS) agonist, GSK3359609 (GSK609), combination with pembrolizumab (PE) in patients (pts) with anti-PD-1/L1 treatment-naïve head and neck squamous cell carcinoma (HNSCC). *First Author: Eric Angevin, Gustave Roussy Institut de Cancérologie, Villejuif, France*

Background: INDUCE-1 (NCT02723955) is a first-in-human study investigating GSK609, an IgG4 ICOS agonist non-T-cell depleting antibody, as monotherapy and combination therapy with anti-cancer agents that includes PE. A range of GSK609 dose levels (≥0.1–1 mg/kg) having biological and clinical activity were identified and evaluated in the expansion phase with GSK609 0.3 mg/kg selected as the dose for further investigation. Results from the HNSCC expansion cohorts (ECs) showed GSK609 has single agent activity in pts with relapsed/refractory disease, and early clinical activity in combination with PE in pts with anti-PD-1/L1 treatment-naïve disease (Rischin, et al. *Annals of Oncol* 2019;30[Supplement_5]:v454–5). Updated results from the GSK609/PE HNSCC EC are presented. **Methods:** Eligible pts for the HNSCC EC had anti-PD-1/L1 treatment-naïve disease, ≤5 prior lines of therapy, measurable disease, and no active autoimmune disease. Pts received GSK609 0.3 mg/kg + PE 200 mg every 3 weeks (wks) until disease progression or unacceptable toxicity, up to 2 years (yrs)/35 cycles. Disease assessments were performed every 9 wks through wk 54 then every 12 wks thereafter. Pts were followed for survival and subsequent anti-cancer therapy. **Results:** As of 11 October 2019, 34 pts were enrolled and evaluable for efficacy analyses. The median age of this population was 61.5 yrs (range: 37–77); 85% were male; 53% received ≥1 prior line of therapy in the metastatic setting. ORR was 26% (95% CI: 12.9, 44.4; n = 9 with 4 complete and 5 partial responses); disease control rate was 68% (95% CI: 49.5, 82.6; n = 23). Among pts with PD-L1 IHC status by 22C3 pharmDx assay (n = 24; 71%), the majority of pts with a response or stable disease (SD) had PD-L1 CPS status < 20 (11 of 15 pts including 1 SD pt with CPS < 1). Median PFS was 5.6 months (95% CI: 3.9, 6,2). Median OS was not reached at time of analysis (95% CI: 8.2, NR); 6-month OS rate was 84% (95% CI: 66, 93). Treatment-related adverse events were reported in 66% of pts; the majority of events were Grades 1 or 2 with < 10% of pts experiencing ≥ Grade 3 events. **Conclusions:** This updated analysis with a more mature dataset shows promising clinical activity that supports further randomized investigation of GSK609 in combination with PE with an OS endpoint in HNSCC. Clinical trial information: NCT02723955. Research Sponsor: Study is funded by GlaxoSmithKline and in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

6518 Poster Discussion Session; Displayed in Poster Session (Board #179), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A prospective phase II open-label randomized controlled trial to compare mandibular preservation in upfront surgery to neoadjuvant chemotherapy followed by surgery in operable oral cavity cancer. *First Author: D. Chaukar, TMH, Mumbai, India*

Background: The study objective was to evaluate the non-Inferiority of survival and ability to preserve mandible with the use of neoadjuvant chemotherapy (NACT) in locally advanced oral cancers compared to upfront surgery alone without compromising survival. **Methods:** This study was a randomized, single centre, non-inferiority trial. Eligibility criteria included treatment naïve histologically confirmed cancer of the oral cavity; cancers requiring segmental resection for paramandibular disease without clinicoradiological evidence of bone erosion, clinical T2, T3 and T4, any N, M0 as per TNM (AJCC) 7th edition, age at least 18 years; and written informed consent. The patients were randomly assigned (1:1) to receive either upfront surgery followed by adjuvant treatment (Standard arm-SA) or receive two cycles of three drugs NACT (Docetaxel, Cisplatin, 5-Flurouracil) at three weekly interval (Intervention arm-IA). Depending on the response after two cycles, the patient would either receive an additional third cycle or undergo surgery followed by adjuvant treatment as decided by the tumour board. The primary endpoint was mandible preservation rate at 30% in the experimental arm. The secondary end points being Loco regional control and treatment related toxicity. **Results:** Between September 2010 and April 2013, 68 patients were enrolled and randomized to SA (34 patients) and IA (34 patients) with a median follow-up of 3.6 years (IQR 0.95- 7.05 years). Majority of the patients were T4 (n = 40, 58.8%) In the IA 28 patients had partial response (n = 28,82.4%), with a mandible preservation (Marginal Mandibulectomy) rate of 48% (n = 16/34). There were no close or positive margins in the IA. All patients received adjuvant treatment. The number of recurrences was similar in both the arms. All patients in the IA developed toxicities with the majority developing Grade III-IV toxicities (Grade III: 14, 41.2%, Grade IV: 11, 32.4%) (p = 0.739). The disease free survival (DFS) (p = 0.715, HR 0.911[0.516-1.607]) and overall survival (OS) (p = 0.747, HR 0.899 [0.510-1.587]) were similar in both the arms. **Conclusions:** NACT seems to be a feasible option for mandibular preservation with acceptable toxicities in a select group of patients without compromising survival. However this needs to be tested in a larger phase III randomized trial. Clinical trial information: CTRI/2015/11/006396. Research Sponsor: Tata Memorial Centre Intramural Funds.

6519 Poster Discussion Session; Displayed in Poster Session (Board #180), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A multicenter phase II trial of the combination cisplatin/ docetaxel/ durvalumab/tremelimumab as single-cycle induction treatment in locally advanced HNSCC (CheckRad-CD8 trial). *First Author: Markus Hecht, Department of Radiation Oncology, Universitatsklinikum Erlangen, Friedrich-Alexander-Universitat Erlangen-Nürnberg, Erlangen, Germany*

Background: PD-1/PD-L1 inhibitors are efficient in head and neck squamous cell cancer (HNSCC). Combination with anti-CTLA4 agents may enhance anti-tumor activity compared to anti-PD-1/PD-L1 monotherapy in different tumor types. In the CheckRad-CD8 trial the typical induction treatment consisting of Cisplatin/Docetaxel was combined with Durvalumab/Tremelimumab. Patients with pathological complete response (pCR) in the re-biopsy after induction treatment or at least 20% increase of intratumoral CD8 density in the re-biopsy compared to baseline entered radioimmunotherapy with concomitant Durvalumab/Tremelimumab. **Methods:** In this prospective multicenter phase II trial, patients with HNSCC stage III-IVB received a single cycle of Cisplatin 30mg/m² d1-3, Docetaxel 75mg/m² d1, Durvalumab 1500mg fix dose d5 and Tremelimumab 75mg fix dose d5. Objectives of this interim analysis were to quantify the effect of the induction treatment on intratumoral CD8 density and the pCR rate and to generate safety data. **Results:** Between Sep 2018 and Dec 2019, 57 patients were enrolled. Median age was 59 years, 22 patients (37%) were current smokers, 27 patients (47%) had oropharyngeal tumors (52% p16 positive). The median pre-treatment intratumoral CD8 density was 335 CD8+ cells/mm². After induction treatment 27 patients (47%) had a pCR in the re-biopsy and further 25 patients (44%) had a relevant increase of intratumoral CD8+ cells (median increase by factor 3.0). Response according to RECIST criteria was CR in 1 (2%), PR in 19 (33%) and SD in 20 patients (35%) (17 patients not evaluable). Adverse events (AE) grade 3-4 appeared in 39 patients (68%) and mainly consisted of leucopenia (43%) and infections (28%). 6 patients (11%) developed grade 3-4 immune-related AEs. In multivariable analysis the intratumoral CD8 density was the only independently significant predictor of pCR (odds ratio 1.0013 per cell/mm², 95%-CI 1.00023-1.0023, p=0.017). 42 patients (74%) continued with Durvalumab/Tremelimumab concomitant to radiotherapy. **Conclusions:** Single cycle induction treatment with Cisplatin/Docetaxel/Durvalumab/Tremelimumab is feasible and achieves a high pCR rate. CD8 density may have a predictive role for further treatment planning in locally advanced HNSCC. Clinical trial information: NCT03426657. Research Sponsor: Astra Zeneca.

6521 Poster Discussion Session; Displayed in Poster Session (Board #182), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

GEM20110714: Final overall survival results of the phase III study of first-line gemcitabine plus cisplatin versus fluorouracil plus cisplatin in recurrent or metastatic nasopharyngeal carcinoma. *First Author: Shaodong Hong, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: GEM20110714, the first randomized, phase III study (NCT01528618) of systemic chemotherapy in recurrent or metastatic (R/M) nasopharyngeal carcinoma (NPC), reported significant reduction of disease progression with gemcitabine plus cisplatin (GP) versus fluorouracil plus cisplatin (FP; hazard ratio [HR], 0.55; 95% CI, 0·44–0·68; P < .001). This study establishes GP as the standard-of-care for first-line treatment of R/M NPC. We present the final overall survival (OS) analysis here. **Methods:** In this multicenter, open-label study conducted in China, patients who had an Eastern Cooperative Oncology Group performance status of 0 or 1 and R/M NPC were randomly assigned (1:1) to receive up to six cycles of either GP or FP once every 3 weeks. The primary endpoint was PFS, which has been previously reported; OS was a secondary endpoint. The final OS analysis was conducted with the data cutoff date of December 17, 2019. **Results:** After a median follow-up time of 64.4 months (95% CI, 61.1-67.6), 148 (81.8%) and 165 (91.2%) deaths occurred in the GP and FP arms, respectively. The estimated hazard ratio for OS was 0.723 (95% CI, 0.578 to 0.904; two-sided P = .004). The median OS was 22.1 months with GP versus 18.6 months with FP. The OS probabilities at 1, 3, and 5 years were 79.9% vs. 71.8%, 31.0% vs. 20.4%, and 18.5% vs. 7.6%, respectively. Un-predefined subgroup analyses based on baseline characteristics were consistent with the primary OS analysis. Postdiscontinuation systemic therapy use was similar: GP, 52%; FP, 57%. No new safety signals emerged. **Conclusions:** In patients with R/M NPC, GP is the first regimen to show significant improvement in OS in a phase III randomized study compared with a traditional chemotherapy regimen (i.e. FP). GP should be considered the standard treatment option for these patients. Clinical trial information: NCT01528618. Research Sponsor: None.

6522 Poster Discussion Session; Displayed in Poster Session (Board #183), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Development and validation of a gene expression-based signature predicting efficacy of induction chemotherapy in locoregionally advanced nasopharyngeal carcinoma: A multicenter cohort study. *First Author: Yuan Lei, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: Induction chemotherapy (IC) followed by concurrent chemoradiotherapy is the mainstay treatment for patients with locoregionally advanced nasopharyngeal carcinoma (LA-NPC). However, some patients obtain little benefit and experience unnecessary toxicities from IC. We intended to develop a gene expression signature that can identify patients who will benefit from IC. **Methods:** We screened chemoresistance-related genes by comparing gene expression profiles of patients with short-term tumor response or non-response to IC (n = 95) using microarray analysis. Chemoresistance-related genes were quantified by digital expression profiling in a training cohort (n = 342) to obtain a gene signature. We then validated this gene signature in the clinical trial cohort (n = 187) and an external independent cohort (n = 240). **Results:** We identified 43 chemoresistance-related genes associated with the short-term tumor response to IC. In the training cohort, a 6-gene signature was developed that was highly accurate at predicting the short-term tumor response to IC (area under the curve [AUC] 0.87, sensitivity = 87.5%, specificity = 75.6%). We then apply the 6-gene signature to classify patients into the benefit group and the no-benefit group. In the benefit group, patients could benefit from IC in terms of failure-free survival (hazard ratio [HR] 0.54 [95% confidence interval 0.34-0.87]; p = 0.01), while patients in the no-benefit group could not (HR 1.25 [95%CI 0.62-2.51]; p = 0.53). In the clinical trial cohort, the developed 6-gene signature was also highly accurate at predicting the response to IC (AUC = 0.82; sensitivity = 87.5%; specificity = 71.8%). Additionally, IC conferred failure-free survival benefits only on patients in the benefit group (HR 0.37 [95%CI 0.18-0.75], p = 0.004) and not on those in the no-benefit group (HR 0.70 [95%CI 0.27-1.82]; p = 0.46). In the external independent cohort, similar results were observed. **Conclusions:** The 6-gene signature can help select patients who will benefit from IC and thus lay a foundation for a more individualized therapeutic strategy for LA-NPC patients. Research Sponsor: This study was supported by grants from the Key-Area Research and Development Program of Guangdong Province (2019B020230002), the National Natural Science Foundation of China (81930072; 81922057), the Natural Science Foundation of Guangdong Province (2017.

6523 Poster Discussion Session; Displayed in Poster Session (Board #184), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Network-meta-analysis of chemotherapy in nasopharyngeal carcinoma (MAC-NPC): An update on 8,221 patients. *First Author: Claire Petit, Gustave Roussy, Villejuif, France*

Background: Based on an individual patient data (IPD) network meta-analysis (NMA) of 20 randomized trials and 5,144 patients (pts), the MAC-NPC collaborative group has shown that the addition of adjuvant chemotherapy (AC) to chemo-radiotherapy (CRT) achieved the highest survival benefit in nasopharyngeal carcinoma (NPC; Ribassin-Majed JCO 2017). Here, we updated the meta-analysis with the addition of 8 trials. **Methods:** Trials of Radiotherapy (RT) with or without chemotherapy (CT) in patients with non-metastatic NPC were identified and updated IPD obtained. Both Western and Chinese medical literatures were searched. Overall Survival (OS) was the main endpoint. Fixed and random-effects frequentist NMA models were applied, network heterogeneity and consistency were evaluated. P-score was used to rank the treatments. R software - netmeta package was used to perform the analyses. Treatments were grouped in the following categories: RT alone (RT), induction chemotherapy followed by RT (IC-RT), induction chemotherapy without taxanes followed by concomitant chemoradiotherapy (ICtax(-)-CRT), induction chemotherapy with taxanes followed by concomitant chemoradiotherapy (ICtax(+)-CRT), concomitant chemoradiotherapy (CRT), concomitant chemoradiotherapy followed by adjuvant chemotherapy (CRT-AC) and RT followed by adjuvant chemotherapy (RT-AC). **Results:** Overall 28 trials and 8,214 pts were included. Median follow-up was 7.2 years. There was no heterogeneity in the NMA. There was inconsistency in the main analysis, which disappeared after the exclusion of 2 outlier trials. ICtax(+)-CRT ranked the best treatment for OS with a P-Score of 91%. Hazard ratio [HR, 95% Confidence Interval] for ICtax(+)-CRT was 0.75 [0.59-0.96] compared to CRT and 0.92 [0.69-1.24] compared to CRT-AC (second best treatment in raking with a P-Score of 85%; see league table below). When the 2 types of IC were merged, CRT-AC ranked the first followed by IC-CRT with P-Scores of 93% and 86% respectively, with a HR of 0.97 [0.84-1.14] for CRT-AC vs. IC-CRT. **Conclusions:** This IPD NMA of the treatment of locally advanced NPC demonstrates that the addition of IC or AC to CRT improves disease control probability and survival over CRT alone. Data on progression-free survival, locoregional and distant control will be presented at the meeting. Research Sponsor: french LNCC, PHRC.

ICtax(+)-CRT p-score = 91%			
0.92	CRT-AC		
[0.69-1.24]	p-score = 85%		
0.87	0.94	ICtax(-)-CRT	
[0.65-1.17]	[0.79-1.13]	p-score = 74%	
0.75	**0.82**	0.87	CRT
[0.59-0.96]	**[0.69-0.97]**	[0.74-1.02]	p-score = 45%

6524 Poster Session (Board #185), Fri, 8:00 AM-11:00 AM

Phase II study of consolidative intensity-modulated radiation therapy following first-line palliative systemic chemotherapy for de novo previously untreated metastatic (M1) nasopharyngeal carcinoma. *First Author: Victor Ho-Fun Lee, Department of Clinical Oncology, Queen Mary Hospital, The University of Hong Kong, Hong Kong, Hong Kong*

Background: The prognosis of de novo previously untreated metastatic (M1) nasopharyngeal carcinoma (NPC) at diagnosis is poor, and the role of consolidative intensity-modulated radiation therapy (IMRT) to the primary tumor and the neck following first-line palliative chemotherapy remains unknown. We report a phase II study of consolidative IMRT after first-line chemotherapy in previously untreated M1 NPC. **Methods:** Consolidative IMRT was given in prospectively recruited patients whose previously untreated M1 NPC did not progress after 6 cycles of first-line chemotherapy with gemcitabine and cisplatin. The primary study objective was overall survival (OS). Secondary objectives included progression-free survival (PFS), local relapse-free survival (LRFS), regional relapse-free survival (RRFS), response and toxicity. **Results:** Sixty-nine consecutive patients were enrolled. Sixty-four (92.8%) patients received first-line chemotherapy, of which 8 (12.5%) developed progressive disease and another 8 (12.5%) did not receive IMRT despite non-progression to first-line chemotherapy. The remaining 48 patients whose disease controlled after chemotherapy received IMRT, including 18 (37.5%) who received concurrent chemoradiation. OS was significantly better in those who received IMRT (35.1 *versus* 14.2 months; $P < 0.001$), after a median follow-up duration of 3.40 years (range 0.43 years to 12.14 years). PFS, LRFS, and RRFS were also significantly longer in those who received IMRT. Multivariable analyses revealed that IMRT was the only prognostic factor of all survival endpoints. Grade 3 adverse events were observed in 10 (20.8%) patients, mainly mucositis, dysphagia and desquamation. **Conclusions:** Consolidative IMRT was associated with an OS benefit and favorable tolerability among previously untreated M1 NPC patients who had non-progressive disease following first-line chemotherapy. These results support the rationale to further investigate IMRT as part of the initial treatment in this setting. Clinical trial information: NCT02476669. Research Sponsor: SK Yee Medical Foundation.

6526 Poster Session (Board #187), Fri, 8:00 AM-11:00 AM

Association between calcitonin and efficacy of anlotinib in medullary thyroid carcinoma: An analysis based on the ALTER01031 trial. *First Author: Ming Gao, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin's Clinical Research Center for Cancer, Tianjin, China*

Background: Calcitonin (Ct) is the most important biomarker for medullary thyroid carcinoma (MTC). In a randomized, placebo-controlled phase IIb trial (ALTER01031, NCT02586350) for MTC, anlotinib exhibited a strong capability not only in PFS prolongation but also in decreasing Ct level. This subanalysis explored the relationship between Ct level and anlotinib efficacy in this trial. **Methods:** Serum Ct of patients (pts) were tested at baseline and on week 6 (after 2 treatment cycles). Correlation between changes in Ct level and changes in target lesion diameters was explored. The influence of baseline Ct level on median PFS for anlotinib treated pts was estimated. Finally, pts in anlotinib arm were divided into two subgroups based on the percentage decline of Ct levels ($>$ 50% vs. $\leq$50%) at week 6. Median PFS (mPFS), median OS (mOS) and objective response rate (ORR) of two groups were compared. **Results:** 86 of 91 enrolled pts (58 in anlotinib arm and 28 in placebo arm) were recorded their serum Ct levels at baseline and no significant difference was observed between two arms (7990.0 ng/L vs. 10891.5 ng/L, $P = 0.192$). After 2 treatment cycles, the Ct level decreased to 4597.5 ng/L in anlotinib arm (n = 50) while increased slightly in placebo arm (12640.0 ng/L, n = 24, $P = 0.006$). For 49 pts in anlotinib arm who had complete assessments at baseline and week 6, roughly linear relationship was observed between Ct levels (X-axis) and target lesion diameters (Y-axis) in percent changes from baseline to week 6 ($y = 0.175x - 0.049$; $r = 0.352$, $P = 0.016$, excluding 3 outliers). Pts with less baseline Ct level ($\leq$ median value vs. $>$ median value) did not show more PFS benefit (17.7 vs. 22.4 months, $P = 0.802$). However, after 2 treatment cycles, a trend of better survival and higher response was observed in pts with high percentage decline of Ct level ($>$ 50%, n = 25) than those with low percentage decline ($\leq$50%, n =25) although without statistical difference (data presented in the table below). **Conclusions:** In ALTER01031, anlotinib showed a strong capability in rapidly decreasing serum Ct. Lower baseline Ct level does not mean better prognosis while a rapid Ct decrease may predict improved survival and treatment response to MTC pts received anlotinib. Clinical trial information: NCT02586350. Research Sponsor: None.

Percentage decline of Ct level	> 50% (events/ censored)	< 50% (events/ censored)	HR (95% CI)	*P* value
mPFS (months)	25.7 (10/15)	17.5 (15/10)	0.665 (0.304, 1.46)	0.302
OS (months)	not reached (5/20)	34.6 (10/15)	0.464 (0.169, 1.29)	0.149
ORR (%)	64	40		0.089

6527 Poster Session (Board #188), Fri, 8:00 AM-11:00 AM

Influence of Eastern Cooperative Oncology Group performance status (ECOG PS), tumor size and age on patient outcomes after anlotinib treatment: A subgroup analysis based on ALTER01031 trial for medullary thyroid carcinoma (MTC). *First Author: Ming Gao, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin's Clinical Research Center for Cancer, Tianjin, China*

Background: Anlotinib is a newly developed TKI achieved a nearly 2-fold PFS prolongation in a randomized, placebo-controlled phase 2b trial (NCT02586350) for MTC, the results of which were firstly published in 2019 ASCO annual meeting. This subanalysis examined the influence of baseline demographic (ECOG PS score, age) and tumor size on efficacy in this study. **Methods:** Kaplan-Meier method was applied to estimate the median PFS (mPFS) for subgroups of patients (pts) received anlotinib or placebo based on ECOG PS score (0 vs. 1), median tumor lesion diameter ($<$ 67 vs. $\geq$67mm) and age ($<$ 55 vs. $\geq$55 years old). **Results:** 91 eligible pts were randomly assigned in a 2:1 ratio to receive anlotinib or placebo. The numbers of pts in each subgroup were summarized in the table below. In placebo arm, mPFS did not differ significantly between pts with ECOG PS 0 and 1 (11.3 vs. 11.1months; HR = 0.895 [95% CI 0.347, 2.312], P = 0.821) or between pts with tumor lesion diameter $<$ 67mm and $\geq$ 67mm (7.0 vs. 11.1 months; HR = 1.168 [95% CI 0.463, 2.945], P = 0.737). Conversely, pts in anlotinib arm with ECOG PS 0 obtained more PFS benefits (34.6 vs. 14.0 months; HR = 0.331 [95% CI 0.163, 0.671], P = 0.002). Similarly, anlotinib treated pts with tumor lesion diameters $<$ 67mm achieved a longer mPFS (Not reached vs. 14.0 months, HR = 0.567 [95% CI 0.280, 1.147], P = 0.111). Consistent with that has been verified in differentiated thyroid cancer, high age predicted poor prognosis as mPFS were 14.3 months and 6.8 months in pts $<$ 55 and $\geq$ 55 years old respectively in placebo arm (HR = 0.322 [95% CI 0.116, 0.893], P = 0.007).). Anlotinib treatment exhibited PFS improvement to pts in both age groups but higher PFS prolongation was observed in pts $<$ 55 years old (22.4 vs. 14.0 months; HR = 0.720 [95% CI 0.321, 1.614], P = 0.381). **Conclusions:** This analysis showed that for pts in placebo arm, PFS was similar regardless of functional status (ECOG PS) or tumor size while older pts had higher progression risk. Treatment with anlotinib exhibited greater PFS benefits for pts with better functional status (ECOG PS = 0), younger age or lower tumor burden. These results indicated that it is reasonable to start anlotinib treatment at a relative earlier disease stage before the worsen of ECOG PS, increase of tumor size or ageing. Clinical trial information: NCT02586350. Research Sponsor: None.

Number of pts	ECOG PS (0/1)	Tumor lesion diameter ($<$ 67/$\geq$ 67 mm)	age ($<$ 55/ $\geq$ 55)
Placebo	10/19	12/17	18/11
Anlotinib	25/37	34/28	38/24

6529 Poster Session (Board #190), Fri, 8:00 AM-11:00 AM

A phase II study on the efficacy and toxicity of cabozantinib in recurrent/metastatic salivary gland cancer patients. *First Author: Wim van Boxtel, Radboud University Medical Center, Nijmegen, Netherlands*

A phase II study on the efficacy and toxicity of cabozantinib in recurrent/metastatic salivary gland cancer patients. **Background:** Because c-MET and VEGFR are often overexpressed in salivary gland cancer (SGC), this study evaluated the efficacy and safety of cabozantinib in recurrent/metastatic (R/M) SGC pts. **Methods:** A single center, single arm, phase II study was conducted. Immunohistochemical c-MET positive (H-score $\geq$10) R/M SGC pts were included in 3 cohorts: adenoid cystic carcinoma (ACC), salivary duct carcinoma (SDC), and other SGCs. Objective growth or complaints due to the disease were required before inclusion in the ACC and other SGC cohort. No prior systemic treatments were required. Pts started 60 mg cabozantinib tablets OD. Primary endpoint was the objective response rate (ORR). A Simon two-stage design was used. In case of $\geq$1 objective response in the first 9 pts/cohort, 8 additional pts would be included in the cohort. **Results:** In total 25 pts were included from Sep. 2018 until premature closure due to severe toxicity in Nov. 2019. Median age was 56 years (range 49-72), prior treatments included: primary tumor resection (n=19), radiotherapy $\geq$50Gy (n=24), systemic therapy (n=10; adjuvant in 2 pts, palliative in 8 pts). Six pts had grade 3 (n=4), grade 4 (n=1), or grade 5 (n=1) wound/fistula complications, occurring at a median of 7.2 mths on cabozantinib (range 2.1-12.8). This resulted in a severe wound complication rate of 32% in 19 pts on treatment for $\geq$2 mths. Remarkably, 4 out of 6 pts developed this complication in the area exposed to high-dose Rx; 2/4 had a pre-existing fistula in this area. Median interval between Rx and start of cabozantinib was 71.3 mths (range 10.6-94.7). Other grade $\geq$3 adverse events in $>$1 pt were: hypertension (5 pts), diarrhoea (2 pts) and dehydration (2 pts). Current median follow-up is 6.8 mths. The ORR was 6% (1/17 pts) in the ACC cohort, 20% (1/5 pts) in the SDC cohort, and 0% (0/3 pts) in other SGC pts; median PFS is 12.6 mths (95% CI 6.8 – 18.4 mths), 9.0 mths (insufficient events for 95% CI), and 6.9 mths (95% CI 0 – 15.2 mths), respectively. Median OS is not reached in any cohort. **Conclusions:** This phase II study on cabozantinib in R/M SGC pts demonstrated severe wound and fistula complications in 32% of pts on treatment for $\geq$2 mths, mostly (4/6 pts) within the radiotherapy field. Because of this toxicity the study was closed prematurely. Furthermore, cabozantinib showed minimal clinical activity in SGC pts. Research funding: Ipsen Pharmaceuticals Clinical trial information: NCT03729297. Research Sponsor: Ipsen Pharmaceuticals.

6530 Poster Session (Board #191), Fri, 8:00 AM-11:00 AM

Pembrolizumab (P) or P + chemotherapy (C) versus EXTREME (E) as first-line (1L) therapy for recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): analysis of KEYNOTE-048 by disease state. *First Author: Danny Rischin, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia*

Background: In the phase 3 KEYNOTE-048 trial (NCT02358031) in R/M HNSCC (N = 882), 1L P vs E showed superior OS in PD-L1 CPS $\geq$20 and CPS $\geq$1 populations, noninferior OS in the total population, no PFS benefit, and favorable safety; 1L P+C vs E showed superior OS in CPS $\geq$20, CPS $\geq$1, and total populations, no PFS benefit, and comparable safety. Results of P or P+C vs E in incurable recurrent only, metastatic only, and R/M subgroups are shown. The metastatic only and R/M subgroups were combined and classified as metastatic. **Methods:** Patients with incurable recurrent (local and/or regional node recurrent disease) or metastatic HNSCC were randomly assigned 1:1:1 to P, P+C, or E. OS and PFS were estimated using the Kaplan-Meier method. Hazard ratios and 95% CIs were based on a Cox regression model with Efron s method of tie handling with treatment as a covariate stratified by ECOG performance status, HPV status, and PD-L1 status. Data cutoff: Feb 25, 2019. **Results:** In the incurable recurrent only subgroup (n = 252), median OS was 11.5 vs 12.1 mo (P vs E) and 13.0 vs 11.1 mo (P+C vs E). In the metastatic subgroup (n = 620), median OS was 11.4 vs 9.7 mo (P vs E) and 13.0 vs 10.1 mo (P+C vs E). Median follow-up, OS, and PFS are shown in Table. Treatment-related adverse events (TRAE) in the incurable recurrent only subgroup: 49.4% (P), 94.7% (P+C), and 97.8% (E); grade 3-5 TRAEs rates: 16.0%, 78.7%, and 73.3%, respectively. TRAE rates in the metastatic subgroup: 61.6% (P), 96.4% (P+C), and 96.4% (E); grade 3-5 TRAEs rates: 17.6%, 69.5%, and 67.0%, respectively. **Conclusions:** P and P+C vs E were efficacious in the metastatic subgroup; in the relatively smaller subgroup of patients with incurable recurrent only HNSCC, the effect was less pronounced. Consistent with the total study population and regardless of disease state, the safety profile was favorable with P vs E and comparable with P+C vs E. These data further support use of 1L P or P+C in patients with R/M HNSCC. Clinical trial information: NCT02358031. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Disease State	Treatment	Median follow-up, mo	Median OS, mo	HR (95% CI) for OS	Median PFS, mo	HR (95% CI) for PFS
Incurable recurrent only	P (n = 82) vs E (n = 94)	11.5 vs 12.1	11.5 vs 12.1	1.09 (0.79-1.51)	2.6 vs 6.3	1.81 (1.32-2.49)
Incurable recurrent only	P+C (n = 76) vs E (n = 88)	13.0 vs 11.1	13.0 vs 11.1	0.92 (0.66-1.28)	4.8 vs 6.2	1.22 (0.88-1.70)
Metastatic	P (n = 216) vs E (n = 203)	11.5 vs 9.8	11.4 vs 9.7	0.73 (0.59-0.91)	2.3 vs 4.9	1.11 (0.90-1.36)
Metastatic	P+C (n = 201) vs E (n = 187)	13.0 vs 10.1	13.0 vs 10.1	0.66 (0.53-0.83)	5.0 vs 4.9	0.82 (0.66-1.02)

6531 Poster Session (Board #192), Fri, 8:00 AM-11:00 AM

Initial analyses of a phase I/II trial of durvalumab (D) plus tremelimumab (T) and stereotactic body radiotherapy (SBRT) for oligometastatic head and neck carcinoma. *First Author: Houda Bahig, Centre Hospitalier de l'Universite de Montreal, Montreal, QC, Canada*

Background: PD-1/PD-L1 +/- CTLA-4 blockade in head-and-neck carcinoma (HNSCC) has shown signs of clinical activity. SBRT aims to reduce tumor burden and perhaps be immune-stimulatory. This analysis seeks to assess the safety and efficacy signal of the triple treatment combination (TTC) consisting of SBRT sandwiched between cycles of D (αPD-L1) and T (αCTLA-4) in oligometastatic (2-10) HNSCC. **Methods:** This is a single arm multi-institutional phase I/II trial (NCT03283605). D (1500 mg) and T (75 mg) were given for 4 monthly cycles, followed by monthly D. SBRT to 2-5 lesions was administered during cycle 2. The median prescribed and maximum SBRT doses were 40 Gy (range:18-50) and 49 Gy (range:28-61), respectively, given in 3-5 fractions. Global health status was derived from EORTC QLQ C30 questionnaires. **Results:** At data cut-off (Dec 31, 2019), 20 patients were recruited, of which 16 had a study treatment and were analyzed. Table describes the patient characteristics. There were 1 CTCAE V5.0 Grade 2 and 1 Grade 3 (both GI) serious adverse event (SAE) attributable to D and T. Two patients had unrelated SAEs (1 Grade 3-hypercalcemia and 1 Grade 5-GI). The Grade 5 SAE was a gastric hemorrhage that occurred the night of the first D + T infusion. There was no Grade 3+ AE secondary to SBRT. Thus, SBRT did not add to the 2/16 patients who had D + T related SAEs. Global health status scores did not differ statistically between baseline (75) and cycle 3 (73). Of the 14 patients that received SBRT, 7 patients had RECIST target lesions untreated by SBRT. The best responses for these 7 patients were: 1 CR, 3 PR, and 3 SD. When SBRT treated lesions are included and analyzed per RECIST (n = 14), there were 9 PR, 3 SD and 2 PD. The estimated median progression free survival was 7.2 months. **Conclusions:** The first 16 evaluable patients demonstrated tolerable profiles to the TTC (D + T + SBRT) for the treatment of oligometastatic ($\leq$10 lesions) HNSCC. Best response rates were encouraging and could be due to the addition of SBRT during immunotherapy that served to either stimulate the immune system or annihilate slow responding or immunotherapy resistant lesions. Smaller overall tumor burden and 7/16 patients being treated in first line could also have contributed to better results. Clinical trial information: NCT03283605. Research Sponsor: AstraZeneca.

Covariate		n = 16
Gender	Female: Male	3: 13
Age	Median (Min, Max)	63.5 (42,84)
Rx lines prior to entering trial	0	7
	1	4
	2	5
	Prior immunotherapy	*2*
Treatment duration	Median months (Min, Max)	5.88 (0.13,13.3)
Total number of lesions	Median (Min, Max)	4 (2,8)
SBRT treated lesions	1	1
	2	11
	3	2

6532 Poster Session (Board #193), Fri, 8:00 AM-11:00 AM

HANNA: Real-world outcomes from an observational study with nivolumab in patients with recurrent or metastatic squamous cell carcinoma of the head and neck in Germany. *First Author: Andreas Dietz, Universitaetsklinikum Leipzig, Leipzig, Germany*

Background: Nivolumab has demonstrated efficacy in clinical trials of recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN). As only limited real-world data are available, we describe the use of nivolumab and its outcomes in routine clinical practice. **Methods:** HANNA is a prospective, observational study of patients with R/M SCCHN treated with nivolumab in 56 hospitals and practices in Germany. In total, 385 patients will be followed for $\leq$ 5 years from treatment initiation until death, withdrawal of consent, loss of follow-up/record, or end of study. The primary objective is overall survival (OS). Secondary objectives include baseline characteristics, safety profiles, and quality of life (QOL) assessment. **Results:** By November 2019, data from 311 patients were available. Median follow-up was 3.5 months. Baseline characteristics were male, 81.7%; median age, 63 years; history of smoking, 73.3%; Eastern Cooperative Oncology Group performance status (ECOG PS) 0/1, 60.8%; ECOG PS 2/3, 29.6%. Location of primary tumor was oropharynx, 38.3%; hypopharynx, 20.9%; oral cavity, 22.8%; larynx, 11.6%; others, 6.4%. 55.6% of R/M SCCHN patients progressed $\leq$ 6 months after platinum-based therapy, whereas 43.4% were platinum-sensitive (progressed $>$ 6 months after platinum-based therapy). Nivolumab was received by 25.1% of patients as first therapy after platinum-based chemo- or radiochemotherapy, by 62.1% as second therapy, and by 12.9% as later line therapy. Median treatment duration was 4.6 months. OS at 1 year was 43.3%. 1-year OS for patients with ECOG PS 0 was 75.9%; ECOG PS 1, 41.2%; and ECOG PS 2, 27.3%. Platinum-sensitive patients had higher 1-year OS probability (51.6%). Drug-related adverse events (grade 1/2) and serious adverse events (grade 3/4) were observed in 28.9% and 10.0% of patients, respectively. Interim QOL data (per FACT-H&N and EQ-5D questionnaire) indicated a tendency toward stabilization or slight improvement. We will present an update of the data with longer follow-up (data cut March 2020). **Conclusions:** HANNA represents one of the largest real-world datasets for nivolumab in R/M SCCHN and comprises a more diverse set of patients than the phase 3 CheckMate 141 trial, including patients with higher ECOG PS, age, and platinum sensitivity. Outcomes from HANNA show that the improved OS, safety, and QOL seen with nivolumab in the real-world setting are consistent with the outcomes from CheckMate 141. Clinical trial information: NCT03114163. Research Sponsor: Bristol-Myers Squibb.

6533 Poster Session (Board #194), Fri, 8:00 AM-11:00 AM

Selection of patients for surveillance imaging after radiotherapy for squamous cell carcinoma of oral cavity and oropharynx. *First Author: Johnathan Zeng, Cleveland Clinic, Cleveland, OH*

Background: NCCN guidelines do not recommend routine surveillance imaging for distant failure (DF) after definitive treatment of head & neck squamous cell carcinoma (SCC). We hypothesized that there exists a subset of patients with sufficiently high enough risk for DF to benefit from surveillance imaging. This study attempts to define high risk cohorts of oropharynx (OP) and oral cavity (OC) patients. **Methods:** A retrospective review was conducted of patients with SCC of the OP or OC at a single tertiary care institution from 1994-2019. Patients were staged according to AJCC 7th edition and included in this study if they completed definitive-intent treatment and received 60 Gray or higher of radiotherapy (RT). Local, regional, and distant failure were estimated with cumulative incidence. Univariable & multivariable risk factors for DF were identified with Fine & Gray competing risk regression. Significant variables were compiled to calculate a risk score. **Results:** 863 patients were included (676 OP/187 OC). OC patients were 60.4% male, median age 61, with median follow up of 77.5 months. Smoking status was 27.3% current, 44.4% former, 28.3% never, with 30 median pack years. Disease was 57.3% T1-2, 42.7% T3-4, 55.6% N0-2a, 44.4% N2b-3. 94.1% had surgery & 34.3% had concurrent systemic therapy. OP patients were 87.9% male, median age 58, 96.3% HPV+, with median follow up of 60.8 months. Smoking status was 20.9% current, 44.5% former, 34.6% never, with 20 median pack years. Disease was 67.9% T1-2, 32.1% T3-4, 29.9% N0-2a, 70.1% N2b-3. 11.5% had surgery & 87.3% had concurrent systemic therapy. Specifically, 52.2% of OP patients received concurrent cisplatin, 10.6% concurrent cetuximab, and 24.5% other systemic therapies. 11.7% of patients experienced DF, of which 77% failed in the lung. Within the OC cohort, nodal stage 2b or higher was the only predictive factor (HR 3.26, $p < 0.001$), conferring a 3 year risk of DF of 34% vs 10%. Within the OP cohort, a high risk cohort of 87 patients (12.9%) was identified with a 3 year incidence DF of 22%, compared to 10% or less in lower risk cohorts. This high risk cohort consisted of active smokers treated with definitive RT and either concurrent cisplatin or no concurrent therapy, with at least T3 and N2b disease, as well as any patients treated with definitive RT and concurrent cetuximab. **Conclusions:** We identified groups of OC & OP patients with greater than 20% risk of developing DF at 3 years, the majority of which occurred in the lung. Surveillance imaging of the chest should be considered for patients meeting these criteria. Research Sponsor: None.

6534 Poster Session (Board #195), Fri, 8:00 AM-11:00 AM

Distinct transcriptional profiles in plasma exosomes associated with recurrence of nasopharyngeal carcinoma patients with standard treatment. *First Author: Yongjiang Li, West China Hospital, West China Medical School, Sichuan University, Chengdu, China*

Background: Nasopharyngeal carcinoma (NPC) is endemic with a high prevalence in Southern China, Asia,cetuximab and North Africa. Exosomes are small vesicles containing a wide range of functional proteins, mRNA and miRNA. In the progression of NPC, the tumor cells constantly release exosomes into the surrounding environment and also into the circulating blood. The aim of this study was to explore the association between RNA expression in plasma exosomes and prognosis of NPC patients after standard treatment. **Methods:** In this retrospective study, a total of 25 eligible NPC patients were included: 12 patients in the recurrence (R) subgroup and 13 patients in the no recurrence (NR) subgroup. RNA was extracted from the exosomes of plasma specimens which were collected at West China Hospital, Sichuan University. Gene expression profiles were conducted by using the RNA-sequencing platform. The DESeq2 package was used to analyze the differentially expressed genes (DEGs) between R and NR subgroups. The gene set variance analysis (GSVA) was performed to explore C5 gene sets enrichment related to the recurrence after standard treatment. **Results:** We observed 332 DEGs between R and NR subgroups, which include 125 up-regulated and 207 down-regulated genes (R vs. NR,|log2fold change|$>$1, $p$$<$0.05). Moreover, hierarchical clustering analysis of the 332 DEGs revealed that all samples clustered into two subgroups, with cluster 1 containing 82% (9/11) recurrence patients and cluster 2 containing 79% (11/14) no recurrence patients. Further, univariate Cox regression analysis showed that 293 out of 332 DEGs were significantly correlated with DFS ($p$$<$0.05), such as TRAM1, CAPN1, SAT1 and ACTB. GSVA and Log Rank test of survival data demonstrated that a total of 824 pathways/biological processes were significantly different between R andNR subgroups ($p$$<$0.05). Specifically, the top 9 pathways/biological processes, such lipoxygenase pathway, rough endoplasmic reticulum membrane and low density lipoprotein particle clearance, was mainly enriched in the NR subgroup (p $<$0.001). **Conclusions:** Profiling of plasma exosomes RNA in NPC patients reveals distinctive gene expression pattern between patients with or without recurrence. Further functional analysis revealed that top enriched 9 pathways/biological processes may correlate with a favorable prognosis and are worth investigating. Moreover, for the prognosis of patients with NPC, RNA expression of plasma exosomes may be a potentially valuable research object. Research Sponsor: the research and data on the evaluation method of stereotactic radiotherapy equipment (subject No: 2017YFC0113701), Research and development of tumor real-time monitoring molecular diagnostic products based on liquid biopsy – a major science and technology project of guangdong province 2019B020232003;Dalian municipal Science and technology innovation projects (2018 j12sn063): a new method for the detection optical flow control chip peripheral blood tumor cells research Science and technology innovation project of Dalian City (No: 2018 j12sn063).

6535 Poster Session (Board #196), Fri, 8:00 AM-11:00 AM

Dendritic cell therapy with CD137L-DC-EBV-VAX in locally recurrent or metastatic nasopharyngeal carcinoma (NPC). *First Author: Robert John Walsh, Department of Haematology-Oncology, National University Cancer Institute, National University Health System, Singapore, Singapore*

Background: Epstein-Barr virus (EBV) is associated with non-keratinising (NK) NPC, a disease prevalent in Southeast Asia, and provides a potential target for dendritic cell (DC) vaccine therapy. CD137 ligand (CD137L) expressed on antigen presenting cells costimulates CD137 expressing T cells upon receptor/ligand interaction. CD137L signalling differentiates monocytes to CD137L-DC, a novel type of DC, which are more potent than classical DC in stimulating autologous T cells. Here, we explore the safety and efficacy of autologous CD137L-DC pulsed with EBV peptides spanning Epstein Barr nuclear antigen 1, latent membrane protein 1 (LMP1) and LMP2 (CD137L-DC-EBV-VAX) in patients with locally recurrent or metastatic NPC. **Methods:** In this single centre, phase I study, eligible patients (pts) with locally recurrent or metastatic NK-NPC and clinical benefit (CB) from their prior treatment (stable disease [SD], partial [PR] or complete response[CR]), underwent apheresis to isolate monocytes which were differentiated to CD137L-DC through CD137L agonist exposure. CD137L-DC were pulsed with EBV antigens during maturation to obtain CD137L-DC-EBV-VAX which was administered intradermally every 2 weeks (w) for up to 7 injections following site preconditioning with Tetanus and Diphtheria vaccine. **Results:** 14 pts were enrolled of which 2 progressed rapidly and did not begin treatment. Mean age was 58 years. Median lines of prior treatment for metastatic NPC was 1 (range 1-6), the most common being cisplatin and gemcitabine. 9 pts received 7 vaccine doses (range 2-7) with a mean administered cell count of 23.9x10^6. CB was seen in 5 cases (42%) with 1 PR and 4 SD beyond 1 year. Median progression free survival (mPFS) was 26w (95% CI, 23-43). The lowest PFS (8w) was in a pt with 6 prior lines of treatment including a checkpoint inhibitor. Mean pretreatment neutrophil: lymphocyte ratio (NLR) was 3.4 and a value of less than 3 was associated with prolonged mPFS (42 *vs* 14w, p = 0.01). Enzyme linked immune absorbent spot (ELISPOT) analysis in 5 pts with CB showed a rise in interferon-γ secreting peripheral T cells prior to the 3rd vaccine versus baseline. Treatment was well tolerated with only 4 cases of grade 1 related adverse events reported, most commonly injection site reaction (3pts). **Conclusions:** CD137L-DC-EBV-VAX is safe and exhibits promising efficacy when administered following CB from chemotherapy. A rise in activated peripheral blood mononuclear cells after 2 vaccinations in selected patients showing benefit suggests immunological correlates with efficacy. Clinical trial information: NCT03282617. Research Sponsor: National Medical Research Council (Singapore) - NMRC/BnB/0018c/2015.

6536 Poster Session (Board #197), Fri, 8:00 AM-11:00 AM

Cisplatin every three weeks versus weekly cisplatin or carboplatin with definitive radiotherapy for squamous cell carcinoma of the head and neck is associated with improved overall survival in a representative national population. *First Author: Michael Gerard McCusker, University of Maryland Medical Center, Baltimore, MD*

Background: For patients with primary untreated locally advanced head and neck squamous cell carcinoma (PULA-HNSCC), high dose once every 3 weeks cisplatin (HDC; 100 mg/m^2) added to curative radiotherapy (RT) prolongs survival, but is associated with severe toxicities. Concurrent chemoradiation (CRT) with low dose weekly cisplatin (LDC; 30-40 mg/m^2), carboplatin (C), or RT alone is often substituted for HDC. We estimated and compared overall survival (OS) and acquired toxicities among Medicare beneficiaries treated with CRT using HDC, LDC, C, or RT. **Methods:** Patients diagnosed from 2004-2011 with PULA-HNSCC (stages III-IVB AJCC 6th and 7th editions) of the oropharynx (OPC), hypopharynx (HP), or larynx (L) who received definitive RT or CRT were identified using the linked SEER-Medicare database. An analytic cohort of patients receiving CRT with HDC, LDC, or C was constructed using well-established eligibility criteria. OS was estimated and compared between patients grouped by treatment received utilizing a multivariable stratified propensity scores weighted Cox regression model, including demographic and disease characteristics. Toxicities were compared using exact common odds-ratio and Fisher's tests. **Results:** We identified 1,335 patients that received RT: OPC (n = 731), HP (n = 174), or L (n = 430). Out of those, patients were treated with HDC (n = 264), LDC (n = 259), C (n = 353), or RT alone (n = 459). Median OS (years) was 5.61 (95% CI = 4.58-7.69) for HDC, 3.7 (95% CI = 3.1-4.79) for LDC, 3.1 (95% CI = 2.48-3.86) for C, and 1.36 (95% CI = 1.19-1.58) for RT, respectively. OS was significantly greater for HDC than for LDC (HR = 1.35, 95% CI = 1.06-1.72, p= 0.02), C (HR = 1.41, 95% CI = 1.12-1.76, p= 0.003), or RT (HR = 2.1, 95% CI = 1.68-2.61, p= $<$ 0.001). Treatment with HDC compared to LDC was not associated with increased prevalence of dysphagia or neutropenia. HDC was associated with hearing loss when assessed at 9-12 months post-diagnosis (p =0.03). **Conclusions:** In SEER-Medicare beneficiaries with PULA-HNSCC of the OPC, HP, or L, OS was significantly better for HDC than LDC when accounting for baseline clinical and demographic characteristics and propensity score weights. Toxicities were similar between regimens, except for an increased incidence of the late acute toxicity of hearing loss in HDC. A regimen of HDC improves OS, but needs to be carefully assessed against increased toxicity risk, with hearing loss in particular. Research Sponsor: None.

6537 Poster Session (Board #198), Fri, 8:00 AM-11:00 AM

Association of autoimmunity with survival in patients with recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) treated with immune checkpoint inhibitors (ICIs). *First Author: Panagiota Economopoulou, Attikon University Hospital, Athens, Greece*

Background: ICIs are associated with immune-related adverse events (irAEs) that occur as a consequence of enhanced immune response due to T-cell activation. The objective of this observational cohort study was to investigate the association between irAEs and disease outcome in pts with R/M HNSCC. **Methods:** 110 pts treated with ICIs were reviewed. Overall survival (OS) was calculated from the date of initiation of ICI to the date of death. To overcome guarantee-time bias, we calculated post-irAEs survival from the date of first irAE presentation in patients who developed irAEs or from the date of ICI initiation in pts without irAEs. **Results:** Primary site was the oral cavity (N = 51), oropharynx (N = 20), larynx (N = 29), hypopharynx (N = 1), paranasal sinuses (N = 5) and nasopharynx (N = 4). 41 (37.3%) had metastatic and 69 (62.7%) recurrent disease. 32 pts (29.1%) developed irAEs, with more common thyroiditis (N = 15, 13.6%). Of 100 pts with evaluable disease, 14 (14%) responded. 6/31 (19.4%) with irAEs vs. 8/69 (11.6%) without irAEs responded to ICI (p = 0.354). After a median follow-up of 16.4 months, 69 pts died. Median OS was 10 mo (95%CI, 6.7-13.4), 10 mo (95%CI, 5.6-14.5) for pts with recurrent and 10 mo (95%CI, 7.7-12.3) for pts with metastatic HNSCC (p = 0.966). Median OS was 17.9 mo (95%CI, 7.9-27.9) for pts with irAEs and 6.6 mo (95%CI, 3.3-9.9) for pts without irAEs (p = 0.001). Median post-irAEs survival was 16.3 (95%CI, 7.1-25.5) for pts with irAEs vs. 6.6 mo (95%CI, 3.3-9.9) for pts without irAEs (p = 0.020). Responders to ICI did not differ in median post-irAEs survival irrespective of whether they developed irAEs (p = 0.561), while among non-responders, those who developed irAEs had significantly longer median post-irAEs survival compared to those who did not (10 vs. 6 mo, respectively, p = 0.044). Multiviariate Cox proportional hazard models showed that independent favorable prognostic factors for post-irAEs survival were the development of irAEs (HR 0.54, 95%CI 0.30-0.97, p = 0.039) and response to ICI (HR 0.16, 95%CI 0.05-0.50, p = 0.002). **Conclusions:** The development of irAEs is a strong predictor of improved survival in patients with advanced HNSCC treated with ICIs. Research Sponsor: None.

6538 Poster Session (Board #199), Fri, 8:00 AM-11:00 AM

Immune checkpoint inhibitor in nasopharyngeal carcinoma: Multi-institution experience. *First Author: Jong Chul Park, Massachusetts General Hospital Cancer Center, Boston, MA*

Background: The current standard treatment for unresectable recurrent/metastatic (R/M) nasopharyngeal carcinoma (NPC) is cytotoxic chemotherapy but prognosis remains poor. Recent phase I-II trials of anti-PD-1 therapy (aPD-1) have demonstrated promising activity in R/M NPC, but the published experience is primarily limited to Epstein-Barr virus (EBV) positive tumors in the Asian population. Here we report our three institutional real-world experience with aPD-1 in patients (pts) with R/M NPC. **Methods:** A retrospective analysis was conducted after IRB approval at the Massachusetts General, Johns Hopkins, and University California San Francisco Hospitals. Demographic and clinical data was collected on pts with R/M NPC who received aPD-1 at the participating institutions. Objective response rate (ORR) was the primary outcome of interest and progression free survival (PFS) and overall survival were secondary outcomes. Univariate and multivariate analyses were conducted to assess association between clinicopathologic factors and outcomes, using logistic regression models. **Results:** A total of 36 pts were identified: 20 pts were treated with pembrolizumab and 16 with nivolumab. Median age was 50 (15-74). Twenty-nine (81%) were male. Twenty pts (56%) were Asian. Twenty-nine pts (81%) had EBV positive disease. Nine (25%) had aPD-1 as first-line therapy (1L). Molecular profiling results were available in 16 pts: TP53 mutation was the most common alteration (25%) and was limited to EBV negative tumors. Median total mutational burden (TMB) was 3/Mb (1-28). Median PD-L1 expression was 10% (0-90). Median follow up was 13.9 months (mos). Objective response was evaluable in all 36 pts: 9 pts achieved objective response (ORR 25.0%, 95% CI 12.1-42.2) with 2 complete responses: EBV positive vs. negative (27.6% vs. 14.2%, P=0.472), Asian vs. non-Asian (25% vs. 25%, P=1.000), and 1L vs. >1L (33.3% vs. 22.2%, P=0.511). Thirteen pts had stable disease (disease control rate 61.1%). Responses were seen in both TMB high (28/Mb) and low (1/Mb) tumors and no association with PD-L1 expression was observed. One-year survival rate was 81.3%. EBV positive pts had a trend towards better survival (84.8 vs. 66.7, P=0.640). Median PFS was 5.5 mos and not different between EBV positive vs. negative pts (5.6 vs. 4.0 mos, P=0.919). **Conclusions:** Our multi-institutional real-world experience with checkpoint inhibitor therapy in R/M NPC confirms that a similar degree of activity is seen as reported in the phase I-II experience in diverse races, but efficacy seems more prominent in EBV positive disease. Research Sponsor: None.

6539 Poster Session (Board #200), Fri, 8:00 AM-11:00 AM

Efficacy and tolerance of carboplatin-cetuximab in patients with metastatic or recurrent head and neck squamous cell carcinoma unfit for extreme regimen. *First Author: Charlotte Le Roy, Tenon Hospital, Paris, France*

Background: Head and neck squamous cell carcinoma (HNSCC) is the fourth cause of death by cancer in France. For metastatic patients, the standard first line treatment is the EXTREME regimen. However, a lot of these patients have a poor performance status (PS) and/or several comorbidities making them unfit for this regimen. We have treated them with carboplatin and cetuximab (simplified EXTREME regimen) since 2007. The aim of this study is to assess the efficacy and tolerance of this regimen in this frail population. **Methods:** We retrospectively reviewed the medical charts of all patients treated with simplified EXTREME regimen for recurrent or metastatic HNSCC in three French academic hospitals between 2007 and 2017. The primary endpoint was overall survival (OS) and secondary endpoints were progression free survival (PFS), overall response rate (ORR), identification of prognostic factors, and toxicity. **Results:** 103 patients were included with a median age of 63 y.o., 60% had a PS 0-1 and 40% a PS 2-3. With a median follow-up of 30.2 months, median OS was 7.2 months and median PFS 3.7 months. ORR was 39% and 24% of patients had disease stabilization. On univariate analysis, a PS of 2 or more was significantly associated with a worse OS (median OS 10.1 months if PS 0-1 versus 4.6 months if PS 2-3; HR = 1.68; 95%CI = 1.11-2.57; p = 0.01). Acute grade 3-4 hematologic and non-hematologic toxicity rates were 25.2% and 27.2%, respectively, with 11.8% of thrombopenia, 9.7% of neutropenia, 10% of skin toxicity, and 12.6% of asthenia. Patients with grade 1 or more skin toxicity had a higher ORR (HR = 3.44; 95%CI = 1.16-10.23; p = 0.03) and a prolonged OS (HR = 0.37; 95%CI = 0.23-0.58; p $<$ 0.0001) and PFS (HR0.29; 95%CI = 0.19-0.47; p $<$ 0.0001). During treatment, 29% of patients had a pain decrease, 13.5% a gain of weight, and 17.2% an improvement in PS. **Conclusions:** This is the largest cohort of patients treated with simplified EXTREME for HNSCC. Simplified EXTREME was well tolerated in this frail population with a high ORR. Patients with a good PS had prolonged survival. Interestingly, skin toxicity of any grade was significantly correlated with treatment efficacy. Research Sponsor: Merck Serono.

6540 Poster Session (Board #201), Fri, 8:00 AM-11:00 AM

Final results of the multicenter, open-label, randomized phase II trial PAZOTHYR evaluating continuous versus intermittent administration of pazopanib in radio-iodine-refractory thyroid cancers (NCT01813136). *First Author: Christelle De La Fouchardiere, Leon Berard Cancer Centre, Lyon, France*

Background: Multikinase inhibitors (MKI) targeting angiogenesis, including pazopanib (P), have shown efficacy in progressive radioiodine refractory thyroid cancers (RAIR-TC) but are accompanied by adverse effects, leading to dose adjustments/interruptions. We aimed to investigate the efficacy and tolerance of a discontinuous scheme of pazopanib administration in this situation. **Methods:** This randomized phase II study enrolled RAIR-TC patients (pts) in first or second-line of MKI with documented disease progression within 12 months (m). After a 6-m pazopanib continuous induction phase, pts with stable disease (SD) or tumor response were randomly assigned in a 1:1 ratio to receive continuous pazopanib (CP) or intermittent pazopanib (IP) until progression and restart. They were stratified by best tumor response [stable disease vs. objective response] and prior MKI treatment [yes vs. no]). Primary endpoint was time to treatment failure (TTF) defined as time between randomization and permanent discontinuation of pazopanib (either for disease progression or intolerance); secondary endpoints included overall response rate (ORR), progression-free survival (PFS) and safety. **Results:** 168 pts (66.5 years median age; 51.8% female) were included and 100 pts randomized (CP: 50, IP: 50). The median number of metastatic sites was 2.0 (1-7) and 50 pts (29.8%) were pretreated with MKI. With a median follow-up of 31.3 m, we did not show any statistically significant difference in the TTF, 80% (66.0-88.7%)] of the pts being under P at 6 m after randomization in the IP arm *versus* 78% (63.8-87.2%) in the CP arm. Median TTF was 14.7 m 95% CI [9.3; 17.4] and 11.9 m 95% CI [7.5; 15.6] respectively (HR 0.79 [0.49-1.27]). The best response with P was 35.6% (95% CI [28.2; 43.6]) and the disease control rate was 89.4% 95% CI [83.5; 93.7]. Median time to progression under P was not statistically different between 2 arms (5.7m 95% CI [4.8;7.8] in the IP arm vs. 9.2m 95% CI [7.3;11.1] in the CP arm (HR 1.36 [0.88; 2.12]). 36/100 pts (36%) experienced pazopanib-related grade 3/4 AEs (CP: 17; IP: 19) mainly represented by gastrointestinal disorders, hypertension, cardiac disorders and asthenia. Five pazopanib-related deaths were reported (CP:1;IP: 4). **Conclusions:** The intermittent administration of pazopanib study did not significantly demonstrate superiority in efficacy or tolerance over continuous treatment. Continuous administration of MKI remains the standard in RAIR-TC. Clinical trial information: NCT01813136. Research Sponsor: PHRC11-089.

6541 Poster Session (Board #202), Fri, 8:00 AM-11:00 AM

A phase I/Ib study of lenvatinib and cetuximab in patients with recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). *First Author: Lara Dunn, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Despite overexpression of EGFR in HNSCC, cetuximab monotherapy has limited benefit. Fibroblast growth factor receptor (FGFR) signaling is a known resistance mechanism to EGFR inhibition. Lenvatinib is a multi-targeted receptor tyrosine kinase inhibitor (RTKI) and has unique activity against FGFR 1,2,3, and 4. We are evaluating inhibition of EGFR and RTKs including FGFR through the combination of cetuximab and lenvatinib in patients (pts) with R/M HNSCC. **Methods:** In this phase I/Ib, single-institution study, pts with measurable disease per RECIST v1.1 that is incurable with surgery and radiation are eligible regardless of prior cetuximab therapy. The dose de-escalation phase included pts with HNSCC and cutaneous squamous cell carcinoma (cSCC) treated with standard cetuximab dosing and lenvatinib in 3 potential dose levels (DL): (0) 24mg, (-1) 20mg, (-2) 14mg oral daily in a standard 3+3 design. The primary objective was to determine the MTD of lenvatinib in combination with cetuximab. The expansion phase included an additional 5 pts with HNSCC treated at the MTD. Exploratory endpoints include ORR and PFS in HNSCC pts treated at the MTD. **Results:** 12 evaluable pts were treated on the dose de-escalation phase. There were no DLTs on DL 0; however, 3/6 pts were removed immediately following the 28-day DLT period due to toxicity that included extensive thrombotic events and athlerosclerotic disease. On DL -1, 0/6 pts (5 HNSCC/1 cSCC) had a DLT establishing lenvatinib 20mg daily as the MTD. 7 pts were enrolled onto the expansion phase; 4 are currently evaluable for response and 2 are unevaluable because of withdrawal due to a cetuximab reaction and required surgery. Of the 9 evaluable HNSCC pts treated with lenvatinib 20mg daily, 6 pts had a PR with a 67% ORR. For the 8 pts who have completed treatment, the median PFS is 3.6 months (range 1.6-10.4). Grade 3 AEs regardless of attribution included hypertension (3), oral mucositis (3) and oral cavity fistula (1). The most common AEs were acneiform rash (7), fatigue (6), and hypertension/hypothyroidism/oral mucositis (5 each). **Conclusions:** The MTD of lenvatinib 20mg daily with cetuximab appears to be active in R/M HSNCC with an impressive preliminary ORR, warranting further evaluation of the efficacy of this combination. Clinical trial information: NCT03524326. Research Sponsor: Eisai Pharmaceuticals.

6542 Poster Session (Board #203), Fri, 8:00 AM-11:00 AM

Clinical response and biomarker analysis of POLARIS-02 a phase II study of toripalimab, a humanized IgG4 mAb against programmed death-1 (PD-1) in patients with metastatic nasopharyngeal carcinoma. *First Author: Fenghua Wang, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: Metastatic nasopharyngeal cancer (mNPC) patients progressed after standard therapy have limited treatment options. This study is to evaluate the clinical efficacy and safety of toripalimab in mNPC patients refractory to standard chemotherapy treatment (Clinical trial ID: NCT02915432). **Methods:** Patients receive 3 mg/kg toripalimab Q2W via IV infusion until disease progression, unacceptable toxicity, or voluntary withdrawal. Clinical response is assessed every 8 weeks according to RECIST v1.1. Tumor PD-L1 expression, plasma EBV titer and other biomarkers will be evaluated for correlation with clinical response. **Results:** From Dec 2016 to Feb 2019, 190 mNPC patients were enrolled from 17 participating centers in China. The median age was 46 years with 83% male. Patients were heavily pretreated with a median of 2 lines of prior systemic treatments. By the cutoff date of Jan 17, 2020, 97% patients experienced treatment related adverse events (TRAE). Most common TRAE included anemia, hypothyroidism, AST increased, proteinuria and fever. Grade 3+ TRAE occurred in 28% patients. Among 190 patients assessed by Independent Review Committee per RECIST v1.1, 6 CR, 33 PR and 40 SD were observed for an ORR of 20.5% and a DCR of 41.6%. The median DOR was 12.9 months. The median PFS and median OS were 1.9 months and 18.6 months respectively. PD-L1+ patients (n=48) had higher ORR than PD-L1- patients (n=134), 27.1% versus 19.4%. By tumor histology, ORR was higher in keratinizing NPC (n=8) than non-keratinizing NPC (n=168), 62.5% versus 19.0%. 144 patients had valid plasma EBV titer measured every 28 days during the study. An average drop of 101-fold plasma EBV titer from baseline was observed in patients with objective responses. Patients with 2-fold+ drop in plasma EBV titer on day 28 (n=60) went on to have 48.3% ORR and 76.7% DCR, whereas patients with less than 2-fold drop (n=88) had 5.7% ORR and 25.0% DCR. 14 responding patients who later developed progressive disease had at least 2-fold+ increase of plasma EBV tier 3-months (median) before radiographic identification of disease progression. **Conclusions:** Toripalimab demonstrated encouraging clinical activity with a manageable safety profile in mNPC patients refractory to standard chemotherapy. Patients with 2-fold+ drops in plasma EBV titer on day 28 from baseline had favorable clinical response of 48.3% ORR, which might be used as a predictive biomarker. Clinical trial information: NCT02915432. Research Sponsor: Shanghai Junshi Biosciences Co., Ltd.

6543 Poster Session (Board #204), Fri, 8:00 AM-11:00 AM

Phase I dose escalation of stereotactic body radiation therapy and concurrent cisplatin for re-irradiation of unresectable, recurrent head and neck squamous cell carcinoma. *First Author: Michelle Echevarria, Department of Radiation Oncology, Moffitt Cancer Center and Research Institute, University of South Florida, Tampa, FL*

Background: For patients with unresectable, previously radiated, locoregionally recurrent head and neck cancer, stereotactic body radiation therapy (SBRT) has become an attractive option. The use of high daily doses of radiotherapy may overcome the inherent radioresistance of these recurrent cancers. Given the resistant and advanced nature of many of these cancers, the addition of chemotherapy to radiotherapy is typically recommended as a radiosensitizer. We therefore performed a phase I clinical trial in order to establish a maximum tolerated dose of SBRT with concurrent chemotherapy in locoregionally recurrent head and neck cancer. **Methods:** Major inclusion criteria were recurrence of previous squamous cell carcinoma of the head and neck in patients who had previously undergone radiotherapy to doses $\geq$ 45 Gy to the area of recurrence, $\geq$ 6 months prior to enrollment, and who were medically unfit for surgery, deemed unresectable, or refused surgery. Patients were treated with radiation therapy every other day for five fractions at three dose levels; 30 Gy, 35 Gy, and 40 Gy. Cisplatin was given prior to every SBRT fraction at a dose of 15 mg/m2. Patients were monitored for safety and tolerability for any grade 4 or greater toxicity (per CTCAE v4.0) that occurred within 3 months from the start of SBRT. Primary end point was maximum tolerated dose (MTD). **Results:** Twenty patients were enrolled and of those 17 patients were evaluable for the primary endpoint. Nine patients had a primary tumor in the oropharynx, four patients in the oral cavity, three in the neck, one in the larynx, and one simultaneously in the larynx and neck. Of the three patients that were not evaluable two withdrew consent, and one patient in the 30 Gy dose level died of unknown causes two weeks following completion of treatment. Due to safety concerns the 30 Gy dose level was expanded an additional three patients, and no further dose limiting toxicities (DLTs) were observed. At the 35 Gy and 40 Gy dose level there were no reported grade 4 or 5 adverse events (per CTCAE v4.0). There were 5 (27%) reported grade 3 toxicities and 12 (66%) grade 2 toxicities. **Conclusions:** This phase I study demonstrates that 40 Gy SBRT with concurrent cisplatin at a dose of 15mg/m2 is feasible, safe, and well tolerated. Patients continue to be followed for secondary outcomes of local control and overall survival. Clinical trial information: NCT02158234. Research Sponsor: H. Lee Moffitt Cancer Center Department of Radiation Oncology.

6544 Poster Session (Board #205), Fri, 8:00 AM-11:00 AM

INDUCE-1: Report on safety run-in cohorts combining Inducible T-cell co-stimulatory receptor (ICOS) agonist GSK3359609 (GSK609) with platinum+5-FU chemotherapy (5-FU/plat), with or without pembrolizumab (PE), for the treatment of advanced solid tumors. *First Author: Erminia Massarelli, City of Hope Helford Clinical Research Hospital, Duarte, CA*

Background: The KEYNOTE-048 study (Burtness, at al. *Lancet* 2019;394: 1915–28) led to approval of PE in combination with 5-FU/plat for first-line (1L) treatment of head and neck squamous cell carcinoma (HNSCC). The Phase I INDUCE-1 study (NCT02723955) has shown that GSK609±PE has a manageable safety profile in patients (pts) with advanced solid tumors (Hansen, at al. *Annals of Oncology* 2018;29[suppl_8]:viii404) and that GSK609 combined with PE has anti-tumor activity in pts with anti-PD-1/L1-naïve HNSCC (Rischin, et al. *Annals of Oncol* 2019;30[Supplement_5]:v454–5). To evaluate the safety of GSK609±PE in combination with 5-FU/plat, we initiated additional safety cohorts. **Methods:** Pts eligible for GSK609+5-FU/plat had a diagnosis of advanced selected solid tumors and ≤5 prior lines of systemic therapy. Pts eligible for GSK609+PE+5-FU/plat had a diagnosis of recurrent or metastatic 1L HNSCC deemed incurable by local therapies. 5-FU/plat was administered every 3 weeks (Q3W) for 4-6 cycles (Burtness, at al. *Lancet* 2019;394:1915–28); GSK609 24 or 80 mg ±PE 200 mg were administered Q3W for up to 2 years/35 cycles or until disease progression or unacceptable toxicity. **Results:** Twenty-nine pts were enrolled in the 5-FU/plat safety cohorts: 10 pts in the GSK609+5-FU/plat cohort and 19 pts in the GSK609+PE+5-FU/plat cohort. With GSK609+5-FU/plat, 9/10 (90%) pts experienced ≥ 1 adverse event (AE). Of 32 AEs of any grade, 9 were Grade ≥3 and 3 were serious AEs (SAEs). Two of the 3 SAEs were related to study treatment (oral mucositis and febrile pancytopenia). With GSK609+PE+5-FU/plat, 18/19 (94.7%) pts experienced ≥ 1 AE. Of 119 AEs of any grade, 24 were Grade ≥3 and 15 were SAEs. Of the 15 SAEs, 11 were related to study treatment (febrile neutropenia [n=4], colitis [n=2], diarrhea [n=1], vomiting [n=1], acute kidney injury [n=1], cardiac chest pain [n=1] and lung infection [n=1]). For all cohorts, no Grade 5 AEs were observed. For 10 pts evaluable for confirmed best overall response in all cohorts, 2 pts had partial response, 6 pts had stable disease and 2 pts were nonevaluable. No difference in GSK609 exposure was observed relative to GSK609 monotherapy. **Conclusions:** The safety profile of GSK609 in combination with 5-FU/plat±PE is manageable. Most AEs were Grades 1 or 2 and consistent with PE and chemotherapy toxicities. Continued follow-up to investigate long-term safety and efficacy of this combination is warranted. Clinical trial information: NCT02723955. Research Sponsor: Study is funded by GlaxoSmithKline and in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

6545 Poster Session (Board #206), Fri, 8:00 AM-11:00 AM

Radiomic response evaluation of recurrent or metastatic head and neck squamous cell cancer (R/M HNSCC) patients receiving pembrolizumab on KEYNOTE-012 study. *First Author: Kirsty Taylor, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Immunotherapy has become a standard of care in the treatment of R/M HNSCC, however only a subset of patients respond, highlighting the need for predictive and prognostic biomarkers. Radiomics is a non-invasive method to quantitatively analyze tumors through conventional imaging. **Methods:** The pre-treatment and first-on-treatment (after 8 weeks) computed tomography (CT) scans from 132 R/M HNSCC patients treated with single-agent Pembrolizumab (10mg/kg Q2W or 200mg Q3W IV) on the KEYNOTE-012 study were analyzed. Identified target lesions, per RECIST 1.1, were manually contoured, and radiomic features from the tumor and peritumoral region (3 mm expansion of the tumor) were extracted using PyRadiomics. All combinations of image filters and feature classes, not including shape descriptors of peritumoral region, were extracted. Feature space dimensionality was reduced by clustering features (hierarchical clustering using Pearson-based distance and complete linkage) and selecting the medoid of each cluster. Correlation with lesion-level response (LLR) at first-on-treatment CT and overall response (OR) was evaluated using concordance index (CI) with Benjamini-Hochberg multiple testing correction. **Results:** A total of 406 lesions were included (45 head & neck (HN), 207 lung, 57 liver, 86 lymph nodes (LN), 11 other). 3562 features were extracted from pre-treatment scans (2246 tumor, 1316 peritumor). Considering all lesion sites collectively, 27 of 110 feature clusters were significantly correlated with LLR (false discovery rate (FDR) < 0.05) but not with best overall RECIST response per patient on study. However, when grouped by organ, a number of feature cluster medoids were significantly associated (FDR < 0.05) with LLR (HN: 1, lung: 28, liver: 8, LN: 1) and OR (liver: 18). Feature clusters predictive of LLR and OR included descriptors of both tumor-specific and tumor/peritumoral gray-level intensity and texture (e.g. 74% tumor and 26% peritumoral features in clusters significantly associated with OR in liver). **Conclusions:** Tumor and peritumoral radiomic features at baseline correlate with LLR and OR to immunotherapy in R/M HNSCC. Despite significant heterogeneity in lesion site, both global and site-specific significant feature clusters could be identified. Research Sponsor: Merck.

6546 Poster Session (Board #207), Fri, 8:00 AM-11:00 AM

The impact of tumor hypoxia on the clinical efficacy of anti-PD-1 mAb treatment in recurrent/metastatic HNSCC patients (R/M). *First Author: Dan Paul Zandberg, UPMC Hillman Cancer Center, Pittsburgh, PA*

Background: Anti-PD-1 mAbs have changed the landscape of R/M HNSCC treatment, but physical, immunologic, and metabolic barriers present in the tumor microenvironment are likely drivers of low response rates. Hypoxia is a well-established feature of the tumor microenvironment and may act as a barrier to T cell infiltration and function. We evaluated the effect of hypoxia on the efficacy of anti-PD-1 mAb treatment in R/M HNSCC patients. **Methods:** We conducted a retrospective analysis of R/M patients treated with anti-PD-1 mAb that had consented to the UPMC Hillman tissue banking protocol (HCC 99-069). Pre-treatment archival FFPE samples were analyzed via immunofluorescent imaging for number of CD8+ T cells (CD8), Tregs, and the percent area (% CAIX) and mean intensity (Int) of carbonic anhydrase IX, a well-described marker of hypoxia. Tissue sections stained with PanCK, CAIX, CD8, Foxp3, and DAPI were imaged with an Olympus IX 83 microscope. ImageJ software and custom software plugins were used to determine %CAIX, Int, CD8, and Treg. PD-L1 by IHC was reported as a combined positive score (CPS) defining positive as CPS $>$ 1. We compared non-responders (NR) i.e. PD to responders (R) i.e. PR or SD, and analyzed OS, PFS. All data were analyzed using GraphPad Prism software. Two-tailed unpaired t test was used when comparing 2 groups, 1-way ANOVA was used for multiple comparisons, and log-rank test was used for survival analysis. **Results:** The 36 patients included were 69% male, median age 59, 58% smokers. 61% were platinum failure. Primary site included 39% OC, 22% OPC (38% HPV positive), 17% Larynx, 17% other, 5% hypopharynx. Low %CAIX/Int, high CD8, and high CD8/Treg were all significantly associated with R. Patients with low %CAIX/Int (12 month OS Low: 75% vs. Mid: 17% vs. High:8%, p = 0.02) and high CD8/Treg had a significant increase in OS. Only high CD8 was associated with significantly higher PFS. Low %CAIX alone showed a non-significant trend towards increased R and no difference in PFS/OS. There was no difference in CD8, CD8/Treg, PD-L1 and Treg between %CAIX/Int groups. **Conclusions:** To our knowledge this is the first evaluation of tumor hypoxia as a predictive biomarker in anti-PD-1 mAb treated R/M HNSCC patients. Lower hypoxia by %CAIX/Int was associated with significantly increased response and OS. While further analysis in a larger dataset is needed to confirm, the lack of significant difference in CD8, Treg, PD-L1, and CD8/Treg between %CAIX/Int groups (Low, Mid, High) suggests that hypoxia may be an independent predictive marker. Research Sponsor: U.S. National Institutes of Health.

6548 Poster Session (Board #209), Fri, 8:00 AM-11:00 AM

Molecular biomarkers to identify patients (pts) who may benefit from durvalumab (D; anti-PD-L1) ± tremelimumab (T; anti-CTLA-4) in recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) from HAWK and CONDOR studies. *First Author: Weimin Li, Astrazeneca, Gaithersburg, MD*

Background: Baseline tumor and germline biomarkers in R/M HNSCC were analyzed for predictive potential in pts benefitting from D or D+T. **Methods:** In HAWK (NCT02207530), 112 pts (PD-L1 tumor cells [TC]≥25%) received D (10 mg/kg Q2W for ≤12 m); in CONDOR (NCT02319044), 67 pts (PD-L1 TC $<$ 25%) received D (10 mg/kg Q2W for ≤12 m), 133 pts received D+T (D 20 mg/kg Q4W, T 1 mg/kg Q4W for ≤12 m), and 67 pts received T (10 mg/kg Q4W [7 doses] then Q12W [2 doses] for ≤12 m) VENTANA PD-L1 (SP263) Assay determined PD-L1 status. Paired FFPE archival tumor and PBMC samples (as germline control) in the HAWK and CONDOR trials were evaluated by whole exome sequencing (WES). Tumor mutation burden (TMB) was number of somatic mutations/megabase. HLA class I types were obtained via WES of PBMCs (CONDOR only). HPV and neutrophil-to-lymphocyte ratio (NLR) were tested locally in CONDOR. Wilcoxon, log-rank tests, and COX-PH models were used. Pooled D & D+T data were analyzed unless noted. **Results:** 153 pts had paired evaluable FFPE tumor and PBMC samples (HAWK, n = 48; CONDOR, n = 105). TMB distributions were similar between studies (P= 0.43). TMB correlated with smoking (P= 0.02) but not HPV (P= 0.24), NLR (P= 0.66), or PD-L1 status (P= 0.43). Overall, high TMB (≥upper tertile) trended with longer OS vs low TMB in all evaluable pts (N = 153; 9.0 vs 5.6 m; HR = 0.70; 95% CI = 0.48-1.01); P= 0.06). In HAWK, there was no association of TMB with OS. In CONDOR, pts (D and D+T arms) with high TMB vs low had significantly longer OS (N = 76; 16.3 vs 5.3 m; HR = 0.53; 95% CI = 0.31-0.92). TMB and OS association was further assessed by increasing TMB cutoffs. Improved HRs trended with higher cutoffs; cutoffs ≥upper quartile significantly linked to OS.TMB was not associated with PFS or ORR. Pts with low PD-L1 and low TMB had worse OS compared to pts with high PD-L1 or high TMB. Pts with high NLR (≥median) and low TMB had significantly worse OS than pts with low NLR and high TMB (HR = 2.63, P< 0.001). Analysis of germline HLA alleles revealed significantly poorer survival for carriers of the HLA-B*15:01 allele (9.4%) (HLA-B variant status did not affect TMB and OS association in CONDOR). Germline HLA heterozygosity did not impact OS. Pts with mutations in *ATM* (5%), a DNA damage repair gene, also trended with prolonged OS. **Conclusions:** TMB is a possible predictive biomarker of IO HNSCC therapy. Combined analysis of NLR and TMB may provide additional PD-L1 data in assessing pts most likely to have long-term benefit. Clinical trial information: NCT002207530, NCT02319044. Research Sponsor: AstraZeneca.

6549 Poster Session (Board #210), Fri, 8:00 AM-11:00 AM

Overall survival modeling and association with serum biomarkers in durvalumab-treated patients with head and neck cancer. *First Author: Vadryn Pierre, Astrazeneca, Gaithersburg, MD*

Background: Optimal patient selection for immunotherapy remains a challenge as most patients fail to respond. We aim to assess baseline factors for association with long-term survival from durvalumab treatment in patients with recurrent/metastatic head and neck squamous cell carcinoma (HNSCC)[1,2]. **Methods:** Pooled longitudinal tumor size, survival, and dropout data from four trials (1108: NCT01693562, CONDOR: NCT02319044, HAWK: NCT02207530, and EAGLE: NCT02369874) involving 467 HNSCC patients were used to develop tumor size-driven hazard models. A panel of 66 serum protein biomarkers at baseline and 4 relevant clinical markers from 346 out of 413 patients treated with durvalumab (all studies except 1108) were initially screened to select a pool of 21 candidate covariates. The criteria for dimensionality reduction comprised correlation strength between biomarkers and pharmacological hypotheses pertaining to a prior analysis[3] (inflammation, immunomodulation, tumor burden and angiogenesis). **Results:** The final tumor model highlighted that high tumor burden, elevated LDH and neutrophil-lymphocyte ratio were associated with faster tumor growth while patients with lower baseline tumor burden had an increase in net tumor shrinkage. For overall survival, the model suggested that high levels of immunomodulators (IL23, Osteocalcin), low inflammation (IL6, NLR), low tumor burden, and low angiogenesis factors (von Willebrand factor (vWF), plasminogen activator inhibitor-1 (PAI-1)) were associated with survival benefits for patients treated with durvalumab. Specifically, these patients had baseline serum IL23 $>$ 2.1 pg/mL and Osteocalcin $>$ 32 pg/mL or serum PAI-1 $<$ 229 pg/mL and serum IL6 $<$ 5.4 pg/mL which corresponded to a hazard ratio estimate (HR and 95%CI) of 0.36 (0.27- 0.47), logrank p-value: $2.3x10^{-14}$. The median (n, 95%CI) overall survival time for the patients with favorable biomarker profile was 14.6 months (n = 129, 11.2-21.4) vs. 4.4 months (n = 217, 3.6-5.3). **Conclusions:** Our results corroborate the prior hypothesis highlighting the prognostic value of inflammation, disease burden, tumor angiogenesis, and immunomodulatory factors on the clinical outcomes of HNSCC patients treated with durvalumab[3]. Collectively, we identified a serum biomarker profile of HNSCC patients with median survival times exceeding 1 year which may potentially be used for patient enrichment following further validation in prospective studies. References: [1]Yanan CPT 2017, [2]Baverel, 2018 ENA, [3]Guo, X, 2019 Asco P6048 Clinical trial information: NCT01693562, NCT02319044, NCT02207530, NCT02369874. Research Sponsor: AstraZeneca.

6551 Poster Session (Board #212), Fri, 8:00 AM-11:00 AM

CD3 and CD20 immune cell densities in primary tumors, lymph node metastasis, and recurrent disease samples of head and neck squamous cell carcinoma. *First Author: Simon Laban, Department of Otolaryngology - Head and Neck Surgery, University Hospital Ulm, Universität Ulm, Ulm, Germany*

Background: Immune cell (IC) infiltrates in primary tumors (PT) have been identified as prognostic markers in head and neck squamous cell carcinoma (HNSCC). IC densities may differ among PT, lymph node metastasis (LNM) and recurrent disease (RD) and by primary disease site (oral cavity- OC, oropharynx- OP, hypopharynx- HP, larynx- L). Here, we compare CD3 and CD20 IC densities in PT, LNM and RD in paired samples from different disease sites and determine the prognostic impact of IC infiltrates. **Methods:** Tissue microarrays with 425 PT, 198 LNM and 46 RD samples--each in triplicate--were stained immunohistochemically for CD3 and CD20 in the same slide. Immune cell densities per mm^2 were determined using a digital image analysis software (QuPath). Individual means were calculated from triplicates of each sample. IC infiltrates from different sample types (PT, LNM, RD) and primary tumor sites were compared using Kruskal-Wallis and Mann-Whitney-U tests. Paired samples were compared using Wilcoxon signed rank test. IC densities were classified as CD3 high/low and CD20 high/low for each primary tumor site using the individual median as a cut-off. Overall survival (OS) was calculated using the Kaplan-Meier method. P-values for each hypothesis were corrected using a false discovery rate of 5%. **Results:** CD3 and CD20 IC densities differed significantly by sample type (both $p<0.0001$) and primary site (CD3: p=0.012, CD20: p=0.0017). CD3 and CD20 densities were significantly lower in PT compared to LNM or in RD compared to PT and LNM. Paired samples (n=172) revealed a significantly higher CD3 and CD20 density (both $p<0.0005$) in LNM compared to PT, but no significant differences between PT and RD (n=28, $p>0.05$). CD3 densities were significantly higher than CD20 densities in all sample types. $CD3_{high}$ patients had the best prognosis in all sites except for OC ($q<0.05$) independent of CD20 status. In OC, CD3 density was not prognostic, but $CD3_{low}/CD20_{high}$ patients had the worst OS compared to $CD3_{low}/CD20_{low}$ and $CD3_{high}/CD20_{high}$ or even $CD3_{high}/CD20_{low}$ patients (p=0.018) who had the best prognosis. **Conclusions:** IC densities of CD3 and CD20 vary by sample type and primary site. Except for OC, in all sites the prognostic impact is determined by $CD3_{high}$, whereas in OSCC only the combination of CD3 and CD20 IC densities achieves a good prognostic value. Interestingly, $CD3_{low}/CD20_{high}$ patients have the worst overall survival in OC patients. Further work is needed to understand the interaction of B- and T cell infiltrates in the tumor, especially in OC. Research Sponsor: Clinician Scientist Program, Other Foundation.

6552 Poster Session (Board #213), Fri, 8:00 AM-11:00 AM

Correlation of tumor mutational burden (TMB) with CDKN2A and TP53 mutation in HPV-negative head and neck squamous cell carcinoma (HNSCC). *First Author: Barbara Burtness, Yale School of Medicine and Yale Cancer Center, New Haven, CT*

Background: The tumor suppressors *TP53* and *CDKN2A* are commonly mutated or lost in HNSCC, impairing G1 checkpoints. This reduces ability to repair DNA damage arising from hypoxia, replication stress, and mutagen exposure, thus increasing TMB, a potential predictive biomarker for immunotherapy benefit. *TP53* mutations can be classified as loss-of-function (LOF) with or without dominant negative (DNE) activity, gain-of-function (GOF) and benign. We investigated whether specific categories of *TP53* mutation were associated with increased TMB, and whether these cooperated with *CDKN2A* mutation to elevate TMB. **Methods:** We analyzed 1010 HPV- HNSCC tumor samples (246 female) profiled with a 592-gene panel by Caris Life Sciences from 2015 to 2019. Predominant subsites were oral cavity (285), oropharynx (225) and larynx (153). TMB reflected all somatic nonsynonymous missense mutations detected. We report mean TMB per megabase (MB). Pathogenicity of *TP53* and *CDKN2A* mutations was determined according to American College of Medical Genetics (ACMG) guidelines. We also used four alternative methods of characterizing *TP53* mutations based on analysis of protein structure, public databases (IARC, ClinVar, InterVar), and publications (PMID: 25108461 and others) assessing structure-function relations. **Results:** 60% of cases had *TP53* mutations ($TP53^{mut}$) designated pathogenic by ACMG guidelines. Estimates of frequency of LOF/DNE mutations ranged from 30-42.8% of cases among the alternative classification methods. Damaging *CDKN2A* mutations were present in 20%. Average TMB per MB varied from 8.2/8.6 (females/males) in oral cavity cancers to 26.5/27.7 (females/males) in cancer of the lip. Mean TMB was typically higher in the presence of damaging LOF/DNE *TP53* mutations or *CDKN2A* mutations, but not *TP53* GOF mutations. Based on ACMG, for tumors with *TP53* and *CDKN2A* wild type (WT) TMB was 8.03, for those with $CDKN2A^{mut}$ only 9.82, for $TP53^{mut}$ only 10.56, and $TP53^{mut}/CDKN2A^{mut}$ 17.6 ($p < 0.001$). For disruptive $TP53^{mut}$ (Poeta algorithm), mean TMB for WT/WT was 8.67, for $TP53^{mut}$ 11.31, $CDKN2A^{mut}$ 17.9 and $TP53^{mut}/CDKN2A^{mut}$ 15.83 ($p < 0.001$). **Conclusions:** Mutation of *TP53* and/or *CDKN2A* is associated with increased mean TMB relative to WT; mean TMB was highest for tumors bearing damaging mutations in both genes. GOF *TP53* mutation was not clearly associated with increased TMB. As TMB is evaluated as a predictive biomarker in the immunotherapy of HNSCC, specific *TP53/CDKN2A* mutational status should also be evaluated. Research Sponsor: Caris Life Sciences.

6553 Poster Session (Board #214), Fri, 8:00 AM-11:00 AM

Prognostic role of pre-treatment magnetic resonance imaging (MRI) radiomic analysis in patients with squamous cell carcinoma of the head and neck (SCCHN). *First Author: Salvatore Alfieri, Head and Neck Cancer Medical Oncology 3 Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: Emerging data suggest that radiomics can be used to predict outcomes in SCCHN. At present, only few data are available for pre-treatment MRI. **Methods:** Study population was retrieved from an ongoing multicenter, randomized, prospective trial (NCT02262221, HETeCo) evaluating health and economic outcomes of two different follow-up (FUP) strategies (intensive vs non-intensive) in effectively cured stage III-IV (VIII TNM ed.) SCCHN. We selected only patients with both pre- and post-contrast enhancement T1 and T2-weighted baseline MRI (b-MRI) and at least 2 years (2y) of FUP. A radiomic model was developed to identify high risk (HR) and low risk (LR) of disease recurrence. Radiomic features (RF) were extracted from the primary tumor in the b-MRI. The best RF combination was selected by Least Absolute Shrinkage and Selection Operator (LASSO). Ten-fold cross-validation was used to compute sensitivity, specificity and area under the curve (AUC) of the classifier. Kaplan-Meier (KM) curves were estimated for HR and LR, for both overall survival (OS) and disease-free survival (DFS) and log rank test was performed. Three years (3y)-DFS and OS were also estimated for the two groups. The radiomic risk class was used as a new variable in a multivariate Cox model including well established prognostic factors in SCCHN (TNM stage, subsite and HPV). **Results:** Out of 155 enrolled HETeCO patients, 98 baseline imaging were retrieved of which 57 b-MRI. Of these, 51 met the eligibility criteria (25 in intensive and 26 in non-intensive arm). Baseline patients' characteristics were: median age 66 yr (38-86); sex (M 42; F 9); median smoking history: 30 packs/y (1-100); 25 oral cavity (49%), 18 oropharynx (35%, 14 HPV+), 6 larynx (12%), 2 hypopharynx (4%). At a median FUP of 42 months (25-64), 45 (88%) patients are still alive. The recurrence rate was 20% (10/51, of which 2 distant). In total, 1608 RF were extracted. The sensitivity, specificity and AUC of the classifier were 90%, 76%, and 80%, respectively. The radiomic risk class was found to be an independent prognostic factor for both DFS and OS (p=0.01 and p=0.046, respectively). KM curves for DFS and OS were significantly different between HR and LR groups (p=0.002 and p=0.04, respectively). In HR vs LR, 3-y DFS and OS were: 78% [61-100%] vs 97% [90-100%], and 88% [75-100%] vs 96% [88-100%], respectively. **Conclusions:** Radiomics of pre-treatment MRI can predict outcomes in SCCHN. External validation of this preliminary radiomics-based model is currently ongoing. Research Sponsor: BRI (Bando Ricerca Istituzionale) 2018. This project has received funding (Fondi 5x1000 Ministero della Salute 2015) from Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy under grant agreement N. D/17/1SA (statement n. 511 on December, 21th, 2.

6554 Poster Session (Board #215), Fri, 8:00 AM-11:00 AM

HPV ctDNA analysis in unresectable recurrent/metastatic oropharyngeal cancer. *First Author: Catherine T Haring, University of Michigan Department of Otolaryngology-Head and Neck Surgery, Ann Arbor, MI*

Background: There is an increasing incidence of human papillomavirus associated (HPV+) oropharyngeal cancer (OPC). While HPV + portents improved prognosis, survival for patients with unresectable recurrent/metastatic (R/M) OPC remains poor. Extant data suggest that HPV ctDNA levels correlate with disease burden and treatment outcomes in patients with HPV + OPC in the primary setting but scant data exists in the metastatic setting. Objective: To develop a highly precise droplet digital (ddPCR) assay for quantification of plasma HPV ctDNA and to evaluate whether HPV ctDNA predicts treatment response in patients with HPV+ R/M OPC. **Methods:** Patients with HPV + R/M OPC starting systemic therapy were enrolled in a biorepository in which blood was collected prior to each cycle of therapy. PCR probes were created for the most common high-risk HPV subtypes, 16 and 18. HPV ctDNA was extracted from plasma and quantified with ddPCR. Percent change in HPV ctDNA was calculated after 1 and 2 cycles of treatment. Treatment response was assessed per standard of care or study protocol after 2-3 cycles of treatment. ROC curve analyses were performed. **Results:** A precise ddPCR assay was developed to identify plasma HPV ctDNA in 10 patients who underwent 16 distinct treatment courses. On ROC curve analysis, percent change in HPV ctDNA after 2 cycles of treatment was predictive of radiographic response (AUC 0.82, p = 0.03). The optimal cutoff point to optimize sensitive and specificity was identified as 30% change in HPV ctDNA (Table). Changes in HPV ctDNA after 1 cycle of treatment were also predictive of radiographic response (AUC 0.82, p = 0.05). **Conclusions:** Changes in HPV ctDNA may be predictive of treatment response in patients with R/M HPV + OPC. Furthermore, HPV ctDNA predicts response earlier than conventional imaging. While validation is needed, this assay shows promise in identifying poor responders who can be directed early towards clinical trials or alternative therapies. Research Sponsor: Internally funded by University of Michigan.

	Stable Disease or Partial Response	Disease Progression	
< 30% increase in HPV ctDNA	6	1	PPV 85.7% (95% CI 48-98%)
≥30% increase in HPV ctDNA	1	8	NPV 88.9% (95% CI 56-98%)
	Sensitivity 85.7% (95% CI 42-100%)	Specificity 88.9% (95% CI 52-100%)	

6556 Poster Session (Board #217), Fri, 8:00 AM-11:00 AM

Molecular correlates of response to preoperative olaparib alone or with cisplatin or with durvalumab in head and neck squamous cell carcinoma (HNSCC): A Hellenic Cooperative Oncology Group study. *First Author: Amanda Psyrri, Hellenic Cooperative Oncology Group (HeCOG), Athens, Greece*

Background: Poly(ADP-ribose) polymerase (PARP) inhibitors drive increased DNA damage and tumor cell death, particularly in tumors with existing defects in DNA repair. Furthermore,they promote immune priming, through a range of molecular mechanisms. Foremost, among candidate intracellular pathways is STING (stimulator of interferon genes), an innate immune response activated by cytosolic DNA (perhaps a consequence of DNA damage) that can lead to enhanced interferon (IFN) production. PARP inhibitor-induced DNA damage also leads to adaptive upregulation of programmed death ligand 1 (PD-L1) expression. To this end, there is increasing rationale for testing PARP inhibitors alone or in combination with chemotherapy or PD1 checkpoint inhibitors in HNSCC. **Methods:** 39 patients were enrolled in OPHELIA phase II trial in which pts were randomized 3: 3:3:1 to Cisplatin (C) 60 mg/m2 on d1 followed by Olaparib (O) 75mg d 1-5 (Arm A), O 300 mg bid for 21-28 days (Arm B), no treatment (ARM C) orD 1500 mg on d1 followed by O 600 mg daily for 21-28 days (Arm D). Response was defined as tumor reduction noted on exam, imaging or pathology. Pretreatment biopsies were subjected to 310 gene OncoDNA NGS panel. Double Stranded Brakes/Repair (DSB/R) was measured by evaluating phosphorylation of histone H2AX by immunochistochemistry (IHC). In addition, IHC for PD-L1 (CPS) and STING was performed in paired pre- and post-treatment biopsies. **Results:** 17/36 pts in (O) treatment arms (6/11 evaluable pts Arm A, 9/11 evaluable pts Arm B, 2/11evaluable\ pts arm D) developed a response. One patient in D+O arm developed path CR. Low γH2AX staining at pretreatment biopsies was associated with progression (p=0.029). Higher PD-L1 expression (CPS≥1) was associated with disease progression (p=0.014). CPS PD-L1 was upregulated following (O) treatment. STING expression was not significantly upregulated post treatment in (O) treatment arms. Alterations in genes that have been previously reported to be associated with (O) sensitivity, namely DNA damage Response/Repair (DDR) genes and genes involved in chromatin remodeling (*CHK2, KMT2D, KMT2C, ARID2 and AJUBA*), were identified in responders. **Conclusions:** This window study demonstrated promising signs of activity of (O) in HNSCC, particularly in tumors with high expression of γH2AX and alterations in DDR or chromatin remodeling genes. Clinical trial information: NCT02882308. Research Sponsor: Preoperative Administration of Olaparib With Cisplatin or With Durvalumab or Alone or no Tratment in Patients Who Are Candidates for Surgery of Carcinoma of the Head and Neck. (OPHELIA).

6557 Poster Session (Board #218), Fri, 8:00 AM-11:00 AM

Exome scale liquid biopsy characterization of putative neoantigens and genomic biomarkers pre- and post anti-PD-1 therapy in squamous cell carcinoma of the head and neck. *First Author: Charles Abbott, Personalis Inc, Menlo Park, CA*

Background: The reduced scope, and number of genes profiled by typical liquid biopsy panels can result in missed biomarkers including neoantigens, which may change with treatment, as well as potentially undetected resistance mechanisms and pathways beyond the scope of targets typically captured by panels. To address these limitations, we used a whole-exome scale liquid biopsy monitoring platform, NeXT Liquid Biopsy, to analyze head and neck squamous cell carcinoma (HNSCC) patients that have received anti-PD1 therapy. Presently, we sought to (1) monitor neoantigen changes in cfDNA as a complement to tumor biopsy-derived neoantigens, (2) compare the impact of tumor escape mechanisms, including HLA-LOH, on neoantigens identified in tissue and cfDNA and (3) to identify novel biological signatures that combine information from both solid tumor and liquid biopsies. **Methods:** Pre- and post-intervention matched normal, tumor and plasma samples were collected from a cohort of 12 patients with HNSCC. Following baseline sample collection all patients received a single dose of nivolumab, followed by resection approximately one month later when feasible, or a second biopsy where resection was impractical. Solid tumor and matched normal samples were profiled using ImmunoID NeXT, an augmented exome/transcriptome platform and analysis pipeline. Exome-scale somatic variants were identified in cfDNA from plasma samples using the NeXT Liquid Biopsy platform. Data from these two platforms were compared with corresponding clinical findings. **Results:** Concordant somatic events were detected between plasma and tumor at pre- and post-treatment timepoints. Neoantigens predicted to arise from these somatic events were reduced in solid tumor post-treatment, but increased in cfDNA, when compared to pre-treatment timepoints. HLA LOH was identified in a number of subjects, likely resulting in reduced neoepitope presentation in those cases. Immune cell infiltration increased in the tumor following treatment, with no changes to the $CD8^+$/Treg cell ratio, suggesting consistent immunoregulation. **Conclusions:** Exome-wide neoantigen burden was reliably predicted from cfDNA, providing additional insight complementing data from solid tumor. Analyzing HLA LOH, and neoantigen burden from both solid and liquid biopsies together over the course of treatment creates a more comprehensive profile of therapeutic response and resistance mechanisms in HNSCC patients missed with typical liquid biopsy panels. Research Sponsor: Personalis, Inc.

6558 Poster Session (Board #219), Fri, 8:00 AM-11:00 AM

Association of radiation treatment failure in head and neck cancer with differential immune infiltrate. *First Author: Mohamed Abdelhakiem, UPMC Hillman Cancer Center, Pittsburgh, PA*

Background: Previously we have shown that PD-L1 expression is associated with treatment failure in Head and Neck Cancer (HNSCC) treated with radiation. We have further evaluated the effect of pre-treatment immune infiltrate on treatment failure following radiation. **Methods:** A total of 75 patients with HPV negative HNSCC treated with surgery and post-operative radiation were included in this study. Pre-treatment tumors were examined via RNA-Sequencing utilizing an Illumina platform. These data were then subjected to immune profiling utilizing publicly available software (xCell) to infer relative enrichment of immune cell infiltrate per sample. Each immune cell type detected at any level in at least 15 tumors was then evaluated for effect on loco-regional recurrence using Cox-regression analysis. Clinical variables included in this analysis include tumor stage, nodal stage and treatment site. Survival analysis was performed utilizing the method of Kaplan Meier, with log rank statistics used to test for significant comparisons. **Results:** The majority of HNSCCs analyzed in this study were from the oral cavity (65.3%), followed by the larynx and hypopharynx (28%) and oropharynx (6.7%). The total median dose of radiation delivered was 60 Gy (range: 36-79.2) and median follow up in living patients was 80.5 months (range: 7-190). On univariate analysis, no measured clinical variable was significantly associated with loco-regional recurrence (LRR). Similar to our previous studies in other HNSCC cohorts treated with radiation, PD-L1 expression was negatively associated with LRR (p = 0.005). Additionally, multiple immune cell infiltrates were negatively associated with LRR including: Th2 helper cells (p = 0.007), CD8+ central memory T cells (p = 0.02), immature dendritic cells (p = 0.037), CD4+ memory T cells (p = 0.043). In a multivariate model including these immune cell subsets, Th2 helper cells, CD8+ central memory T cells and immature dendritic cells remained significantly negatively associated with LRR following radiation. **Conclusions:** This analysis demonstrates the importance of pre-treatment immune infiltrate on outcomes in HNSCC and points to potential avenues to explore to augment response to radiation. Research Sponsor: NIH.

6559 Poster Session (Board #220), Fri, 8:00 AM-11:00 AM

Computerized features of spatial interplay of tumor-infiltrating lymphocytes predict disease recurrence in p16+ oropharyngeal squamous cell carcinoma: A multisite validation study. *First Author: Germán Corredor, Case Western Reserve University, Cleveland, OH*

Background: While overall, patients with p16+ oropharyngeal squamous cell carcinoma (OPSCC) have a favorable prognosis, subsets of patients experience disease recurrence (DR) and death despite aggressive multimodality treatment. Aside from routine staging criteria, there are no biomarkers of tumor behavior routinely employed in OPSCC to identify patients at higher risk of DR. In this study we sought to evaluate whether the interplay between tumor-infiltrating lymphocytes (TILs) & cancer cells, in both stromal and epithelial compartments from digitized H&E-stained slides, can predict DR in OPSCC patients. **Methods:** OPSCC resected specimens from 354 patients (66 with DR) were retrospectively collected from 3 different sites. 107 (16 DR) patients from site 1 formed the training set and 247 (50 DR) patients from sites 2 & 3 formed the independent validation cohort. Computerized algorithms automatically identified 4 types of nuclei (TILs & non-TILs in both stromal & epithelial regions), defined clusters for each nuclei type based on cell proximity, and used network graph concepts to capture measurements relating to the arrangement of these clusters. The top 10 features determined by a statistical selection method (LASSO) were used to train a Cox regression model that assigns a risk of DR to each patient on the training set. The median risk score was used as threshold for stratifying patients on the validation set into low and high-risk of DR. Survival analysis was used to evaluate the stratification given by the trained model. **Results:** Patients identified by the TIL interplay model as high risk for DR had statistically worse disease specific survival. Univariate analysis yielded an HR=2.49 (95% CI: 1.22-5.07, p=0.04) for site 2 and HR=3.62 (95% CI: 1.39-9.43, p=0.03) for site 3. Multivariate analysis controlling the effect of different clinical variables is shown in the attached table. **Conclusions:** We introduce a prognostic model based on the automated quantification of the interplay between tumor microenvironment cells that is able to help distinguish OPSCC patients with higher DR risk from those who will experience longer disease-free survival. Research Sponsor: U.S. National Institutes of Health.

	p-val site 2	HR site 2	p-val site 3	HR site 3
O-stage (8th ed) 1,2 vs. 3,4	0.88	1.07 (0.45-2.52)	0.11	2.78 (0.80-9.60)
T-stage (8th ed) 1,2 vs. 3,4	0.11	1.93 (0.86-4.37)	0.96	1.03 (0.31-3.49)
N-stage (8th ed) 0,1 vs. 2,3	0.01	2.75 (1.31-5.74)	0.90	1.07 (0.34-3.34)
TIL interp. Low vs. High	0.02	2.81 (1.15-6.87)	0.05	3.45 (0.99-12.07)

6560 Poster Session (Board #221), Fri, 8:00 AM-11:00 AM

Prognostic value of radiological extranodal extension detected by computed tomography for predicting outcomes in head and neck squamous cell cancer patients treated with radical chemoradiotherapy. *First Author: Abhishek Mahajan, Tata Memorial Centre, Mumbai, India*

Background: As per the AJCC 8th edition ENE/ECS is the most important predictor for N staging of HNSCC and is one of the key predictor of outcomes. Because ENE/ECS is based on pathological findings after surgery and it is difficult to predict outcomes for locally advanced squamous head and neck cancer (LASHNC) treated radically with CCRT. We hypothesized that ENE assessed by CT imaging (rENE) may directly correlate with outcomes in LASHNC treated radically with CCRT. **Methods:** This open-label, investigator-initiated, phase 3, randomized trial was conducted from 2012 to 2018. Adult patients with LASHNC who were fit for radical chemoradiation were randomized 1:1 to receive either radical radiotherapy (66-70 grays) with concurrent weekly cisplatin (30 mg/m^2) (CRT) or the same schedule of CRT with weekly nimotuzumab (200 mg) (NCRT). 536 patients were accrued,182 were excluded due to non-availability DICOM CT scan, 354 patients were analysed for rENE (based on 6 criterion for metastasis and 3 for rENE). Near equal distribution of patients was achieved in CRT arm (170 patients) and NCRT arm (184 patients). There were 181 (51.1%) oropharynx and 173(48.9%) larynx and hypopharynx patients. We evaluated association of radiological ENE and clinical outcomes.The endpoints were disease-free survival (DFS), duration of locoregional control (LRC), and overall survival (OS). **Results:** There were 244(68.9%) patients with radiologically metastatic nodes, out of which 140(57.3%) had rENE. There was no significant association between rENE and CRT (p value 0.3) or NCRT (p value 0.412). The median follow-up was 33.0 months (95%CI 30.7-35.2 months). Complete response was achieved in 204 (57.6%) cases, PR/SD in 126(35.6%) cases and PD in 24(6.8%) cases. rENE positive patients had poor overall 3-year survival (46.7%), poor DFS (48.8%) and LRC (39.9%) than rENE negative cases (63.6%, 87%, 60.4%). rENE positive cases had 1.71 times increase chances of incomplete response than rENE negative cases. Overall stage, clinical positive node, response, rENE and site were the only significant factors for predicting OS, DFS and LRC. **Conclusions:** In conclusion, pre-treatment rENE can be regarded as an independent prognostic factor for survival (OS, DFS, LRC) in patients with LASHNC treated radically with CCRT. Pre-treatment rENE is not only associated with CCRT response but is also associated with poor prognosis and hence rENE, as an imaging biomarker, can stratify responder's vs non-responders. Clinical trial information: CTRI/2014/09/004980. Research Sponsor: This study was funded by Biocon Ltd, Science and Engineering Research Board grant EMR/2015/001591, and by the Tata Memorial Center Research Administration Council.

6561 Poster Session (Board #222), Fri, 8:00 AM-11:00 AM

Immune functional portraits of head and neck cancer using next generation sequencing. *First Author: Susan Raju Paul, Massachusetts General Hospital, Boston, MA*

Background: The addition of biomarkers as companion diagnostics and Next Generation Sequencing (NGS) have dramatically increased therapeutic efficacy and have aided precision medicine development. The unique genomic profile and tumor microenvironment (TME) composition of each patient can be ascertained through NGS. Using TCGA and Geo datasets, we characterized head and neck cancers (HNC) according to the cellular and functional state of their TME and conducted a pilot validation study using prospectively collected HNC tumors. **Methods:** To stratify the TME of HNC tumors into molecular functional portraits, we analyzed the sequencing data of 1,486 HNC tumor samples and 143 controls (normal, oral leukoplakia) from TCGA and GEO data sets. For the prospective pilot study, resected tissue from oropharyngeal carcinomas independent of HPV status were processed for whole exome (WES) and RNA-seq (n = 6; HPV-positive = 1). **Results:** To characterize the cellular composition and functional state of HNC tumors and their TMEs, we created 26 separate molecular signatures related to functional processes such as immune checkpoint inhibition, immune infiltration, immunosuppression, and stromal activities represented by angiogenesis and mesenchymal stromal cells. Unsupervised clustering of these signatures delineated tumors into 4 types: immune infiltration with increased stromal signatures (type A), immune infiltration with decreased stromal signatures (type B), no immune infiltration with increased stromal signature (type C), and no immune infiltration and decreased stromal signatures (type D). Most HPV-positive tumors were type B (p = 1e-27) and associated with increased survival compared to the HPV-negative tumors (types C and D; p = 3e-05). Type B HPV-positive tumors had reduced *FAT1* and *TP53* mutations, whereas type B HPV-negative tumors had increased *caspase 8* mutations/loss. In the validation cohort, actionable mutations were found in *PI3KCA* and *TSC2* in types A and B HPV-negative tumors. Moreover, while the HPV-positive tumor was classified as type C, we identified a *caspase 8* homozygous deletion and absence of *FAT1* and *TP53* mutations, supporting the TCGA and GEO analysis. **Conclusions:** Exome and transcriptome analyses with cellular deconvolution from bulk RNA-seq enrich tumor characterization by including major TME components, providing a comprehensive biomarker profile for precision therapy and clinical decision making. Our prospective analysis identified TME parameters comparable with the large datasets and revealed targetable genomic alterations. Research Sponsor: None.

6562 Poster Session (Board #223), Fri, 8:00 AM-11:00 AM

Detection of somatic mutations in saliva of patients with oral cavity squamous cell carcinoma. *First Author: Evgeny Izumchenko, University of Chicago, Chicago, IL*

Background: Oral cavity squamous cell carcinoma (OCSCC) frequently presents as clinically advanced disease with poor prognosis. When diagnosed at early stages, survival rates approach 80%, underscoring the need for validated, cost-effective detection methods. OCSCC is driven by the serial acquisition of genetic alterations. Tumor-defining somatic mutations are attractive biomarkers and hence their presence in saliva may be associated with malignancy as shown in a few proof-of-concept studies, including our previous work. Based on this premise, we present a low-cost, accurate, next generation sequencing (NGS) test with high clinical utility aimed at detecting mutations in the saliva for early diagnosis and potential screening of OCSCC. **Methods:** We have designed a custom NGS panel that covers exons of 7 most frequently mutated genes in OSCC. This minimal gene set derived from the analysis from 3 public datasets, predicted incidence of at least one somatic aberration in 89% of patients. We recruited 91 treatment-naïve OCSCC patients and profiled DNA from tissue and matched pre-operative saliva using this test. We also tested DNA from 12 subjects with premalignant lesions with high-grade oral dysplasia and matched saliva. **Results:** Using stringent variant calling criteria, at least one somatic variant was detected in 88 (96%) of the 91 primary tumors. 90.9% of the matched saliva were concordant, with only a minor decrease in early stage disease. Tumor-specific mutations (≥5% AF) in driver genes were detected in 10 (83.3%) dysplastic lesions, suggesting that driving clonal events may occur early in disease development. Interestingly, in 3 matched saliva of the dysplastic samples, the same mutations were detected. To ensure a variant is not a false positive call, we performed a vigorous multistep analytical validation of this saliva-based test: (i) independent re-sequencing of 24 saliva confirmed 94% reproducibility; (ii) no functionally relevant variants were detected in saliva from 12 of 13 healthy subjects without history of tobacco and alcohol usage; (iii) reproducibility, sensitivity, and specificity were confirmed using a positive control with 7 loci at 0.25% AF across 8 independent saliva sequencing runs and a certified negative control and was found to be on par with droplet digital PCR. **Conclusions:** These data highlight the feasibility of saliva-based testing for early diagnosis of OCSCC and premalignant lesions. Research Sponsor: Tata Centre for Development (TCD) at University of Chicago, Philanthropic - Jill and Ozzie Giglio.

6563 Poster Session (Board #224), Fri, 8:00 AM-11:00 AM

18 FDG PET/CT prediction of treatment outcomes in patients with p16-positive, non-smoking associated, locoregionally advanced oropharyngeal cancer (LA-OPC) receiving deintensified therapy: Results from NRG-HN002. *First Author: Rathan M Subramaniam, 290 Great King Street, Dunedin, New Zealand*

Background: To determine the negative predictive value (NPV) of 12-14 week post-treatment PET/CT for 2-year progression-free survival (PFS) and 2-year locoregional control (LRC) in NRG-HN002, which is a two-arm phase II trial for patients with low-risk, non-smoking associated p16-positive LA-OPC randomized in a 1:1 ratio to reduced-dose IMRT with or without cisplatin. **Methods:** PET/CT scans were reviewed both centrally and locally by participating institutions. Tumor response evaluations for primary site, right neck, and left neck were carried out using a 5-point ordinal scale ('Hopkins Criteria'). Overall scores were then assigned as 'Negative,' Positive,' or 'Indeterminate.' Patients who had a 'Negative' score for all three evaluation sites were given an overall score of 'Negative.' The endpoints were NPV for LRC and PFS at 2 years testing NPV $\leq$ 90% vs $>$ 90% (1-sided alpha 0.10 and 76% power). **Results:** There were 316 patients enrolled, of whom 306 were randomized and eligible. Of these, 131 (42.8%) patients consented to a post-therapy PET/CT, and 117 (89.3%) patients were eligible for PET/CT analysis. The median time from end of treatment to PET/CT scan was 94 days (range 52-139). The rates of 2-yr PFS and LRC in the analysis subgroup were 91.3% and 93.8%, respectively. Based on central review, post-treatment scans were negative for residual tumor for 115 patients (98.3%) and positive for 2 patients (1.7%). The NPV for 2-year LRC was 94.5% (90% lower confidence bound [LCB] 90.6%; p = 0.07). NPV for 2-year PFS was 92.0% (90% LCB 87.7%; p = 0.30). Similar NPV results were obtained based on analysis of local reviews. **Conclusion:** Within the context of deintensification with reduced-dose radiation, the NPV of a 12-14 week post-therapy PET/CT for 2-year LRC is statistically $>$ 90%, similar to that reported for patients receiving standard chemoradiation. However, in this study, there was not enough evidence to conclude that the NPV of a 12-14 week post-therapy PET/CT for 2-year PFS is $>$ 90%. Grant acknowledgement: This project was supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology SDMC), U24CA180803 (IROC), UG1CA189867 (NRG Oncology NCORP) from the National Cancer Institute (NCI). This project is funded, in part, under a Grant with the Pennsylvania Department of Health. The Department specifically disclaims responsibility for any analyses, interpretations or conclusions. Clinical trial information: NCT02254278. Research Sponsor: U.S. National Institutes of Health.

6564 Poster Session (Board #225), Fri, 8:00 AM-11:00 AM

Computational discovery of non-mutational tumor-restricted antigens reveals evidence of immunoediting in head and neck squamous cell carcinoma. *First Author: Jan Ole Kemnade, Baylor College of Medicine, Houston, TX*

Background: We previously identified 107 expression-based tumor antigens (EbTAgs) defined as genes with negligible expression in healthy tissue and overexpression in cancer. EbTAgs present novel targets for the adaptive anti-tumor immune response and exhibit evidence of immunoediting in highly immune infiltrated oral cavity tumors. To detail the landscape of EbTAgs in head and neck squamous cell carcinoma (HNSC) and further elucidate EbTAg immunoediting, we compared the expression EbTAgs in the context of tumor immune infiltration among four HNSCC subtypes: oral cavity (OC), HPV+ oropharyngeal (HPV+OP), HPV- oropharyngeal (HPV-OP), and laryngeal/hypopharyngeal (LH). **Methods:** Upper quartile FPKM gene expression values of all protein coding genes were calculated for all HNSC samples using RNAseq data from The Cancer Genome Atlas (TCGA). TCGA HNSC tumors were divided into subtypes and analyzed for EbTAg expression. Individual tumor sample immune infiltrate was determined using unsupervised clustering of 14 immune cell signature ssGSEA scores for the HNSC dataset as a whole and for each subtype. **Results:** LH tumors expressed significantly more EbTAgs than other subtypes (p=0.0014), specifically HPV+OP (p=0.0008, Tukey's test). Immune clustering analysis showed that LH tumors were significantly more likely to be in the low than the high immune cluster whereas the reverse was true for HPV+OP tumors ($p<0.0001$). Hypothesizing that EbTAg expression was a function of tumor immune infiltration rather than HNSC subtype, we compared EbTAg expression between tumors in low and high immune clusters of the entire HNSC dataset as well as of each HNSC subtype. Significantly more EbTAgs were expressed in low immune tumors compared to high immune tumors of the HNSC dataset ($p<0.0001$). Similarly, significantly more EbTAgs were expressed in low immune tumors compared to high immune tumors of the OC, OP-all tumors, and HPV+OP datasets (p=0.0003, $p<0.0001$, p=0.0006) with a trend of more EbTAgs in the immune low versus high tumors in the HPV-OP and LH datasets (p=0.12, p=0.095). **Conclusions:** EbTAg expression in TCGA HNSC samples correlates with tumor immune infiltration resulting in lower expression under greater immunological pressure. These results reinforce the hypothesis that EbTAgs undergo immunoediting and are immunologically relevant. Exploration of EbTAgs as antigenic targets of modular vaccines or adoptive T-cell therapy as well as biomarkers of immune checkpoint inhibition therapy response is warranted. Research Sponsor: U.S. National Institutes of Health.

6565 Poster Session (Board #226), Fri, 8:00 AM-11:00 AM

Does sinonasal cancer survival differ based on human papillomavirus status? *First Author: Shreya Pusapadi Ramkumar, Saint Louis University School of Medicine, St. Louis, MO*

Background: The sinonasal tract is a lesser known "hot spot" for the human papillomavirus (HPV), compared with the oropharynx. Additionally, unlike the oropharynx, the role of HPV tumor status in the survival and overall prognosis of the sinonasal tract and other non-oropharyngeal head and neck cancer sites remains inconclusive. Understanding differences in survival based on HPV status could be useful clinically, as it has been for HPV-positive oropharyngeal disease. This study examined whether there are survival differences in sinonasal cancer based on HPV status. **Methods:** This study included adult sinonasal cancer cases diagnosed between 2010 and 2015 in the National Cancer Database. A multivariable Cox proportional hazards model estimated the association between sinonasal cancer HPV status (HPV-positive, HPV-negative) and all-cause mortality while controlling for covariates (sex, age, race/ethnicity, insurance status, urban/rural, county-level household income, county-level percentage without high school diploma, comorbidity score, stage, histology, facility type, and treatment). A second multivariable proportional hazards model stratified HPV-positive tumor status by high-risk HPV (16, 18, 26, 31, 33, 35, 36, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, 82, and 85) vs. low-risk HPV (6, 11, 32, 34, 40, 42, 44, 54, 61, 62, 64, 71, 72, 74, 81, 83, 84, 87, and 89) and compared their all-cause mortality to HPV-negative patients. **Results:** There were 1,750 sinonasal cancer patients included in this study, and 484 (27.7%) had HPV-positive disease. Among patients with HPV-positive disease, 75.6% had high-risk types. Mortality risk among all HPV-positive patients combined was 23% lower than HPV-negative patients (aHR = 0.77; 95% CI 0.64, 0.93). After stratifying by high-risk vs. low-risk HPV, high-risk HPV positive patients had 30% lower mortality risk than HPV-negative patients (aHR = 0.70; 95% CI 0.57, 0.88) while risk of mortality did not significantly differ between low-risk HPV-positive patients and HPV-negative sinonasal cancer patients. **Conclusions:** Sinonasal cancer shows differential survival based on HPV status, and sinonasal cancer patients positive for high-risk HPV had a significantly greater survival advantage than low-risk strains and those with HPV negative disease. HPV status might yet play a role in prognostication of sinonasal cancer, if future studies confirm these findings. Research Sponsor: None.

6566 Poster Session (Board #227), Fri, 8:00 AM-11:00 AM

Combination of tumor multinucleation and spatial arrangement of tumor-infiltrating lymphocytes to predict overall survival in oropharyngeal squamous cell carcinoma: A multisite study. *First Author: Can Koyuncu, Case Western Reserve University, Cleveland, OH*

Background: Oropharyngeal squamous cell carcinoma patients can have major morbidity from current treatment regimens, necessitating accurate identification of patients with aggressive versus indolent tumors. In this study, we sought to evaluate whether the combination of computer extracted features of tumor cell multinucleation (MN) and spatial interplay of tumor-infiltrating lymphocytes (TILs) is prognostic of overall survival (OS) in OPSCC patients. **Methods:** OPSCC specimens from 688 patients were retrospectively collected from 3 different sites. 141 patients from site 1 formed the training set (D1) and 322 patients from site 2 and 225 patients from site 3 formed the independent validation cohort (D2, n = 547). A machine learning (ML) model was employed to automatically calculate a Multi-nucleation risk index (MNI), which is the ratio of the number of MN to the number of epithelial cells, to each patient. A separate ML model was also used to capture measurements related to the interplay between TILs and tumor cells (SpaTIL), which were then used to compute a risk score using a Cox regression model. The median value of both the MNIs and the SpaTIL risk scores in D2 were used to identify patients as either low- or high-risk. A definitive label was assigned to each patient by combining the class labels obtained from the MNI and SpaTIL models using a logical AND operation. **Results:** In D2, the patients with high-risk scores had statistically significantly worse survival in univariate analysis. The univariate analysis yielded an HR = 1.91 (95% CI: 1.25-2.93, p = 0.0027) for D. Multivariate analysis controlling the effect of different clinical variables is shown in the table. **Conclusions:** We presented a computational pathology approach to prognosticate disease outcome in OPSCC by combining features relating to density of multinucleation and spatial arrangement of TILs and validated the approach on a large multi-site dataset. With additional validation the approach could potentially help identify OPSCC patients who could benefit from de-escalation of therapy. Research Sponsor: U.S. National Institutes of Health.

	p-val	HR
Age (< 56)	0.18	1.32 (0.88 - 1.97)
O-stage (8th ed)	0.28	1.32 (0.80 - 2.20)
1 2 vs 3 4		
T-stage (8th ed)	0.024	1.69 (1.07 - 2.67)
1 2 vs 3 4		
N-stage (8th ed)	0.995	1.00 (0.65 - 1.54)
0 1 vs 2 3		
MNI + SpaTIL	0.018	1.62 (1.09 - 2.4)
Low vs High		

6567 Poster Session (Board #228), Fri, 8:00 AM-11:00 AM

Machine learning guided adjuvant treatment of head and neck cancer. *First Author: Frederick Howard, Section of Hematology/Oncology, Department of Medicine, University of Chicago, Chicago, IL*

Background: A combined analysis of the EORTC 22931 and RTOG 95-01 trials confirmed that patients (pts) with head and neck squamous cell carcinoma (HNSCC) and positive margins or extracapsular extension (ECE) benefit from adjuvant chemoradiotherapy (CRT), but the best treatment of pts with other risk factors is unclear. We hypothesized that deep learning models could identify the margin/ECE negative pts who benefit from CRT. **Methods:** We abstracted pts from the NCDB diagnosed from 2004-2016 with resected HNSCC who received radiotherapy (RT). We reserved 20% of pts for validation and used the remaining 80% for feature selection and model training. Features were chosen based on independent significance in a Cox proportional hazards model, and included demographics, tumor stage, site, grade, RT dose, and receipt of chemotherapy. HPV status was included, and imputed when unknown. We generated survival predictions with DeepSurv (DS), random survival forest (RSF), and neural network multitask (NNM) models. We consider CRT to be recommended by a model if predicted survival is longer with CRT than RT. We calculated the median overall survival (mOS) difference and hazard ratio (HR) for receipt of treatment in line with model recommendations. This was repeated with inverse probability of treatment weighting (IPTW) to account for confounding. As a comparator, we used the intermediate risk factors in the EORTC (T3-4 except T3N0 larynx, N2-3, LVI, deep nodes with oral / oropharynx cancer) and RTOG (2 involved nodes) trials as decision rules. **Results:** 36,831 pts from the NCDB met the inclusion criteria. 92% had T3-4 or node positive disease, and 40% received CRT. RTOG, EORTC, DS, NNM, and RSF models recommend CRT for 32%, 74%, 63%, 61%, and 35% of pts. The concordance index in the validation set was 0.696, 0.692, and 0.699 for DS, NNM, and RSF. Treatment according to model recommendations in the validation cohort was associated with a mOS benefit of 18.4 months (7.6 to 29.3, 95% CI) for DS, 20.5 months (8.8 to 32.2, 95% CI) for NNM, and 5.8 months (-6.6 to 18.3, 95% CI) for RSF. Similar results were seen with IPTW. **Conclusions:** Machine learning models can predict benefit from CRT in margin/ECE negative pts, and outperform treatment according to EORTC or RTOG inclusion criteria in this cohort. External validation of these models is warranted. Research Sponsor: None.

	HR (95% CI)	p-value	HR, IPTW (95% CI)	p-value
RTOG	0.94 (0.87 – 1.01)	0.10	0.84 (0.70 – 1.00)	0.06
EORTC	0.91 (0.84 – 0.98)	0.01	0.88 (0.74 – 1.04)	0.13
DS	0.85 (0.79 – 0.92)	< 0.01	0.81 (0.68 – 0.95)	0.01
NNM	0.83 (0.77 – 0.90)	< 0.01	0.79 (0.67 – 0.93)	< 0.01
RSF	0.89 (0.83 – 0.97)	< 0.01	0.81 (0.68 – 0.97)	0.02

6568 Poster Session (Board #229), Fri, 8:00 AM-11:00 AM

Association of sarcopenia with higher toxicity and poor prognosis in nasopharyngeal carcinoma. *First Author: Xin Hua, SunYat-sen University Cancer Center, Guangzhou, China*

Background: Given the growing evidence that sarcopenia is associated with toxicity and survival in various cancers, we investigated its significance in patients with nasopharyngeal carcinoma (NPC) receiving concurrent chemoradiotherapy (CCRT). **Methods:** In this retrospective analysis, we studied 862 NPC patients who had received CCRT between 2010 and 2014. Sarcopenia was determined using routine pre-radiotherapy computed tomography (CT) simulation scans at the third cervical (C3) vertebral level. Receiver-operating characteristic (ROC) curve analyses were used to determine the optimal cutoff values. Propensity score matching (PSM) was applied to develop comparable cohorts of patients with or without sarcopenia. **Results:** A total of 862 patients were included as the primary cohort, and 308 patients were matched and regarded as the matched cohort. In the primary cohort, the five-year overall survival (OS), locoregional recurrence-free survival (LRFS), and distant metastasis-free survival (DMFS) rates for the sarcopenia group vs. non-sarcopenia group were 78.2% vs. 93.6% ($P < 0.001$), 89.4% vs. 87.9% ($P = 0.918$), and 82.5% vs. 89.0% ($P = 0.007$), respectively. Univariate and multivariate survival analyses revealed that sarcopenia was an independent predictor of OS ($P < 0.001$ and $P < 0.001$) and DMFS ($P = 0.009$, $P = 0.034$). Patients with sarcopenia experienced significantly higher rates of treatment-related toxicities compared with patients without sarcopenia ($P = 0.032$). In addition, patients with sarcopenia also experienced significantly worse treatment response than those without sarcopenia ($P = 0.004$). Similar results were found in a PSM cohort. **Conclusions:** The current findings support that sarcopenia is a promising indicator for predicting clinical outcomes in NPC patients receiving CCRT. A simple and rapid analysis on CT simulation images can provide information about the therapeutic toxicity and survival prognosis, consequently guiding personalized multi-modality interventions during CCRT. Research Sponsor: National Natural Science Foundation of China (Nos. 81772877, 81773103, 81572848).

6569 Poster Session (Board #230), Fri, 8:00 AM-11:00 AM

SNOW: Sitravatinib and nivolumab in oral cavity cancer (OCC) window of opportunity study. *First Author: Marc Oliva Bernal, Catalan Institute of Oncology (ICO), Barcelona, Spain*

Background: Sitravatinib (receptor TKI against TYRO3, AXL, MERTK and VEGF family of receptors) is predicted to increase M1-type tumor-associated macrophages (TAMs) and decrease MDSCs in the tumor microenvironment. SNOW is a window-of-opportunity study evaluating the immunogenic and antitumor effects of preoperative sitravatinib and nivolumab in patients (pts) with OCC. Early results demonstrated the combination was safe and active (Oliva et al, SITC 2019). Biomarker analyses and updated results are presented. **Methods:** Pts with untreated T2-4a, N0-2 or T1>1cm-N2 OCC are eligible. All pts receive oral sitravatinib 120mg daily from day (D) 1 up to 48h pre-surgery and 1 dose of Nivolumab 240mg on D15. Surgery planned between D23-D30. Standard of care adjuvant radiotherapy given based on clinical stage. Tumor pictures, fresh tumor biopsies, blood samples taken at baseline, D15 and pre-surgery. Tumor flow cytometry and multiplex immunofluorescence staining performed on all biopsies to study changes in immune-cell populations. Tumor whole-exome sequencing (WES) performed on baseline biopsies. **Results:** As of Jan 31st 2020, 10 out of 12 planned pts were enrolled. Study treatment was well-tolerated: only 1 pt had grade (G) >3 toxicity (hypertension) and 1 pt required surgery delay due to G2 thrombocytopenia. None had intraoperative complications. 1 pt had wound infection and tracheostomy bleeding 11 days post-surgery, possibly-related to study drugs. All pts had tumor reduction, 9/10 had pathological downstaging, including 1 complete response (Table). All had clear margins with no extranodal extension; none required adjuvant chemotherapy. All pts are alive with no recurrence (median follow-up= 69 weeks). Lower % of MDSCs and increased % of M1-TAMs and M1:M2 ratio trend was seen at D15 and pre-surgery, with stronger effect in major responders. Best responders (Pts S1-S2) had higher % of PD-L1+ TAMs at baseline. Tumor WES revealed an HRAS G12D mutation in pt S2 and a BLM mutation (DNA repair) in pt S6 (no downstaging). **Conclusions:** Pharmacodynamic analyses support the antitumor and immune effects of sitravatinib and nivolumab in OCC. Immune pathological response assessment and transcriptomics are on-going. Clinical trial information: NCT03575598. Research Sponsor: Tumor Immunotherapy Program, Princess Margaret Cancer Centre, Pharmaceutical/Biotech Company.

Pt	S1	S2	S4	S6	S7	S8	S9	S10	S11	S13
Primary tumor	Alveolus	Alveolus	Tongue	Tongue	Floor of the Mouth	Tongue	Alveolus	Tongue	Tongue	Gingiva
PD-L1 CPS	79	90	34	100	<1	7	27	*	*	*
Clinical stage	T4aN2b	T4aN2b	T3N1	T3N1	T4aN2c	T2N0	T4aN0	T2N2b	T3N0	T4aN0
Pathological stage	ypT0N0	ypT4aN0**	ypT2N0	ypT3N1	ypT4aN0	ypT1N0	ypT3N0	ypT1N2a	ypT1N1	ypT2N0

* Pending **Only residual tumor in bone

6573 Poster Session (Board #234), Fri, 8:00 AM-11:00 AM

Phase I trial of hafnium oxide nanoparticles activated by radiotherapy in cisplatin-ineligible locally advanced HNSCC patients. *First Author: Christophe Le Tourneau, Institut Curie, Saint-Cloud, France*

Background: The standard of care non-surgical approach for locally advanced head and neck squamous cell carcinoma (LA HNSCC) patients (pts) is concurrent chemoradiation with high dose cisplatin or cetuximab in case of contra-indication. Older age is a contra-indication to cisplatin, and cetuximab might not improve survival in older pts. It is therefore urgently needed to develop new treatment options for elderly pts with LA HNSCC. NBTXR3 are hafnium oxide nanoparticles that can enhance the efficacy of radiotherapy (RT) by increasing locally the deposited dose. In this phase I clinical trial we aimed to evaluate the feasibility and safety of NBTXR3 administered as intratumoral (IT) injection prior to RT in LA HNSCC elderly pts. **Methods:** Pts with stage III-IV LA HNSCC of the oropharynx or oral cavity ineligible for platinum-based chemoradiation received a single IT injection of NBTXR3 into a selected primary tumor and intensity modulated RT (IMRT; 70 Gy/35 fractions/7 weeks) [NCT01946867]. A 3+3 dose escalation design, tested NBTXR3 dose levels equivalent to 5, 10, 15, and 22% of baseline tumor volume, followed by a dose expansion at the Recommended Phase II Dose (RP2D). Primary endpoints included RP2D determination, and early dose limiting toxicities (DLT). NBTXR3 intratumoral bioavailability and anti-tumor activity (RECIST 1.1) were also evaluated. **Results:** Enrollment was completed at all dose escalation levels: 5% (3 pts), 10% (3 pts), 15% (5 pts), and 22% (8 pts). No early DLT or SAE related to NBTXR3 or injection were observed. The median follow-up from NBTXR3 administration is 7.6 months. One AE (Grade 1) related to NBTXR3 and four AEs (Grade 1-2) related to the injection were observed. RT-related toxicity was as expected with IMRT. CT-scan assessment showed a good dispersion of NBTXR3 throughout the injected tumor and not in surrounding healthy tissues. The RP2D was determined to be 22%. Preliminary efficacy was evaluated in pts who received the intended dose of NBTXR3 and RT. A complete response of the injected lesion was observed in 9/13 (69%) evaluable pts at doses ≥10% (2 unconfirmed) and an overall complete response in 5/13 (38%) evaluable pts at doses ≥10%. Preliminary safety and efficacy data of the dose expansion cohort at the RP2D will also be presented. **Conclusions:** NBTXR3 activated by RT was well tolerated at all tested doses and demonstrated promising preliminary anti-tumor activity. Recruitment is ongoing in the dose expansion cohort. These results demonstrate that further testing of NBTXR3 in this population is warranted. Clinical trial information: NCT01946867. Research Sponsor: Nanobiotix, SA.

6574 Poster Session (Board #235), Fri, 8:00 AM-11:00 AM

DURTRERAD: A phase II open-label study evaluating feasibility and efficacy of durvalumab (D) and durvalumab and tremelimumab (DT) in combination with radiotherapy (RT) in non-resectable locally advanced HPV-negative HNSCC—Results of the preplanned feasibility interim analysis. *First Author: Konrad Friedrich Klinghammer, Charite Comprehensive Cancer Center, Berlin, Germany*

Background: DURTRERAD is a randomized phase II study evaluating feasibility and efficacy of durvalumab (anti-PD-L1) vs. durvalumab and tremelimumab (anti-CTLA-4) in combination with radiotherapy as primary treatment for locally advanced HPV negative HNSCC**.** (NCT03624231). Concurrent chemo-RT with a platinum-based regimen is considered the standard treatment, although efficacy and long-term toxicity are not satisfactory. Combining immunotherapy with RT might result in improved efficacy with limited long-term toxicity. **Methods:** The phase II study planned to enroll 120 pts, 60 pts (1:1) in each treatment arm. Treatment with DT (1500mg/75 mg, arm DT),or D (1500mg, arm D) both in combination with RT (70Gy) was considered to be feasible if less than 10% of the patients treated will discontinue treatment due to on-treatment toxicities. A first interim analysis for feasibility and efficacy was planned after randomisation of 20 patients. **Results:** So far 23 patients have been screened, 16 patients have been randomised and started their allocated treatment, 10 in arm D and 6 in arm DT. Of 10 patients in arm D 1 patient stopped infusional treatment due to immune related toxicity. Out of 6 patients in the DT arm, however, 5 patients stopped treatment due to treatment related AEs, 2 pts due to immune related toxicity with one Grade 5 AE. Three patients stopped due to non-immune related AE. The grade 5 AE prompted the interim analysis, which revealed non-feasibility as well as safety-issues of the DT+radiotherapy combination . As a result, the DT arm was prematurely terminated. **Conclusions:** Even though in the recurrent/metastatic setting DT was not associated with increased toxicity, DT in combination with RT was not feasible in our poor prognostic, vulnerable patient cohort of advanced HPV negative unresectable HNSCC, warranting early disclosure of these results. No increase in toxicity was observed in the D monotherapy arm, and the trial continued with D monotherapy in combination with RT. Clinical trial information: NCT03624231. Research Sponsor: AstraZeneca.

6575 Poster Session (Board #236), Fri, 8:00 AM-11:00 AM

Dose and volume de-escalation for HPV-associated oropharyngeal cancer: Long-term follow-up of the OPTIMA trial. *First Author: Ari Rosenberg, University of Chicago, Chicago, IL*

Background: Human papilloma virus (HPV) associated oropharyngeal cancer is associated with a favorable prognosis, but standard multimodality treatment is associated with substantial treatment related toxicity. A de-escalation treatment paradigm that optimizes oncologic outcomes while reducing toxicity is needed. We sought to further expound on our published OPTIMA data with long-term follow-up and additional pts subsequently treated using the OPTIMA treatment paradigm. **Methods:** Long-term follow-up of our institutional de-escalation OPTIMA trial (NCT02258659) and retrospective review of additional patients treated subsequently per OPTIMA outline was performed. Pts were classified as low-risk (LR) ($\leq$T3, $\leq$N2B, $\leq$10PYH) or high-risk (HR) (T4, $\geq$N2c, $>$ 10PYH). Pts received induction chemotherapy (IC) of 3 cycles of dose dense carboplatin and nab-paclitaxel (OPTIMA) or paclitaxel (subsequently treated). LR with $\geq$50% response received low-dose radiotherapy (RT) to 50 Gy. LR with 30-50% response or HR with $\geq$50% response received intermediate-dose chemoradiotherapy (CRT) to 45Gy. All others received full-dose CRT to 75Gy. **Results:** 108 pts consented and 107 were treated (61 on study; 46 subsequently) from October 2014 through November 2019. 1 pt transferred care post-enrollment. Median follow-up was 36 months (interquartile range 17-45). Median age was 63 years (range 33-84) and 95% were male. 47% were LR and 53% were HR. $\geq$50% tumor shrinkage occurred in 78/107 (73%) of pts overall, and 37/51 (73%) among LR; 41/56 (73%) among HR. 82% of pts received de-escalated (C)RT. Overall, 94% of pts were alive at last follow-up (98% LR; 89% HR). 3 pts (2 HR and 1 LR) developed disease recurrence (2.7%), with 2 local recurrences and 1 distant recurrence. Likelihood of G-tube placement was 3% in low-dose RT, 35% in intermediate-dose CRT, and 84% in full-dose CRT. **Conclusions:** IC followed by risk-adapted dose and volume de-escalated treatment for HPV+ oropharyngeal cancer demonstrates excellent oncologic and functional outcomes with long-term follow-up. Supported by Celgene, Alinea benefit supported by Grant Achatz/Nick Kokonas, and National Cancer Institute of the National Institutes of Health (NIH) through Grant Number P30 CA14599. Clinical trial information: NCT02258659. Research Sponsor: Celgene, U.S. National Institutes of Health, Alinea benefit supported by Grant Achatz/Nick Kokonas, and National Cancer Institute of the National Institutes of Health (NIH) through Grant Number P30 CA14599.

6576 Poster Session (Board #237), Fri, 8:00 AM-11:00 AM

Single-cell multiplexed proteomics to identify novel polyfunctional CD8+ T cell signatures induced by nivolumab in head and neck cancer patients after salvage surgery. *First Author: Shuchi Gulati, University of Cincinnati Medical Center, Cincinnati, OH*

Background: Immune checkpoint inhibitors (ICIs) are FDA approved for use in head and neck squamous cell cancer (HNSCC), however, only ~20% patients achieve a response. Identification of biomarkers of response or toxicity remains a challenge. Polyfunctional T-cells, or T-cells producing multiple cytokines, have been recognized as contributors to durable immunity against various cancers. However, their role has not been studied prospectively in HNSCC patients receiving ICIs. To look for an early predictor of response, we used single-cell functional proteomic profiling (IsoPlexis) on blood samples pre- and post- first dose of nivolumab (nivo) in patients on our phase-II study of locally recurrent HNSCC (NCT03355560). **Methods:** HNSCC patients who failed definitive radiation +/-chemotherapy and were subsequently treated with curative intent salvage resection were enrolled to receive 6 months of nivo beginning 4 to 11 weeks after surgery. Blood samples were collected before and after the first dose of nivo. Peripheral blood mononuclear cells were isolated, enriched for CD8+ T cells and using the 32-plex IsoCode technology, single-cell cytokine signals were captured and polyfunctional strength of CD8+ T cells was evaluated across four groups (effector, stimulatory, regulatory, inflammatory). A comparison analysis was performed between pre- and post- nivo treatment and between patients who relapsed (non-responders) vs those who did not (responders). **Results:** Thirty-three of 39 planned patients have been enrolled, of which 28 are evaluable and 5/28 (18%) developed recurrence. Median age is 68 years (range 51-85), 9/28 (32%) patients are female, 26/28 (93%) are white, disease sites include oropharyngeal 6/28 (21%), oral cavity 11/28 (39%) and larynx 11/28 (39%). Samples were evaluated at a median follow up of 5.9 months from enrollment. Single-cell analysis demonstrated a strong upregulation of polyfunctional human CD8+ T cell subsets in responders. Polyfunctional Strength Index (PSI) was enhanced in CD8+ T cells across the responders' samples, composed largely of effector cytokines (granzyme-β, IFN-γ, MIP-1α, perforin, TNF-α). **Conclusions:** Single-cell functional proteomic analysis revealed significantly upregulated polyfunctional profiles and an increase in effector cytokines in patients who responded to nivo. This data provides important insights into PD-1 inhibitor triggered T-cell activity and may be used to predict response to ICIs in HNSCC patients using a blood test. Clinical trial information: NCT03355560. Research Sponsor: BMS.

6577 Poster Session (Board #238), Fri, 8:00 AM-11:00 AM

Nivolumab (Nivo) and ipilimumab (Ipi) in combination with radiotherapy (RT) in high-risk patients (pts) with locally advanced squamous cell carcinoma of the head and neck (LA SCCHN). *First Author: Jennifer Maria Johnson, Thomas Jefferson University, Department of Medical Oncology, Philadelphia, PA*

Background: Immune checkpoint inhibitors (ICI) are the standard of care in recurrent/metastatic SCCHN but their role in the curative therapy setting with RT is under study. We evaluated the novel approach of combining Nivo, a PD-1 inhibitor, and Ipi, a CTLA-4 inhibitor, in lieu of chemotherapy, with concurrent RT in pts with high-risk LA SCCHN. **Methods:** We enrolled newly diagnosed, chemotherapy eligible pts with AJCC 7th edition stage IVA-IVB SCCHN of the oral cavity, oropharynx (OP), hypopharynx, and larynx. HPV+ OP were T4, N2c or N3 OP. Nivo (3 mg/kg every 2 weeks IV x 17 doses) and Ipi (1 mg/kg every 6 weeks x 6 doses) were administered starting 2 weeks prior to the start of RT. RT was prescribed to a dose of 70 Gy delivered in 2 Gy/fraction/day using VMAT. The primary objective was safety of combination ICI with RT. Secondary objectives included 1-year progression-free survival (PFS), overall survival, and correlative studies. **Results:** 24 pts were enrolled; median age of 60 (range 48-77); 20 were male; 16 oropharynx (14 HPV+), 2 hypopharynx, and 6 larynx; AJCC 7th edition stage IVA (23), IVB (1). Grade 3 acute in-field adverse events (AEs) occurred in 17/24 (71%) of patients during concurrent ICI-RT (9 mucositis, 6 dysphagia, 5 dermatitis, 4 odynophagia, 1 dysphonia); there were no grade 4/5 AEs during ICI-RT. During ICI maintenance 5 pts developed in-field ulcerations at the primary site detected at an average of 3 months post RT; 1 of them died of bleeding due to erosion into the carotid artery with no evidence of active cancer; 4 additional pts developed in-field necrosis. 7 pts discontinued ICI treatment at $>$ 3 months post-RT: 1 due to immune AE, 5 due to in-field ulcerations, 1 due to persistent mucositis without ulceration. 4 pts (17%) had grade 3 immune AEs: 1 elevation of lipase, 1 colitis, and 2 rash. There were no grade 4/5 immune AEs. The median follow-up is 16 months (range, 6.3-30.6). 21 of 24 pts (87.5%) are alive with no evidence of disease progression. 2 pts recurred at distant sites: 1 had a solitary lung lesion at 11 months and was treated with RT; 1 in mediastinal lymph nodes at 9 months and was treated with chemo-RT. Locoregional control remains at 100%. **Conclusions:** RT plus dual ICI combination was feasible and resulted in no locoregional relapses so far in 24 high-risk LA SCCHN pts. Longer follow-up is needed to fully assess PFS and locoregional control as well as post-treatment in-field ulceration/necrosis that may be attributed to the potent radiosensitizing effect of dual PD-1 and CTLA-4 blockade. Clinical trial information: NCT03162731. Research Sponsor: Bristol Myers Squibb.

6578 Poster Session (Board #239), Fri, 8:00 AM-11:00 AM

Prospective, longitudinal digital activity monitoring before and after treatment of low-risk oropharyngeal squamous cell carcinoma: A feasibility study. *First Author: Gary Brandon Gunn, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Given the expected excellent prognosis of low-risk oropharyngeal squamous cell carcinoma (OPSCC), consideration of long-term toxicity and functional outcomes has become increasingly important. Activity monitors (e.g. FITBIT) are imperfect but have been shown to have reasonable validity in healthy adults. Here we aimed to test the feasibility of using medical grade longitudinal digital activity monitoring to better define objective functional outcomes after treatment of low-risk OPSCC. **Methods:** This prospective, observational parallel cohort study included patients with previously untreated stage I-III (AJCC 7) OPSCC eligible for standard of care single-modality treatment with either Intensity-Modulated Proton Therapy (IMPT) or TransOral Robotic Surgery (TORS). Objective Actigraph accelerometer data (Actigraph, Pensacola, FL) were collected continuously for 1 week at baseline, 3, 6 and 12 months after treatment along with subjective patient-reported outcome (PRO) measures. **Results:** Forty-four patients (34M, 10F) enrolled with median age 59 years (range: 42-78). Baseline, 3 and 6 month activity data were available for 40 patients (91%): 16 IMPT and 24 TORS. There was a significant decrease in mean percent of day performing moderate to vigorous physical activity (MVPA) (-0.78, 0.021) mean number of steps/minute (-1.1, $p = 0.035$), and mean kcals/day (-115.9, $p < 0.001$) from baseline to 3 months after treatment for the overall cohort. A significant decrease in mean kcals/day (-82.2, $p = 0.004$) persisted for the overall cohort at 6 months with no significant difference between groups. **Conclusions:** Longitudinal digital activity monitoring is feasible before and after treatment of low-risk OPSCC. This approach may offer objective functional endpoints for future de-escalation trials. Similar short-term decreases in objective activity measurements were observed after IMPT and TORS. Long-term (12 month) activity data and correlations to subjective PRO measures will be available at the time of presentation. Clinical trial information: 02663583. Research Sponsor: Philanthropy, U.S. National Institutes of Health.

6579 Poster Session (Board #240), Fri, 8:00 AM-11:00 AM

Risk of chronic opioid use after radiation for head and neck cancer: A systematic review and meta-analysis. *First Author: Sondos Zayed, Department of Radiation Oncology, London Health Sciences Centre, London, ON, Canada*

Background: Opioid overuse is a major international public health concern. The prevalence and risk factors for chronic opioid use (COU) in radiation-induced head and neck pain are poorly understood. The aim of this study was to estimate the rates of COU and to identify risk factors for COU in head and neck cancer (HNC) patients undergoing curative-intent radiotherapy (RT) or chemoradiotherapy (CRT). **Methods:** We performed a systematic review and meta-analysis based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, using the PubMed (Medline), EMBASE, and Cochrane library databases, queried from dates of inception until present. COU was defined as persistent opioid use ≥3 months after treatment completion. Studies in the English language that reported on COU in HNC patients who received RT/CRT were included. Meta-analyses were performed using random effects models. Heterogeneity was assessed using the I^2 value. **Results:** A total of 134 studies were identified, with 7 retrospective studies (reporting on 1841 patients) meeting inclusion criteria. Median age was 59.4 years (range 56.0-62.0) with 1343 (72.9%) men and 498 (27.1%) women. Primary tumour locations included oropharynx (891, 48.4%), oral cavity (533, 29.0%), larynx (93, 5.1%), hypopharynx (32, 1.7%), and nasopharynx (29, 1.6%). 846 (46.0%) patients had stage I/II disease and 926 (50.3%) had stage III-IV disease. 301 (16.3%) patients had RT alone, 738 (40.1%) received CRT, and 594 (32.3%) underwent surgery followed by adjuvant RT/CRT. The proportion of HNC patients who received radiotherapy and developed COU was 40.7% at 3 months (95% CI 22.6%-61.7%, $I^2 = 97.1\%$), 15.5% at 6 months (95% CI 7.3%-29.7%, $I^2 = 94.3\%$) and 7.0% at 1 year. There were significant differences in COU based on primary tumor sites ($P < 0.0001$), with the highest rate (46.6%) in oropharyngeal malignancies. Other factors associated with COU included history of psychiatric disorder (61.7%), former/current alcohol abuse (53.9%), and start of opioids prior to radiation treatment (51.6%). There was no significant difference in the proportion of COU by gender ($P = 0.683$), disease stage (I/II vs III/IV; $P = 0.443$), or treatment received (RT, CRT, or adjuvant RT/CRT; $P = 0.711$). **Conclusions:** A significant proportion of patients who undergo radiotherapy for head and neck cancer suffer from COU. High-risk factors for COU include an oropharyngeal primary tumour, history of psychiatric disorder, former/current alcohol abuse, and pre-treatment opioid use. New strategies to mitigate opioid use are needed. Research Sponsor: None.

6580 Poster Session (Board #241), Fri, 8:00 AM-11:00 AM

Upfront DPYD genotyping and toxicity associated with fluoropyrimidine-based concurrent chemoradiotherapy for oropharyngeal carcinomas. *First Author: Antoine Desilets, CHUM, Montreal, QC, Canada*

Background: The combination of carboplatin and 5-fluorouracil (5-FU) is effective when used concurrently with radiotherapy for locoregionally advanced oropharyngeal carcinomas (Calais et al. 1999). DPYD polymorphisms can be associated with an increased risk of severe toxicity to fluoropyrimidines (Deenen et al. 2016). Upfront screening for the DPYD*2A allele is available in the province of Québec, Canada since March 2017. This study aimed to determine the effect of upfront genotyping on grade ≥3 toxicities. **Methods:** The studied population included all consecutive cases of oropharyngeal carcinomas treated with 5-FU based chemoradiotherapy one year before and after the implementation of upfront DPYD*2A genotyping. All patients were treated at the Centre Hospitalier de l'Université de Montréal (CHUM) between March 2016 and April 2018. Clinical data were extracted from chart review. Extended screening for 3 supplemental at-risk DPYD variants was also retrospectively performed in August 2019. **Results:** 181 patients were included in the analysis (87 patients before and 94 patients after DPYD*2A screening implementation). 91% of patients (n = 86) were prospectively genotyped for the DPYD*2A allele. Of those screened, 2% (n = 2/87) demonstrated a heterozygous DPYD*2A mutation. Those two patients received cisplatin-based treatment and thus avoided 5-FU toxicities. Extended genotyping of DPYD*2A-negative patients later allowed for the retrospective identification of 6 additional patients with alternative DPYD variants (two c.2846A > T and four c.1236G > A allele mutations). **Conclusions:** The DPYD*2A, c.2846A > T and c.1236G > A polymorphisms are associated with an increased risk of G3-4 toxicity to 5-FU, as well as higher hospitalization rates. Upfront DPYD genotyping can identify patients in whom fluoropyrimidine-related toxicity should be avoided. This represents an interesting addition in terms of pharmacovigilance. Research Sponsor: None.

Adverse events of interest are summarized in the table below.

	Pre-DPYD*2A screening	Post-DPYD*2A screening	*p*	DPYD-mut (non-DPYD*2A) (n = 6)	DPYD WT (n = 78)	*p*
Grade ≥3 toxicity	71%	62%	0.18	100%	60%	0.046
Mucositis	54%	47%		100%	44%	
Dysphagia	39%	26%		66%	23%	
Radiation-induced dermatitis	15%	14%		0%	14%	
Neutropenia	8%	9%		17%	9%	
Hospitalization	29%	21%		33%	23%	
Enteral feeding	41%	30%		50%	32%	

6582 Poster Session (Board #243), Fri, 8:00 AM-11:00 AM

A novel multiple-catheter implantation method for advanced head and neck cancer. *First Author: Masatoshi Ohmae, Rinku General Medical Center, Izumisano, Japan*

Background: We previously developed a super-selective intra-arterial chemotherapy (iaCT) approach for head and neck cancer (HNC), by which, an intra-arterial catheter is retrogradely inserted via either the superficial temporal artery (STA) or occipital artery (OA) and connected to a subcutaneous reservoir. As a result, since this approach overcomes the need for frequent fluoroscopy sessions, the infusion frequency can be increased and the therapeutic effectiveness improved. However, since the anticancer effect is limited to the region supplied by the selected blood vessel, it is often difficult to control an advanced HNC by single-catheter iaCT. Subsequently, a novel multiple-catheter implantation method (MCIM) for super-selective iaCT has been developed using, both, the STA and OA. **Methods:** A total of 21 patients with stage III or IV HNC were enrolled in this study and treated via MCIM for iaCT between 2009 and 2017. The catheters were super-selectively placed in the tumor-feeding arteries after having entered the STA or OA. The first catheter was introduced into one of the target branches. Next, a second catheter was introduced into another target branch. If a third catheter was required, the procedure was repeated. The extra-arterial portions of the catheters were subcutaneously connected to an implanted juxta-mastoidal infusion reservoir. **Results:** The response rate was 100%; particularly, 20 cases of complete response and 1 of partial response were confirmed. Although the partial responder underwent salvage surgery and two complete responders ultimately died (due to either delayed recurrence or brain metastases), the other 18 patients have been living cancer-free for 2-9 years. **Conclusions:** The MCIM method allows to expand the infusion region while maintaining the main advantages of super-selective iaCT. As a consequence, due to the lack of need for patient confinement in the catheter room and for frequent fluoroscopy sessions, patients' mental and physical distress, medical expenses, and treatment time are all ultimately reduced. Research Sponsor: None.

6583 Poster Session (Board #244), Fri, 8:00 AM-11:00 AM

Neoadjuvant nivolumab (N) plus weekly carboplatin (C) and paclitaxel (P) in resectable locally advanced head and neck cancer. *First Author: Ralph Zinner, University of Kentucky, Department of Medical Oncology, Lexington, KY*

Background: Despite multimodality standard therapy, patients (pts) with resectable locally advanced squamous cell carcinoma of the head and neck (LA SCCHN) are at high risk for recurrence. Pts with pathologic complete response (pCR) or major pathologic response (MPR) to neoadjuvant chemotherapy have improved overall survival. PD-1 checkpoint inhibitors are approved in combination with platinum-based chemotherapy in the 1st-line treatment of recurrent/metastatic SCCHN. We hypothesize the addition of N to wkly carboplatin C and P will increase the pCR rate at the primary site compared to historical controls. **Methods:** This is an investigator-initiated trial for pts with newly diagnosed (AJCC 8^{th}) stage III-IV HPV- (oral cavity (OC), oropharynx (OP), hypopharynx (HP), and larynx (L) or stage II-III HPV+ OP SCCHN without distant metastasis who are surgical candidates. Neoadjuvant chemo starting d1 is C AUC 2 IV wkly x 6 plus P 100 mg/m2 IV wkly x 6 plus N 240 mg IV q 2 wks x 3 with surgery on wk 8. The primary endpoint is pCR at the primary site. To estimate pathologic response, the resected pathology specimens are cut >1 section/cm. Using the Aperio Digital scanning system, slides are imaged, and then annotated by at least 2 pathologists for viable tumor vs. treatment effect with areas automatically calculated to yield the percentage of viable tumor. Our primary endpoint will be reached if 11/37 planned pts have a pCR at the primary site. **Results:** From 11/17-12/19, 27 pts received the study regimen and had surgery (1/27 had an unknown primary; thus, inevaluable for the primary endpoint). Of 27 pts, median age was 59 (46-83), women 31%, HPV+ 15%, OC 73%, OP 19%, HP 7%, L 4%; stage III 33%, stage IVA 67%. Gd 3 toxicities were in 37% pts; 1 pt febrile neutropenia, 3pts anemia, 1pt diarrhea, 1pt cellulitis and 1pt rash. Four pts had gd 3-4 neutropenia. Dose reductions were in 2 pts, and 4 pts had 1 wkly dose dropped. All 27 pts went to surgery, none with PD by CT; all with negative margins. One pt died with rapid recurrence; no other recurrences (median f/u 13 mos). Our primary endpoint was met; 11/26 (42%) pts (excluding pt with unknown primary) had a pCR at the primary site. 9/23 (39%) HPV- pts, had a pCR. MPR or pCR was 18/26 (69%) and in HPV- pts, 15/23 (65%). 2/11 pts had microscopic residual disease in 1 LN each. **Conclusions:** The combination of N and wkly PC was well tolerated. The primary endpoint of pCR at the primary site in > 11/37 pts was met with the 27^{th} pt. Accrual continues. Exploratory outcomes assessing markers of immune bias in tumor tissue and plasma are in process. Clinical trial information: NCT03342911. Research Sponsor: Bristol-Myers Squibb.

6584 Poster Session (Board #245), Fri, 8:00 AM-11:00 AM

***RAS*-mutated sporadic medullary thyroid cancer: A single-center experience.** *First Author: Spandana Brown, Houston Methodist Hospital, Houston, TX*

Background: Activating *RAS* mutations are recognized as important drivers in sporadic medullary thyroid cancer (sMTC), with a reported prevalence between 0-43%. However, few studies have looked at correlations between *RAS*-mutated sMTC and clinicopathologic features. **Methods:** Patients with sMTC diagnosed between 1992 – 2019 with NGS testing for *RET* and *RAS* mutations seen at a tertiary cancer center were retrospectively evaluated. The objective was to analyze demographic and clinical features among patients with *RAS*-mutated sMTC and to evaluate associations between these features and overall survival (OS). Analyses were performed to correlate patient demographics and pathologic staging with treatment characteristics, disease course, and OS. **Results:** We identified 42 patients (50% female) with *RAS*-mutated sMTC out of 218 pts with sMTC. Median age at diagnosis was 50 years (range 24-78 years). 26 (62%) patients had stage IV disease at time of diagnosis. 28 (67%) of patients had *HRAS* mutations and 14 (33%) had *KRAS* mutations. *HRAS Q61R* was the most common *HRAS* mutation type (n = 19, 45%). Median follow-up time was 64 months (range 23-274 months) during which 11 (26%) patients died. The median OS was 16.2 years, with 5- and 10- year OS of 88% and 73% respectively. Of the 20 (48%) patients who received systemic therapy, 79% had stage IV disease and tended to be older (median age 54). Median time from diagnosis to initiation of systemic therapy was 33 months. Factors associated with worse OS included distant metastases at diagnosis, shorter time interval between diagnosis and treatment, and Ctn/CEA doubling times < 6 months. *HRAS Q61R* mutations were associated with a better prognosis, with 100% 10-year OS compared with 10-year OS of 39% and 51% (p = 0.02) for other *HRAS* and *KRAS* mutations respectively. **Conclusions:** At a tertiary cancer center, patients with *RAS*-mutated sMTC had a 10-year OS rate of 73%, with significantly worse OS in patients with *HRAS/KRAS* mutations other than *HRAS Q61R*. In comparison, prior studies have reported 10-year OS rates between ~71-90% in sMTC and 10-year OS rates as low as 56% for more aggressive *RET M918T* sMTC mutations. The findings here are consistent with other studies that have suggested patients with *RAS*-mutated sMTC are at intermediate risk for aggressive disease, though there are limited data on OS rates in *RAS* or RAS-/RET- sMTC. Future research comparing outcomes between various *RAS* mutations and in comparison to *RET+* and RAS-/RET- patients is needed, especially as systemic therapy use in *RAS*-mutated sMTC evolves. Research Sponsor: None.

6585 Poster Session (Board #246), Fri, 8:00 AM-11:00 AM

ELLA01-1: A study to determine the utility of TP53 mutations as a prognostic biomarker in adenoid cystic carcinoma. *First Author: Robert Metcalf, The Christie NHS Foundation Trust, Manchester, United Kingdom*

Background: TP53 mutations are reported in 5% of patients with adenoid cystic carcinoma (ACC). Whilst TP53 mutations are associated with adverse clinical outcomes across multiple tumour types, their prognostic significance in ACC is unknown. We sought to determine the utility of TP53 mutations as a prognostic biomarker in a prospective cohort of ACC patients. **Methods:** From April 2017 to September 2019, 146 patients with ACC were prospectively recruited to an ethically approved study. DNA was extracted from archival FFPE samples and underwent targeted next generation sequencing (Qiagen GeneRead DNAseq Targeted Panel V2 n = 134; Foundation Medicine; n = 12). Clinical, pathological and outcome data were collected on all patients and Kaplan-Meier survival analysis was performed to test for survival differences between TP53 mutated and wild-type ACC. **Results:** 146 ACC patients (mean age 48 years, range 16-79) underwent DNA extraction and next generation sequencing for TP53 mutations. The primary site was major salivary gland in 47% and minor salivary gland in 48% (other 5%). Analysis was successful in 122/146 patients (84%). Recurrent or metastatic disease was present in 94% (115/122) at study entry. TP53 alterations were identified in 9% (11/122), most frequently within the DNA binding domain (9/11). Non-pulmonary visceral metastases were seen more frequently in TP53 wild-type than in TP53 mutated ACC (44% vs. 10%; p = 0.042), and other clinical parameters were balanced between groups. During follow-up from diagnosis (median follow up 6.6 years), death occurred in 45% of patients with TP53 mutation and in 23% with TP53 wild-type ACC (p = ns). In TP53 mutated ACC, median overall survival was significantly shorter (5.3 vs. 16.3 years), and 10-year survival rate significantly lower (42% vs. 82%) than TP53 wild-type ACC (log-rank p = 0.013). **Conclusions:** In this cohort of patients with ACC, TP53 mutations were seen with a higher frequency than previously reported. This may be explained by the high frequency of recurrent or metastatic disease at study entry. TP53 mutation was associated with a statistically significant reduction in overall survival in patients with recurrent and metastatic ACC. These findings suggest that stratifying by TP53 status may be of clinical value to inform follow-up strategy in addition to established clinical, pathological and genomic biomarkers. Research Sponsor: The Christie Charity, University of Manchester, Syncona Foundation, Infrastructure Industry Foundation.

6586 Poster Session (Board #247), Fri, 8:00 AM-11:00 AM

Recurrent or metastatic salivary gland tumor (MSGT) patients treated with selinexor, a first in class selective exportin-1 (XPO1) inhibitor. *First Author: Eoghan Ruadh Malone, Princess Margaret Hospital, Toronto, ON, Canada*

Background: MSGT are rare with limited systemic treatments. This single institution, prospective study in recurrent or metastatic (RM) MSGT involved 2 phases: genomic profiling followed by treatment with either genomically-matched or unmatched therapy. Here we present the results of the unmatched arm for patients (pts) treated with S an oral selective inhibitor of XPO1 that leads to activation of tumor suppressor proteins and retention of oncoprotein mRNAs in the cell nucleus, inducing cancer cell apoptosis. **Methods:** Patients (pts) with RM-MSGT had archived paraffin embedded tumor samples profiled with targeted next generation sequencing, immunohistochemistry for androgen receptor (AR) and fluorescent in-situ hybridization for HER-2 and ALK. If no actionable mutations were identified or if no matched agents were available, pts with progressive disease could receive S (60mg given twice weekly Q28 days). The study had a simon-2 stage design; 1 partial response in the first 18 pts treated with S, would trigger an additional 7pts to receive S in stage 2. **Results:** Between July 2014 and April 2019 85 pts were enrolled on study: 73 had sequencing which identified 41 with no actionable mutations and 32 with actionable mutations. 18 pts (10F/8M, median age 61 years [40-79]) were treated with S and included adenoid cystic (n = 8), salivary duct (n = 4), acinic cell (n = 2) and other subtypes (n = 4). Of these 18, 4 pts had actionable aberrations: AR amplification (n = 2), mutations in SMARCB1 (n = 1) and CDKN2A (n = 1). 13pts were treatment naïve, 3pts and 2pts received 1 and 2 or more lines of treatment respectively prior to enrollment: androgen deprivation therapy (n = 2), chemotherapy (n = 3), early phase clinical trials (n = 3). The median number of cycles of S received were 3 (range: 1-19). The best response by RECIST was SD in 13pts (72%) (SD > 6 months (range: 6-18 months) in 5pts (28%); tumor reduction measured in 7pts (39%)), no PRs, PD in 3pts (17%), and 2pts (11%) were not evaluable for response due to insufficient duration of treatment coming off early due to toxicity. The median PFS (95% CI) was 7.6 (3.5-NA) months and the median OS (95% CI) was 15.4 (7.3-NA) months. The most common drug-related toxicities were grade 1-2 fatigue 14pts (78%), nausea 13pts (72%) and dysguesia 10pts (56%). 5 (28%) pts had a dose reduction and 6 (33%) in total had a dose interruption due to toxicity. **Conclusions:** Single agent antitumor activity was limited and the side effect profile was tolerable. No specific genomic aberration was associated with response to S. Clinical trial information: NCT02069730. Research Sponsor: Karyopharm.

6587 Poster Session (Board #248), Fri, 8:00 AM-11:00 AM

Radioiodine (RAI) in combination with durvalumab for recurrent/metastatic thyroid cancers. *First Author: Bharat Burman, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Immune checkpoint blockade (ICB) has limited efficacy for radioiodine-refractory thyroid cancer. The high incidence of autoimmune thyroid disease and ICB-induced hypothyroidism suggests that loss of T cell tolerance to thyroid protein epitopes is common and can be activated by ICB to induce immune responses. We hypothesize that RAI can enhance presentation of thyroid protein immunogens and putative neoantigens in thyroid cancers to amplify the effectiveness of ICB. We studied the safety and efficacy of RAI plus the anti-PD-L1 agent durvalumab (durva) in recurrent/metastatic (R/M) patients (pts). **Methods:** Pts. had at least one RAI-avid tumor on the most recent RAI scan or one tumor on FDG PET with an SUVmax < 10. RECIST measurable disease was required. Any number of prior therapies was allowed. Pts were treated with durva 1500 mg IV every 4 weeks with recombinant human TSH (rhTSH)-stimulated RAI (100 mCi) administered in Cycle 1. Treatment beyond progression was allowed. The primary objective was to assess safety. Durva related dose limiting toxicities (DLTs) were monitored for 6 weeks after the first dose. Since no durva DLTs were observed in the first 6 pts, per protocol rules the trial accrued 11 pts total. Secondary objectives were assessing best overall response (BOR) per RECIST and progression-free survival (PFS). **Results:** 11 pts (7 female) were enrolled. Eight had prior drug therapy. No DLTs or $>$ Grade 3 durva related adverse events (AEs) were observed. The most common non-laboratory AEs (regardless of attribution) were cough (7), hypertension (7), pain (6), edema (5), and fatigue/nausea/diarrhea/arthralgia/dry skin/dyspnea/edema (4 each). As of 2/6/20, 2 had partial response, 7 stable disease, and 2 progression of disease as BOR. Six pts had tumor regression. Four pts received treatment for $>$ 6 months. Six are still on treatment. Analyses of research biopsies (bxs) (8 had pre-treatment bxs, 6 had an additional on-treatment bx) will be presented. **Conclusions:** Durva plus RAI is safe and well tolerated. The preliminary efficacy signal in this small cohort is promising. Understanding how RAI plus PD-L1 targeting impacts the tumor immune microenvironment may guide how RAI should be evaluated in future ICB trials. Clinical trial information: NCT03215095. Research Sponsor: AstraZeneca, U.S. National Institutes of Health.

6588 Poster Session (Board #249), Fri, 8:00 AM-11:00 AM

Effect of ARMS-qPCR on detection sensitivity of earlier diagnosis of papillary thyroid cancers with worse prognosis determined by BRAF V600E and TERT promoter mutation coexisting. *First Author: Peng-cheng Yu, Fudan University Shanghai Cancer Center, Shanghai, China*

Background: Co-existing of *BRAF* V600E and *TERT* promoter C228T/C250T mutation has been extensively related to prognosis in thyroid cancer. Our study aimed to establish a more sensitive method for mutation detection and explore the correlation more in-depth. **Methods:** *BRAF* and *TERT* promoter mutation status of 250 papillary thyroid cancer was detected by both Amplification Refractory Mutation System quantitative PCR (ARMS-qPCR) and Sanger sequencing to compare the sensitivity. The associations between the mutation status and the clinicopathological features were analyzed. **Results:** ARMS-qPCR displayed higher sensitivity than Sanger (*BRAF* V600E: 75.2% vs. 52.4%, $p< 0.001$; *TERT* promoter C228T/C250T: 12.0% vs. 3.6%, $p= 0.001$; Co-mutation (9.6% vs. 3.2%, $p= 0.005$). Both methods indicated that patients with *BRAF* V600E and *TERT* promoter co-mutation were higher in age at diagnosis (ARMS-qPCR: 51.0 ± 14.2 vs. 40.2 ± 12.6, $p<0.001$; Sanger: 64.3 ± 7.1 vs. 40.5 ± 12.6, $p <0.001$), and the recurrence rate (16.7% vs. 3.1%, $p= 0.014$; 50.0% vs. 2.9%, $p< 0.001$), besides, the co-mutation group were related to more advanced TNM stage ($p< 0.001$; $p< 0.001$) and higher MACIS score (5.1 ± 1.5 vs. 4.2 ± 0.7, $p= 0.006$; 6.6 ± 1.1 vs. 4.2 ± 0.8, $p< 0.001$). In addition, compared with the co-mutation results of Sanger, it seems that ARMS-qPCR has identified an earlier stage of group, which were younger (43.3 ± 10.1 vs. 66.4 ± 6.1, $p< 0.001$), and with smaller tumor (1.8 ± 1.5 vs. 4.0 ± 1.3, $p= 0.002$), as well as lower recurrence rate (0.0% vs. 50%, $p= 0.007$). Besides, the newly identified group were lower in MACIS score (4.2 ± 0.8 vs. 6.9 ± 0.7, $p= 0.002$) and with lower TNM stage ($p= 0.001$). **Conclusions:** Patients with *BRAF* V600E and *TERT* promoter C228T/C250T co-mutation have a worse prognosis. Using ARMS-qPCR, the more sensitive method could identify earlier stages of patients with a potentially worse prognosis. Research Sponsor: National Science Foundation of China.

	ARMS-qPCR Co-Mut			Sanger Co-Mut			ARMS-qPCR(+)		
	+(n = 24)	-(n = 226)	p	+ (n = 8)	- (n = 242)	p	Sanger + (n = 8)	Sanger-, (n = 16)	p
Age at diagnosis ± SD	51.0±14.2	40.2±12.6	**< 0.001**	66.4±6.1	40.4±12.5	**< 0.001**	66.4±6.1	43.3±10.1	**< 0.001**
Size(cm) ± SD	2.5±1.8	1.8±1.0	0.057	4.0±1.8	1.8±1.0	**< 0.001**	4.0±1.3	1.8 ±1.5	**0.002**
Recurrence, n (%)	4(16.7)	7(3.1)	**0.014**	4(50.0)	7(2.9)	**< 0.001**	4(50.0)	0(0.0)	**0.007**
MACIS score ± SD	5.1±1.5	4.2±0.7	**0.006**	6.9±0.7	4.2±0.8	**< 0.001**	6.9±0.7	4.2±0.8	**< 0.001**
TNM stage, n (%)			**< 0.001**			**< 0.001**			**0.001**
I+II	23(95.8)	225(99.5)		7(87.5)	241(99.6)		6(87.5)	17(100.0)	
III+IV	1(4.2)	1(0.4)		1(12.5)	1(0.4)		1(12.5)	0(0.0)	

TPS6589 Poster Session (Board #250), Fri, 8:00 AM-11:00 AM

Phase III LEAP-010 study: first-line pembrolizumab with or without lenvatinib in recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). *First Author: Lillian L. Siu, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada*

Background: The PD-1 inhibitor pembrolizumab is currently approved as first-line monotherapy for patients with R/M HNSCC whose tumors express PD-L1 combined positive score (CPS) $\geq$1. In a phase 1b/2 trial (NCT02501096) of pembrolizumab plus lenvatinib (multikinase inhibitor of VEGFR 1-3, FGFR 1-4, PDGFRa, RET, and KIT) in solid tumors, the combination demonstrated promising antitumor activity and a manageable safety profile in patients with HNSCC. LEAP-010 (NCT04199104) is a randomized, double-blind, placebo-controlled, phase 3 study that will evaluate the efficacy and safety of first-line pembrolizumab with or without lenvatinib in patients with PD-L1–positive R/M HNSCC. **Methods:** Key eligibility criteria include histologically confirmed R/M HNSCC incurable by local therapies, PD-L1–positive tumor (CPS $\geq$1) as determined by central laboratory, measurable disease as assessed by blinded independent central review (BICR) per RECIST v1.1, and ECOG performance status (PS) 0 or 1. Patients will be randomly assigned 1:1 to pembrolizumab plus lenvatinib or pembrolizumab plus placebo. Randomization will be stratified by PD-L1 status defined by tumor proportion score ($<$ 50% vs $\geq$50%), human papillomavirus status for oropharynx cancer (positive vs negative), and ECOG PS (0 or 1). Patients will receive intravenous pembrolizumab 200 mg every 3 weeks for 35 cycles (~2 years) and oral lenvatinib 20 mg or placebo once daily; patients may continue to receive lenvatinib or placebo after pembrolizumab treatment is complete. Treatment will continue until BICR-verified disease progression or unacceptable toxicity. Pembrolizumab retreatment (second course) for 17 additional cycles will be allowed for eligible patients who stop pembrolizumab and subsequently experience BICR-verified disease progression. These patients could have stopped treatment with stable disease, partial response, or complete response or after 35 cycles of pembrolizumab for reasons other than disease progression or toxicity. Tumor imaging assessment will be performed at week 6, then every 6 weeks until 1 year, and thereafter every 9 weeks. Primary end points are objective response rate and progression-free survival, assessed by BICR per RECIST v1.1, and overall survival. Secondary end points are duration of response and safety and tolerability. Recruitment is ongoing; planned enrollment is ~500 patients. Clinical trial information: NCT04199104. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; and Eisai Inc., Woodcliff Lake, NJ, USA.

TPS6590 Poster Session (Board #251), Fri, 8:00 AM-11:00 AM

Single-arm study of bimiralisib in head and neck squamous cell carcinoma (HNSCC) patients (pts) harboring *NOTCH1* loss of function (LOF) mutations. *First Author: Faye M. Johnson, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Effective targeted therapies are needed for HNSCC that is lethal despite recent advances with immunotherapy. A major challenge to personalize treatment is that most genomic alterations are in tumor suppressors, including *NOTCH1* that is mutated in ~20% of HNSCC. We recently published that HNSCC cell lines harboring *NOTCH1* LOF mutations undergo cell death *in vivo* and *in vitro* following PI3K inhibition, in contrast to *PIK3CA* mutant cell lines that merely undergo cell cycle arrest when exposed to the same drugs. Based on these results we initiated a novel genomic biomarker-driven phase II clinical trial treating *NOTCH1* mutant HNSCC pts with the dual PI3K/mTOR inhibitor bimiralisib (PQR309). **Methods:** The primary objective is to determine the objective response rate (ORR) of recurrent/metastatic HNSCC harboring *NOTCH1* LOF mutations to bimiralisib. Pts who have already received standard platinum chemotherapy and immunotherapy will receive bimiralisib orally twice per wk unless progression or intolerable toxicity occurs. Tumors will be evaluated using RECIST q 6 wks. A Simon's optimal two-stage design is used. To have 80% power to detect an ORR of 30%, (one-sided $\alpha = 0.05$, $\beta = 0.20$) 10 pts will be enrolled in the first stage. If $\leq$1 pts respond, the trial will be closed for futility. If $\geq$2 pts have an OR, the study will enroll an additional 19 pts in the second stage. The null hypothesis (ORR $\leq$ 10%) will be rejected if $\geq$ 6 in 29 pts have an OR. Seven pts have enrolled. The algorithm for determining *NOTCH1* mutation function is based on the patterns of mutations in HNSCC vs. leukemia where mutations are activating. It may be difficult to determine whether *NOTCH1* mutations are homo- or heterozygous due to normal cell contamination. Therefore, levels of activated NOTCH1 in pretreatment tumors may be assessed by IHC with an antibody against activated NOTCH1 (NICD). In parallel with the trial, to further confirm *NOTCH1* LOF, we can use site-directed mutagenesis to re-create *NOTCH1* mutations from trial pts that will then be introduced into NOTCH1-null cell lines to assay for NICD and growth inhibition with culture on NOTCH1 ligand. All pts will have serial collection of blood for pharmacokinetics and for ctDNA to examine clonal evolution associated with acquired resistance. Samples with high *NOTCH1* mutation ctDNA VAF will be analyzed by WES and compared with pretreatment tissue. In the second stage, IHC and WES may be performed on pre- and post- treatment (day 15 and progression) tissue to examine pharmacodynamics and mechanisms of resistance. Clinical trial information: NCT03740100. Research Sponsor: PIQUR.

TPS6591 **Poster Session (Board #252), Fri, 8:00 AM-11:00 AM**

INDUCE-3: A randomized, double-blind study of GSK3359609 (GSK609), an inducible T-cell co-stimulatory (ICOS) agonist antibody, plus pembrolizumab (PE) versus placebo (PL) plus PE for first-line treatment of PD-L1-positive recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC). *First Author: Aaron Richard Hansen, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Pembrolizumab as part of first-line treatment for patients (pts) with R/M HNSCC has improved survival. However, in order to further improve outcomes in this population investigation of rational combinations targeting different mechanisms that cancers exploit to evade the immune system is required. ICOS, a member of the CD28/B7 immunoglobulin receptor superfamily, provides a co-stimulatory signal augmenting T-cell proliferation, cytokine production, cytotoxic function and survival. GSK609 is a humanized IgG4 antibody selected for its potent agonist activity and non-depleting properties. The rationale for targeting ICOS with GSK609 plus PD-1 blockade with PE is supported by preclinical and clinical evidence (Rischin, et al. *Annals of Oncol* 2019;30[Supplement_5]: v454–5). INDUCE-3 trial (NCT04128696) will explore if the addition of GSK609 to PE improves outcomes of pts with R/M HNSCC. **Methods:** INDUCE-3 uses a 2-in-1 adaptive design that has the option to seamlessly expand from an initial Phase 2 to a Phase 3 study. Pts (n = 600) will be stratified by PD-L1 status and HPV status (oropharynx only) then randomly assigned in a 1:1 ratio to receive GSK609 plus PE or PL plus PE, every 3 weeks until progression, unacceptable toxicity, or up to 35 cycles. GSK609 plus PE will be assessed for superiority versus PL plus PE in overall survival (OS) and progression-free survival (PFS) per RECISTv1.1 as dual primary endpoints; secondary endpoints include PFS per immune-based RECIST; milestone OS; safety and tolerability; time to deterioration in patient-reported physical function and pain. Efficacy and patient-reported outcome endpoints will be assessed in the PD-L1 combined positive score (CPS) $\geq$1 and $\geq$20 populations. Key eligibility criteria are aged $\geq$18 years; locally incurable R/M HNSCC of the oral cavity, oropharynx, hypopharynx, or larynx; no prior systemic therapy in the R/M setting; PD-L1 CPS $\geq$1 by central testing; measurable disease per RECIST v1.1 and ECOG PS 0/1. Recruitment is ongoing in countries across the globe. Funding: Study is funded by GlaxoSmithKline and in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. Clinical trial information: NCT04128696. Research Sponsor: GSK.

TPS6592 **Poster Session (Board #253), Fri, 8:00 AM-11:00 AM**

CCTG HN.10: A phase II single-arm trial of elective volume adjusted de-escalation radiotherapy (EVADER) in patients with low-risk HPV-related oropharyngeal squamous cell carcinoma (NCT03822897). *First Author: Scott Victor Bratman, Department of Radiation Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Treatment for HPV positive(+) oropharyngeal squamous cell carcinoma (OSCC) is highly effective but associated with significant short and long term treatment related morbidity. We hypothesize that decreasing the regions of elective nodal irradiation (ENI) in the neck will lead to less toxicity and better quality of life/functional outcomes while maintaining high disease control rates in patients with favourable prognosis HPV+ OSCC. **Methods:** HN.10 is a Canadian Cancer Trials Group phase II trial with a primary objective to evaluate the efficacy of primary definitive radiotherapy (RT) or chemoradiotherapy (CRT) utilizing volume reduced ENI as measured by 2-year event-free survival (EFS) in patients with low-risk HPV+ OPSCC. Secondary objectives include to evaluate overall survival, local control, regional control, locoregional control, out-of-field regional control, distant metastasis free survival, early and late toxicities of treatment, subjective swallowing functions, quality of life, utilization of healthcare resources, work productivity, and prognostic biomarkers. An imaging and biospecimen bank will be compiled as part of trial conduct. Key eligibility criteria include: pathologically proven diagnosis of HPV+ OPSCC; HPV association determined locally by either p16 immunohistochemistry or direct detection of HPV DNA sequences (e.g. by PCR or in situ hybridization) performed on a core needle or surgical biopsy specimen of the primary tumour or involved cervical lymph node; clinical stage T1-3 N0-1 M0 (UICC/AJCC 8th Ed.); fit for radiotherapy +/-chemoradiotherapy. Statistical Design: The primary endpoint is 2-year EFS. Assuming 2-year EFS to be 91% (Ha) for low-risk HPV-related OPSCC with standard treatment, and that the experimental treatment will be considered as ineffective if the 2-year EFS is $\leq$ 85% (H0), with one-sided alpha of 0.1, a sample size of 100 patients will have 80% power to detect a 6% difference of 2-year EFS. With 3 years of accrual and 2 years of follow-up, the total duration of this study will be 5 years. A total of 304.7 person-years of follow-up is needed for the final analysis. The null hypothesis (H0) will be rejected when the observed survival rate is 88.85% or higher (i.e. if there are 18 or fewer EFS events observed). Conduct to Date: Study activation February 20, 2019. Enrollment as of January 29 2020: 23. Clinical trial information: NCT03822897. Research Sponsor: CIHR Project Scheme.

TPS6593 **Poster Session (Board #254), Fri, 8:00 AM-11:00 AM**

The AIM-HN and SEQ-HN study: A pivotal study evaluating the efficacy of tipifarnib in patients with head and neck squamous cell carcinoma (HNSCC) with *hras* mutations (AIM-HN) and the impact of *hras* mutations on response to first line systemic therapies for HNSCC (SEQ-HN). *First Author: Robert I. Haddad, Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, MA*

Background: *HRAS* mutations define a unique molecular subset of ~ 5% of HNSCC. Evidence suggests that these tumors respond poorly to standard systemic therapy but the impact of *HRAS* missense mutations on clinical outcomes has not been formally characterized. Tipifarnib is a potent and selective inhibitor of farnesyltransferase, a critical enzyme for *HRAS* activity. Phase 2 Proof of concept for tipifarnib in *HRAS* mutant HNSCC was recently achieved in study KO-TIP-001 (NCT02383927, Ho et. al. ESMO 2018). **Methods:** The AIM-HN and SEQ-HN Study (KO-TIP-007, NCT03719690) is an ongoing international, multicenter, open-label, 2 cohort (AIM-HN and SEQ-HN), pivotal trial designed to determine the Overall Response Rate (ORR) of tipifarnib in patients (pts) with *HRAS* mutant HNSCC (AIM-HN). SEQ-HN will retrospectively investigate how the ORR to first line treatment compares between the accrued *HRAS* mutant pts to matched-case control *HRAS* wild type (wt) HNSCC pts. Information on subsequent lines of therapy for *HRAS* mutant and wt pts will also be collected. AIM-HN will enroll at least 59 pts (oral cavity, pharynx, larynx, sinonasal, nasopharyngeal, or unknown primary) who are refractory or have relapsed from at least one prior line of systemic platinum-based therapy and have measurable disease by RECIST 1.1. AIM-HN pts must have tumors with $>$35% *HRAS* mutant variant allele frequency (VAF) or $>$20% VAF if serum albumin is $>$3.5 g/l. AIM-HN pts will receive treatment with tipifarnib at 600 mg bid on days 1-7 and 14-21 of 28-day cycles. Using Simon's Two-Stage Minimax design, if true ORR is $>$ 30%, the study will have 80% power to detect ORR $>$ 15% at 0.025 significance level. Both interim (after first 31 pts) and final analysis, 2-sided 95% CI on ORR, will be performed on the modified intent to treat population. The SEQ-HN observational cohort will enroll ~225 control pts who will receive standard of care treatment. A subset of SEQ-HN pts will be matched to the *HRAS* mutant AIM-HN pts according to defined patient characteristics and compared for responses to therapy. Clinical trial information: NCT02383927. Research Sponsor: Kura Oncology.

TPS6594 **Poster Session (Board #255), Fri, 8:00 AM-11:00 AM**

Randomized, phase II study of ficlatuzumab with or without cetuximab in patients with pan-refractory, recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). *First Author: Julie E. Bauman, University of Arizona Cancer Center, Tucson, AZ*

Background: Patients with pan-refractory R/M HNSCC, with clinical resistance to cytotoxic therapy, anti-EGFR molecular targeting, and immunotherapy, have poor survival. An established tumor-intrinsic resistance mechanism to cetuximab, an anti-EGFR IgG1 monoclonal antibody (mAb), is activation of the hepatocyte growth factor (HGF)/cMet pathway, which converges with the EGFR network at both the PI3K/Akt and MAPK nodes allowing for reciprocal compensation. Moreover, over-expression of HGF in the tumor microenvironment is immunosuppressive. Convergent data suggest that HGF/cMet pathway inhibition concurrent with EGFR blockade may overcome cetuximab resistance. We previously reported a Phase I study of ficlatuzumab, a humanized anti-HGF IgG1 mAb, with cetuximab in cetuximab-resistant R/M HNSCC. The combination showed promising safety, overall response rate (ORR) and progression-free survival (PFS). Preliminary biomarker analyses showed that high circulating cMet was associated with poor PFS whereas serum Veristrat, a proteomic classifier associated with worse prognosis in the setting of anti-EGFR monotherapy, was not. An increase in total peripheral T cells, particularly the $CD8^+$ subset, was associated with treatment response while progression was associated with expansion of a unique myeloid population. We designed a follow-on randomized phase II trial evaluating ficlatuzumab with or without cetuximab in pan-refractory, R/M HNSCC with signaling and immune correlatives. **Methods:** This is a multicenter phase II trial with a randomized, non-comparative, two-arm design (ficlatuzumab 20 mg/kg with or without cetuximab 500 mg/m^2 every 2 weeks) in patients with pan-refractory R/M HNSCC. Key eligibility criteria include: R/M HNSCC; cetuximab resistance (progression during or within 6 months of cetuximab-radiation or palliative cetuximab); platinum resistance; prior exposure to anti-PD1 mAb; ECOG 0-1; consent to baseline research biopsy. The primary objective is to evaluate the efficacy of each arm as measured by PFS. To test the hypothesis that either regimen improves historical PFS from 2 to 3.33 months requires 66 eligible patients. Key secondary endpoints are ORR and survival. Mechanistic biomarkers include tumor HGF/cMet pathway activation, tumor and peripheral immune profiles, soluble cMet, and serum Veristrat. Thirty-five of 66 subjects have enrolled at 6 centers. A Bayesian continuous monitoring rule for futility has not been triggered for either arm. Clinical trial information: NCT03422536. Research Sponsor: Aveo.

TPS6595 Poster Session (Board #256), Fri, 8:00 AM-11:00 AM

Window-of-opportunity trial of nivolumab with or without the IDO inhibitor BMS-986205 in patients with resectable squamous cell carcinoma of the head and neck (SCCHN). *First Author: Adam Luginbuhl, Thomas Jefferson University, Department of Otolaryngology, Philadelphia, PA*

Background: Indoleamine 2,3-dioxygenase (IDO1) catabolizes tryptophan to kynurenine and is highly expressed in multiple malignancies including SCCHN. Elevated IDO1 activity may contribute to an immunosuppressive tumor microenvironment and compromise therapeutic responses to immune checkpoint therapy. We designed a window-of-opportunity trial to test whether the IDO inhibitor BMS-986305 improves treatment responses and T cell function in SCCHN patients treated with nivolumab. **Methods:** Patients with previously untreated, resectable, pathologically confirmed SCCHN are eligible. Primaries of the oral cavity, oropharynx, larynx, hypopharynx, or nasal cavity/paranasal sinuses must be AJCC 8th edition stage II or higher (M0). Stage I oropharyngeal cancers with lymphadenopathy are also eligible. Patients are randomized 3:1 to receive either A) nivolumab 480 mg IV x 1 plus BMS-986205 100 mg PO daily starting a week prior to nivolumab and continuing for 4 more weeks (total of 5 weeks) or B) nivolumab 480 mg IV alone for 4 weeks. At the 5th week of treatment patients are assessed for response with physical exam and repeat CT scans for tumor volumes: if there is greater than 10% reduction in volume of either primary tumor or lymph node metastases, patients will be considered responders and receive another cycle of their originally assigned treatment, i.e. nivolumab 480 mg IV for a second dose +/- BMS-986205 100 mg PO daily for an additional 4 weeks followed by surgery in week 9. If tumor volume is stable or progression is noted in either the primary site or lymph nodes, patients are considered non-responders followed by definitive surgery in week 5 (i.e. after only one cycle of treatment). The primary endpoint of this study is the response rate after cycle 1 (using the criteria defined above). The projected sample size is 48 patients (36 in arm A and 12 in arm B). Secondary endpoints include safety, pathologic treatment effect and metabolic and molecular correlates of treatment in the tumor microenvironment. Clinical trial information: NCT03854032. Research Sponsor: Bristol Myers Squibb.

TPS6596 Poster Session (Board #257), Fri, 8:00 AM-11:00 AM

ROMAN: Reduction in oral mucositis with avasopasem manganese (GC4419)–Phase III trial in patients receiving chemoradiotherapy for locally advanced, nonmetastatic head and neck cancer. *First Author: Jon Holmlund, Galera Therapeutics, Malvern, PA*

Background: Approximately 70% of patients receiving intensity-modulated radiotherapy (IMRT) plus cisplatin for locally advanced head and neck cancer (HNC) develop SOM, defined as WHO Grade 3 or 4, which limits patients' ability to eat solids (Gr 3) or liquids (Gr 4, requiring enteral nutrition). An RT-induced burst of superoxide initiates oral mucositis (OM) development. GC4419, a superoxide dismutase mimetic, interrupts this process by converting superoxide to H2O2. It showed promising reduction of SOM in a published open-label Phase 1b/2a trial (IJROBP 1 Feb 2018). In a subsequent randomized, double-blind placebo-controlled trial in 223 patients receiving IMRT/cisplatin for HNC (ASCO 2018), 90 mg of GC4419 administered M-F prior to IMRT demonstrated statistically significant reduction in SOM duration (p=0.024, median 1.5 days @ 90 mg vs. 19 days placebo) and meaningful reductions @ 90 mg in SOM incidence (43% vs. 65%) and severity (incidence of Grade 4, 16% vs. 30%). The safety results were acceptable and consistent with the known toxicities of IMRT/cisplatin. **Methods:** 335 patients at multiple centers in the U.S. and Canada with locally-advanced, nonmetastatic head and neck cancer (oral cavity/oropharyngeal) receiving 70 Gy IMRT (>50 Gy to > 2 oral sites) plus cisplatin (40 mg/m2 qwk x 6-7, or 100 mg/m2 q3wk x 3) are being randomized (double-blinded) 3:2 to 90 mg of GC4419 or placebo, M-F before each RT fraction. Enrollment is stratified by cisplatin schedule and treatment setting (definitive vs. post-op). OM by the WHO scale will be assessed twice weekly during RT & weekly for 2 weeks post RT. The primary efficacy endpoint is incidence of SOM through the end of IMRT. Secondary efficacy endpoints include severity (incidence of Grade 4 OM through the end of IMRT), & days of SOM (days from first to last SOM for all patients, with patients never developing SOM having 0 days of SOM by definition). Days of SOM for the subset developing SOM will be analyzed descriptively. Patients will be followed for one year post IMRT for tumor progression/recurrence and for two years for survival. Clinical trial information: NCT03689712. Research Sponsor: Galera Therapeutics, Inc.

TPS6597 Poster Session (Board #258), Fri, 8:00 AM-11:00 AM

A phase II open-label, multicenter, study to evaluate the efficacy and safety of rivoceranib in subjects with recurrent or metastatic adenoid cystic carcinoma. *First Author: Hyunseok Kang, University of California, San Francisco, San Francisco, CA*

Background: Adenoid cystic carcinoma (ACC) is a rare salivary gland malignancy, also found in other secretory gland sites (tracheobronchial tree, esophagus, breast, lungs, prostate, uterine cervix and vulva). Initial disease is typically treated with surgical resection and radiation, but recurrent or metastatic disease remain to be a significant challenge. There is no standard systemic therapy option for advanced ACC, although recent studies with tyrosine kinase inhibitors have shown moderate objective response and disease stabilization rates. Rivoceranib (also known as apatinib) is a potent selective inhibitor of VEGFR-2 and has been evaluated in a single arm phase II study of 59 recurrent or metastatic ACC patients in China and has demonstrated an (ORR) of 47.1% and disease control rate of 98.1. **Methods:** This is a phase II, open-label, multicenter[HGJ3], single arm clinical trial of oral rivoceranib (700 mg daily) in patients with recurrent or metastatic ACC of any anatomic site, not amenable to curative surgery or radiotherapy to confirm activity of rivoceranib. Subjects must have at least one evaluable lesion by RECIST v1.1 and have evidence of disease progression within the 6 months prior to study entry. Fifty-five subjects will be enrolled at 7 US sites and 4 South Korean sites. The primary endpoint is ORR assessed by investigators with a target ORR of 25% to detect a difference of 15% from the historical ORR of 10% at 1-year (this achieves 80% power with a 5% significance level). Secondary endpoints include overall survival, disease control rate, progression free survival at 6, 12 and 24 months and time to progression. Exploratory objectives include correlation between ORR and the presence of MYB/MYB-L1 fusion, pharmacokinetics evaluation, and patient-reported quality of life assessments by FACT-G. This study is open and enrolling at the time of submission. References: 1. Tchekmedyian V, Sherman EJ, Dunn L, et al. Phase II Study of Lenvatinib in Patients With Progressive, Recurrent or Metastatic Adenoid Cystic Carcinoma. Journal of clinical oncology: official journal of the American Society of Clinical Oncology 2019;37:1529-37. 2. Zhu G, Zhang L, Li R, Dou S, Yang W, Zhang C. Phase II trial of apatinib in patients with recurrent and/or metastatic adenoid cystic carcinoma of the head and neck: Updated analysis. Journal of Clinical Oncology 2018;36:6026. Clinical trial information: NCT04119453. Research Sponsor: Elevar therapeutics.

7000 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

The oncology hospital at home: Health care utilization outcomes from the huntsman at home trial. *First Author: Kathi Mooney, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT*

Background: Unplanned hospitalizations and emergency department (ED) visits are common during cancer care. Providing acute hospital level care at home may add value by decreasing hospital and ED use. We conducted the first evaluation of an oncology Hospital-at-Home program, Huntsman at Home (H@H). **Methods:** The Huntsman Cancer Institute began H@H services in 2018 and accepts referral of cancer patients for acute-medical or post-surgical care at home. Patients are admitted who require continued acute level medical care after hospitalization or have emergent unstable symptoms related to treatment or disease progression that would otherwise require ED evaluation or hospitalization. Prospectively, patients referred to H@H from 8/2018 through 10/2019 were compared to a usual care comparison group (UC) drawn concurrently from patients living within the Salt Lake City metropolitan area who qualified for admission to H@H, but lived outside the service zip codes. Probability of H@H enrollment propensity scores were constructed via random forest from patient descriptors and health care utilization at admission. We used an intent-to-treat approach for analysis. Primary outcomes were hospitalizations, length of stay (LOS), ED visits and cumulative charges over 30 and 90 days post admission to either group. Comparisons were made by generalized linear models, stratified by tertiles of H@H vs. UC propensity score. **Results:** 367 patients, 169 H@H and 198 UC, were evaluated. The average age was 62 yrs, 85% were Caucasian, and 77% had stage IV cancer. Propensity score distributions were overlapping, demonstrating group comparability. A variety of cancers were represented; the most common being colon, gynecologic, prostate and lung cancers. Compared to UC, H@H patients were more likely to be female (61% vs 43%) and during the month prior to admission, showed a trend towards longer LOS if hospitalized (6.7 vs 5.5 days). During the first 30 days after admission, propensity stratified comparisons showed H@H patients with lower hospital LOS (mean reduction 1.19 days, p=0.022), 56% lower odds of unplanned hospitalizations (OR 0.44, p=0.001), 45% lower odds of ED visits (OR 0.55, p=0.037) and 50% lower cumulative charges (mean ratio 0.50, $p<0.001$) compared to UC. Results over 90 days were similarly robust. **Conclusions:** In the first reported trial of an adult oncology Hospital at Home program, there was strong evidence for reduced hospitalizations, ED visits, and cost. Oncology Hospital at Home programs show promise for increased patient-centered care while simultaneously improving value. Research Sponsor: Cambia Foundation.

7001 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A multicenter study comparing granulocyte-colony stimulating factors to antibiotics for primary prophylaxis of taxotere/cyclophosphamide-induced febrile neutropenia in patients with early-stage breast cancer. *First Author: Mark J. Clemons, Cancer Research Group, Ottawa Hospital Research Institute, Ottawa, ON, Canada*

Background: Docetaxel-cyclophosphamide (TC) adjuvant chemotherapy is commonly used in patients with early stage breast cancer (EBC). Due to the risk of febrile neutropenia (FN) with TC, primary prophylaxis with either ciprofloxacin (cipro) or granulocyte-colony stimulating factors (G-CSF) is recommended. Despite significant differences in costs (7-120 $US/course [cipro] vs. 2100-7000 $US/dose [G-CSF]) and toxicity profiles, optimal primary FN prophylaxis is unknown. We performed a pragmatic randomised trial comparing the superiority of G-CSF to cipro. **Methods:** EBC patients receiving TC chemo were randomized to receive cipro or G-CSF as primary FN prophylaxis. The primary outcome is a composite of either treatment-related hospitalisations or FN. Secondary outcomes included: chemo dose reductions, delays, discontinuations and incidence of *C. difficile* infections. Primary analysis was performed with the intention to treat (ITT) population. **Results:** 455 eligible patients were randomized to cipro (227) or G-CSF (228). 37/227 (16.3%) patients on cipro had a hospitalization, compared with 25/228 (11.0%) on G-CSF (Fisher's exact test p-value=0.10). Relative risk (RR) of hospitalization for patients on G-CSF:0.68, 95%CI=0.42 to 1.09. Patients on cipro were statistically significantly more likely to be hospitalized for FN (30/227, 13.2%) vs 9/228 (4.0%) patients on G-CSF($p<0.001$). RR of developing FN and being hospitalized for patients on G-CSF: 0.44, 95%CI=0.26 to 0.76. There was no significant difference between groups for chemo dose reductions, delays, and *C. difficile* rates. Twenty patients on cipro (8.8%) and 9 on G-CSF (3.9%) discontinued chemo early (p=0.036). RR of discontinuing chemo: 0.43, 95% CI=0.19 to 0.96. **Conclusion:** G-CSF was superior to cipro at reducing FN. While a trend towards reduced hospitalizations was also observed with G-CSF, it did not attain statistical significance. However, as 18 patients would need to be treated with G-CSF to prevent one hospitalization compared to cipro, this would suggest a cost of over $100000 $US to prevent a hospitalization. A formal cost-effectiveness analysis will be performed. Clinical trial information: NCT02173262, NCT02816112. Research Sponsor: Canadian Institute of Health Research - Strategy for Patient Oriented Research Grant, Cancer Care Ontario Clinical Programs and Quality Initiatives grant.

7002 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase III randomized controlled trial of eRAPID (electronic patient self-Reporting of Adverse-events: Patient Information and advice)—An eHealth intervention during chemotherapy. *First Author: Galina Velikova, Leeds Institute of Medical Research at St James's, University of Leeds, Leeds, United Kingdom*

Background: Routine monitoring of patients' symptoms can improve symptom management, quality of life (QOL) and survival. eRAPID is an online system for patients to report symptoms, uniquely providing automated severity-dependent advice (self-management or alerts for hospital contact). We evaluated eRAPID impact on patient experiences & clinical care. **Methods:** A prospective randomized two-arm parallel group trial (1:1 allocation Usual Care (UC): UC+eRAPID). Eligible patients started chemotherapy for colorectal, breast & gynecological cancers at Leeds Cancer Centre. In eRAPID arm, patients completed weekly online symptoms for 18 weeks. Primary outcome: QOL/symptom control (FACT-PWB Physical Wellbeing Scale) at 18 weeks. Secondary outcomes: process of care (admissions/ chemotherapy delivery), patient self-efficacy (Lorig Self-Efficacy Scale) & global QOL (EQ5D).Mixed effects repeated measures models were employed. **Results:** During Jan 2015-June 2018, we screened 1484 patients; 508/690 eligible patients (73.6%) consented & were randomized (256 eRAPID:252 UC). No statistically significant effect of eRAPID on FACT-PWB score was found at 18 weeks (difference in means 0.20 95% CI -0.81, 1.20; p = 0.699). There was a positive impactat 6 & 12 weeks (1.08, 95% CI 0.12, 2.05; p = 0.028 & 1.01, 95% CI 0.05, 1.98; p = 0.039).In responder analysis lower proportion of eRAPID patients had clinically meaningful deterioration 47.5% at 12 weeks vs 56.3% UC. Pre-planned subgroup analysis found no effect in metastatic disease, but better FACT-PWB in non-metastatic/adjuvant group at 6 & 12 weeks (1.45, 95% CI 0.32, 2.58; p = 0.011 & 1.13; 95% CI 0.07, 2.19; p = 0.036). eRAPID patients reported better self-efficacy (p = 0.007) & QOL EQ5D-VAS at 12 (p = 0.030) & 18 weeks (p = 0.010). There were no differences for admissions/chemotherapy delivery. 3314 online reports were completed, median per patient 14.0 (range 0-117). Emergency alerts were activated in 29/3314 cases (0.9%), self-management advice 2714/3314 (81.9%). Post-hoc analysesshowed high patient adherence was associated with clinicians' use of the data, high baseline FACT-PWB & older age. High adherence patients had better FACT-PWB scores at 12 weeks. **Conclusions:** Online symptom monitoring with immediate advice improved symptom control early during adjuvant chemotherapy (6 &12 weeks), helping patient education & self-efficacy. The results support its utility as an improved model for patient care during adjuvant chemotherapy. Clinical trial information: ISRCTN88520246. Research Sponsor: National Institute for Health Research.

7004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Early discontinuation to adjuvant endocrine therapy in the ECOG-ACRIN TAILORx Trial. *First Author: Betina Yanez, Northwestern University Feinberg School of Medicine, Chicago, IL*

Background: The TAILORx study demonstrated women with an intermediate Oncotype DX score receive the same benefit with endocrine therapy (ET) compared to chemoendocrine therapy (CET). However, early discontinuation of adjuvant ET is problematic among breast cancer survivors, with previous studies suggesting that up to 50% of women do not adhere to the full 5 years of recommended ET treatment. The aim of this study was to identify patient-level risk factors associated with early discontinuation of ET in the TAILORx study. **Methods:** TAILORx was coordinated by the ECOG-ACRIN Cancer Research Group. Participants were a subgroup of 954 women who completed additional measures on health-related quality of life (HRQoL) including endocrine symptoms (ES) physical well-being (PWB) and social well-being (SWB) prior to initiating ET, which categorized into three groups by tertile for analysis. All participants were diagnosed with hormone-receptor–positive, human epidermal growth factor receptor 2–negative, axillary node–negative breast cancer who started ET within a year of study entry. Early discontinuation of ET, defined as discontinuation less than 4 years from initiation for reasons other than death or recurrence, was assessed by clinician report. Rate of discontinuation was calculated using Kaplan-Meier estimates, and Cox-proportional hazards joint models were used to analyze the association between rates of adherence to ET with patient-level factors. **Results:** In a joint model, receipt of CET therapy (vs receipt of ET only; HR = .59, 95% CI .38-.94, p = .02) and age above 40 (versus age < = 40; HR = .30, 95% CI .14-.66, p = .003) were associated with a lower probability of early discontinuation of ET. Adjusted for these factors, a history of depression compared to no history of depression (HR 1.82, 95% CI 1.19-2.77, p = 0.005), worse ES compared to better ES (HR 1.70, 95% CI 1.06-2.74, p = 0.03), worse PWB compared to better PWB (HR 2.12, 95% CI 1.30-3.45,p = 0.003), and worse SWB compared to better SWB (HR 1.94, 95% CI 1.20-3.13, p = 0.007) were individually and significantly associated with a higher probability of early discontinuation of ET, although none reached statistical significance when all were included in a joint model. **Conclusions:** Younger women are at risk for early discontinuation and modifiable characteristics such as HRQoL and history of depression are potential risk factors for early discontinuation of ET. These results support systematic screening for HRQoL and depressive symptoms to identify women at risk for discontinuation of ET. Clinical trial information: NCT00310180. Research Sponsor: U.S. National Institutes of Health.

7005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

U.S. trends and racial/ethnic disparities in opioid access among patients with poor prognosis cancer at the end of life (EOL). *First Author: Andrea Catherine Enzinger, Dana-Farber Cancer Institute, Boston, MA*

Background: Heightened US opioid regulations may limit advanced cancer patients' access to effective pain management, particularly for racial/ethnic minority and other vulnerable populations. We examined trends in opioid access, disparities in access, and pain-related emergency department (ED) visits among cancer patients near end of life (EOL). **Methods:** Using a 20% random sample of Medicare FFS beneficiaries, we identified 243,124 patients with poor prognosis cancers who died between 2007-2016. We examined trends in outpatient opioid prescription fills and pain-related ED visits near EOL (30 days prior to death or hospice enrollment), for the overall cohort and by race (white, black, other). Per-capita opioid supply by state was obtained from the federal Drug Enforcement Agency ARCOS database. Geographic fixed-effects models examined predictors of opioid use near EOL, opioid dose in morphine milligram equivalents (MMEs), and pain-related ED visits, adjusted for patient demographic and clinical characteristics, state, opioid supply, and year. **Results:** From 2007-2016 the proportion of patients with poor prognosis cancers filling an opioid prescription near EOL fell from 41.7% to 35.7%, with greater decrements among blacks (39.3% to 29.8%) than whites (42.2% to 36.5%) and other races (38.2% to 32.4%). The proportion of patients receiving long-acting opioids near EOL fell from 17% to 12% overall (15% to 9% among blacks). Among patients receiving EOL opioids, the median daily dose fell from 40MMEs (IQR 16.5-98.0) to 30MMEs (IQR 15.0–78.8). In adjusted analyses, blacks were less likely than whites to receive EOL opioids (AOR 0.85; 95% CI, 0.80 to 0.91) and on average received 10MMEs less per day (b -9.9; 95% CI -15.7 to -4.2). Patients of other race were also less likely to receive EOL opioids (AOR 0.92; 95% CI, 0.85-0.95), although their dose did not differ significantly from whites. Rates of pain-related ED visits near EOL increased from 13.2% to 18.8% over the study period. In adjusted analyses, blacks were more likely than whites to have pain-related ED visits (AOR 1.29, 95% CI, 1.16-1.37) near death, as were those of other races (AOR 1.30; 95% CI, 1.17-1.37). **Conclusions:** While lawmakers have sought to mitigate the impact of opioid regulations upon cancer patients, access to EOL opioids have decreased substantially over time with concomitant increases in pain-related ED visits. There are significant racial/ethnic disparities in opioid access, with blacks receiving fewer opioids at lower doses and having more ED-based care for pain near EOL. Research Sponsor: U.S. National Institutes of Health.

7006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Relationships among skeletal muscle, symptom burden, health care use, and survival in hospitalized patients with advanced cancer. *First Author: Chinenye C. Azoba, Massachusetts General Hospital, Boston, MA*

Background: Loss of skeletal muscle mass (quantity) is common in patients with advanced cancer, but little is known about muscle density (quality). Hospitalized patients with advanced cancer are a highly symptomatic population at risk for the adverse effects of muscle loss. Thus, we sought to describe associations between muscle mass and density, symptom burden, health care use, and survival in these patients. **Methods:** We prospectively enrolled hospitalized patients with advanced cancer from 9/2014-4/2017. Upon admission, patients reported their physical (Edmonton Symptom Assessment System [ESAS]) and psychological (Patient Health Questionnaire 4 [PHQ4]) symptoms. We used computed tomography (CT) scans performed per routine care ≤45 days prior to enrollment to evaluate muscle mass and density at the level of the third lumbar vertebral body. We categorized patients as sarcopenic using validated sex specific cutoffs. We used regression models to examine associations between muscle mass and density and patients' symptom burden, health care use, and survival. **Results:** Of 1,121 patients enrolled, 677 had evaluable CT scan data (mean age = 62.86±12.95 years; 51.1% female). The most common cancer types were gastrointestinal (36.8%) and lung (16.7%) cancer. Most met criteria for sarcopenia (64.0%). Older age and female sex were associated with lower muscle mass (age: B = -0.16, $p < .01$; female: B = -6.89, $p < .01$) and density (age: B = -0.33, $p < 0.01$; female: B = -1.66, p = .01), while higher BMI was associated with higher muscle mass (B = 0.58, $p < .01$) and lower muscle density (B = -0.61, $p < .01$). Higher muscle mass was significantly associated with improved survival (HR = 0.97, $p < .01$), but not with symptom burden or health care use. Higher muscle density was significantly associated with lower ESAS physical (B = -0.17, p = .02), ESAS total (B = -0.29, $p < .01$), PHQ4 depression (B = -0.03, $p < .01$) and PHQ4 anxiety (B = -0.03, $p < .01$) symptoms. Higher muscle density was also associated with decreased hospital length of stay (B = -0.07, $p < .01$), risk of readmission or death in 90 days (OR = 0.97, $p < .01$), and improved survival (HR = 0.97, $p < .01$). **Conclusions:** Most hospitalized patients with advanced cancer have muscle loss consistent with sarcopenia. We found that muscle mass (quantity) correlated with survival, whereas muscle density (quality) was associated with patients' symptoms, health care use, and survival. These findings underscore the added importance of assessing muscle quality when seeking to address the adverse effects of muscle loss in oncology. Research Sponsor: Massachusetts General Hospital Cancer Center.

7007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Associations between psoas muscle area (PMA) and density (PMD) with phase I oncology clinical trial outcomes. *First Author: Pritish Iyer, Fox Chase Cancer Center, Philadelphia, PA*

Background: Malnutrition and cancer cachexia can lead to loss of muscle mass (sarcopenia) and are associated with poor outcomes. Muscle status can be evaluated by computed tomography (CT)-based radiographic measures, specifically at the L3 vertebrae where the psoas and other core muscles reside. We previously found that baseline malnutrition was associated with worse phase 1 clinical trial outcomes including increased toxicity and reduced survival (Jain et al. Oncologist, 2019). We sought to evaluate the relationship between muscle status and phase 1 trial outcomes. **Methods:** CT-based psoas muscle area (PMA) and psoas muscle density (PMD) were evaluated in 83 patients who enrolled in a phase 1 trial. We localized the L3 vertebral body on axial imaging and manually outlined the psoas muscle to calculate PMA (standardized to height) and PMD. Two reviewers independently conducted the analyses. We stratified patients by having a PMA or PMD above or below the group's median. We evaluated for associations between PMA/PMD and the following clinical trial outcomes: rates of grade ≥ 3 toxicity, frequency of dose reductions/interruptions, hospitalizations, tumor response, duration on study (DOS), and overall survival (OS). We also evaluated for correlations between PMA/PMD and a validated measure of nutritional status, the PG-SGA. Chi-square analysis was used to determine statistical significance between groups. Kaplan-Meier curves were used to compare DOS and OS. **Results:** 83 patients were included (38 male, 45 female), with a median age of 60 (range 28-85). The most common cancer type was gastrointestinal (33%). Mean PMA was 2.89 cm^2/m^2 (range 1.41-5.72) and mean PMD 37.77 Hounsfield units (range 13.27-56.18). PMA above the median was associated with a reduced risk of grade ≥ 3 toxicity (32.5% vs 67.4%, p = 0.001). There was no association between PMD and grade ≥ 3 toxicity, or between PMA/PMD and other phase 1 trial outcomes. There was a significant correlation between nutritional status and PMA (r = -0.278, p = 0.01) but not PMD. **Conclusions:** PMA and PMD are readily available CT-based measures of muscle status. In oncology phase 1 clinical trial participants, lower baseline PMA was associated with a two-fold increased risk of grade ≥ 3 toxicity. Baseline PMA was moderately correlated with nutritional status which was previously shown to be associated with poor trial outcomes. More research is necessary to further understand the specific mechanisms by which nutritional status and muscle mass may influence toxicity risk in this population. Research Sponsor: None.

7008 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Benefits of an early mobility program for hospitalized cancer patients: A pilot study. *First Author: Cardinale B. Smith, Icahn School of Medicine at Mount Sinai, New York, NY*

Background: Cancer patients are often hospitalized with complications from cancer and cancer treatment. Many experience a decline in physical functioning which likely contributes to increased length of stay (LOS) and excess days, increased readmissions and decreased patient experience. We aimed to determine whether a mobility program project would improve quality of care and decrease healthcare utilization. **Methods:** We implemented a mobility aide program on an oncology unit in a large academic medical center between April 2, 2019 to December 31, 2019. The program consisted of nursing evaluation using the Activity Measure for Postacute Care (AMPAC), an ordinal scale ranging from bed rest to ambulating ≥250 feet, was used to quantify mobility. Plan of care was determined in a multidisciplinary manner with physical therapy (PT), nursing and a mobility aide, a medical assistant with enhanced rehabilitation training. Patients were then mobilized two times per day seven days a week. Using descriptive statistics we evaluated the programs impact on excess days, readmissions, changes in mobility and patient experience as measured by Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) during this time period compared to the 6 month interval prior to implementation. **Results:** During the study interval, 988 patients were admitted and received the mobility program. There was a 6% reduction in excess days (p = 0.04). Similarly, readmission rates decreased from 25% to 19% (p = 0.03). Overall 76% of patients wither maintained or improved their mobility score. During this time period HCAHPS scores (willingness to recommend hospital) increased from 63% at baseline to 91% (p = 0.01). **Conclusions:** Use of this mobility program resulted in a significant decrease in healthcare utilization and improvement in patient experience. This demonstrates that non-PT professionals can mobilize hospitalized cancer patients decreasing the burden of PT and nursing resources. Future work will evaluate the sustainability of the program and evaluate association with healthcare costs. Research Sponsor: None.

7009 Poster Discussion Session; Displayed in Poster Session (Board #281), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Survival outcomes among older adults (OA) receiving second-line therapy for metastatic CRC (mCRC): 5,289 patients (pts) from the ARCAD Clinical Trials Program. *First Author: Nadine Jackson McCleary, Dana-Farber Cancer Institute, Boston, MA*

Background: Survival outcomes of 2nd line mCRC therapy for OA are poorly understood. We evaluated the rates and survival outcomes of 2nd line therapy among OA age 70+ compared to younger adults (YA) age < 70 following progression on 1st line clinical trials. **Methods:** Associations between clinical characteristics of pts with available treatment data after progression on 10 of 23 1st line ARCAD trials, time to initial progression (TTiP) and 2nd line therapy were evaluated. Time to progression (TTP) and overall survival (OS) were compared between OA and YA enrolled on 2nd line trials by Cox regression, adjusting for age, sex, ECOG PS, number of metastatic sites, presence of metastasis in lung/liver/peritoneum. **Results:** Sixteen percent of 1st line ARCAD trial participants were age 70+ (n = 870). Data for 2nd line therapy was available for 60.6% pts (3206/5289). Each additional decade of life was associated with 11% lower odds of receiving 2nd line therapy in multivariate analysis (p = 0.0117). OA participating in 2nd line trials (7.9% age 75+ of 7921) experience similar TTP and OS to YA (mTTP: 5.1 vs. 5.2mos; mOS 11.6 vs 12.4mos, respectively). **Conclusions:** We did not observe a statistical difference in survival outcomes by age following 2nd line mCRC therapy. Further study is needed to examine unmeasured comorbidity and use of geriatric assessment to select OA likely to benefit from 2nd line therapy. Research Sponsor: NIH/NCI Gastrointestinal SPORE Dana-Farber/Harvard Cancer Center.

Multivariate analysis of survival outcomes for mCRC OA vs. YA following initial progression.

		1st line therapy TTiP N = 5289 (5121 evaluable)			2nd line therapy TTP N = 7921 (7408 evaluable)			2nd line therapy OS N = 8280 (7764 evaluable)	
Characteristic			**OR (95% CI)**	**P-value**		**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Enrollment age – mean (SD)		59.8 (10.7)	1.11 (1.02, 1.21)	0.012	Age, per 10 yrs	0.97 (0.94,0.99)	0.005	0.99 (0.97,1.02)	0.618
Sex – no. (%)	Male	2880 (87.2)	1.15 (0.96,1.38) (Female Referent)	0.121		0.98 (0.94,1.04)	0.54	0.97 (0.92,1.02)	0.204
ECOG PS – no. (%)	0	2566 (90.4)	Referent						
	1	1815 (85.8)	1.55 (1.30,1.84)	< 0.0001		1.22 (1.16,1.28)	< 0.001	1.51 (1.43, 1.59)	< 0.0001
	> 1	115(69.7)	4.07 (2.85, 5.82)			1.59 (1.38,1.83)		3.54 (3.13,4.02)	
Metastasis	Lung	1562 (87.4)	1.03 (0.86,1.23)	0.761		1.10 (1.04,1.18)	0.003	1.08 (1.01,1.16)	0.02
	Liver	3421 (88.0)	0.90 (0.75, 1.09)	0.291		1.36 (1.28,1.45)	< 0.001	1.62 (1.52,1.74)	< 0.001
	Peritoneum	407 (88.1)	0.92 (0.68, 1.24)	0.571		1.27 (1.03,1.57)	0.025	1.42 (1.14,1.75)	0.001

7010 Poster Discussion Session; Displayed in Poster Session (Board #282), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Cumulative incidence of financial hardship in metastatic colorectal cancer patients: Primary endpoint results for SWOG S1417CD. *First Author: Veena Shankaran, Fred Hutchinson Cancer Research Center, Seattle, WA*

Background: Despite evidence that rising cancer care costs are contributing to "financial toxicity" in cancer pts, no studies, to our knowledge, have prospectively assessed the financial impact of cancer diagnosis (dx) using both self-reported and objective financial measures. S1417CD, led by the SWOG Cancer Research Network and conducted in the NCI Community Oncology Research Program (NCORP), was the first national prospective cohort study to evaluate time-to-first evidence of major financial hardship (MFH) in pts with newly diagnosed mCRC. We present results of the primary endpoint analysis. **Methods:** Pts age ≥ 18 within 120 days of mCRC dx receiving systemic treatment completed surveys every 3 months (mo) for 12 mo. MFH was defined as ≥ 1 occurrence of self-reported increase in debt, new loans, selling home, refinancing home, or ≥ 20% income decline during the 12 mo study period. Cumulative incidence (CI) of MFH was estimated to account for competing risk of death. Additional endpoints, not reported here, included quality of life, caregiver strain, and changes in credit status over 12 mo. **Results:** In total, 380 pts (median age 59.9) across 126 clinic sites were enrolled, with 377 eligible and evaluable for the primary endpoint (reached 12 mo assessment, death, or MFH endpoint); complete data were available for 92% of pts as of Jan 23, 2020. Most pts were white (78%), male (61%), and insured (98%), with annual income ≤ $50,000 (56%). Cumulative incidence of MFH at 12 mo was 71.5% (95% CI: 65.9%-76.3%), with 24.6%, 52.4%, and 61.8% at 3, 6, and 9 mo. The dominant components of MFH were new debt (12-mo CI, 56.7%) and >20% decline in income (26.7%); 104 (41%) pts reported ≥ 2 elements of MFH. In a secondary analysis excluding new debt, 12 mo cumulative incidence of MFH was 42.9% (95% CI: 37.2%-48.5%), with 10.3%, 24.4%, and 31.9% at 3, 6, and 9 mo. **Conclusions:** In a national sample of mCRC pts on systemic tx, financial hardship, most commonly in the form of increased debt, accumulates progressively over time. Nearly 3 out of 4 pts experiencing MFH at 12 mo despite access to health insurance coverage. These findings underscore the need for clinic and policy solutions such as early financial navigation and elimination of cost sharing to protect pts from financial devastation as they continue with tx. Clinical trial information: NCI-2015-01885. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology, Other Foundation, U.S. National Institutes of Health.

Cumulative incidence of MFH in mCRC.

	3 mo	6 mo	9 mo	12 mo
Any MFH n(%)	**24.6%**	**52.4%**	**61.8%**	**252 (71.5%)**
Debt	19.2%	39.7%	48.6%	56.7%
New loans	8.7%	20.1%	23.7%	25.8%
≥ 20% income decline	2.4%	6.8%	11.8%	26.7%
Refinancing home	0.3%	1.9%	2.2%	3.4%
Selling home	0.5%	1.6%	1.9%	2.6%

7011 Poster Discussion Session; Displayed in Poster Session (Board #283), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Reassessing the net health benefit (NHB) of FDA approved cancer drugs with evolution of evidence using the American Society of Clinical Oncology Value Framework (ASCO-VF). *First Author: Seanthel Delos Santos, Sunnybrook Research Institute, Toronto, ON, Canada*

Background: Regulatory approval of oncology drugs are often based on data presented in the primary publication of clinical trials (CT). However, clinically relevant data, such as long-term overall survival (OS) and quality of life (QOL), are often reported in subsequent publications. Therefore, this study aimed to evaluate the ASCO-VF NHB at the time of drug approval and over time as further evidence is published. **Methods:** All FDA approved oncology drug indications from 01/06-12/16 were reviewed to identify CTs that were scorable using the ASCO-VF version 2. Subsequent publications of included CTs relevant for scoring were identified from Web of Science with a follow-up time of 3 years from approval. Using ASCO-defined threshold scores of ≤40 for low benefit and ≥45 for substantial benefit, changes in classification of benefit were assessed at 3-years post-FDA approval. **Results:** We identified 57 FDA approved indications (40.4% OS, 59.6% progression-free survival (PFS) as primary endpoints) with scorable ASCO-VF CTs. Among those 57 indications, 36.8% at the time of FDA approval demonstrated substantial benefit, 10.5% demonstrated intermediate benefit, and 52.6% demonstrated low benefit. We then identified 96 subsequent publications relevant to scoring within 3-years of FDA approval, consisting of primary endpoint updates (29.2%; 14.6% OS, 12.5% PFS), secondary endpoint updates (44.8%; 16.7% OS, 7.3% PFS), new reporting of secondary endpoint (4.2% OS), safety updates (28.1%), and QOL reporting (43.8%). Upon reassessment of the NHB in subsequent publications, there was an overall change from initial classification of benefit in 36.8% of trials (17.5% became substantial, 8.8% became low, and 10.5% became intermediate). Changes in scores were mainly the result of an updated hazard ratio (35.1%), change in scoring endpoints from PFS to OS as per ASCO-VF endpoint hierarchy (8.8%), toxicity updates (57.9%), new tail of the curve bonus (12.3%), palliation bonus (14.0%), or QOL bonus (22.8%). Overall, at reassessment at 3 years post-FDA approval, 42.1% were substantial, 10.5% were intermediate, and 47.3% were low benefit. **Conclusions:** Only a modest proportion of FDA approved drugs have demonstrated substantial NHB at time of approval. As further evidence was published, a substantial proportion of indications have a change in classification of NHB, resulting in a small increase in the overall proportion of indications being deemed to have substantial benefit at 3 years post-approval. Research Sponsor: None.

ABSTRACT WITHDRAWN

7013 Poster Discussion Session; Displayed in Poster Session (Board #285), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Saving the best to the last: Can we wait for second-line? *First Author: Renana Barak, Institute of Oncology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel*

Background: A common perception of some oncologists is that the vast majority of their patients with metastatic disease will receive 2nd line treatment upon progression. Therefore, "saving" good treatment options for the future may be acceptable. We aimed to examine whether this perception correlates with real-life. **Methods:** Using an oncology electronic database, consisting of >27,000 patients treated at our institution, we selected consecutive patients with metastatic or locally advanced lung, colon, pancreatic, bile duct and gastric cancers who started standard 1st line, consisting of at least doublet therapy. We then assessed the correlation between proceeding to 2nd line therapy and demographic and clinical variables, including age, gender, initial BMI, hemoglobin, WBC, creatinine, glucose, calcium, as well as survival. **Results:** A total of 553 patients met the inclusion criteria. Their median age was 66 and 317 were men. Their diagnoses were colon (197), lung (129), pancreas (101), bile duct (71) and gastric (55) cancers. Only 59% received at least one course of 2nd line treatment (61.9% colon, 65.1% lung, 66.3% pancreas, 35.2% bile duct and 54.5% gastric). Probability of reaching 2nd line treatment was associated with disease site (P=0.0002) as well as with age, with patients who received 2nd line being 2.5 years younger compared to those who did not (65 vs. 67.5 years, P=0.008). No other factor, including gender, BMI or standard laboratory values at presentation could predict chances of proceeding to 2nd line, for either the whole group or by primary cancer origin. Survival of patients not starting 2nd line was also significantly shorter across all tumor types. **Conclusions:** These real-life data indicate that only 60% of patients starting standard doublet or triplet treatment for advanced cancers will commence 2nd line therapy; and this cannot be reliably predicted in advance using standard clinical and laboratory characteristics. Our data challenge the practice of saving good treatment options for subsequent lines, and call for the development of tools enabling prediction of response and tolerance to treatment, pursuing for better patient selection and patient-tailored therapy. Research Sponsor: None.

7014 Poster Discussion Session; Displayed in Poster Session (Board #286), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Going off pathway: Problem or good care? *First Author: Stephen B. Edge, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: Clinical oncology pathways (COP) provide decision support and benchmarking against national standards. Some organizations provide financial incentives for using COP-recommended treatment (on pathway: OnP). Treatment (Rx) other than COP recommended Rx (off pathway: OffP) is appropriate for some cases. There are limited data on the appropriateness of OffP Rx. This study examines rates and reasons for OffP Rx in one cancer center. **Methods:** All systemic Rx decisions entered in the ClinicalPath COP from 10/1/18 - 9/30/19 were classified as OnP (including Rx on a clinical trial) or OffP and as adjuvant/neoadjuvant therapy (ADJ) or for metastatic cancer (MET). Oncologists must provide free text reasons for OffP Rx. Records of all OffP care were reviewed by a senior nurse-led team and physician to verify and classify OffP reasons. Cases without clear documentation were referred to the treating oncologist and/or multidisciplinary team for review. Justified OffP reasons (R1-6) were classified as: R1. Documented drug toxicity and/or treatment-limiting co-morbidity; R2. Prior treatment precluding pathway Rx; R3. New drug indication or molecular targeted therapy not in COP; R4. Continuation of Rx started prior to referral; R5. Other clearly documented and reviewed provider or multidisciplinary team rationale; and R6. Patient preference. **Results:** There were 2,997 COP treatment decisions for 2,389 patients. The OnP rate was higher for ADJ than for MET Rx (87% vs. 78%). Non-justified OffP care accounted for 1% of cases. 69% of OffP Rx was because of known drug toxicity, co-morbidity limiting therapy, prior therapy precluding COP choice, and new drug indications (Table). **Conclusions:** COPs provide decision support and practice benchmarking. Lower OnP rates for MET Rx likely reflect the nuances of Rx for advanced cancer. Most OffP care was justified and appropriate. Financial incentives that focus on the percentage of COP OnP care could paradoxically harm the quality of care, especially given the high percentage of OffP decisions for reasons of drug toxicity, co-morbidity and new drug indications. Research Sponsor: None.

OVERALL and Representative cancer sites + # COP Decisions	*OnP Rate*		*Overall OffP Rate - ADJ + MET*	*Reasons for OffP Rx - % of OffP Rx*	*See methods for key to reasons*				
	Adj	Met		R1	R2	R3	R4	R5	R6
OVERALL - 2997	87%	78%	16%	44%	13%	12%	2%	11%	18%
Breast - 750	92%	80%	12%	53%	10%	16%	0	2%	19%
NSCLC - 485	83%	85%	16%	47%	10%	8%	1%	19%	14%
Colorectal - 245	96%	77%	16%	24%	16%	21%	3%	5%	32%
Gastric / Esoph - 138	89%	68%	25%	46%	11%	14%	0	17%	11%
Pancreas - 127	98%	93%	6%	43%	43%	0	0	0	14%
Melanoma - 286	88%	64%	27%	39%	11%	36%	4%	7%	4%
Myeloma - 286	78%	-	22%	52%	15%	6%	5%	3%	19%

7015 Poster Discussion Session; Displayed in Poster Session (Board #287), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Impact of utilization management policy on uptake of hypofractionated radiation in early-stage breast cancer. *First Author: Winnie Chi, Healthcore, Inc, Wilmington, DE*

Background: While hypofractionated radiation (HFR) after breast-conserving surgery is a cost-effective, patient-centered treatment in early-stage breast cancer (ESBC), less than 40% of eligible women received it in 2013. In 2016, a large commercial payer implemented a utilization management policy to encourage HFR for eligible women through denying reimbursement for extended-course radiation. We assessed the impact of the policy on HFR use and associated spending. **Methods:** We conducted a retrospective, adjusted difference-in-differences analysis using administrative claims of women continuously enrolled in 14 geographically diverse commercial health plans covering 6.9% of US adult women. The study population included women aged 18 or older with ESBC who were eligible for HFR according to 2011 guidelines from the American Society for Radiation Oncology. Women who received mastectomy, brachytherapy, or < 11 or > 40 external beam fractions were excluded. We compared HFR use and associated spending between women in fully-insured and Medicare Advantage (fully-insured) plans for whom the policy applied vs. self-insured or Medicare supplemental insurance (self-insured) plans for whom the policy did not apply. We adjusted for age, comorbidity, region, Medicare enrollment, and prior chemotherapy. **Results:** Among 10,540 eligible women, 3,619 (34%) were in fully insured plans and thus subject to the policy. There were no meaningful differences in mean age (63.8 vs. 65.0), Charlson comorbidity index (3.0 vs. 3.2), or practice setting between the fully-insured and self-insured groups. The policy was associated with an increase in HFR (4.2 adjusted percentage point difference-in-difference [ppd], 95% CI 0.0 to 8.4, p = 0.051) and a non-significant decrease in radiotherapy-associated expenditures (-$2,275, p = 0.09). Spillover analyses revealed significantly higher uptake of HFR among self-insured patients who were indirectly exposed to the policy through seeing the providers who also treated fulled insured women (8.5 adjusted ppd, 95% CI 3.6 to 13.5, p = 0.001), compared to those who were not exposed. **Conclusions:** A payer's utilization management policy was associated with direct and spillover increases in HFR use, even after accounting for a strong secular trend towards increased hypofractionation use. However, policymakers must balance the impact of this and similar policies against their additional administrative costs. Research Sponsor: None.

7016 Poster Discussion Session; Displayed in Poster Session (Board #288), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Effect of mammography screening frequency on false-positive biopsy rates and detection of local recurrence among breast cancer survivors. *First Author: Julia E McGuinness, Columbia University Irving Medical Center, New York, NY*

Background: Current guidelines recommend that women with a history of early-stage breast cancer treated with breast-conserving therapy (BCT) continue screening mammography after treatment. One strategy is semi-annual ipsilateral mammography for the first 3 years after diagnosis, when risk of local recurrence is highest. However, a potential harm of more frequent screening is false-positive breast biopsy. We examined the association between screening frequency and rates of false-positive biopsy and local recurrence among breast cancer survivors. **Methods:** We conducted a retrospective cohort study at Columbia University Irving Medical Center (CUIMC) in New York, NY, of women diagnosed with stage 0-III breast cancer from 2007 to 2017, who were treated with BCT and had at least 2 screening mammograms at CUIMC within the first 3 years after diagnosis. Demographic and clinical information were collected from the electronic health record. Frequency of mammography screening was defined as the median interval between two consecutive mammograms (every 6 months vs. yearly). False-positive biopsy and local recurrence were identified by review of breast pathology reports. A false-positive biopsy was defined as a breast biopsy without evidence of invasive or non-invasive cancer. Descriptive statistics and logistic regression models were conducted to examine relationships between covariates and either false-positive biopsy or local recurrence. **Results:** In our study cohort (n = 1404), the median age at breast cancer diagnosis was 61 years (range, 24-94), including 45% white, 14% black, 32% Hispanic, and 8% Asian. Eighty percent of women had screening mammography of the ipsilateral breast every 6 months during the first 3 years after diagnosis. Comparing women who screened every 6 months vs. yearly, there was no difference in local recurrence rates (4.0% vs. 4.1%), including screen-detected and invasive recurrences, but a higher rate of false-positive biopsy (13.5% vs. 7.5%). In multivariable analysis, women who screened every 6 months had about a 2-fold increased risk of having a false-positive biopsy (OR 1.93; 95% CI 1.17-3.19); no other factors were significantly associated with false-positive biopsy. **Conclusions:** We observed that women with early-stage breast cancer treated with BCT who underwent more frequent screening mammography had more false-positive breast biopsies, but no difference in local recurrence rates. Future studies are needed to determine optimal screening strategies for breast cancer survivors. Research Sponsor: U.S. National Institutes of Health.

7017 Poster Discussion Session; Displayed in Poster Session (Board #289), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The potential cost-effectiveness of a risk-based pancreatic cancer screening strategy in new-onset diabetes. *First Author: Naomi RM Schwartz, University of Washington, Seattle, WA*

Background: There are no established methods for pancreatic cancer (PC) screening, but the National Cancer Institute and the Pancreatic Cancer Action Network (PanCAN) are investigating risk-based screening strategies in new-onset diabetes (NOD)—a group with elevated PC risk. Preliminary estimates of the cost-effectiveness of these strategies can provide insights about potential value and inform supplemental data collection. Using data from the Enriching New-Onset Diabetes for Pancreatic Cancer (ENDPAC) risk model validation study, we assessed the potential value of CT screening for PC in those determined to be at elevated PC risk, as is being done in a planned PanCAN Early Detection Initiative (EDI) trial. **Methods:** We created an integrated decision tree and Markov state-transition model to assess the cost-effectiveness of screening those age ≥50 and with NOD for PC using CT imaging vs. no screening. PC prevalence, sensitivity, and specificity were derived from the ENDPAC validation study. PC stage distribution in the no screening strategy and PC survival were derived from SEER. Background mortality for diabetics, screening and cancer care expenditure, and health state utilities were derived from the literature. The base case assumed 40% of screen-detected PC cases were resectable, and a threshold analysis explored the fraction required for screening to be <$100,000 per QALY gained. Life years (LYs), quality-adjusted life years (QALYs), and costs were tracked over a lifetime horizon and discounted at 3% per year. Results are presented in 2019 USD, and we took a U.S. payer perspective. **Results:** In the base case, screening resulted in 0.0055 more LYs, 0.0045 more QALYs, and $305 in additional expenditure for a cost per QALY gained of $68,059 (Table). Among PC cases, screening resulted in 0.67 more LYs, 0.55 more QALYs, and $22,691 in additional expenditure. In probabilistic analyses, screening resulted in a cost per QALY gained of <$50,000 and <$100,000 in 34% and 99% of simulations, respectively. In the threshold analysis, >25% of screen-detected cases needed to be resectable for the cost per QALY gained with screening to be <$100,000. **Conclusions:** We found that risk-based pancreatic cancer screening in NOD is likely to be cost-effective in the U.S. if even a modest fraction (>25%) of screen-detected cases are resectable. Future studies should reassess the value of this intervention once PanCAN EDI data become available. Research Sponsor: Pancreatic Cancer Action Network (PanCAN) Grant.

Strategy	QALYs	Cost	Cost per QALY
Screening	14.711	$65407	
No Screening	14.706	$65102	
Difference	0.0045	$305	$68059

7018 Poster Discussion Session; Displayed in Poster Session (Board #290), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Composite grading algorithm for National Cancer Institute's PRO-CTCAE. *First Author: Amylou C. Dueck, Mayo Clinic, Scottsdale, AZ*

Background: Standard reporting of symptomatic adverse events (AEs) in oncology relies on clinicians to rate patient (pt) experience using CTCAE; each symptom is represented by a single graded item. To capture direct pt experience, NCI developed PRO-CTCAE to supplement CTCAE. In PRO-CTCAE, the pt answers up to 3 questions per AE about a symptom's frequency, severity and interference with daily activities. To align PRO-CTCAE with CTCAE, we developed an algorithm for mapping sets of questions for an AE to a single composite numerical grade. **Methods:** We used a 5-step process. (1) All 187 possible PRO-CTCAE score permutations were presented to clinical investigators to subjectively map permutations to single numerical grades (range 0-3). (2) Permutations with < 75% agreement were presented to investigator committees at a National Clinical Trials Network meeting to gain majority consensus via anonymous voting. (3) The resulting algorithm was refined via graphical and tabular approaches to assure directional consistency. (4) Validity, reliability and sensitivity were assessed in a national study dataset. (5) Accuracy for delineating AEs between study arms was measured in 2 phase III clinical trials (Alliance for Clinical Trials in Oncology A091105 and Exelixis COMET-2). **Results:** (1) 12/187 score permutations had < 75% initial agreement. (2) Majority consensus was reached for all permutations. (3) 5 mappings were adjusted to assure directional consistency. (4) Composite grades for 46/59 (78%) AEs were higher in pts with ECOG performance status 2-4 vs 0-1 (median effect size 0.23 [range -0.49-0.73]; 32/59 effect size ≥0.2; 25/59 $p< 0.05$), similar to when conducting analysis on individual unmapped items. The test-retest reliability for 24 selected composite grades ranged from 0.57-0.96 (median intraclass correlation coefficient [ICC] 0.77) with 18/24 (75%) grades having ICC ≥0.7. Median (range) standardized response means in pts reporting worsening, no change, and improvement were 0.20 (0.03-0.34), -0.06 (-0.20-0.03) and -0.12 (-0.32-0.06). (5) Pattern, directionality and statistical significance of between-arm differences in both trials were preserved with composite grades as compared to individual unmapped items. **Conclusions:** A composite grading algorithm for PRO-CTCAE was rigorously developed and validated. PRO-CTCAE composite grades may be useful in analyses to provide a single metric for each pt-reported AE for trial and real-world reporting. Support: UG1CA189823; U01CA233046; HHSN261200800043C; Bayer (A091105); https://acknowledgments.alliancefound.org. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

7019 Poster Discussion Session; Displayed in Poster Session (Board #291), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Predictive survival ability of patient-reported in comparison to physician-reported performance status in solid malignancies. *First Author: Abdulla Al-Rashdan, Tom Baker Cancer Centre, Calgary, AB, Canada*

Background: Performance status (PS) is an important prognostic tool in cancer management that is mainly generated by physicians. In oncology, the Eastern Cooperative Oncology Group (ECOG) measure is commonly used. Patient-reported functional status (PRFS) is an emerging method that allows patients to provide an estimate of their function; however, there is limited information about its prognostic significance in solid tumors. We explored the prognostic value of PRFS in comparison to ECOG on survival. **Methods:** 13,045 newly diagnosed cancer patients in Ontario, Canada, who had information from both PRFS and ECOG on the same day of an outpatient visit between March 2013 and March 2018 were included. The dataset were randomly divided into 60% training (n = 7,827) and 40% validation (n = 5,218) cohorts. Covariates were similar at baseline for both training and validation datasets. Survival was estimated by modeling clinical characteristics with PRFS, with ECOG, and alone. **Results:** PRFS and ECOG scores were statistically significant predictors of overall survival. Both higher PRFS and ECOG scores tended to be associated with inferior survival, hazard ratio (HR) = 1.71 (P < .0001), and HR = 1.90 (P < .0001) respectively. Models that included either PRFS or ECOG scores outperformed the model with baseline clinical characteristics only. C statistics were 0.836, 0.839, and 0.811 respectively. **Conclusions:** Patient-reported functional status adds to survival modeling and is equally predictive as the ECOG scale at various stages of solid malignancies. PRFS may be used instead of ECOG in clinical or research setting for survival estimation. Research Sponsor: Study done by Cancer Care Ontario that is funded by Government of Ontario.

7020 Poster Discussion Session; Displayed in Poster Session (Board #292), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Subjective cognition in chimeric antigen receptor T-cell therapy recipients. *First Author: Anna Barata, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL*

Background: Chimeric antigen receptor T-cell (CAR-T) therapy can lead to durable responses in chemorefractory patients with hematologic malignancies. CAR-T, however, can be associated with neurotoxicity. There is a significant body of literature describing patient-reported concerns with cognition in hematopoietic cell transplant (HCT) recipients, a similar treatment group. However, little is known about subjective cognition in CAR-T patients. This study examined changes in subjective cognition over time in CAR-T recipients and compared their outcomes with allogeneic HCT recipients. **Methods:** At baseline and 90 days after infusion, participants completed the Everyday Cognition Questionnaire (ECog). The ECog provides scores for total cognition, memory, language, visuospatial abilities, planning, organization, divided attention, and satisfaction with cognition. Comparison data from allogeneic HCT recipients came from a previous observational study. Linear mixed models compared changes in subjective cognition between recipients of CAR-T and allogeneic HCT over time. Models were adjusted by age, marital status, education, and Karnofsky performance status. **Results:** Participants were 111 CAR-T recipients (mean age 60 years, 37% female) and 190 allogeneic HCT recipients (mean age 53, 42% female). Linear mixed models indicated CAR-T recipients' subjective cognition didn't change within the 90 days after infusion (p's > .05). At baseline, there were no group differences between CAR-T and allogeneic HCT recipients in subjective cognition (p's > 0.05). Over time, however, subjective cognition between groups differed. Specifically, CAR-T recipients reported stable subjective cognition whereas allogeneic HCT recipients reported worsening total subjective cognition (p = 0.04), memory (p = 0.02), visuospatial abilities (p = 0.01), planning (p = 0.01), and divided attention (p = 0.01). At follow-up, CAR-T recipients reported better total subjective cognition (p < 0.01), memory (p < 0.01), language (p = 0.01), visuospatial abilities (p < 0.01), planning (p < 0.01), and divided attention (p < 0.01) than allogeneic HCT recipients. **Conclusions:** Despite the neurotoxicity associated with CAR-T, patients can expect to perceive similar subjective cognition at day 90 compared to baseline. Future studies should also evaluate objective cognition in CAR-T recipients. Research Sponsor: U.S. National Institutes of Health, 2017 Moffitt Team Science Award.

7021 Poster Session (Board #293), Fri, 8:00 AM-11:00 AM

Global perspectives on clinical cancer research: A comparison of randomized controlled trial (RCT) design and outcomes across high income and low-middle income countries. *First Author: Connor Wells, Queen's University, Kingston, ON, Canada*

Background: Cancer clinical trials have become increasingly international in scope. There are limited data regarding trial variation based on the economic status of the country in which they are conducted. Here we describe trial characteristics, design, and results of all RCTs published globally during 2014-2017. **Methods:** A structured literature search was designed using PUBMED to identify all RCTs evaluating anti-cancer therapies published during 2014-2017. Data captured included authorship, participants, study characteristics, design, and results. RCTs were classified based on the World Bank country-level economic classification of the first author [low-middle/upper-middle income countries (LMIC) and high-income countries (HIC)]. Among superiority RCTs that met the primary endpoint (i.e. statistically "positive"), we calculated the ESMO-MCBS to identify trials with substantial clinical benefit (MCBS scores 4/5 or A/B). Outcomes were compared with Chi Square or Fisher's Exact tests. **Results:** The study cohort included 694 RCTs; 636 (92%) were led by HIC and 58 (8%) were led by LMIC. Compared to LMIC, RCTs in HICs were more likely to be funded by industry [73% vs 41%, $p<0.001$] and more likely to test novel systemic therapies [87% vs 78%, p=0.027]. LMIC studies were typically smaller (median N=220 vs N=474 participants, $p<0.001$) and more likely to meet their primary endpoints [66% vs 44%, p=0.002]. In "positive" superiority trials, the effect size was larger in LMICs compared to HICs (median HR 0.62 vs HR 0.84, $p<0.001$). The proportion of trials identifying treatments with substantial clinical benefit (ESMO MCBS 4/5/A/B) was 45% (LMIC) and 31% (HIC, p=0.291). Studies from LMIC were published in journals with lower impact factors (IF) (median IF 7 vs 21, $p<0.001$); a publication bias persisted when adjusted for whether a trial was positive or negative: median IF LMIC negative trial=5 vs HIC negative trial=18 ($p<0.001$); median IF LMIC positive trial=9 vs HIC positive trial= 26 ($p<0.001$). **Conclusions:** Only a small minority of oncology RCTs are led by investigators in LMIC; these trials are less likely to be funded by industry and more likely to meet their primary endpoint. "Positive" RCTs from LMIC identify therapies with a substantially larger effect size than HIC. These data identify a substantial publication bias against RCTs conducted in LMIC. Research Sponsor: None.

7022 Poster Session (Board #294), Fri, 8:00 AM-11:00 AM

Videos improve patient understanding of misunderstood chemotherapy terms in a rural population. *First Author: Eli Rowe Abernethy, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: Rural communities can have low health literacy, which impacts the adequacy of informed consent, adherence to treatment, and outcomes. We had previously created and tested educational videos about basic chemotherapy terminology for use in an underserved population at our inner-city hospital. This study aimed to determine if these videos increased understanding of these terms in rural communities. **Methods:** Through patient and provider interviews in an underserved urban setting, 20 basic cancer treatment terms were identified as frequently misunderstood. As a pilot, 6 of these terms were explained in short, animated one-minute videos using VideoScribe (Sparkol).To determine if these videos improved understanding in the rural setting, 50 rural patients, specified as patients living in a county ranked 4-9 on the USDA Rural Urban Continuum Code (RUCC) scale, were asked to define each term before and after viewing the video. All answers were audiotaped and double coded for correctness of definition pre and post video screening, using the video definition as the correct definition. Before video and after video correct definition rates were calculated, along with 95% exact binomial confidence intervals using the Clopper-Pearson method. The videos for all 20 terms can be viewed on CancerQuest (https://www.cancerquest.org/media-center/videos/cancer-treatment-terms). **Results:** Participants were mostly white (79%), female (52%), resided in the more rural counties RUCC ranked 6-9 (62%), had < a high school degree (56%) and had a family income of <$40K (59%). **Conclusions:** Improving health literacy is a critical component in improving care. Our study establishes that a simple and easily disseminated intervention can significantly increase patient understanding of basic chemotherapy terminology in a rural setting. Research Sponsor: U.S. National Institutes of Health, Research reported in this publication was supported in part by the Biostatistics and Bioinformatics Shared resource of Winship Cancer Institute of Emory University and NIH/NCI under award number P30CA138292. The content is solely the responsibility of the.

The percentages of patients who provided correct definitions pre and post video intervention.

Term	Before – Rate (95% CI)	After – Rate (95% CI)	McNemar p-value
Cancer	32% (20% – 47%)	76% (62% – 87%)	<0.001
Chemotherapy	52% (37% – 66%)	84% (71% – 93%)	<0.001
Palliative chemotherapy	10% (3% – 22%)	76% (62% – 87%)	<0.001
Curative treatment	35% (22% – 50%)	76% (62% – 87%)	<0.001
Blood count	55% (40% – 69%)	90% (78% – 97%)	<0.001
Risk of infection	54% (39% – 68%)	82% (69% – 91%)	<0.001

7023 Poster Session (Board #295), Fri, 8:00 AM-11:00 AM

Project facilitate: A review of the FDA oncology center of excellence expanded access pilot program. *First Author: Natasha L Kormanik, U.S. Food and Drug Administration, Silver Spring, MD*

Background: Expanded Access (EA), also known as "compassionate use," is a regulatory pathway in which a patient with an immediate life-threatening condition or disease can gain access to an investigational product for treatment when no satisfactory therapy is available. Oncology practices may lack the regulatory experience or administrative support to use EA. In response, FDA OCE launched Project Facilitate (PF), a call center to assist oncology healthcare providers requesting EA. An analysis of single-patient investigational new drugs (IND) was performed to assess the first 10 months of PF compared to the period prior to its launch. **Methods:** Preliminary data was extracted from the FDA's central database that yielded 719 single-patient INDs between May 31-November 30, 2018 & 2019 in the Office of Oncologic Diseases (OOD). Data collected included IND receipt date, acknowledgment date, application status, drug name, underlying malignancy of patient, address of requesting physician, withdrawal date, and patient demographics. A manual review of INDs was performed to assess for actual processing dates and to capture demographics not captured by the database. A total of 28 INDs were excluded due to duplications, cancellation by Sponsor prior to issuance of FDA decision, or coding errors in the database. Industry denial explanations were reported by the provider by emails. **Results:** Data from 692 INDs were analyzed and 692 (100%) were granted safe to proceed. The median processing time was 1.5 days (mean = 2) in 2018 and 0.5 day (mean = 0.5) in 2019. Our findings indicate that the volume of oncology EA requests increased by 76 (19%) in 2019 vs 2018. A total of 207 unique drugs were requested. Malignancies most frequently involved included: Acute myeloid leukemia (n = 84, 8.3%), soft tissue sarcoma (n = 77, 7.6%), and non-small cell lung cancer (n = 60, 5.9%). States with the highest requests included: California (n = 82, 11.8%), New York (n = 81, 11.7%), and Massachusetts (n = 42, 6.1%). A majority of requests were from major academic centers (77%). All denied requests (N = 9) by industry were due to company's decision to not provide products outside of a clinical trial. **Conclusions:** The positive trends in decreased processing times and increased number of requests are consistent with OCE's mission to improve efficiency of the EA program and ensure equitable access to all oncology patients. Research Sponsor: None.

Demographics		OOD EA Requests n (%)
Age (N = 563)	< 2	29 (5.2%)
	3-11	49 (8.7%)
	12-17	31 (5.5%)
	18-54	184 (32.7%)
	55-64	102 (18.1%)
	> 65	168 (29.8%)
Gender (N = 626)	Male	322 (51.4%)
	Female	304 (48.6%)

7024 Poster Session (Board #296), Fri, 8:00 AM-11:00 AM

Breast and cervical cancer screening disparities among transgender patients. *First Author: Oluwadamilola Temilade Oladeru, Harvard Radiation Oncology Program, Boston, MA*

Background: Over a million Americans identify themselves as transgender and this population is growing. Transgender status was a pre-existing condition prior to the Affordable Care Act (ACA), and transgender individuals faced unique disparities in gender-specific cancer screening in part due to discrimination in health insurance coverage. Modern literature for transgender adults' adherence to cancer screening is limited. To fill this knowledge gap, we conducted a cross sectional study to investigate transgender individuals' self-reported adherence to cancer screening and access to primary care compared to cisgender individuals. **Methods:** The Behavioral Risk Factor Surveillance System database was queried for transgender (either male-to-female [MTF] or female-to-male [FTM]) and cisgender adults from 2014-2016 and 2018. Primary endpoints were adherence to breast and cervical cancer screening guidelines and access to primary health care. Those with prior hysterectomy, breast and cervical cancer were excluded. Multivariable logistic regression was performed to evaluate the association of transgender status with cancer screening and healthcare access, after adjusting for demographic characteristics and survey weights. **Results:** A total of 219,665 and 206,446 participants were eligible for breast and cervical cancer screening, respectively. Of those, 614 (0.28%) and 587 (0.29%) transgender participants were eligible for each cancer screening type, respectively, representing a weighted estimate of nearly 200,000 transgender participants total. When compared to cisgender counterparts, transgender participants were less likely to adhere to breast cancer screening (FTM: OR 0.47, $p < 0.001$; MTF: OR 0.04, $p < 0.001$) and to have received any breast cancer screening (FTM: OR 0.32, $p < 0.001$; MTF: OR 0.02, $p < 0.001$). Similarly, FTM participants were less likely to adhere to cervical cancer screening (OR 0.42, $p < 0.001$) and to have received any cervical cancer screening (OR 0.26, $p < 0.001$). In addition, transgender participants were more likely to have no primary care physician (FTM: OR 0.79, $p < 0.001$; MTF: OR 0.58, $p < 0.001$) and to be unable to see a physician when needed within the past year due to medical cost (FTM: OR 1.44, $p < 0.001$; MTF: OR 1.36, $p < 0.001$). **Conclusions:** Despite the implementation of the ACA, limited primary care access and poor adherence to breast and cervical cancer screening are evident for transgender populations. Further research efforts to improve the utilization of preventive cancer services are needed for this underserved population. Research Sponsor: None.

7025 Poster Session (Board #297), Fri, 8:00 AM-11:00 AM

Racial disparities in immune-related adverse events (irAE) of immune checkpoint inhibitors (ICPi) and association with survival based on clinical and biochemical responses. *First Author: Monica Peravali, MedStar Washington Hospital Center, Washington, DC*

Background: ICPi cause various irAE with thyroid dysfunction as a commonly reported abnormality. There is increasing evidence showing positive association with development of irAE and survival. However, prior trials with ICPi had underrepresentation of minorities with <5% African Americans (AA). **Methods:** We retrospectively reviewed patients (pts) with stage IV solid malignancies treated with PD1/PDL1 blockers between 1/2013-12/2018 across MedStar Georgetown Cancer Institute facilities. Pts treated with CTLA-4 inhibitors were excluded. Progression free survival (PFS) and overall survival (OS) were primary endpoints and were calculated using Kaplan-Meier methods and Wilcoxon rank sum test for comparison. **Results:** 293 pts met eligibility criteria. 91 pts (31%) had any grade irAE; most common AE were endocrine (40.7%) specifically TSH elevation, dermatological (23.1%) and rheumatologic (18.7%). Proportion of irAE was significantly higher in Caucasians versus AA (60.4% vs 30.8%), in pts with low PDL1, lower LDH, older age, and those who had more treatment cycles with ICPi. Rate of progression was lower in pts with irAE (30.8% vs 46.0%, p-0.0140). Median PFS (5.8 vs 3.0 months (mo), p- 0.0204) and OS (17.1 vs 7.2 mo, p value- <0.0001) were higher with irAE. Statistically significant difference in OS (17.1 vs 8.6 mo, p- 0.0002) but not in PFS (5.8 vs 3.3 mo, p: 0.0545) was noted with endocrine irAE. No differences in survival were observed among other commonly reported irAE. Differences in survival among subgroups of pts with irAE are detailed in table. **Conclusions:** Development of irAE positively correlated with improved PFS and OS as reported in previous studies. To our knowledge, this is the first study observing differences in OS favoring endocrine AE and Caucasian race. These factors may be potential surrogate markers of prognosis pending replication of these results in large-scale studies. Research Sponsor: None.

		Overall N (%)	irAE N (%)	irAE Median PFS (mo)	P value	irAE Median OS (mo)	P value	Endo irAE N (%)	Endo irAE Median PFS (mo)	P value	Endo irAE Median OS (mo)	P value
Gender	Female	129 (44)	41 (45.1)	6.3	0.8977	16.3	0.4756	18 (48.7)	7.7	0.8542	17.0	0.9495
	Male	164 (56)	50 (54.9)	5.7		18.5		19 (51.4)	5.7		17.0	
Race	White	140 (47.8)	55 (60.4)	7.7	0.4601	20.6	0.0237	23 (62.2)	10.4	0.2243	21.8	0.0356
	Black	122 (41.6)	28 (30.8)	5.8		12.9		13 (35.1)	5.2		15.8	
	Others	31 (10.6)	8 (8.8)	2.2		16.0		1 (2.7)			6.2	
PDL1 Expression	<50%	69 (23.5)	16 (17.6)	5.2	0.6985	14.2	0.6468	3 (25.0)	5.2	1.000	16.5	1.0000
	>50%	32 (10.9)	14 (15.4)	6.3		16.6		9 (75.0)	6.3		15.8	

7026 Poster Session (Board #298), Fri, 8:00 AM-11:00 AM

Health insurance status and cancer stage at diagnosis and survival in the United States. *First Author: Jingxuan Zhao, American Cancer Society, Atlanta, GA*

Background: While previous studies demonstrated associations between Medicaid coverage or no health insurance with both advanced stage at cancer diagnosis and worse survival, access to health care in the U.S. has changed substantially in the past decade. This study examined associations of health insurance status with stage at diagnosis and survival among 17 common cancers using recent national data. **Methods:** We identified 1,427,532 cancer patients aged 18-64 years newly diagnosed with 17 common cancers from the 2010-2013 National Cancer Database. Multivariable logistic regression models were used to examine the distribution of stage at diagnosis by health insurance status (private, Medicare, Medicaid, dual Medicare/Medicaid, and uninsured) overall and for each cancer site. Cox models compared stage-specific survival by health insurance for each site. **Results:** Compared to privately insured patients, Medicaid and uninsured patients were significantly more likely to be diagnosed with advanced-stage cancer (III/IV) for all the 17 cancers combined (adjusted odds ratio [AOR]: 2.27, 95% confidence interval [95CI]: 2.24-2.29; AOR: 2.39, 95CI: 2.36-2.42, respectively) and for all included cancer sites separately. Medicare and Medicare-Medicaid patients were also more likely to be diagnosed at advanced-stage for all the 17 cancers combined, but results varied by cancer site. Compared to the privately insured patients, worse survival was observed for patients with all other insurance types and uninsured at each stage for all the 17 cancers combined and most cancer sites. For example, among patients diagnosed at stage I, adjusted mortality hazard ratios for Medicare, Medicaid, Medicare-Medicaid, and uninsured patients were 1.72 (95CI: 1.70-1.75), 1.73 (95CI: 1.71-1.76), 2.07 (95CI: 2.02-2.17) and 1.56 (95CI: 1.53-1.58), respectively, compared with privately-insured patients. **Conclusions:** Patients with non-private insurance were more likely to be diagnosed with cancer at advanced stage and have worse survival. Improving access to health insurance with adequate coverage is crucial for receiving appropriate cancer screening, diagnosis, and quality care. Research Sponsor: None.

7027 Poster Session (Board #299), Fri, 8:00 AM-11:00 AM

Effect of shorter time to treatment on survival in rural patients with breast cancer. *First Author: Suneel Deepak Kamath, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH*

Background: Rural cancer care in the United States has unique challenges from variable access to care. This study examined differences in time to first treatment (TTT), a potential surrogate for access, and predictors of overall survival (OS) between rural and non-rural patients with breast cancer. **Methods:** Women with stage I-III breast cancer from 2004-2012 in the National Cancer Database of Commission on Cancer (CoC)-accredited facilities were included and categorized as rural and non-rural. Differences in demographic, disease and treatment characteristics, socioeconomic factors and TTT (< 4 weeks, 4-8 weeks and > 8 weeks) between rural and non-rural patients were assessed by Chi-square test. The effect of age, insurance status, cancer center type, community median income, community % no high school, and TTT on OS were assessed using univariate and multivariate Cox models. **Results:** The study included 1,205,031 patients, 18,417 (2%) of whom were rural. Compared to non-rural patients, rural patients were more likely to be age > 65, Caucasian, receive care at non-academic centers, have government insurance, have lower income and less education ($p < 0.0001$ for all). Significant demographic and socioeconomic differences are shown in Table. Rural patients had shorter mean TTT (3.72 vs. 4.35 weeks, $p < 0.0001$). More rural patients had TTT < 4 weeks (67% vs. 57%) and < 8 weeks (94% vs. 90%), $p < 0.0001$ for both. Shorter TTT (both < 4 weeks vs. 8 weeks and 4-8 weeks vs. > 8 weeks) was associated with improved OS (HR: 0.84, 95% CI: 0.82-0.86, $p < 0.0001$ and HR: 0.82, 95% CI: 0.81-0.83, $p < 0.0001$, respectively). After adjusting for demographic, socioeconomic, disease stage and treatment factors, rural status was associated with significantly better OS compared to non-rural status (HR: 0.92, 95% CI: 0.89-0.96, $p < 0.0001$). **Conclusions:** Despite several adverse socioeconomic factors, rural patients with breast cancer with access to CoC-accredited facilities had significantly shorter TTT and better OS compared to non-rural patients. These data suggest improving TTT can mitigate disparities in rural cancer care. It is unclear whether our data apply to non-CoC-accredited facilities in rural United States. Research Sponsor: None.

Characteristic	Rural	Non-Rural	P value
Age > 65	45%	40%	< 0.0001
Race			
Caucasian	91%	85%	< 0.0001
African American	6%	11%	
Other	2%	3%	
Academic Center	15%	28%	< 0.0001
Private vs. Government Insurance	43% vs. 53%	53% vs. 43%	< 0.0001
Community Median Income < $38,000	42%	15%	< 0.0001
% No High School Degree ≥ 13%	61%	38%	< 0.0001
Time to Treatment (weeks)	3.72	4.35	< 0.0001

7028 Poster Session (Board #300), Fri, 8:00 AM-11:00 AM

Geographic and demographic disparities in breast cancer outcomes: A population-based study. *First Author: Rohit Gosain, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: Breast cancer (BC) is one of the leading causes of cancer-related mortality worldwide, with over 2 million new cases diagnosed each year. Area of residence has been shown to affect survival, but its impact on BC is unknown. The purpose of this study is to address the potential disparities in BC outcomes between the urban area (UA) and rural area (RA). **Methods:** We obtained data based on BC patients' (pts) area of residence; UA vs RA, using the Surveillance, Epidemiology, and End Results (SEER) database treated from 1975-2016. Different socio-demographic variables and tumor characteristics (cts) from both groups were analyzed. Disease specific survival (DSS) and overall survival (OS) were analyzed by Kaplan-Meier methods. Multivariable analyses were conducted using Cox regression models. **Results:** A total of 99,339 and 872,742 pts were analyzed from RA and UA respectively. Pt cts, including age, sex, marital status, insurance status were similar across both RA and UA. There were a higher number of Black and Hispanic pts in the UA compared to RA. A total of 264,191 pts had receptor subtype data available. A slightly higher percentage of triple negative BC (TNBC) pts was seen in the RA compared to UA (13.5% v 12.7%) whereas UA had a higher percentage of HER2+ BC (18% v 17.3%). There were 95.4% early/locally advanced (stage I-III) and 4.6% metastatic pts. UA pts had significantly improved DSS and OS regardless of stage, grade or other tumor cts compared to RA pts. When stratified by receptor subtype, UA had significantly improved DSS and OS in hormone positive (HR+) (OS HR of 0.86; DSS HR of 0.87; $p < 0.05$) and HER2+ pts (OS HR of 0.87; DSS HR of 0.83; $p < 0.05$). However, there were no significant differences seen between UA and RA pts with TNBC. **Conclusions:** To our knowledge, this is the first study to report BC outcomes based on geographic disparities. Interestingly, HR+ and HER2+ UA pts had better outcomes than RA pts, whereas TNBC pts had similar survival regardless of residence area. Perhaps this disparity is partly due to the longer duration of treatment needed with hormonal therapy in the adjuvant setting making compliance an important factor to take into account in RA pts, in addition to complicated decision making with upcoming data in HER2 + cancer in the early stage setting. Access to healthcare, differences in surgical and systemic approaches of pt care, management of treatment-related toxicities and environmental factors are all potential factors that may affect outcomes in BC pts. Based on the above data, further studies are needed to further evaluate and reduce such disparities. Research Sponsor: None.

7029 Poster Session (Board #301), Fri, 8:00 AM-11:00 AM

Socioeconomic disparities in *MGMT* promoter methylation testing for glioblastoma patients. *First Author: Bryan Iorgulescu, Dana-Farber Cancer Institute, Boston, MA*

Background: *MGMT* promoter methylation holds important prognostic and predictive implications for glioblastoma (GBM) patients. Herein we evaluate whether any barriers faced *MGMT* testing. **Methods:** Adults with newly-diagnosed GBMs were identified from the U.S. National Cancer Database (2010-2016). Patient socioeconomic, tumor, and cancer program features were evaluated for association with *MGMT* testing by multivariable logistic regression. **Results:** Of 12,380 GBM patients, only 57% had *MGMT* testing–a rate that increased to 74% by 2016. Testing was independent of patients' sex or race/ethnicity (all $p > 0.05$); and was largely independent of GBM histology, size, and location. Older patients were less likely to receive testing (54% of ≥70-years-olds vs 62% of those in their 40s, $p = 0.01$). Insurance status was an independent predictor of testing: only 43% of uninsured patients had testing, vs 61% of privately-insured or 55% of Medicare patients ($p \leq 0.01$). The uninsured rate dropped from 3.6% in 2010 to 2.5% in 2016 and was associated with Medicaid expansion under the Affordable Care Act. Patients from non-expansion states had the lowest rates of testing (55%), vs patients from expansion states (58%, $p < 0.001$). Additionally, household incomes were independently associated with testing: only 50% of patients living in the poorest quartile of households had testing vs 61% in the richest quartile ($p = 0.001$). Diagnosing hospital type was also an independent predictor of testing: patients diagnosed at academic/NCI-designated cancer programs were most likely to have testing (65%), vs only 45% of community and 44% of comprehensive community cancer program patients were provided testing (all $p < 0.001$). By 2016, testing rates had improved in all program types–particularly at comprehensive community (67%) and academic (80%) programs, but lagged at community programs (56%, $p < 0.001$). Patients without *MGMT* testing received less chemotherapy (mOR = 0.66, $p < 0.001$) and were associated with worse overall survival (mHR = 1.08, $p = 0.002$). **Conclusions:** Newly-diagnosed GBM patients in the U.S. who were uninsured, from the poorest quartile of households, or diagnosed at community cancer programs faced significant barriers to receiving *MGMT* testing. Medicaid expansion under the ACA was associated with reduced uninsurance, increased Medicaid insurance, and improved rates of testing. Reduced testing rates were associated with less chemotherapy and worse OS. Together our results indicate that substantial socioeconomic and care setting disparities exist in *MGMT* testing for GBM patients. Research Sponsor: None.

7030 Poster Session (Board #302), Fri, 8:00 AM-11:00 AM

Association between Medicaid expansion status and metastatic disease at diagnosis in patients with melanoma. *First Author: Jesus C. Fabregas, Harvard TH Chan School of Public Health, Boston, MA*

Background: The Affordable Care Act (ACA) expanded Medicaid coverage in 2010. It is unknown what impact the ACA expansion has had on a timely diagnosis for patients with melanoma. We hypothesize Medicaid ACA expansion has decreased the odds of being diagnosed with Stage IV melanoma. **Methods:** The National Cancer Database was queried. Analysis was restricted to patients diagnosed (dx'd) in or after 2010. Stage IV dx was the outcome variable. Predictors were dx'd at an already expanded ACA state (ES) or not (NES). Covariates were age, race, sex, education status, income, rural setting, and Charlson comorbidity index. Univariate and Multivariate analyses were performed using logistic regression (table). The outcome model was adjusted using a generated Propensity Score as a continuous variable. An interaction term was used to evaluate for effect modification of ES on the association between race and Stage IV. **Results:** 219,475 patients diagnosed in 2010 or later were included. Median age was 62 years. By Univariate analysis, NES, age >= 65, black race, male sex, lower educational and income level, rural area, and a higher Charlson score were significantly associated with increased odds of being dx'd with Stage IV melanoma (all $p < 0.001$). By Multivariate Analysis, these associations persisted except for rural area and age. After adjusting for propensity score, ES patients were 9% less likely to be diagnosed with Stage IV melanoma as compared with NES patients (OR = 0.91 $p < 0.001$; 95% CI 0.867 – 0.959). ACA expansion status was an effect modifier on the association between race and late diagnosis ($p = 0.004$ for interaction term). For NES patients, black race had 3.26 odds ($p < 0.001$ 95% CI 2.56 – 4.18) of being diagnosed with Stage IV as compared with white patients. The odds dropped to 1.76 (p 0.004; 95% CI 1.20 – 2.57) for ES patients. **Conclusions:** ES patients were less likely to be diagnosed with Stage IV melanoma as compared to NES patients. Medicaid expansion decreased the likelihood for black patients to be diagnosed with Stage IV as compared with whites. This suggests Medicaid expansion improves access to care and earlier diagnosis of melanoma and decreases racial gaps. Research Sponsor: None.

Multivariate model.

	OR	95% CI	P
Expansion/No	0.91	0.87 – 0.96	< 0.001
Age > = 65/ < 65	0.91	0.86 – 0.95	< 0.001
Black/White	2.67	2.17 – 3.27	< 0.001
Male/Female	1.60	1.52 – 1.69	< 0.001
Education (Vs > 17.5% dropout rate) < 6.3%	0.60	0.54– 0.66	< 0.001
Income (Vs < $40,227) > = $63,333	0.79	0.72 – 0.88	< 0.001
Metro/Rural	1.01	0.86 – 1.20	0.874
CCI 1/0	1.57	1.47– 1.68	< 0.001
2/0	2.40	2.15 – 2.69	< 0.001
+3/0	3.20	2.75 – 3.72	< 0.001

7031 Poster Session (Board #303), Fri, 8:00 AM-11:00 AM

Disparities by race, socioeconomic status, and insurance type in the receipt of NCCN guideline concordant care for select cancer types in California. *First Author: Kiran Clair, University of California Irvine Medical Center, Orange, CA*

Background: There are a limited number of studies that have evaluated the association between National Comprehensive Cancer Network (NCCN) guideline adherence and survival across different cancers. We aim to assess the relationship between race/ethnicity, socioeconomic status (SES), insurance type and the receipt of NCCN guideline concordant cancer care and survival. **Methods:** This is a retrospective population-based cohort study of patients with 7 types of invasive cancer using the California Cancer Registry. Adherence with NCCN guidelines was defined by appropriate surgical, radiation, and chemo- or hormonal therapies. Multivariate logistic regression was used to evaluate the relationship between the patient, insurance type, tumor, and guideline adherence. Disease-specific survival analysis was performed using multivariate proportional hazards model. **Results:** A total of 543,198 patients were identified with invasive cancer between 2004-2017 (cases by disease type: breast 189,311, prostate 156,502, colon 80,102, liver 25,857, gastric 22,066, ovary 22,551, and cervix 16,691). The proportion of patients receiving NCCN guideline-concordant care varied by disease type. Non-concordant guideline treatment was associated with increased disease-specific mortality across all cancer types: breast (HR 1.28, 95%CI 1.23-1.33), prostate (HR 1.31, 95%CI 1.22-1.41), colon (HR 1.73, 95%CI 1.67-1.78), liver (HR 2.52, 95%CI 2.42-2.63), gastric (HR 2.38, 2.28-2.49), ovary (HR 1.32, 95%CI 1.26-1.38), and cervical cancer (HR 1.17, 95%CI 1.08-1.26). In multivariate models, compared to White, black patients were less likely to receive guideline concordant care for breast (OR 0.88, 95%CI 0.84-0.92), prostate (OR 0.90, 95%CI 0.86-0.93), colon (OR 0.85, 95%CI 0.79-0.92), and ovarian cancer (OR 0.71, 95%CI 0.62-0.82). Compared to Managed care insurance patients, Medicaid payer status was also associated with lower guideline concordant care for breast (OR 0.81, 95%CI 0.78-0.84), prostate (OR 0.91, 95%CI 0.86-0.97), colon (OR 0.70, 95%CI 0.65-0.75), gastric (OR 0.69, 95%CI 0.63-0.75), and liver cancer (OR 0.66, 95%CI 0.61-0.72). **Conclusions:** Less than half of cancer patients received NCCN guideline concordant care. There was an incremental relationship observed between SES and the likelihood of receiving guideline concordant care. Patients receiving non-guideline concordant care had worse disease-specific survival. Research Sponsor: None.

7032 Poster Session (Board #304), Fri, 8:00 AM-11:00 AM

The impact of census-tract socioeconomic status on survival in stage III colon cancer. *First Author: Amina Dhahri, University of Maryland Capital Regional Health, Cheverly, MD*

Background: Socioeconomic status (SES) has been associated with worse outcomes in stage III colon cancer. However, these studies have used large geographic areas (zip codes or counties) as a proxy for SES which may bias results. To overcome this challenge, we used a national database with census-tract level SES to assess the impact on cancer-specific (CSS) and overall survival (OS). **Methods:** Using the SEER Census-Tract Dataset from 2004-2015, we identified 8th edition AJCC stage III colon adenocarcinoma patients who underwent curative-intent surgery and initiated adjuvant chemotherapy. The predictor variable was census-tract level SES, consisting of 7 variables such as income, housing, and education. SES was analyzed as quartiles. Statistical analysis included chi square tests for association and Kaplan-Meier and Cox regression for survival analysis. **Results:** We identified 27,222 patients who met inclusion criteria. Lower SES was associated with younger age, Black or Hispanic race/ethnicity, Medicaid or uninsured status, higher T stage, <12 lymph nodes examined and lower grade tumors. Median CSS was not reached; the 25th percentile CSS time was 54 months for the lowest SES (LSES) quartile and 80 months for the highest (HSES). Median OS was 113 months for LSES and not reached for HSES. The 5-year CSS rate was 72.4% for the LSES quartile compared to 78.9% in the HSES ($p<0.001$). The 5-year OS rate was 66.5% for LSES and 74.6% in the HSES ($p<0.001$). After adjusting for potential confounders (age, sex, race, insurance, pathologic T and N stage and grade), LSES was associated with increased cancer-specific death relative to the HSES (HR 1.22; 95% CI [1.114-1.327]) **Conclusions:** This is the first study to evaluate CSS and OS in a national cohort of stage III colon cancer patients using a granular, standardized measure of SES. Despite receipt of guideline-based treatment, low SES remained a predictor of increased cancer-specific mortality. These data suggest that investigating treatment barriers beyond adjuvant therapy is needed to address colon cancer survival disparities. Research Sponsor: None.

Relative hazard of death: multivariable cox proportional regression for cancer-specific survival for stage III colon cancer

	Hazard Ratio	95% Confidence Interval		p-value
Highest SES (80th Percentile)	1.000	-	-	-
Higher SES (60th percentile)	1.178	1.087	1.277	<0.001
Middle SES (40th Percentile)	1.170	1.079	1.269	<0.001
Lower SES (20th Percentile)	1.181	1.088	1.283	<0.001
Lowest SES (0th Percentile)	1.212	1.111	1.322	<0.001

Model adjusted for age, sex, race, insurance status, grade, and pathologic T and N stage

7033 Poster Session (Board #305), Fri, 8:00 AM-11:00 AM

A randomized controlled trial of a self-administered, online decision-aid ("Navya Patient Preference Tool") to reduce decisional conflict in women with early breast cancer. *First Author: Shalaka P Joshi, Tata Memorial Centre, Mumbai, India*

Background: Shared decision making to confront choices with clinical equipoise, has been the privilege of those patients with access to time intensive consults with oncologists. We conducted a randomized controlled trial for breast cancer patients to use an online, self-administered, out-of-the-medical-encounter decision aid (DA) to choose between breast conserving surgery (BCS) and mastectomy. **Methods:** Navya Patient Preference Tool (Navya PPT) is a multilingual DA based on adaptive conjoint analysis of tradeoffs between cost, adverse effects of radiation, and breast conservation. Prior analysis established high internal reliability and external validity of the Navya PPT. Eligible cT1/2, cN0 breast cancer patients planned for surgery were block randomized, in 1:1:1 ratio, to receive the research questionnaire (RQ) to measure decisional conflict on choice of surgery (control, arm 1), Navya PPT followed by RQ (experimental, arm 2) or Navya PPT followed by RQ administered with key male family member (experimental, arm 3). Groups were stratified with respect to age, socio-economic status (SES) and educational level. The study was powered to detect a decrease in Decisional Conflict Index (DCI) by 0.25 (β-0.8, two sided α- 0.01). **Results:** Between June 2017 and December 2019, 247/255 patients were randomized to arm 1 (83), arm 2 (84), and arm 3 (80). Median age was 48 years (IQR 23-76), and median pT size was .5 cm (0.5-6 cm). 59% of patients were middle or lower SES and 46.2% had $\leq$ 12th grade education. DCI was significantly reduced in arm 2 as compared with arm 1 (1.34 vs. 1.65, Cohen's d 0.49 ($\pm$ 0.31) $p<0.05$) as well as in arm 3 as compared with arm 1 (1.30 vs. 1.65, Cohen's d 0.54 ($\pm$ 0.31) $p<0.05$). 80% ($\pm$ 6%) of patients underwent surgery of choice as determined by Navya PPT. BCS rate was similar in all three arms (85.2, 88.9 and 86.5% respectively (p=0.779). **Conclusions:** Online, self-administered, adaptive DAs used out of the medical encounter can reduce decisional conflict and increase access to shared decision making for every patient; especially in practices with low doctor to patient ratios. Clinical trial information: IEC/0116/1619/001. Research Sponsor: Intramural Institutional Funding.

7035 Poster Session (Board #307), Fri, 8:00 AM-11:00 AM

Impact of the affordable care act and early Medicaid expansion on head and neck cancer mortality in the United States. *First Author: Nosayaba Osazuwa-Peters, Saint Louis University School of Medicine, St. Louis, MO*

Background: Medicaid expansion has been associated with increased access to care and earlier stage at diagnosis among patients with head and neck cancer (HNC). However, it is unclear whether Medicaid expansion has impacted HNC mortality rates. We examined the associations between early Medicaid expansions (2010-2011) with mortality rates for HNC in the United States. **Methods:** Data were obtained from the Surveillance, Epidemiology, and End Results (SEER) program. SEER*Stat was utilized to obtain mortality rates for early expansion (CA, CT, DC, MN, NJ, and WA) and non-early expansion states (all others) in the year ranges as available in SEER: 2005-2007 (pre-expansion) and 2012-2016 (post-expansion). Deaths in 2008-2011 were excluded as a phase-in/washout period. Difference-in-differences analyses were utilized to compare mortality rates pre- and post-early expansion in early expansion vs. non-early expansion states. The parallel trends assumption was tested comparing changes in HNC mortality rates between early expansion and non-early expansion states from 2002-2004 to 2005-2007 and from 2005-2007 to 2008-2011. **Results:** There were 6882 and 35459 deaths due to HNC in early expansion and non-early expansion states, respectively. HNC mortality rates (deaths per 100,000) decreased from 2005-2007 to 2012-2016 in both early expansion (2.17 to 1.85, difference = -0.32, 95% CI = -0.42 to -0.22) and non-expansion states (2.59 to 2.43, difference = -0.16, 95% CI = -0.22 to -0.11). Relative to non-expansion states, there was a reduction of 0.16 deaths per 100,000 (95% CI = 0.05 to 0.27, p = 0.007) after early Medicaid expansion in expansion states. However, in parallel trends testing, there was no difference in the change in mortality rates between early expansion and non-expansion states from 2002-2011 ($p > 0.37$). **Conclusions:** In this quasi-experimental analysis, there was an association between early Medicaid expansion with decreased HNC mortality. Thus, Medicaid expansion might help decrease disparities associated with access to care among HNC survivors. As longer-term data emerges, additional follow-up will be necessary to understand the mechanisms that underlie the HNC mortality benefits seen in early Medicaid expansion. Research Sponsor: None.

7037 Poster Session (Board #309), Fri, 8:00 AM-11:00 AM

Feasibility of switching to S-1 after other fluoropyrimidine-related cardiotoxicity during chemotherapy for solid tumors. *First Author: Pia J. Osterlund, Tampere University and Central Hospital, Tampere, Finland*

Background: Fluoropyrimidines (FP) are the cornerstone of chemotherapy in many solid tumors and linked to cardiotoxicity (CarTx) in about 5% (Polk, Cancer Treat Rev 2013), often leading to FP discontinuation. CarTx may be less common with S-1 and successful switch from other FP has been reported (Kwakman, EJC 2017). **Methods:** This 6-country, 12-center, cohort study included patients with solid tumors (ICD10 C15-C21, C24-25, C50, C80) who experienced FP-related CarTx. Primary endpoint was recurrent (R) CarTx during S-1 therapy after switch from any other FP. **Results:** CarTx during capecitabine (n = 124), continuous (n = 13) or bolus 5-fluorouracil (n = 4) was reported for 141 patients who switched to S-1 therapy. CarTx was chest pain including vasospasm without cardiac findings (55%), acute coronary syndrome or myocardial infarction (32%), atrial fibrillation (4%), heart failure/cardiomyopathy (4%), tachy-/bradycardia (3%), and/or other (15%). CarTx was grade 3-4 in 55%, appeared on cycle 1-2 in 89%, and at median 4 days (range 0-466) from FP initiation (Table). Causality was judged related in 26%, probable in 60%, and possible in 14%. Action with FP causing CarTx was permanent discontinuation in 91%. Treatment intent was curative in 70%. Cumulative incidence of RCarTx with S-1 was 3.5% ($CI_{95\%}$, 1.2-8.4%) and median time to R-CarTx was 11 (range 6-195) days. Four (out of 141) had grade 1 and one grade 2 R-CarTx. Three were judged possibly related to S-1 and 2 not related. S-1 was discontinued in one patient and continued in 4 (for 63-252 days) without action (n = 2), with dose reduction (n = 1), or delay (n = 1). There were no differences in demographic or risk factors regarding R-CarTx on S-1 (Table). **Conclusions:** FP-related CarTx is often severe, occurs early, and leads to permanent FP discontinuation. Switching to S-1-based therapy is safe, with, at the most, grade 1-2 R-CarTx in only 3.5%, and rarely leads to treatment discontinuation (0.7%), allowing patients to continue on an FP-based regimen. Clinical trial information: NCT04260269. Research Sponsor: None.

	During FP causing CarTx n = 141	Switched to S-1		
		No R-CarTx n = 136	R-CarTx n = 5	OR (95%CI)
Age, median yrs (range)	68 (19-86)	66 (51-72)	68 (19-86)	1.00 (0.92-1.07) per yr
Male/Female, %	60/40	60/40	60/40	1.02 (0.16-6.30)
ECOG 0/1/2, %	13/75/12	13/74/13	20/80/0	0.58 (0.06-5.60); 0 vs 1-2
Cardiovascular comorbidity: Yes/No/missing, %	49/50/1	49/50/1	60/40/0	1.55 (0.25-9.55)
Worst CarTx grade 1-2/3-4, %	45/55	44/56	60/40	0.53 (.09-3.25)
Cycle number for CarTx: 1/2/3-14, %	78/11/11	79/11/10	60/20/20	1.33 (1.03-1.71); per cycle

7038 Poster Session (Board #310), Fri, 8:00 AM-11:00 AM

Patient-reported health literacy and numeracy among new patients seeking consultation at a comprehensive cancer center. *First Author: Nadine Jackson McCleary, Dana-Farber Cancer Institute, Boston, MA*

Background: Health literacy and numeracy are essential for patients to make informed cancer treatment decisions. Oncologists do not typically evaluate literacy and numeracy and vary in their ability to adapt health discussions to meet patients' needs. Systematic ascertainment of literacy and numeracy may provide oncologists with useful information to help guide initial oncology consultations. **Methods:** We deploy an electronic new patient intake questionnaire (NPIQ) that includes health literacy and numeracy, basic demographics and cancer risk screening. Patients are considered to have limited health literacy and/or numeracy if they respond with either "somewhat", "a little bit" or "not at all" to a single question: "How confident are you filling out medical forms?" or "How confident are you in understanding medical statistics?" respectively. **Results:** Between January 2018 and August 2019, 8418 (24.6%) of patients presenting for a new patient consultation responded to the NPIQ. Among respondents with non-missing data, limited health literacy was reported by 19.4% respondents with 13.9% reporting "not at all" and 33.1% reporting "not at all" or only "a little bit" of confidence completing medical forms. Limited health numeracy was reported by 33.2% respondents with 9.1% reporting "not at all". Nearly 20% of respondents reported both limited health literacy and numeracy. Patients reporting lack of confidence completing medical forms or understanding medical statistics were older (20.3%, 30.7% ³ 70 years old), male (20.2%, 30.1%), and non-white (21.3%, 32.1%). **Conclusions:** A substantial proportion of cancer patients report lack of confidence in their ability to complete medical forms or understand medical statistics, potentially limiting the ability to actively engage in shared decision-making. Prospective identification of these social determinants of health prior to consultations may provide oncologists with information necessary to tailor health discussions and to provide materials that promote understanding and informed decision-making. Research Sponsor: None.

Health literacy and numeracy among new patient intake questionnaire responders.

ePRO responder N=8418		Limited Health Literacy N=7089		Limited Health Numeracy N=7050	
		Yes (n=1374)	No (n=5715)	Yes (n=2337)	No (n=4713)
Age	< 70	14.9%	71.2%	26.7%	59.2%
	³ 70	20.2%	58.5%	30.7%	47.0%
Sex	Female	13.6%	70.9%	26.1%	57.8%
	Male	20.2%	63.6%	30.1%	53.4%
English Proficient	Yes	15.5%	68.9%	27.1%	56.9%
	No	38.1%	39.1%	45.5%	31.1%
Race	White	15.8%	68.8%	27.3%	56.9%
	Non-white	21.3%	59.6%	32.1%	48.0%

7039 Poster Session (Board #311), Fri, 8:00 AM-11:00 AM

Association of medical comorbidities and cardiovascular disease with toxicity and survival in patients receiving checkpoint inhibitor immunotherapy. *First Author: Andrew Johns, Dept. of Internal Medicine, The Ohio State University Wexner Medical Center, Columbus, OH*

Background: Checkpoint inhibitor immunotherapy (IO) is widely used to treat advanced cancer in pts. with medical comorbidities (MC), but the effect of MC on outcomes is poorly understood. **Methods:** We performed a single institution retrospective cohort study of pts. who received IO from 2011-2018. Immune-related adverse events (irAEs) were graded by Common Terminology for Adverse Events criteria, v4.0. MC were abstracted by query of ICD-10 codes corresponding to diagnoses in the Charlson Comorbidity Index (CCI) at any time prior to IO start. Modified CCI scores excluding points for cancer were calculated for each pt. Bivariate analysis with chi-squared statistics was used to describe characteristics and MC of pts. with vs. without irAEs. Overall survival (OS) was estimated by the Kaplan-Meier method (from start of first-line IO) and compared using the log-rank test. The association of CCI score and individual MC with irAEs and OS was tested with regression models adjusted for pt. characteristics. **Results:** Among 671 pts. with advanced cancer (39.6% melanoma; 21.8% non-small cell lung) treated with IO, median age 65 (IQR 55-74) years, the most common MC were COPD (24%) and diabetes (20%). 33.8% of pts. had CCI score ≥2. Neither CCI score nor any specific MC were associated with any grade or ≥G3 irAEs ($P > 0.05$). Increasing CCI score was significantly associated with decreased OS ($P = 0.002$). CHF (13.9 vs. 8.1 months, $P = 0.008$) and previous MI (14.2 vs. 10.1 months, $P = 0.009$) were associated with decreased median OS but did not remain significant in the regression model. Among pts. without cardiovascular disease (CVD), pts. with ≥G3 irAEs had longer OS than pts. with no ≥G3 irAEs ($P < 0.001$). This OS benefit for ≥G3 irAEs was not seen in pts. with CVD ($P = 0.94$). See table for adjusted HR. **Conclusions:** Risk for irAEs does not appear to be impacted by MC. Pts. with MC have shorter OS, but no specific MC are associated with OS after adjustment for pt. characteristics. OS is significantly increased among pts. without CVD who experience ≥G3 irAEs. CVD may be an important predictor of OS in pts. with irAEs and should be evaluated in patients receiving IO. Research Sponsor: REDCap project and The Ohio State University Center for Clinical and Translational Science grant support (National Center for Advancing Translational Sciences, Grant UL1TR002733); OSU K12 Training Grant for Clinical Faculty Investigators #5K12 CA133250-09.

OS models: CVD and toxicity.

Model	Covariate	HR	95% CI		P-value
1*	No CHF; no MI	Ref.			
	CHF	0.81	0.57	1.16	0.25
	MI	0.87	0.67	1.15	0.34
2**	No CVD, no ≥G3 irAEs	Ref.			
	No CVD; ≥G3 irAEs	0.37	0.25	0.55	< 0.001
	CVD; no ≥G3 irAEs	1.02	0.80	1.31	0.86
	CVD; ≥G3 irAEs	1.02	0.61	1.69	0.94

*adjusted for age, sex, ECOG PS, BMI, race, cancer type, therapy line **adjusted for sex, ECOG PS, BMI, race, cancer type, IO duration, therapy line

7040 Poster Session (Board #312), Fri, 8:00 AM-11:00 AM

Morbidity, mortality and healthcare use among siblings of children with cancer: A population-based study. *First Author: Aditi Desai, The Hospital for Sick Children, Toronto, ON, Canada*

Background: Siblings of children with cancer are at increased risk of adverse mental health outcomes; impact of the childhood cancer experience on these siblings' physical health is unclear. We characterized the long-term risk of adverse physical health outcomes and healthcare use among siblings of children with cancer. **Methods:** Pediatric cancer patients in Ontario diagnosed between 1988 and 2016 were linked to their biological siblings to form the siblings/case cohort. Cases were matched to population controls based on sex, age, and residence area. Index date for cases was the date of their brother's or sister's cancer diagnosis (controls had the same index date as cases). After individual linkage to health services data, we compared several outcomes between these two groups: 1) physical health conditions (e.g. cancer, hypertension, injuries, death); 2) acute healthcare use (hospitalization, emergency department [ED] visits), and; 3) preventative healthcare use (periodic health checkups, influenza vaccinations). Predictors of outcomes, including demographics and characteristics of the cancer-affected child, were examined in cases. Cox proportional hazards, recurrent event, or logistic regression models were used as appropriate. **Results:** We identified 8,529 cases and 30,364 matched controls [median age at index: 6 years, interquartile range (IQR) 0-10; median follow-up time: 9 years, IQR 5-15]. Compared to controls, cases had increased risk of hypertension [hazard ratio (HR) 1.8; 95% confidence interval (95CI) 1.1-2.9; $p = 0.01$]. They also had higher rates of ED visits [rate ratio 1.1; 95CI 1.1-1.2; $p < 0.001$] and increased risk of hospitalization [HR 1.1; 95CI 1.1-1.2; $p < 0.001$]. Cases were more likely to undergo periodic health checkups [odds ratio (OR) 1.1; 95CI 1.0-1.1; $p = 0.01$] and influenza vaccinations [OR 1.5; 95CI 1.4-1.6; $p < 0.001$]. In multivariable analysis restricted to cases, rurality and bereavement, among other predictors, were associated with increased use of acute healthcare. **Conclusions:** Increased risk of hypertension and hospitalization in cases suggests that these siblings are experiencing poorer physical health compared to their peers. Increased rates of ED visits and preventive healthcare suggests parental anxiety surrounding these siblings' health. Siblings at highest risk of adverse outcomes could be identified through demographic characteristics, among others. Siblings would benefit from targeted surveillance and further investigation to elucidate underlying mechanisms influencing their health. Research Sponsor: Canadian Institutes of Health Research.

7041 Poster Session (Board #313), Fri, 8:00 AM-11:00 AM

Breast cancer patients' insurance status correlates with their adherence to endocrine therapy: Analysis of ECOG-ACRIN TAILORx trial. *First Author: Gelareh Sadigh, Emory University, School of Medicine, Atlanta, GA*

Background: Cancer patients spend substantial amounts on their healthcare services, and are at high risk for financial toxicity, a patient-reported outcome shown to be associated with care non-adherence. Even with insurance, cancer patients often face unpredictable or unmanageable costs. In women with breast cancer enrolled in TAILORx trial, we investigated the association between study entry insurance status and adherence to endocrine therapy (ET). **Methods:** Women with hormone-receptor–positive, human epidermal growth factor receptor 2–negative, axillary node–negative breast cancer enrolled in TAILORx clinical trial who started ET within a year of study entry were included. Early discontinuation was defined as stopping ET within 4 years of start for reasons other than distant recurrence or death, and the rate was calculated using Kaplan-Meier estimates. Cox proportional hazards model was used to analyze association between the patients' insurance status at study entry and early discontinuation of ET incorporating patients' treatment, age, race and Recurrence Score in the model. **Results:** A total of 9,475 patients were included (mean age: 55.6; 84% white; 9% Hispanic). A total of 58.0% had private insurance, while 11.7% had Medicare; 5.8% had Medicaid; 0.98% had military/VA insurance; 3.8% were self-pay, and 19.1% were patient recruited from international sites. The rates of 4-year early discontinuation were highest among self-pay (18.7%) and Medicaid patients (18%) and lowest among patients with military/VA insurance (8.6%) and international sites (9.8%). In multivariable analysis, compared to private insurance patients with Medicaid (HR 1.6; 95% CI 1.3-2.0) and self-pay (HR 1.6; 95% CI 1.3-2.1) had higher probability of discontinuing ET within 4 years of start and those at international sites had lower probability of early discontinuation (HR 0.8; 95% CI 0.7-0.9) (All p values < 0.05). **Conclusions:** Patients' insurance status plays an important role in adherence to ET with uninsured and underinsured having a high rate of treatment non-adherence. Early identification of patients at risk and enrollment in insurance optimization programs may improve adherence to therapy. Clinical trial information: NCT00310180. Research Sponsor: U.S. National Institutes of Health.

7042 Poster Session (Board #314), Fri, 8:00 AM-11:00 AM

National estimates of substance use, substance use disorders, and treatment among adolescent and young adult cancer survivors. *First Author: Xu Ji, Department of Pediatrics, Emory University and Aflac Cancer and Blood Disorders Center of Children's Healthcare of Atlanta, Atlanta, GA*

Background: Adolescent and young adult (AYA) survivors of cancer are at an elevated risk of early-life morbidity and mortality due to the disease trajectory and treatment. Engagement in risk behaviors, including substance use, can exacerbate survivors' vulnerabilities and place them at further risk for adverse health outcomes. This study provides national estimates of the prevalence of substance use and misuse, substance abuse or dependence (i.e., substance use disorders [SUD]), and receipt of treatment for SUD among AYA cancer survivors. **Methods:** We used 2015-2018 National Survey of Drug Use and Health data to identify a nationally-representative AYA sample (aged 12-34 years). Outcomes included past-year alcohol use, marijuana use, other illicit drug use, misuse of any prescription psychotherapeutic drugs (including opioid analgesics, stimulants, sedatives, or tranquilizers), and misuse of prescription opioid analgesics. Outcomes also assessed past-year SUD in aforementioned drug classes. Among those with SUD, we evaluated past-year receipt of SUD treatment. Multiple logistic regressions were estimated to compare outcomes between 846 AYAs who reported a cancer history and 142,870 AYAs who did not, adjusting for sociodemographic and need-related characteristics. **Results:** In bivariate analyses, AYAs with a cancer history were *more* likely than noncancer peers to use alcohol (78.6% vs. 63.4%; $p< 0.001$) and illicit drugs other than marijuana (11.2% vs. 7.8%; $p= 0.02$), misuse any prescription psychotherapeutic drugs (16.9% vs. 10.6%; $p< 0.001$) and prescription opioid analgesics (12.0% vs. 5.9%; $p< 0.001$), and have an illicit drug (other than marijuana) SUD (3.7% vs. 1.3%; $p< 0.01$) in the past year. In regression analyses, differences in past-year misuse of any prescription psychotherapeutic drug and prescription opioid analgesics persisted ($p= 0.02$, $p< 0.01$, respectively). Among AYAs with SUD, those with a cancer history were *more* likely than noncancer peers to receive SUD treatment (21.0% vs. 8.1%; $p= 0.01$) in the past year; this difference persisted in regression analyses ($p= 0.03$). **Conclusions:** AYAs with a cancer history had an elevated risk for misusing prescription psychotherapeutic medications, which was driven by misuse of prescription opioids; yet, only one in five AYAs with a cancer history and SUD received treatment. Our findings underscore the need for future interventions designed to reduce substance use and misuse and improve access to SUD treatment in AYA cancer survivors. Research Sponsor: None.

7043 Poster Session (Board #315), Fri, 8:00 AM-11:00 AM

Concurrent and sequential chemoradiation therapy are associated with improved survival among unresected stage III non-small cell lung cancer patients in the United States. *First Author: Zhiyuan Zheng, American Cancer Society, Atlanta, GA*

Background: Concurrent chemoradiation therapy (cCRT) has been shown to improve survival outcomes among inoperable stage III non-small cell lung cancer (NSCLC) patients compared to sequential CRT (sCRT) and single-modality therapy in clinical trials. However, many "real world" patients do not receive CRT, and less is known about the survival benefits of concurrent CRT vs other treatment modalities in pragmatic, non-clinical trial settings. **Methods:** We used the National Cancer Database (2004-2011) to identify unresected stage III NSCLC patients (ages 18-79 years) with Charlson comorbidity score ≤ 1 and 5-year follow up through the end of 2016. cCRT was defined as the initiations of chemotherapy (CT) and radiation therapy (RT) that were ≤ 14 days (n = 30,290) apart, whereas sCRT was defined as $>$ 14 days apart (total n = 10,596). The remaining three treatment groups included CT only (n = 11,216), RT only (n = 7,772), and neither CT/RT during first course treatment (n = 10,694). Cox proportional hazard model was used to examine the 5-year survival by treatment modalities, controlling for patient demographics, comorbidity score, health insurance, facility type, area-level social deprivation index (SDI, a composite measure for area-level socio-economic status), driving time to the treatment facility, diagnosis year, and region. Adjusted hazard ratios (HR), and medium survivals were generated by treatment modalities. **Results:** Among 70,568 unresected stage III NSCLC patients, 61,487 (87.1%) patients died within the 5-year follow-up period. In adjusted analyses, cCRT and sCRT had similar survival (median survivals: 15.3 months), whereas other treatment modalities were associated with worse survival compared to cCRT: CT only (median survival: 10.8 months; HR [95%CI]: 1.46 [1.43-1.50]), RT only (median survival: 6.7 months; HR [95%CI]: 1.93[1.88-1.99]), and no treatment (median survival: 3.2 months; HR [95%CI]: 2.64 [2.58-2.71]), all $p < 0.001$. Higher comorbidity score (Charlson score 1 vs 0, HR [95%CI]: 1.18 [1.16-1.21]), non-private insurance (Medicaid: 1.16 [1.12-1.20]; Medicare: 1.10 [1.08-1.13]; uninsured: 1.21 [1.16-1.26]) were all associated with worse survival (all $p < 0.001$). **Conclusions:** Concurrent CRT and sequential CRT have similar survival outcomes among unresected stage III NSCLC patients with minimum comorbidities, however, single modality and no therapy are associated with much poorer survival among "real world" patients, and should be avoided unless clinically appropriate. Research Sponsor: AstraZeneca.

7044 Poster Session (Board #316), Fri, 8:00 AM-11:00 AM

Nurse, oncologist, and patient impressions of electronic symptom monitoring via patient-reported outcomes in community oncology practices: Qualitative results from the U.S. national PRO-TECT trial (AFT-39, NCT03249090). *First Author: Ethan M. Basch, UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC*

Background: There is growing interest to implement electronic patient-reported outcomes in oncology practices for symptom monitoring. It is not well known what nurse, physician, and patient impressions of benefits, acceptability, and challenges are in routine care use. **Methods:** PRO-TECT is an ongoing U.S. national trial including 26 community oncology practices across 15 states that implemented PRO symptom monitoring [NCT03249090]. Patients complete weekly PROs between visits, nurses receive alerts for severe/worsening symptoms, and oncologists review PROs at office visits. Interviews were conducted with 147 stakeholders including nurses (N = 46), oncologists (N = 27), data managers (N = 15), and patients (N = 59). Each stakeholder group had different interview guides with overlapping topics to explore experiences with the PRO system. Interviews lasted 15-60 minutes, were digitally recorded, transcribed, and entered into a qualitative analysis software program. A codebook was developed from the research questions, interview guides, and discussions with the project team. Standardized coding methods were applied, with transcripts double coded for thematic analysis. Feedback surveys were also completed by nurses (N = 57), oncologists (N = 38), and patients (N = 435). **Results:** Key benefits perceived across stakeholder groups included increased patient self-awareness of symptoms; improved direct communication of patients with care teams; more open and honest conveying of symptom experiences; ability to track symptoms over time; and increased involvement of patients in their own care. Most stakeholders felt PRO symptom monitoring had a positive impact on quality of care delivery, and believed benefits of PROs outweighed necessary staff efforts. Challenges included additional work by nurses to review and respond to alerts, staff turnover requiring retraining, and limited time of oncologists. In the survey, 39/56 (70%) nurses felt the PRO system improved quality of care; 27/33 (82%) oncologists noted PROs were useful for team discussions and care delivery; and 320/434 (74%) patients agreed that weekly PRO reporting improved discussions with their care team. **Conclusions:** Clinicians and patients perceived weekly PRO symptom monitoring between visits to be valuable despite added staff effort. Results of additional analyses are forthcoming. Clinical trial information: NCT03249090. Research Sponsor: Patient-Centered Outcomes Research Institute.

7046 Poster Session (Board #318), Fri, 8:00 AM-11:00 AM

Neoadjuvant treatment with chemotherapy or chemoradiation in stage III non-small cell lung cancer: Analysis of the National Cancer Database. *First Author: Sindhu Janarthanam Malapati, Van Elslander Cancer Center-Ascension St John Hospital, Detroit, MI*

Background: Use of neoadjuvant chemotherapy (Neo-chemo) improves survival in locally advanced NSCLC. However, data regarding the benefit of adding radiation (Neo-CRT) is limited. Meta-analyses suggest that the use of Neo-CRT could lead to significant tumor downstaging but with increase in therapy-related mortality. **Methods:** Patients with resected stage III NSCLC were identified from the NCDB between 2010 and 2015. Patients were divided into two groups based on the type of neoadjuvant therapy received (Neo-chemo vs. Neo-CRT). Surgical and survival outcomes were compared. Kaplan-Meier method and log-rank test were used for survival analysis. **Results:** Of the 136,942 patients with stage III NSCLC, 15,804 patients had definitive surgery. Mean age was higher for those who received Neo-chemo (63.8 vs. 61.8 years, $p<0.0001$). Median overall survival (OS) for Neo-CRT was 49.8 months and for Neo-chemo was 53.6 months. After adjusting for treatment facility, age, gender, race, comorbidity index, insurance status, T and N stage, there was a 12% reduction in mortality with use of Neo-chemo compared to Neo-CRT (p=0.03, 95% confidence interval 0.78-0.98). 3 years OS for Neo-CRT and Neo-chemo was 51.1 and 54.3%, respectively. The 30-day operative mortality rate was slightly higher in the Neo-chemo group (4.6 vs. 3.2%, p=0.004) but 90-day mortality rates were similar (7.41% vs. 6.83%, p=0.37). Length of hospital stay for primary tumor resection was shorter for the Neo-chemo group (5 vs. 6 days, $p<0.0001$); however, there was no significant difference in 30-day readmission rates between the two groups (91.53% vs. 94.01%, p=0.09). **Conclusions:** In this study, neoadjuvant chemotherapy resulted in 12% lower mortality compared to neoadjuvant chemoradiation despite the notable increase in the rate of complete pathologic tumor and nodal response achieved with the addition of neoadjuvant radiation. There was no difference in R0 resection rates, postoperative mortality or readmissions between the two groups. Research Sponsor: None.

	Neo-CRT (%) N=3,022	Neo-chemo N=1,069	HR for death (Neo-chemo compared to Neo-CRT)	p-value for HR
T3	781 (25.8)	278 (26.0)	0.93	0.51
T4	565 (18.7)	213 (19.9)	0.97	0.83
N2	2234 (73.9)	722 (67.5)	0.92	0.24
N3	113 (3.7)	32 (2.9)	1.12	0.67
CDCC* ≤1	2739 (90.6)	950 (88.9)	0.91	0.12
CDCC *>1	283 (9.4)	119 (11.1)	0.95	0.75
Pathologic T0	598 (19.79%)	85 (7.95%)	0.78	0.28
Pathologic N0	1729 (57.21%)	536 (50.14%)	0.86	0.07
Negative surgical margin (R0 resection)	2809 (95.25%)	945 (94.23%)	0.89	0.06

*Charlson Deyo Comorbidity Score

7047 Poster Session (Board #319), Fri, 8:00 AM-11:00 AM

Inclusion of economic outcomes in NCI grants: A portfolio analysis. *First Author: Michael T. Halpern, National Cancer Institute at the National Institutes of Health, Bethesda, MD*

Background: While new interventions have improved cancer screening, treatment, and survivorship, the costs and other economic impacts of interventions may affect their uptake and availability. It is unknown what proportion of recently-funded National Cancer Institute (NCI) grants include economic outcomes. **Methods:** We used the NIH Query/View/Report (QVR) System to determine the number of competitive grants funded by NCI 2015-2020 that included economic outcomes. Grants were identified using the NIH Research, Condition, and Disease Categorization (RCDC) category "Cost Effectiveness Research"; 19 RCDC terms/concepts related to economic analyses; and 18 economic phrases searched for in grant titles, abstracts, and specific aims. The specific aims and abstracts of all grants meeting any of these search criteria were reviewed by an NCI scientist to ensure the presence of economic study outcomes. **Results:** Among over 13,700 competitive grants awarded by NCI 2015-2020, the search identified 149 grants; following abstract/specific aims review, 102 of these grants (0.74% of all grants) included an economic outcome. Most (69 of 102, 67.6%) included cost-effectiveness analysis; 24 included other cost analyses, 7 assessed financial hardship or similar outcomes, and 2 focused on developing economic methods. Among RCDC terms, more than half (53) listed modeling (9 listing Cancer Intervention and Surveillance Modeling Network), 24 randomized controlled trials, 15 QALYs, 11 implementation science, 3 willingness to pay. The most common cancer sites listed were breast (28), lung (23), cervical (19), and colorectal (17) cancer. Almost half (48) mentioned screening and 24 cancer prevention. Risk factors listed included 28 for smoking, 18 HPV, 8 HIV, 8 physical activity, 6 obesity, 4 nutrition. Ten listed treatment efficacy, 6 chemotherapy, 4 radiation therapy, 3 hormone therapy, and 1 chemo-radiation. "Treatment as usual" was listed by 16, symptom management 4, and telehealth 4. Survivors were listed for 15, caregivers 3, health disparity 18, rural 15, young adult 4. The majority of grant mechanisms were R01 (76, 74.5%); 3 were R21/R03, 4 other R mechanisms, 7 K awards, 6 U grants, 6 P, F, or L grants. **Conclusions:** While this search may not have identified all funded NCI grants over the past 5 years involving economic analyses, we found that less than 1% included economic outcomes. Recommendations to assist NCI in supporting health economics research focused on cancer across the entire care spectrum should be considered. Research Sponsor: None.

7048 Poster Session (Board #320), Fri, 8:00 AM-11:00 AM

Long-term financial outcomes and quality of life in partners of colorectal cancer survivors. *First Author: Christine M Veenstra, University of Michigan, Ann Arbor, MI*

Background: Many patients with colorectal cancer face financial toxicity, but little is known about financial outcomes among their partners. Moreover, virtually nothing is known about associations between partners' quality of life and their financial outcomes. **Methods:** In 2019 we surveyed patients who, in 2014-18, underwent resection of Stage III colorectal cancer and were seen at a community oncology practice, an academic cancer center, or reported to Georgia SEER (current RR 46%). Patients gave a separate survey to their partner. 254 partners (68% RR) completed surveys. Partners were asked about financial impacts of the patient's cancer. Partners' quality of life (QOL) was measured with the PROMIS global health scale. Multivariable regression analyses of 3 partner-reported outcomes (1. Perception that their financial status is worse off, 2. Substantial worry about finances, 3. Debt related to patients' cancer) were generated to assess associations between each outcome and key partner and patient variables, and associations between partners' QOL and financial outcomes. **Results:** Among partners, 55% were $<$ age 65, 64% female, 86% white, and 27% had $<$ high school education. 61% were employed at time of patient's diagnosis; 38% of those missed 7-30 days work and 13% missed $>$ 1 month work due to the patient's cancer. 66% patients were employed at diagnosis. Among those, 34% were no longer working at the time of survey. In 14% dyads only the patient was working at diagnosis and among those, 50% were no longer working at the time of survey. 32% partners reported their financial status is worse off, 36% reported substantial worry about finances, and 28% reported current debt, all due to the patient's cancer. After adjustment for partner and patient variables, partners of patients further out from diagnosis and partners of patients who were working at diagnosis were more likely to report substantial worry. Partners $<$ age 50, with $<$high school education, with $>$1 comorbid condition, and partners of patients who were working at diagnosis were more likely to report debt (all $p < 0.05$). Endorsing each of the 3 financial outcomes was associated with lower QOL among partners, after adjustment for partner and patient variables (all $p < 0.01$). **Conclusions:** Nearly 1/3 of partners of survivors of colorectal cancer reported long-term adverse financial outcomes due to the patient's cancer. Partners of patients working at the time of diagnosis were more likely to report substantial worry and debt, perhaps because many patients who were working at diagnosis are no longer working in the survivorship period. Research Sponsor: U.S. National Institutes of Health.

7049 Poster Session (Board #321), Fri, 8:00 AM-11:00 AM

Comparative effectiveness of proton versus photon chemoradiotherapy for patients with private insurance. *First Author: Brian Christopher Baumann, Washington University in St. Louis, St. Louis, MO*

Background: Proton therapy may increase the tolerability/efficacy of concurrent chemoradiotherapy (CRT) but is controversial & generally not covered by private insurers. There is little data on the comparative effectiveness (CE) of proton vs photon CRT among private insurance pts to guide payers on proton coverage policies. **Methods:** We conducted a CE study of adult non-metastatic cancer pts with private insurance treated with curative-intent proton vs photon CRT from 2011-2016 at Penn. The choice of radiation modality was heavily influenced by the insurer's proton coverage policy. Data on adverse events (AEs) & survival were gathered prospectively using standardized templates. Primary endpoint was 90-day AEs associated with unplanned hospitalizations (CTCAEv4 grade $\geq$3 AEs). Secondary endpoints included 90-day grade $\geq$2 AEs, decline in ECOG performance status (PS) during treatment, disease-free survival (DFS) & overall survival (OS). Modified Poisson regression models with inverse propensity score weighting were used for adverse event outcomes. Weighted Cox proportional hazards models were used for survival outcomes. Propensity scores were estimated using an ensemble machine-learning approach. $P<0.01$ was significant. **Results:** 920 pts were included (178 proton/742 photon), with H&N(25 proton/296 photon); CNS(44/128); lung(41/120); upper GI(34/78) & lower GI/GYN(34/120). Median age was 57. Race, comorbidity score, BMI, baseline AEs & baseline PS were similar ($p>0.05$ for all). 11.2% of proton pts had grade $\geq$3 AE's vs 26.8% of photon pts. On propensity score weighted-analyses, proton CRT was associated with significantly lower relative risk (RR) of 90-day grade $\geq$3 AEs (RR 0.51, 95%CI 0.32-0.81, $p<0.01$). 90-day grade $\geq$2 AE's (RR 0.91, 95%CI 0.83-0.99, p=0.03); decline in PS (RR 0.85, 95%CI 0.70-1.04, p=0.11); DFS (HR 0.64, 95%CI 0.27-1.52, p=0.31) & OS (HR 0.53, 95%CI 0.18-1.52, p=0.24) favored protons. Sensitivity analysis showed that a substantial imbalance in an unmeasured confounder would be needed to alter the significance of the primary outcome. Proton accepting insurance status was not associated with a difference in 90-day grade $\geq$3 AE's (RR 1.02, 95%CI 0.95-1.10, p=0.54) for pts treated with photon CRT (608 with non-proton accepting insurance & 134 with proton-accepting insurance). **Conclusions:** In adults with private insurance, proton CRT was associated with significantly reduced acute grade $\geq$3 AE's with similar DFS & OS. Proton-accepting insurance status was not associated with better health outcomes when adjusting for RT modality. Research Sponsor: None.

7050 Poster Session (Board #322), Fri, 8:00 AM-11:00 AM

Prior authorization process improvement for pain medications in an oncology unit: Timely initiation of test claim request form. *First Author: Susy Varghese, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Oncology patients with extensive metastatic disease and advanced-stage cancer frequently require controlled medications for pain managements. Insurers require Prior Authorization (PA) for high-cost specialty medications including: Hydromorphone, Oxycodone, Oxymorphone, Fentanyl, Nucynta, Lyrica and Lidocaine patch. Failure to obtain PA may delay patient hospital discharge and attainment of discharge medications, increase patient medication costs, increase hospital readmissions and emergency visits, and exacerbate clinical complications. In order to avoid delays, providers must submit a Claim Request (CR) to initiate the PA process. PA usually takes 48-72 hours after the CR is submitted; therefore, timely CR submission in anticipation of discharge is imperative. Baseline rates for initiating CR in a timely manner was 15%. A quality improvement project was conducted to increase provider-initiated CRs for prescribed pain medications requiring PA and to demonstrate a sustainable process, anchored by development of new policy. **Methods:** The project revised the provider-initiated CR process by implementing the following interventions: The Electronic Medical Record (EHR) was modified to create a 'quick link' to facilitate CR form submissions. The link was made available to providers via their dashboard for easy access to the CR form.The medication reconciliation process was revised to require nurses to send reminders to providers for any of the seven discharge medications requiring CR submission for PA. A new component was incorporated into the discharge planning process by discussing PA and CR during interdisciplinary rounds. Providers and nurses were educated about the revised process. **Results:** Rates for timely CR submission were collected from the EHR biweekly for 3 months post-intervention. Post-intervention, 77% of timely CR claims increased from baseline of 15% to 87%. Due to the timely initiation of CR, some medications were deemed not to require PA, and the percentage of PA requirement reduced from 95% to 55%. In addition, up to 16% of patients had money refunded as a result of timely CR submission. **Conclusions:** The new process was effective for ensuring an efficient and effective process for patients who require high-cost controlled medications for pain management, reducing waste and providing a quality experience for the patient. As a result of the project, the new process has become policy and is now being used on other units in the institution for additional medications that requires CR and PA. Research Sponsor: None.

7051 Poster Session (Board #323), Fri, 8:00 AM-11:00 AM

Rates of adherence to bone health guidelines for women with breast cancer treated with anti-estrogen therapy. *First Author: Leighton Andrew Elliott, Geisinger Medical Center, Danville, PA*

Background: Long-term use of aromatase inhibitor (AI) therapy has been shown to decrease bone mineral density (BMD) and is associated with at least twice the fracture risk when compared to an age-matched healthy population. AI's are a common treatment in hormone receptor-positive breast cancer for post-menopausal women. Similarly, tamoxifen has been shown to decrease BMD in premenopausal women. As a result, the National Comprehensive Cancer Network (NCCN) recommends BMD screening for women being treated with anti-estrogen therapy (AET), typically via Dual-energy X-ray absorptiometry (DEXA) scan. Previous studies have shown poor adherence to BMD screening with AI therapy, but no known study has evaluated compliance with tamoxifen therapy. **Methods:** We evaluated a retrospective cohort (December 2015 – July 2019) of all women with a breast cancer diagnosis initiating AET using data from the electronic health records of patients throughout a rural integrated health system. We assessed non-adherence to baseline and annual BMD screening using descriptive statistics along with preliminary data regarding fractures associated with AET therapy. **Results:** A total of 3,693 health records of women with a breast cancer diagnosis and documented prescription for AET were evaluated. In the year before AET initiation, 16% of women received BMD screening. Overall, 1,189 women treated with AET had a DEXA scan ordered at any point after drug initiation: 37% for AI's and 12% for tamoxifen. Of those treated with AI, 84% had no DEXA ordered within 12 months of starting drug after a minimum of 9 months of continuous use; this value was 96% for tamoxifen use. Patients complied with the ordered DEXA scan within the first year 81% of the time. Repeat DEXA scans were ordered 34% of the time, and patient compliance decreased to 55%. There was no significant difference in the number of patient comorbidities between patients who did and did not have a DEXA scan ordered. After starting an AI, 131 fractures were documented; 44% occurred within the first year following starting drug treatment with an average of 5 months from drug start to diagnosis. **Conclusions:** A significant proportion of breast cancer patients treated with AET did not receive guideline-recommended BMD screening. These findings should raise awareness of the importance of BMD screening by responsible providers, including oncologists, primary care physicians, care managers and insurance companies in order to decrease avoidable morbidity. Research Sponsor: None.

7052 Poster Session (Board #324), Fri, 8:00 AM-11:00 AM

Factors associated with change in the magnitude of clinical benefit of anti-cancer drugs in the post-marketing period. *First Author: Aida Bujosa Rodríguez, Hospital de Sant Pau, Barcelona, Spain*

Background: Initial drug approval is often based on surrogate endpoints. Definitive outcomes like Overall Survival (OS) or Quality of life (QoL) may not be available. Here, we evaluate changes in the magnitude of clinical benefit using the American Society of Clinical Oncology Value Framework (ASCO-VF) and European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) comparing the time of approval to the most recent available data for cancer drugs approved by the US Food and Drug Administration (FDA) between 2006 and 2015. **Methods:** We examined data on trials supporting FDA accelerated (AA) and regular (RA) cancer drug approvals between January 2006 and December 2015. We performed a systematic search of Pubmed and ClinicalTrials.gov to identify updated OS and/or QoL data, with follow up through April 2019. For AA drugs we analysed initial and confirmatory trials as follow-up. ASCO-VF and ESMO-MCBS grades were applied for trials at approval and after marketing. We explored variables associated with improved clinical benefit scores using multivariable logistic regression. **Results:** We identified 102 trials supporting the approval of 59 drugs for 96 solid tumour indications. Of these indications, 22 (23%) were granted AA and 21 (95%) were converted to RA. At time of approval, 38% of trials showed improved OS and 17% improved QoL. Substantial clinical benefit was observed in 26% of initial approval trials using ESMO-MCSB and in 34% using ASCO-VF. After a median post-marketing period of 3.3 years, updated results changed substantial clinical benefit in 20 trials with ESMO-MCBS (19 upgrades, 1 downgrade) and in 23 trials using ASCO-VF (19 upgrades, 4 downgrades). For 25% of trials no updated information was found. In the palliative setting, multivariable analysis showed association between improved ASCO-VF scores and initial approvals based on single-arm trials (OR 9.21, 95%CI 1.36-62.29, P=0.023), drugs with companion diagnostics (OR 4.95, 95%CI 1.01-24.22, *P*=0.049) and second or later lines (OR 7.80, 95%CI 1.35-45.02, *P*=0.022) while for ESMO-MCBS, drugs with companion diagnostics (OR 6.86, 95% CI 1.82-25.86, *P*=0.004) and immunotherapy drugs (OR 6.42, 95%CI 1.27-32.59, *P*=0.025) were associated with greater clinical benefit. **Conclusions:** Drugs with companion diagnostic tests, immunotherapy as well as approved based on single-arm trials were associated with increased clinical benefit after marketing approval. For a quarter of trials there were no updated data in the post-marketing period. Research Sponsor: None.

7053 Poster Session (Board #325), Fri, 8:00 AM-11:00 AM

Implementing routine patient-reported outcome collection in a large, academic health system. *First Author: Nishant Shah, University of Pennsylvania, Philadelphia, PA*

Background: Patients' symptoms and side effects have traditionally been assessed by clinicians. There is increasing evidence that patient self-reported symptom severity often differs from clinician assessment, and that collecting patient-reported outcomes (PRO) can improve communication, symptom management, and even survival. However, the implementation of routine PRO collection across a large healthcare system poses operational and informatics challenges. **Methods:** Using native electronic health record (EHR) functionality, we implemented a standardized PRO questionnaire across a large academic cancer center and associated community-based practices. The questionnaire is based on the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) developed by the National Cancer Institute. It assesses eleven common side effects of cancer care and is available for completion from home via the EHR patient portal or in clinic via tablet PC. Implementation was stepwise, beginning with a disease-specific patient population in the main academic cancer center and expanding over two years to include all cancer types, three specialties (radiation oncology, hematology/oncology, gynecologic oncology), and multiple satellite practice locations. **Results:** PRO collection was initiated for patients with gastrointestinal malignancies in two clinic locations at the main cancer center in 12/2017. During the first 3 months of implementation (12/2017-2/2018), questionnaires were completed for 1838 (56.3%) of 3267 eligible patient visits. Work with practice managers and staff to refine operational workflows led to improvement to a 75.6% capture rate for the period 3/2018 – 5/2018. From 6/2018 through 6/2019, the program was expanded to all multidisciplinary clinics in the main cancer center, as well as eight satellite practices. Aggregate capture rates from 7/2018 through 12/2019 have shown sustained performance, with 101,082 (76.7%) of 131,720 eligible visits captured. Of twelve total clinics participating, eleven have sustained capture rates above 70%, and nine capture over 80% of eligible visits. Questionnaires were completed through the online patient portal 12.1% of the time, with the remainder completed in clinic via tablet PC. **Conclusions:** Routine PRO collection as standard-of-care is possible across a variety of practice environments in a large, complex health system, with sustained capture of approximately three-fourths of eligible visits. Most patients prefer to complete the questionnaire in clinic. Research Sponsor: None.

7054 Poster Session (Board #326), Fri, 8:00 AM-11:00 AM

NSCLC: Integrating the "Yale model shared decision-making solution" into the practice setting. *First Author: Kerin B. Adelson, Yale University, New Haven, CT*

Background: Lung cancer patients are faced with treatment choices that involve complex decisions that can be preference-sensitive. In 2017 the National Quality Forum initiated a "Call to Action" to integrate shared decision-making (SDM) processes into practice in which clinicians and patients work together to make healthcare decisions that align with what matters most to patients. Projects In Knowledge, @Point of Care, Dartmouth and Yale collaborated to develop a pilot educational initiative to address and improve patient-centered care and SDM processes in the institutional cancer-care setting. **Methods:** Training materials co-developed for the Yale NSCLC team members (oncologists, nurses/NPs, social worker) address SDM, *Checkpoint Inhibitor Therapy in NSCLC,* and clinician-patient role play methods for implementing SDM in treatment discussions/decisions. Qualitative interview and observational methods were used to assess improved SDM performance by the multidisciplinary Yale NSCLC team by comparing baseline pre-intervention to post-intervention interviews and rating observed performance on case study role-play scenarios. Following the training and assessments, a focus group that included all team members was conducted to assess the acceptability, feasibility, and repeatability of the program and to inform future education. **Results:** Training empowered all Yale NSCLC team members to show pre- to post-education improvement in SDM (34% to 88%). Areas of greatest improvement: 1) providing reasonable treatment options to patients (+58%); 2) determining decision style preference – to what extent a patient wants to participate in the treatment decision process with their clinician (+76%); 3) determining patients' risk tolerance regarding treatments that may be more efficacious but may have more side effects (+77); and 4) determining patients' goals/preferences (+88%). **Conclusions:** Educational training improved SDM skills by all Yale NSCLC team members, which can lead to improved clinician-patient decision-making and patient-centric care. The training process also facilitated team building and encouraged ongoing participation in SDM. Research Sponsor: Genentech.

7055 Poster Session (Board #327), Fri, 8:00 AM-11:00 AM

Hyponatremia could be an important prognostic factor for oncology patients: Result of a retrospective study. *First Author: Prantik Das, Derby Teaching Hospitals NHS Trust, Derby, United Kingdom*

Background: Hyponatraemia is the most common electrolyte disorder encountered in clinical practice. Hyponatraemia in hospitalized people is associated with an increased morbidity, mortality and longer hospital stay compared with people with normal serum sodium concentrations. It is a negative prognostic indicator for survival in oncology patients. Incidence of hyponatremia in malignancy is largely underestimated. **Methods:** Retrospective analysis of patients admitted to oncology ward in our institution between August to September 2018 was conducted. Patients were identified from admission register and data were analysed from electronic medical records. Primary aim was to evaluate the incidence of hyponatraemia in oncology in-patients and impact on survival. Data were also analysed for patients demography, cancer types, grade of hyponatremia and treatment approach. **Results:** 119 patients were admitted to oncology ward during study period. Out of them 38% were identified to be Hyponatraemic and 51 % patients were male. Lung cancer was the predominant cancer type followed by breast, upper GI and ovarian respectively. Of hyponatraemic patients, 63% were asymptomatic, among symptomatic patients vomiting, confusion and headaches are common. According to severity, 42% patients had grade 1, 40% grade 2 and 18% grade 3 hyponatraemia respectively. When it comes to status of hydration, 62.2% were noted to be euvolaemic, 6.66% were hypervolaemic and 15.5% were hypovolaemic and the hydration status of the rest of 15.5% were not known. Considering mortality, 53% patients died within 30 days of diagnosis of hyponatremia compared to 17% deaths among non-hyponatraemic patients. Median survival of patients with grade 3, 2 and 1 hyponatremia were 29, 35 and 62 days respectively. Out of 45 patients 14 (31.1%) had acute onset hyponatraemia and they had considerably poorer survival compared to their chronic hyponatraemic counterparts. 80% of acute hyponatraemic patients have died within 30 days of diagnosis, compared to 140 days for chronic hyponatraemics with similar death rate. Out of 48% non-hyponatraemic patients who died within next 6 months, 31% developed hyponatraemia at some point before their death and amongst them, 5.7% had severe, 8.5% had moderate and 17% had mild hyponatraemia respectively. **Conclusions:** Our study indicated that hyponatremia is poor prognostic factor among oncology patients, with mortality being significantly higher when the grade is higher and when acute in onset. Identifying and early intervention could improve patient outcome. Research Sponsor: None.

7056 Poster Session (Board #328), Fri, 8:00 AM-11:00 AM

Improving the delivery of team-based survivorship care after primary breast cancer treatment through a multi-level intervention. *First Author: Lauren P. Wallner, University of Michigan Medical School, Ann Arbor, MI*

Background: The delivery of team-based survivorship care after primary cancer treatment remains challenging, in part due to a lack of effective interventions. We developed a multi-level intervention for breast cancer patients and their primary care and medical oncology providers to improve the delivery of team-based survivorship care called ConnectedCancerCare (CCC). CCC includes a patient-facing, personalized mobile website, and tailored feedback letters to providers. **Methods:** We conducted a pilot randomized controlled trial in a breast oncology clinic to establish the feasibility and acceptability of CCC. Women within one year of completing primary treatment for stages 0-II breast cancer were randomized to CCC (intervention) or a static online survivorship care plan (control). Participants completed online surveys at baseline and 3 months, ascertaining their knowledge about PCP roles in their survivorship care, their communication with their PCP about team-based care, and whether they scheduled a follow-up visit with their PCP. Multiple measures of acceptability were collected among women in the intervention arm (n = 28). Qualitative interviews were conducted at the completion of the study with 5 PCPs, 6 oncology providers, and 10 intervention patients to identify barriers and facilitators to implementing CCC. **Results:** Among 160 eligible women invited to participate, 66 women completed the baseline survey and were randomized (41% participation rate), and 54 completed the 3-month follow-up survey (83% response rate). Women in the intervention arm found the content of the CCC website to be highly acceptable, with 82% reporting it was easy to use, and 86% reporting they would recommend it to other patients. A greater proportion of women randomized to CCC (vs. control) reported scheduling a PCP follow-up visit (64% vs. 42%) and communicating with their PCP about provider roles (67% vs. 18%). Women in the CCC arm also reported higher mean knowledge scores regarding team-based cancer care (3.7 vs. 3.4). Providers noted challenges to implementing CCC, including integration into electronic medical records, and supporting sustained engagement with CCC over time. **Conclusions:** Our findings suggest deploying CCC in medical oncology practices is feasible, and the intervention content is acceptable among breast cancer patients. CCC shows promise for improving understanding and communication about provider roles in survivorship care, and facilitating patients to follow up with their PCP early in the survivorship period. Clinical trial information: NCT03618017. Research Sponsor: U.S. National Institutes of Health, University of Michigan Rogel Cancer Center.

7057 Poster Session (Board #329), Fri, 8:00 AM-11:00 AM

A personalized prediction model for hospital readmission risk for cancer patients. *First Author: Jacob Tyler Shreve, Cleveland Clinic, Cleveland, OH*

Background: Cancer patients (pts) are at high risk of unplanned hospital readmissions. Predicting which cancer patients are at higher risk of readmission would improve post-discharge follow-up/navigation, decrease cost, and improve pt outcomes. **Methods:** We conducted a retrospective cohort study of non-surgical cancer pts hospitalized at our center between 12/2014 to 7/2018. A machine learning algorithm was trained on 348 medical, sociodemographic and cancer-specific variables with a total of 1,801,944 data points. The cohort was randomly divided into training (80%) and validation (20%) subsets. Prediction performance was measured by area under the receiver operator characteristic curve (AUC). **Results:** A total of 5,178 hospitalizations were included, of which 45.1% were women, and 27.6% experienced an unplanned readmission within 30 days. The most frequently represented cancers were hematologic malignancies (30.5%), followed by GI (18.1%), lung (13.7%), and GU (10.9%). Significant variables that impacted the algorithm decision are ranked from the most to the least important, including: days from last admission; planned index chemotherapy admission; number of vascular access lines, drains, and airways in use; length of stay; cancer diagnosis; total ED visits in past 6 months; age; discharge lab values (sodium, albumin, alkaline phosphatase, bilirubin, platelets); number of prior admissions; and discharge disposition. The AUC for the validation subset was 0.80. To ease the translation of this model into the clinic, we developed a web application whereby users can supply the aforementioned variables to the model and receive a personalized prediction that highlights those variables most affecting a subject's readmission risk status: www.Cancer-Readmission.com. **Conclusions:** A cancer-specific readmission risk model with high AUC for 30-days unplanned readmission has been developed. The model is embedded in a freely available web application that provides personalized, patient-specific predictions. Programs that integrate this model can identify cancer patients with a greater risk for unplanned hospital readmission, thus providing a personalized approach to prevent future unplanned readmissions. Research Sponsor: None.

7059 Poster Session (Board #331), Fri, 8:00 AM-11:00 AM

The effect of cardiovascular disease on the association between immune-related adverse events and overall survival. *First Author: Ohad Oren, Mayo Clinic, Rochester, MN*

Background: Preliminary data suggests that immune-related adverse events (irAEs) are associated with lower all-cause mortality, presumably due to improved anti-tumor responses. Investigations of large cohorts are needed to establish better understanding of that association. **Methods:** We reviewed the Mayo Clinic database for all patients who received an immune checkpoint inhibitor (ICI). The primary outcome was all-cause mortality. Descriptive and uni-variate analyses were generated. **Results:** Between March, 2010 and July, 2019, 3,326 patients received an ICI. The most common irAEs were colitis (287, 8.6%), pneumonitis (238, 7.2%) and hepatitis (227, 6.9%). A total of 933 (28.1%) patients developed at least 1 irAE and 176 (5.3%) patients experienced 2 or more irAEs. Survival analysis demonstrated an association between the number of irAEs and all-cause mortality (log-rank, $P < 0.0001$), a relationship which was maintained for the 3 most common cancer types (lung, melanoma, renal) and for the individual ICI agents. In patients with lung cancer, colitis ($P = 0.04$) but not pneumonitis ($P = 0.83$) was associated with improved overall survival. No association between irEA and all-cause mortality was demonstrated in patients with history of stroke (log-rank, $P = 0.12$), peripheral artery disease (PAD) (log-rank, $P = 0.68$) and obesity (log-rank, $P = 0.18$). In an analysis of pre-ICI body-mass index (BMI), an association between irAE and lower overall mortality was shown in patients with BMI < 30 (log-rank, $P < 0.001$) and not in those with higher BMIs (log-rank, $P = 0.09$). The presence of stroke, PAD and obesity were associated with higher all-cause mortality in a survival analysis ($P < 0.001$). The irAE-mortality association was not modulated by the presence hypertension (log-rank, $P < 0.0001$), diabetes mellitus (log-rank, $P < 0.0001$), or heart failure (log-rank, $P = 0.006$). **Conclusions:** The development of any irAE is associated with higher overall survival. The presence of numerous cardiovascular disease states neutralizes that association, likely a result of competing causes of mortality although interaction with immune or inflammatory pathways is possible. In addition, pneumonitis is not associated with better overall survival in patients with lung cancer presumably due to compromise of already-tenuous respiratory status. Research Sponsor: Research funds of mentor.

7060 Poster Session (Board #332), Fri, 8:00 AM-11:00 AM

The association of fitness and body mass index (BMI) on all-cause mortality in cancer survivors: The Henry Ford Exercise Testing Project (The FIT Project). *First Author: Catherine Handy Marshall, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD*

Background: The obesity paradox –i.e. inverse associations between body mass index (BMI) and mortality – has been reported in patients with cancer, heart failure, and diabetes. However, the influence of cardiorespiratory fitness (CRF) on this relationship is not well established. This study assesses the association of BMI and CRF with all-cause mortality among cancer patients. **Methods:** The Henry Ford (HF) FIT Project is a retrospective cohort study of 69,885 consecutive patients who underwent physician-referred exercise stress testing from 1991 through 2009. Cancer diagnosis was identified through linkage to the HF tumor registry. We included patients 40-70 years old, with BMI recorded, at time of exercise test, with a history of cancer > 6 months prior. BMI was categorized as normal (18.5-24.9kg/m^2), overweight (25-29.9kg/m^2), or obese (> = 30kg/m2). All-cause mortality was obtained from the National Death Index. Because of a significant interaction between BMI and cancer type, patients with breast or prostate cancer were excluded. Multivariable adjusted Cox proportional hazard models were used to evaluate the association of CRF andBMI with all-cause mortality; adjusted for age at exercise test, sex, diabetes, smoking, cancer stage, and time from cancer diagnosis to exercise test. **Results:** Included were 676 patients with a mean age of 58 years (SD 7.5), 51% female, 70% White, 25% Black, with a median of 4.8 years from diagnosis to exercise test and median follow up time of 10.3 years. Among patients achieving < 10 METs, those who are overweight and obese had a lower risk of mortality HR 0.47 (95% CI 0.25,0.86) and HR 0.44 (95% CI 0.26, 0.74, respectively), compared to those with normal BMI. Among patients with METs > = 10, those who were overweight had the lowest risk of all-cause mortality (HR 0.23, 95% CI 0.09-0.62) compared to normal weight, while no statistically significant different risk of mortality was observed when comparing those who are obese to normal weight (HR 0.37, 95% CI 0.13-1.06). In an analysis combining BMI and fitness groups (four categories), those with BMI > = 25 and METs > = 10 had the lowest risk of all-cause mortality (Table). **Conclusions:** In non-breast/non-prostate cancer patients, increased BMI is associated with improved overall survival in those with METs < 10, while a U-shaped relationship between BMI and all-cause mortality exists among those with METs > = 10. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology, Other Government Agency, U.S. National Institutes of Health.

BMI Category	< 10 METs	≤ 10 METs
18.5 to < 25	Ref	0.41 (0.20, 0.87)
> = 25	0.47 (0.29, 0.79)	0.13 (0.06, 0.26)

7061 Poster Session (Board #333), Fri, 8:00 AM-11:00 AM

Global oncology authorship and access patterns. *First Author: Maria Teresa Bourlon, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico*

Background: Global Oncology is a movement to improve equitable access to cancer control and care, recognizing challenges due to economic and social factors between high, middle, and low-income countries (HIC, MIC, LIC). Access to local, regional, and global cancer data and analysis is a major driver for building a global oncology community. The JCO Global Oncology (JCO GO) online open access journal was established in 2015 with the mission to be the voice of research relevant to populations with limited resources. To assess its goals of encouraging global interaction and increasing MIC and LIC engagement, we analyzed authorship and accessing data. **Methods:** Logged views of articles published in 2018 were identified by DOI, using Google Analytics during the period 01/01/2018 to 06/30/2019. The country of origin of all authors and the location of downloads were classified according to the 218 economies listed in The World Bank Data (WBC) of 2019. **Results:** 132 articles were published in JCO GO in 2018 with 88152 views, from which the accessing nation was identified for 99%. Views originated from 180 countries: 35% HIC, 51% MIC, and 14% LIC. The most common accessing countries were: USA (37%), India (14%), United Kingdom (3%), Brazil (3%), and Ethiopia (3%). Corresponding authors came from 34 nations: 60% HIC, 32% MIC, and 8% LIC. The most common economies involved in any authorship were: USA (47%), India (10%), Brazil (5%), Mexico (4%), and Nigeria (3%). Reader origin did not differ according to corresponding author WBC. Article authorship was exclusively from one economic category in 49%: 23% HIC 16% MIC, 2% LIC. For 59% of articles, authorship came from mixed economies: 42% HIC + MIC, 11% HIC + LIC, 0% MIC + LIC, 6% HIC + MIC + LIC. **Conclusions:** JCO GO 's reach extends to over 80% of the world´s economies. The majority of articles have authors from mixed WBC countries. Areas identified to address are: low level of LIC corresponding authorship; few papers from authors across all economies; no papers from only LMICs authors; low percentage of views by LIC. This information provides focus for global oncology authorities to target interventions to reduce the academic segregation of LICs, such as global oncology funding opportunities, mentorship and policies to encourage interactions and develop MIC and LIC leaders. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

7062 Poster Session (Board #334), Fri, 8:00 AM-11:00 AM

iStopCancer: A database of 6,016 low pass whole genome sequencing of minimal invasive samples from 21 cancer types of Chinese population. *First Author: Min Yuan, Shanghai Tenth People's Hospital, Shanghai, China*

Background: Cancer is a group of genetic diseases that result from changes in the genome of cells in the body, leading them to grow uncontrollably. Recent researches suggest Chromosome instability (CIN), which is defined as an increased rate of chromosome gains and losses, manifests as cell-to-cell karyotypic heterogeneity and drives cancer initiation and evolution. **Methods:** In the past two years, we initiated iStopCancer project, and characterized 4515 'best available' minimal-invasive samples from cancer patients and 1501 plasma samples from non-tumor diseases by using low-pass whole genome sequencing. DNA from 'best available' minimal-invasive samples, including peripheral plasma, urines, pancreatic juice, bile and effusions were analyzed by low coverage whole genome sequencing followed by the UCAD Bioinformatics workflow to characterize the CINs. In total, 32T bp nucleotide (coverage =1.7X for each sample) were collected. All the data can be visualized on website: http://www.istopcancer.net/pgweb/cn/istopcancer.jsp. **Results:** 3748(83%) of tumors present detectable CIN (CIN score>1000) in minimal-invasive samples. The missed cancer patients were majorly from patients with either tumor size less than 2cm or less-aggressive cancers, including thyroid cancer, low-grade urothelial carcinoma, lung cancer in-situ, et al. Of the 1501 non-tumor individuals, 30(2.0%) present detectable CIN (|Z|>=3) at the time of sample collection, 24(80.0%) was diagnosed as tumor patient in 3-6 months follow-up. There were 9 (0.59%) of non-cancer individuals without detectable CIN were also reported as tumor patients during 6-month following up. In summary, the positive and negative prediction value is 80.0% and 99.4% respectively. The false alarms were majorly from patients with EBV activations, which indicates virus may interference chromosome stability and drove virus-associated carcinogenesis. For the patient with repeated detections, plasma cfDNA CIN dynamics predicted clinical responses and disease recurrences. Quick clearance of plasma cfDNA CIN in 2-3 weeks was found in 153 (83.6%) patients. Meanwhile, no quick clearance was found in majority of SDs/PDs (73/88=83.0%). Furthermore, cfDNA CIN predicts clinical response 2-8 weeks ahead of traditional biomarkers (CEA, CA15-3, CA199, AFP et al). **Conclusions:** Large-scale low coverage whole genome sequencing data provides useful information for cancer detection and managements. Research Sponsor: None.

7063 Poster Session (Board #335), Fri, 8:00 AM-11:00 AM

Linking insurance claims across time to characterize treatment, monitoring, and end-of-life care in metastatic breast cancer. *First Author: Jennifer Lee Caswell-Jin, Stanford University, Stanford, CA*

Background: Treatment and monitoring options for metastatic breast cancer (MBC) are increasing, but little is known about patterns or predictors of their use. Insurance claims are potentially informative, but tracking patient care timelines using episodic claims data has been cumbersome. **Methods:** We used an advanced cohort engine, implementing a temporal query language, to link IBM Marketscan claims over time for > 125 million US individuals from 2007-2014. To select the most common MBC subtype (ER+, HER2-), our criteria were: ≥2 MBC ICD codes, ≥1 year of follow-up, and ≥1 CPT or medication code for endocrine therapy and 0 for HER2-targeted therapy. We defined aggressive MBC as ≥1 ICD code for visceral or central nervous system metastasis < 1 year after the first MBC code. Geographic area was defined by 9 Census-Bureau designated regions. End-of-record was used as a surrogate for death in a Cox regression. We used multivariate logistic regression to determine correlation of factors, including disease aggressiveness and geography, with treatment, monitoring, and end-of-life events. **Results:** 7,335 women met criteria for ER+, HER2- MBC, with median age 59. Nearly half (46%) had aggressive disease, which correlated with shorter survival (hazard ratio (HR) 1.5 [1.4-1.6], P < 0.001). Treatment: first-line was endocrine therapy for 64% versus chemotherapy for 36%. Monitoring: 79% were imaged mostly by CT versus 21% by PET-CT, with median between-scan interval of 81 days; 63% received CA 15-3 serum tumor markers. End-of-life: 10% had a hospice code, of whom 19% had an ICU stay and 34% chemotherapy in the prior 3 months. Correlates of care: Disease aggressiveness correlated with first-line chemotherapy (odds ratio (OR) 2.0 [1.8-2.2], P < 0.001), PET/CT (OR 1.6 [1.4-1.8], P < 0.001), more frequent scans (OR 2.3 [2.1-2.6], P < 0.001), and chemotherapy < 3 months pre-hospice (OR 1.2 [1.1-1.4], P < 0.001), but not with CA 15-3 monitoring or ICU stay. Disease aggressiveness did not vary by region ($\chi 2$ P = 0.8), but region was significantly associated with treatment, monitoring, and end-of-life care (P < 0.001). **Conclusions:** Approximately two-thirds of ER+, HER2- MBC patients receive first-line endocrine therapy and are monitored with CA 15-3 serum tumor markers; 10% had evidence of hospice use, a likely underestimate due to differential follow-up. MBC care patterns vary by geography while disease aggressiveness does not, suggesting that care is not optimally tailored to individuals. These insights from claims data can inform quality improvement for MBC care. Research Sponsor: Breast Cancer Research Foundation, Other Foundation.

7064 Poster Session (Board #336), Fri, 8:00 AM-11:00 AM

Vital status ascertainment in cancerlinq discovery (CLQD): Improvement in mortality capture with a supplemental data source. *First Author: Danielle Potter, American Society of Clinical Oncology, Alexandria, VA*

Background: Overall survival (OS) is the gold standard outcome in clinical cancer research but many clinical trials cannot assess long-term OS. Real-world data sources can be used to calculate long-term OS, but only if vital status is accurately captured. **Methods:** The primary goal was to assess concordance of death dates from CLQD and an external source, and the effect of incorporation of external death data on estimates of OS. CLQD obtains electronic medical record (EMR) data from participating US oncology sites. Underreporting of vital status is a common problem with EMR data; we investigated the value of including death data from a commercially available database, obituarydata.com (OBD) into CLQD. OBD pulls death data from published obituaries across the US. A matching algorithm is used to match patients in CLQD and OBD. OBD death data from breast, lung, ovarian, and pancreatic cancer patients diagnosed between 2010–2018 supplemented the CLQD in this study. OS was calculated using Kaplan-Meier estimation; Pearson correlation was used for comparing time to death. **Results:** The addition of OBD modestly changes OS estimates (see Table). Among a subset of patients with death dates in both CQLD and OBD, dates were highly correlated for breast (r = 0.98), lung (r = 0.93), ovarian (r = 0.99), and pancreatic (r = 0.88) cancers. When date differences existed, they were ≤10 days for > 95% of the patients. These results suggest death dates are reliable in CLQD EMRs. OS curves were as expected, with OS decreasing by stage and age at diagnosis. **Conclusions:** Incorporating OBD modestly improves OS estimates and shows that when death data is present in CLQD, it is reliable. Future enhancements will focus on improving sensitivity of mortality ascertainment with external data linkages, without compromising specificity. Research Sponsor: AstraZeneca.

OS (95% CI) for CLQD EMR alone and with OBD supplemental dates.

		24 Month OS	36 Month OS	48 Month OS	60 Month OS
Breast	EMR	0.96 (0.96-0.96)	0.94 (0.94-0.95)	0.93 (0.93-0.93)	0.91 (0.91-0.91)
	EMR+OBD	0.96 (0.95-0.96)	0.93 (0.93-0.93)	0.91 (0.91-0.91)	0.89 (0.89-0.89)
Lung	EMR	0.59 (0.58, 0.59)	0.51 (0.50, 0.51)	0.46 (0.45, 0.46)	0.42 (0.41, 0.42)
	EMR+OBD	0.54 (0.54, 0.55)	0.46 (0.46, 0.47)	0.40 (0.40, 0.41)	0.36 (0.35, 0.36)
Ovarian	EMR	0.88 (0.87, 0.89)	0.82 (0.82, 0.83)	0.77 (0.77, 0.78)	0.73 (0.72, 0.74)
	EMR+OBD	0.86 (0.85, 0.86)	0.79 (0.78, 0.80)	0.73 (0.72, 0.74)	0.67 (0.66, 0.68)
Pancreatic	EMR	0.42 (0.41, 0.43)	0.34 (0.33, 0.35)	0.31 (0.30, 0.32)	0.29 (0.27, 0.30)
	EMR+OBD	0.37 (0.36, 0.38)	0.29 (0.28, 0.30)	0.25 (0.24, 0.26)	0.23 (0.22, 0.24)

7065 Poster Session (Board #337), Fri, 8:00 AM-11:00 AM

Real-world outcomes of immune-related adverse events in 2,125 patients managed with immunotherapy: A United Kingdom multicenter series. *First Author: Anna Claire Olsson-Brown, Clatterbridge Cancer Centre, Liverpool, United Kingdom*

Background: Immune-related adverse events (irAE) are a recognised complication of immune checkpoint inhibitor (ICI) therapy. Previous characterisation of irAEs has been limited to clinical trial or registry populations and small case series. Here we present a multi-centre, granular, real-world analysis of the prevalence and outcomes of irAEs experienced by patients managed within a single comprehensive public health service. **Methods:** A multi-centre retrospective analysis of 2125 consecutive patients treated with ICIs was undertaken across 12 centres. All patients were managed within the UK National Health Service outside of a trial setting between June 2016 and September 2018. Patients received either ICI monotherapy (MT) or combination therapy (CT). Data were collected using a standardised, pre-piloted, collection tool. IrAEs ≥ grade 2 or endocrinopathies of any grade were considered clinically significant and recorded as per the Common Terminology Criteria for Adverse Events (V5) (CTCAE). Descriptive statistics were employed using Stata v15 (College Station, TX). **Results:** Patients received αPD-1 (1757; 82%), combination αPD-1/αCTLA-4 (285, 13%), αCTLA-4 (51; 2%) and αPD-L1 (31; 1%) immunotherapy for malignant melanoma (961), non-small cell lung cancer (788) or renal cell carcinoma (335). The median age was 66 (MT) and 57 (CT). Clinically significant irAEs occurred in 732 (34%) individuals; 28% (524) on MT and 73% (208) on CT. Colitis (206,10%), thyroiditis (194, 9%), hepatitis (142, 7%) and dermatitis (126, 6%) were most commonly observed. Grade 1 endocrinopathies occurred in 20% (173) of cases. Grade 2 irAEs occurred in 43% (359), grade 3 31% (269) and grade 4 6% (51). The were 3 (0.4%) cases of grade 5 irAE; pneumonitis (2) and hepatitis, all following αPD-1 MT. 93% (680) required corticosteroids with 64% (490) requiring systemic corticosteroids and 11% (80) steroid sparing immunosuppression. 16% (336) of patients had pre-existing autoimmune disease of whom 40% (136) experienced irAEs. IrAEs led to admission in 42% (308) of cases, accounting for 2996 bed days. Length of stay was 7 days (1-67; IQR 4-13). Higher dependency care was required in 0.7% (15) of cases. Colitis (35%, 107) and hepatitis (25%, 77) accounted for the most admissions. Pneumonitis accounted for 3% (66) of irAEs but 12% of admissions. **Conclusions:** One third of patients experienced a clinically-significant irAE resulting in significant morbidity and admission burden highlighting the need for effective management strategies to optimise patient outcomes. Research Sponsor: None.

7066 Poster Session (Board #338), Fri, 8:00 AM-11:00 AM

Perioperative chemotherapy versus adjuvant chemoradiation in resectable gastric cancer: A national cancer database analysis. *First Author: Sindhu Janarthanam Malapati, Van Elslander Cancer Center-Ascension St John Hospital, Detroit, MI*

Background: In patients with resectable gastric cancer, the use of either perioperative chemotherapy (POC) or adjuvant chemoradiotherapy (CRT) are acceptable treatment options in addition to surgical resection. Both approaches improved overall survival (OS) compared to surgery alone. Randomized controlled trials comparing these two modalities are lacking. This study uses real-world data to compare the clinical outcomes of these two approaches. **Methods:** We identified gastric cancer patients in the NCDB who had definitive surgery between years 2004 and 2015. They were divided into two cohorts: POC and adjuvant CRT. We compared the OS and surgical outcomes in both groups. Kaplan-Meier method and multivariable Cox regression model were used to estimate survival. **Results:** Of 75,654 patients who underwent definitive surgical resection, 1,920 had POC and 9,161 had adjuvant CRT. Median OS was 56 months with POC and 38.5 months with CRT. After adjusting for age, gender, race, insurance status, comorbidity index, and treatment facility, patients who received POC had an 18% reduction in all-cause mortality compared to those who received adjuvant CRT ($p < 0.0001$, 95% confidence interval 0.74- 0.88). Although, 30- and 90-day mortality was slightly higher with POC compared to CRT (0.047 vs. 0.03%, $p<0.0001$ and 1.46 vs. 0.45%, $p<0.0001$ for 30 and 90 day mortality, respectively). Length of hospital stay for primary tumor resection was similar between the two groups; but the 30 day readmission rate after surgery was higher with CRT compared to POC (12.74 vs. 8.33%, $p<0.0001$). **Conclusions:** Among patients undergoing definitive surgical resection for gastric cancer, our study shows an association between the use of POC (vs. adjuvant CRT) and improvement in OS. In the POC cohort, while there was a slight increase in postoperative mortality, this was surpassed by the benefit derived from use of POC, resulting in net improvement of survival. These interesting observations warrant confirmation in randomized clinical trials. Research Sponsor: None.

	CRT (%) N=9,161	POC(%) N=1,920	HR for mortality (POC compared to CRT)	p-value for HR
Node positive	1,936 (21.8)	870 (46.1)	0.72	<0.0001
Node negative	3,655 (39.9)	801 (41.7)	0.75	<0.0001
T2	1,246 (13.6)	297 (15.5)	0.92	0.40
T3/T4	1,917 (20.9)	1,121 (58.4)	0.61	<0.0001
CDCC* ≤1	8,457 (92.3)	1,838 (95.7)	0.75	<0.0001
CDCC* >1	7,04 (7.6)	82 (4.2)	0.74	0.07
Positive surgical margin	7,233 (78.9)	1,637 (85.2)	0.95	0.556
Negative surgical margin	1,735 (18.9)	239 (12.4)	0.75	<0.0001

*Charlson Deyo Comorbidity Score

7067 Poster Session (Board #339), Fri, 8:00 AM-11:00 AM

Effectiveness of adjuvant FOLFOX versus 5FU for colon cancer treatment in community oncology practice using a hybrid study approach. *First Author: Jennifer Leigh Lund, Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC*

Background: Treatment effects may differ between trials and community settings, in part due to underrepresentation of certain patient subgroups in trials. We used a hybrid approach combining clinical trial and real-world data to compare the effectiveness of adjuvant FOLFOX vs 5FU for stage II-III colon cancer in community oncology practice. **Methods:** We used Multicenter International Study of Oxaliplatin/5FU-LV in the Adjuvant Treatment of Colon Cancer (MOSAIC) combined with patients who met trial eligibility criteria within US Oncology from 1/1/2008-5/31/2019. In the combined data, we used logistic regression to estimate the probability of trial enrollment as a function of age, sex, substage, body mass index (BMI), and performance status. We estimated inverse odds of sampling weights and weighted MOSAIC participants to reflect three US Oncology populations: 1) patients meeting trial eligibility, 2) stage III patients, and 3) stage III patients initiating FOLFOX. Within the weighted trial populations, we estimated mortality hazard ratios (HRs) and bootstrapped 95% confidence intervals (CIs) comparing FOLFOX with 5FU. **Results:** There were 2246 MOSAIC participants and 9335 US Oncology patients. MOSAIC participants were younger, had more stage II cancer, lower BMI, and worse performance status compared with US Oncology patients. After weighting MOSAIC participants to reflect the US Oncology populations, the HRs were attenuated (Table) compared with the original MOSAIC estimate (HR = 0.84; 0.71,1.00). **Conclusions:** When differences between trial and clinical populations exist and response to therapy varies across subgroups, treatment efficacy can differ from clinical effectiveness. Compared with trial results, we found that effectiveness of FOLFOX versus 5FU was attenuated in community oncology practice. Research Sponsor: Patient-Centered Outcomes Research Institute.

Effectiveness of FOLFOX vs 5FU on mortality in MOSAIC and three US Oncology populations.

Population	Trial Arm	6-Year Mortality	HR (95% CI)
Trial eligible US Oncology patients	5FU	19.3%	1.0
	FOLFOX	20.0%	1.05 (0.80,1.33)
Stage III US Oncology patients	5FU	24.0%	1.0
	FOLFOX	24.8%	0.97 (0.73,1.31)
Stage III US Oncology patients on FOLFOX	5FU	24.5%	1.0
	FOLFOX	24.4%	0.93 (0.71,1.25)

7068 Poster Session (Board #340), Fri, 8:00 AM-11:00 AM

The economic impact of cancer-related premature mortality in Brazil: A human capital approach analysis. *First Author: Marianna De Camargo Cancela, Division of Population Research, Brazilian National Cancer Institute, Rio De Janeiro, Brazil*

Background: One method of calculating indirect costs of cancer is the analysis of productivity loss. Using the human capital approach, we estimate how much cancer-related premature mortality indirectly impacts the economy. Given the diverse causes of cancer death and sociodemographic profiles in Brazil, we estimated lost productivity due to cancer by regions, providing evidence for local decision-makers. **Methods:** Data of all cancers deaths among working-age people (15-64 years for men and 15-60 for women) occurring in 2016 were extracted from the National Mortality System, by region, sex and age-group. Data on life expectancy, workforce participation, unemployment and wages were extracted from the Brazilian National Institute of Geographics and Statistics. Loss of productivity was calculated as the value of time between death and potential retirement age. **Results:** In total 536,827 (men) and 407,737 (women) years of potential productive life (YPPLL) were lost in 2016, corresponding to US$ 6,196,682,092 (PPP) for Brazil. The profile of YPPLL by cancer type varied by region. In the affluent South and Southeast regions, the cancers with higher impact in men were lung (12.4% and 9.9% of total YPPLL) and colorectal (9.6% and 10.4% of total YPPLL) while in the less affluent North and Northeast, stomach cancer was responsible for 17% and 12% of YPPLL, respectively. Among women, breast cancer had the highest impact in all regions (21.7%-26.2%), excepting the North, where cervical cancer was responsible for 31.3% of the YPPLL. Nationally, individual YPPLL was higher for testicular cancer in males (31.3 years) and Hodgkin's disease in females (20.2). In the North and the Northeast, despite lower mortality rates, the economic impact of productivity loss was higher, representing 0.23 and 0.29% of the regional GDP. **Conclusions:** Our results show the indirect economic impact of premature cancer mortality in Brazil, at a total cost of US$ 6,196,682,092 in 2016, representing 0.2% of the entire country's GDP. The regional patterns highlight the need for adaption of public policies, typical from a country in transition, with the impact of lifestyle and infection-related cancers simultaneously and differently affecting economically the regions. Research Sponsor: MSD Brazil - MSD ONCOLOGY POLICY GRANT PROGRAM, Other Government Agency.

7070 Poster Session (Board #342), Fri, 8:00 AM-11:00 AM

Differences in real-world (RW) non-small cell lung cancer (NSCLC) treatment patterns among people living with HIV/AIDS (PLWHA) compared to those without HIV/AIDS (PWoHA). *First Author: Andrew J. Klink, Cardinal Health, Dublin, OH*

Background: NSCLC is the most common non-AIDS-defining cancer in PLWHA with an estimated prevalence 2-5 times that of PWoHA. Guidelines now support treatment of NSCLC among PLWHA to follow those for PWoHA. However, PLWHA have been often excluded from cancer clinical trials that test novel agents including immunotherapy (IO). This study aimed to assess differences in systemic therapy patterns for advanced NSCLC among PLWHA and PWoHA in the RW. **Methods:** Adult patients with ≥2 claims for NSCLC between 1/1/13-12/31/18 (earliest claim = index date), ≥3 months data pre/post index date, and no evidence of clinical trial participation, pregnancy or other malignancy prior to index date were identified from Symphony Health longitudinal prescription and medical claims. Patient characteristics and treatment patterns were summarized by descriptive statistics and comparisons by HIV status made on univariate analyses. Times to discontinuation were estimated by Kaplan-Meier method and compared by log-rank tests. **Results:** There were 60,278 NSCLC PWoHA who received systemic therapy. Of 1,344 PLWHA with NSCLC, 239 (18%) received systemic therapy. PLWHA differed significantly from PWoHA: median age at diagnosis (58 v 68 years), male preponderance (66% v 47%), payer mix (Medicare 26% v 42%; Medicaid 21% v 7%), Charlson Comorbidity Score (median 6 v 1), depression (13% v 5%) and liver disease (8% v 2%), respectively (all $P< 0.01$). Differences in common systemic therapies among PLWHA v PWoHA include use of first line (1L) carboplatin + paclitaxel (28% v 19%; $P< 0.01$), 1L erlotinib (6% v 11%, $P= 0.02$) and 2L gemcitabine (10% v 4%, $P< 0.01$). IOs were used in 1L among 43 (18%) and 7,149 (12%) of PLWHA v PWoHA, respectively ($P< 0.01$). RW surrogates for PFS: median duration of 1L therapy was shorter among PLWHA (1.8 v 2.3 months, $P< 0.01$); median times from 1L initiation to 2L were similar (5.4 v 4.9 months; $P= 0.48$). Similar proportion of patients continued onto 2L (32% and 30%) and 3L (10% and 9%) among PLWHA and PWoHA, respectively (all $P> 0.05$). Total time from diagnosis to last follow-up (RW surrogate for overall survival) was 12.8 v 15.5 months in PLWHA and PWoHA ($P= 0.07$). **Conclusions:** PLWHA are younger at diagnosis of NSCLC and have higher comorbidity. Important differences in regimen selection and IO utilization exist across PLWHA and PWoHA. PLWHA have shorter 1L than PWoHA. Given higher risk and younger age at diagnosis, additional research is needed to establish screening and treatment guidelines for NSCLC in PLWHA. Research Sponsor: Cardinal Health.

7071 Poster Session (Board #343), Fri, 8:00 AM-11:00 AM

The correlation between clinical benefit and financial cost of cancer drugs. *First Author: Aaron Philip Mitchell, Memorial Sloan Kettering Cancer Center, New York City, NY*

Background: The cost of many cancer drugs is very high, but it is unclear if these costs are associated with commensurate improvement in outcomes. We aimed to assess the association between the cost of cancer treatments and their clinical benefit, using the NCCN Evidence Blocks value assessment framework. **Methods:** The NCCN Evidence Blocks include 4 measures of clinical benefit: Efficacy, Safety, Quality of Evidence, and Consistency of Evidence. The NCCN assigns scores on each measure ranging from 1 (least favorable) to 5 (most favorable). We obtained the NCCN Evidence Blocks scores as of December 31, 2018 for all recommended cancer treatments for the 30 most prevalent cancers in the US. For each treatment, we calculated total treatment costs (including drugs, administration fees, and supportive care medications) using Medicare reimbursement rates. We categorized treatments as either "time-limited" or "time-unlimited" according to whether their costs are best reflected as per full treatment course (often, adjuvant/neoadjuvant treatments) (time-limited) or per month of therapy (often, treatments for advanced disease) (time-unlimited). We used generalized estimating equations, with clustering within treatment indications, to estimate the association between Evidence Blocks scores and treatment costs, modeling the expected change in cost associated with a one-unit increase in the score on an Evidence Blocks measure. **Results:** There were 541 time-unlimited and 845 time-limited treatments. Among time-unlimited treatments, monthly treatment cost ranged from $4 to $64,630. Monthly treatment cost was positively associated with Efficacy ($3,036, 95%CI: $1,782, $4,289) and Quality of Evidence ($1,509, 95%CI: $171, $2,847) but negatively associated with Safety (-$1,470, 95%CI: -$2,790, -$151) and Consistency of Evidence (-$2,003, 95%CI -$3,420, -$586). Among time-limited treatments, cost per course of therapy ranged from $0 to $775,559, and no measure was significantly associated with cost. Evidence Blocks scores accounted for little of the variation in treatment cost (linear model R-squared = 0.10 for time-unlimited, and < 0.01 for time-unlimited). **Conclusions:** The association between NCCN Evidence Blocks measures and treatment cost was inconsistent, and accounted for little of the cost variation among treatments for the same indication. The clinical benefit of cancer treatments does not appear to be a primary determinant of treatment cost, suggesting that current pricing models may be inadequate to incentivize the development and utilization of high-value treatments. Research Sponsor: None.

7072 Poster Session (Board #344), Fri, 8:00 AM-11:00 AM

Breast density notification with adjunctive digital breast tomosynthesis (DBT): A cost-effectiveness analysis. *First Author: Jason Semprini, Uni-University of Iowa, College of Public Health, Department of Health Management and Policy, Iowa City, IA*

Background: Dense breasts increase a woman's risk of developing cancer while also raising the likelihood of a missed diagnosis from traditional mammography screening. Digital Breast Tomosynthesis (DBT) has been shown to identify positive breast cancer more accurately in women with dense breasts, but no study has estimated the cost-effectiveness of this screening mode under a notification requirement. **Methods:** Taking the perspective of a healthcare system, we estimated the incremental cost-effectiveness ratio (ICER) of providing DBT as an alternative to mammography for 40-year old women. Model parameters reflecting risk of breast cancer, detection rates, and costs were estimated from recent meta analyses, Tufts' CEA registry, and Medicare Fee Schedules. We used probabilistic Markov Models to estimate the ICER under uncertainty, and a time-variant model in which breast density and cancer risk change over time. Additionally, a heterogeneity analysis included all women between the ages of 40-65, while also using 1st and 2nd degree family history to calculate cancer risk. **Results:** In the probabilistic model, adjunctive DBT has a cost differential of $12,203, with an increase of 0.0382 quality-adjusted life years (ICER = $319,491/QALY) compared to mammography. This result was most sensitive to the probability of a missed diagnosis for women with dense breasts. At a willing-ness to pay of $50,000, adjunctive DBT had a 57% chance of being more costly and less effective than standard mammography. Conversely, DBT only had a 20% chance of being cost-effective and a 9.9% chance of being less costly and more effective. The time-variant model reported an ICER of $174,218, but adjunctive DBT became even more cost-effective after expanding the population and including family history of cancer (ICER_All Ages = $157,146; ICER_FamHist = $153,388). **Conclusions:** Breast density notification laws which provide additional screening via DBT are not cost-effective at a willingness to pay of $50,000. Policymakers, however, should note that many modern cancer therapeutics also exceed this threshold. As an adjunctive screening technique, DBT would result in fewer deaths and increase quality of life, but the effect is minimal and carries a high cost. Including breast density within greater risk stratification protocols, however, may prove highly cost-effective, especially for older women with a family history of cancer. Research Sponsor: None.

7073 Poster Session (Board #345), Fri, 8:00 AM-11:00 AM

A randomized controlled trial (RCT) testing a mobile application (app) to identify cancer treatment-related financial assistance. *First Author: Aaron Tarnasky, Duke University School of Medicine, Durham, NC*

Background: Insured cancer patients face high treatment-related, out-of-pocket costs. While philanthropic- and pharmaceutical-sponsored financial assistance programs exist, patients are often unaware of them. We developed "Bridge", a patient-facing app that identified financial assistance programs for which a patient might be eligible based on treatment, disease, insurance, and financial characteristics. We hypothesized that patients in the Bridge study arm would be more likely than controls to apply for and receive financial assistance. **Methods:** We enrolled patients at a single institution from January 2018-March 2019. Patients were receiving treatment for any cancer, had a life expectancy of ≥6 months, and self-reported out-of-pocket costs. We randomized patients 1:1 to intervention (Bridge) vs. control (financial assistance educational websites). We assessed subjective financial distress with the validated COST measure. Outcomes included application for and receipt of financial assistance. Data on outcomes was collected from the medical record, institutional pharmacy database, and Bridge. We compared patient characteristics between study arms using chi-square and Mann-Whitney-Wilcoxon tests. We used an unadjusted logistic regression model to compare differences in outcomes. **Results:** We randomized 200 patients and found no significant differences between arms in baseline characteristics (Table). At 6 months from enrollment, patients in the Bridge arm were more likely than controls to apply for financial assistance [35% Bridge vs. 10% control, OR 3.53, 95% CI 1.69-7.34, $p < 0.01$]. Bridge patients were also more likely than controls to receive financial assistance (30% Bridge vs. 9% control, OR 3.39, 95%CI 1.78-6.46, $p < 0.01$). **Conclusions:** Among patients with treatment-related out-of-pocket costs, those who interacted with a financial assistance app were significantly more likely to apply for and receive treatment-related financial assistance. Research Sponsor: U.S. National Institutes of Health.

Baseline	Control (n = 100)	Bridge (n = 100)	Total (n = 200)
Median age, years	59	56	57
Female gender	59%	49%	54%
White race	67%	74%	71%
Stage IV/metastatic	48%	57%	53%
Educated past high school	80%	69%	75%
Median income	$55,000 (n = 83) (IQR $35,000-$100,000)	$66,000 (n = 83) (IQR $40,000-$120,000)	$62,000 (n = 166) (IQR $36,000-$100,000)
Private insurance	69%	72%	71%
Median monthly out-of-pocket cost	$775 (n = 93) (IQR $280-$2421)	$1,100 (n = 93) (IQR $413-$2195)	$928 (n = 186) (IQR $330-$2421)
Median financial distress score	24	23 (n = 99)	23 (n = 199)

7074 Poster Session (Board #346), Fri, 8:00 AM-11:00 AM

Venous thromboembolism prophylaxis in ambulatory cancer patients initiating chemotherapy: A cost-effectiveness analysis. *First Author: Emma Ryan, Duke University School of Medicine, Durham, NC*

Background: Venous thromboembolism (VTE) is a major cause of morbidity and mortality among cancer patients. The Apixaban for the Prevention of Venous Thromboembolism in High-Risk Ambulatory Cancer Patients (AVERT) randomized controlled trial concluded that apixaban is a safe and effective option for VTE prophylaxis in high-risk ambulatory cancer patients initiating a new chemotherapy regimen. We performed a cost-effectiveness analysis from a health system perspective to determine if apixaban is a feasible prophylactic strategy for this population. **Methods:** A decision model was created from a third party payer perspective with a time horizon of 6 months, based on the treatment arms of the AVERT trial: (1) apixaban 2.5 mg twice daily for 6 months during active chemotherapy versus (2) placebo. Rates of VTE (4.2% apixaban vs 10.2% placebo), major bleeding (3.5% vs 1.8%) and clinically relevant nonmajor bleeding (CRNMB) (7.3% vs 5.5%) were modeled from the results of the AVERT trial. Cost estimates for treatments and events were obtained from wholesale drug costs, previously published studies and Medicare reimbursement data, and adjusted for inflation to 2018 dollars. Quality adjusted life years were calculated based on previously published utility values for the health states of advanced cancer, DVT, PE, and major bleeding events. An exploratory analysis was performed comparing prophylactic aspirin to no prophylaxis assuming a VTE rate of 7.2%, major bleeding rate of 3.5%, and CRNMB rate of 7.3%, based on the conservative assumptions that while aspirin may not be as effective at preventing VTE, the rate of clinically significant bleeding events would be similar or greater than that of apixaban. **Results:** In the base case model, apixaban is more costly and more effective than placebo (ICER = $5,013,190/QALY), and the cost per VTE prevented in the apixaban arm is $33,000. In one-way sensitivity analysis, if the cost of apixaban were reduced by 40% from $3,197 to $1,250 for a 6 month course, this could potentially be a cost-effective prophylaxis strategy with an ICER less than $100,000/QALY. In the alternative analysis, aspirin dominates placebo as it is both more effective and less expensive, and remains cost-effective even when the rate of clinically recognized bleeding with aspirin exceeds 15%. **Conclusions:** Further investigation into less costly prophylactic options such as generic direct oral anticoagulants (once available) and aspirin is warranted prior to broader implementation of a VTE prophylaxis strategy in this population. Research Sponsor: None.

7075 Poster Session (Board #347), Fri, 8:00 AM-11:00 AM

Cost-effectiveness of genomic profiling in veterans with metastatic lung adenocarcinoma. *First Author: Pradeep Poonnen, Duke University Health System/Durham VA Medical Center, Durham, NC*

Background: Tumor profiling identifies patients who are eligible for targeted anticancer therapies. Common tumor profiling approaches include targeted gene panel testing (TGPT), which tests for common mutations in select genes, and multigene panel sequencing (MGPS), which tests for a broad range of mutations in a comprehensive set of genes. Our objective was to determine the lifetime cost-effectiveness of MGPS and TGPT compared to no tumor profiling for Veterans with metastatic lung adenocarcinoma from the Veterans Health Administration's (VHA) perspective. **Methods:** A decision analytic model was developed to simulate outcomes for a closed cohort of hypothetical Veterans with metastatic lung adenocarcinoma considering anticancer therapy. OncoKB genes with levels of evidence 1 and 2 for guiding therapy were included. Three profiling strategies were studied: TGPT (*ALK, EGFR, ROS1*), MGPS (*ALK, BRAF, EGFR, HER2, MET, NTRK1, NTRK2, NTRK3, RET, ROS1*), and no tumor profiling. We assumed 95% of patients with actionable mutations received targeted therapies. Non-targeted therapy options included chemotherapy and/or immunotherapy, and no anticancer therapy. Model inputs were derived from randomized trials (progression-free survival), VHA and Medicare (drug costs), published studies (non-drug cancer-related management costs, health care utilities), and VHA National Precision Oncology Program and cBioPortal for Cancer Genomics databases (mutation prevalence). Costs (2019 US$) and quality-adjusted life years (QALYs) were discounted at 3%/year. Base-case scenario, one-way sensitivity analyses, and probabilistic sensitivity analyses (PSA) using 1,000 Monte Carlo simulations were completed. **Results:** Base-case results and corresponding 95% credible intervals from the PSA indicated the cost/QALY gained was $309,399 ($280,371-$343,161) for TGPT and $324,707 ($296,086-$359,778) for MGPS compared to no tumor profiling. Of the 3 strategies, MGPS resulted in the highest number of QALYs. One-way sensitivity analyses revealed the cost/QALY estimates were most impacted by changes in health state utility on a targeted therapy (quality of life), costs of alectinib, and non-drug cancer-related costs in patients receiving targeted therapy. Compared to no tumor profiling, cost-effectiveness ratios for both profiling approaches surpassed the $150,000/QALY threshold in 100% of PSA simulations. **Conclusions:** Tumor profiling (TGPT or MGPS) can optimize anticancer therapy selection in patients with metastatic lung adenocarcinoma and improve quality-adjusted survival, but compared to no tumor profiling, is not cost-effective. Research Sponsor: None.

7076 Poster Session (Board #348), Fri, 8:00 AM-11:00 AM

Three versus six months of adjuvant chemotherapy for colorectal cancer: A multi-country cost-effectiveness and budget impact analysis. *First Author: Catherine Hanna, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom*

Background: The international Short Course Oncology Treatment (SCOT) trial demonstrated non-inferiority and significantly less toxicity of 3 versus 6 months of adjuvant chemotherapy for patients with colorectal cancer (CRC). This study assesses the value of shorter treatment and the economic implications of implementing the findings from the perspective of the countries that participated in the SCOT trial. **Methods:** Individual patient level data (n=6055) from the SCOT trial was used in a fully-pooled, cost utility analysis for the six participating countries. The incremental net monetary benefit (INMB) per patient was calculated using a willingness to pay threshold of one Gross Domestic Product per capita for each country. Responses to a clinician questionnaire (n=265 across 21 countries collected in April 2019) were used to estimate extent of practice change. The budget impact over 5 years of using shorter treatment was calculated, using 2019 and US dollars (USD) as the base year and currency, respectively. **Results:** Cost drivers for differences between the SCOT trial arms were reduced chemotherapy costs and fewer hospitalisations in the first treatment year. The INMB per patient of using shorter treatment and subsequent monetary impact on healthcare provider budgets resulting from implementation are shown in Table. This is a cost saving treatment strategy in all countries. The budget impact over 5 years amounts to savings of nearly half a billion USD. **Conclusions:** The economic burden of CRC treatment globally exceeds $39 billion per annum. Understanding the costs and consequences of widespread clinical practice change is important for optimal budget planning. This study has widened the transferability of results from a phase III cancer trial, showing shorter treatment is cost-effective from a multi-country perspective. The vast savings could provide benefit elsewhere within a limited healthcare budget, and justify the investment in conducting the SCOT trial. Research Sponsor: CRUK.

	Australia	Denmark	New Zealand	Spain	Sweden	United Kingdom
INMB	$14 966	$15 578	$12 266	$11 147	$13 868	$14 738
Budget impact ($ million) (55% practice change stage III, 20% practice change stage II)	-$55	-$18	-$8	-$156	-$27	-$208

7077 Poster Session (Board #349), Fri, 8:00 AM-11:00 AM

Total cost of lung cancer care associated with broad panel versus narrow panel sequencing. *First Author: Rogelio Alberto Brito, CVS Health, Woonsocket, RI*

Background: Many lung cancer patients are diagnosed late with advanced or metastatic disease. Targeted therapies can improve quality of life and increase the chances of progression-free survival versus conventional treatments. An understanding that there may be more than one driver mutation associated with a specific lung tumor is crucial for the timing and delivery of the most effective line of therapy. Broad panel sequencing (BPS) minimizes tissue use and enables personalized treatment that decreases the use of ineffective agents and unwarranted side effects, in addition to opening pathways to early clinical trials. However, many payors do not reimburse for BPS. The objective of this study was to determine if BPS leads to lower total cost of care versus narrow panel sequencing (NPS). **Methods:** We identified new lung cancer patients who completed BPS (Current Procedural Terminology (CPT) code 81455, 51+ genomic test) or NPS (CPT code 81445, 5-50 genomic test) using medical claims from January 1, 2018, to March 31, 2019. We defined total cost of care as allowed costs paid for medical and pharmacy claims across a six-month time period from the first gene sequencing panel. We also compared the allowed costs of BPS and NPS. A Student's t-test was used to compare differences and results are presented as mean +/- standard deviation. **Results:** From January 2018 to March 2019, we identified 45 patients who underwent BPS sequencing and 399 patients who underwent NPS. The average BPS cost was $1,977 +/- $2,713 versus the average NPS lab cost $719 +/- $1,087, $p < 0.0001$. The average 6-month per member per month (PMPM) total cost was $11,535 +/- $9,168 among those who underwent BPS compared to $20,039 +/-19,642 in those who underwent NPS. This difference of $8,504 was statistically significant, $p = 0.0022$. **Conclusions:** BPS has been shown to optimize treatments in patients with lung cancer. These initial results of claims suggest that while lung cancer patients undergoing BPS have higher total sequencing costs than those undergoing NPS, BPS significantly reduces overall total cost of lung cancer care. Identifying the broader genomic landscape of a patient's tumor earlier will empower oncology providers and lung cancer patients with information to make timely, precise treatment decisions that are ultimately more cost effective. Research Sponsor: CVS Health.

7078 Poster Session (Board #350), Fri, 8:00 AM-11:00 AM

Hospitalization for complications due to systemic therapy in the United States. *First Author: Muni Rubens, Miami Cancer Institute Baptist Health South Florida, Miami, FL*

Background: Management of complications of systemic therapy for cancer involves significant healthcare burden for both patients and healthcare system. Aim of this study is to estimate trends as well as burden associated with these hospitalizations, using a nationally representative data. **Methods:** National Inpatient Sample data during 2005-2016 was used to identify complications of systemic therapy using ICD-9 and ICD-10 external cause of injury codes. Primary outcome was hospitalization rate while secondary outcomes were cost and in-hospital mortality related to these complications. **Results:** There were 443,222,223 hospitalizations recorded during the study period, of which 2,419,722 were due to complications of systemic therapy. The average annual percentage change of these hospitalizations was 8.1%, compared to -0.5% for general hospitalizations. The 3 most common causes for hospitalization were anemia (12.8%), neutropenia (10.8%), and sepsis (7.8%). During the study period, hospitalization rates had highest relative increases for sepsis (1.9 fold) and acute kidney injury (1.6 fold) and highest relative decrease for dehydration (0.21 fold) and fever of unknown origin (0.35 fold). Complications responsible for highest costs per hospitalization were sepsis ($16,834), acute kidney injury ($13,172), and pneumonia ($13,040). Leading causes of in-hospital mortality associated with systemic therapy were sepsis (15.8%), pneumonia (7.6%), and acute kidney injury (7.0%). **Conclusions:** During 2005-2016, hospitalization rates for systemic therapy complications increased by an annual rate of 8.1%, with anemia, neutropenia, and sepsis as the most common complications requiring hospitalization. Initiatives such as rule OP-35 by the Centers for Medicare and Medicaid Service, improving access and providing coordinated care, early identification and management of symptoms, and expanding urgent care access could decrease these hospitalizations and the burden on healthcare. Research Sponsor: None.

Number of hospitalizations, mortality, and cost for top 8 complications of systemic therapy.

Diagnosis	Number of hospitalizations (%)	Mortality %	Total Charges in Billions USD
Anemia	309,724 (12.8%)	2.8%	12,024
Neutropenia	261,330 (10.8%)	1.6%	9,091
Sepsis	188,738 (7.8%)	15.8%	16,834
Pneumonia	106,468 (4.4%)	7.6%	13,040
Acute kidney injury	87,110 (3.6%)	7.0%	13,172
Nausea with vomiting	77,431 (3.2%)	0.70%	6,059
Dehydration	72,592 (3.0%)	2.8%	6,351
Urinary tract infection	31,459 (1.3%)	1.5%	8460

7079 Poster Session (Board #351), Fri, 8:00 AM-11:00 AM

A cost analysis of managing cancer-related pain among hospitalized US cancer patients. *First Author: Olatunji B. Alese, Winship Cancer Institute, Atlanta, GA*

Background: Pain is a common symptom of cancer, affecting patients' function and quality of life. It is also a common cause of hospitalization for cancer patients. The aim of this study was to evaluate the cost of in-hospital pain management among US cancer patients. **Methods:** A retrospective analysis of data from all US hospitals that contributed to the National Inpatient Sample for 2011-2015 was conducted. All cancer patients admitted for pain management were included in the analysis. Main outcomes were factors significantly associated with hospital length of stay, total charge per hospital stay, and in-hospital mortality. Weighted chi-square test was used for categorical covariates and univariate analysis was performed using a logistic model. **Results:** 122,776 patient discharges were identified. Mean age was 59.3 years and 52.3% were female. 65.9% stayed in the hospital for longer than 72 hours, with a median total hospital charge of $48,156. Conversely, the median total hospital charge for those spending less than 72 hours on admission was $15,966. Median total charge per hospital stay was similar among insured and uninsured/self-pay patients ($32,879 vs. $32,323; p=0.013), but higher in patients without metastatic disease ($33,315 vs. $29,369; $p<0.001$). It was also higher in those with the highest income quartile when compared with lowest income patients ($38,223 vs. $30,047; $p<0.001$). Co-morbid medical illnesses were more prevalent in those with longer hospital stay (15 vs. 12; $p<0.001$) and the overall in-hospital mortality rate was 8.2%. There was no significant difference in median total hospital charges between those who died in, or those discharged from the hospital ($33,746 vs. $32,795; $p<0.001$). On multivariate analyses, gender, race, insurance status, diagnosis of metastatic cancer, age, number of co-morbid medical illnesses, year of diagnosis, and median income were significant predictors of length of stay. Race, insurance payor, metastatic cancer, age, and number of co-morbid medical illnesses were significant predictors of total hospital charges, after adjusting for other covariates. **Conclusions:** In-patient pain management of cancer patients is associated with significant health care costs. Optimization of outpatient pain management strategies could significantly lower the cost of care for cancer. Research Sponsor: None.

7080 Poster Session (Board #352), Fri, 8:00 AM-11:00 AM

Patient-reported benefit from proposed interventions to reduce financial hardship during cancer treatment. *First Author: Emeline Aviki, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Awareness of cancer patients' financial toxicity (FT) has increased substantially over the past decade; however, interventions to minimize financial burden remain underdeveloped and understudied. This survey-based study explores patient beliefs on which potential mitigating strategies could improve their financial hardship during cancer treatment. **Methods:** Interviewer-administered surveys were conducted with consecutive patients in an outpatient, urban, private academic Gynecologic Cancer clinic waiting room for 2 weeks in August 2019. The survey items included patient demographics, disease characteristics, the Comprehensive Score for Financial Toxicity (COST) tool (validated measure of FT with score 0-44; lower scores indicate worse FT), assessment of cost-coping strategies, and patient-reported anticipated benefit from described potential interventions (items that were feasible and relevant to implement in clinic). **Results:** Of 101 patients who initiated the survey, 87 (86%) completed it and were included in this analysis. The median age was 66 (range, 32-87). Thirty-eight patients (44%) had ovarian, 29 (33%) uterine, 5 (6%) cervical, and 15 (17%) an "other" gynecologic cancer. The median COST score was 32 (range, 6-44). Twenty-nine patients (33%) had COST scores $\leq$25 and 16 (18%) had COST scores $\leq$18. The most frequent cost-coping strategy reported was reducing leisure activities (n = 36, 41%) and using savings to pay for medical bills (n = 34, 39%). Six patients (7%) reported not taking a prescribed medication in the past 12 months due to the inability to pay and 0 reported skipping a recommended imaging study. When it came to interventions patients anticipated would improve their current financial hardships, 34 (39%) indicated access to transportation assistance to and from appointments, 31 (36%) said "knowing up front how much I'm going to have to pay for my healthcare", 29 (33%) indicated "minimizing wait time associated with appointments, which keeps me away from work", and 22 (25%) indicated "access to free food during/around appointments and treatments". Only 26 (30%) noted they were not experiencing financial hardship. **Conclusions:** For an outpatient population of gynecologic cancer patients, several focused, feasible interventions could be implemented to potentially decrease patient FT. Our study can help health care providers in the design of interventions to create meaningful improvements in patient financial burden. Next steps should assess the impact of targeted interventions on patient outcomes. Research Sponsor: National Cancer Institute P30 CA008748, Other Government Agency, New York Community Trust.

7081 Poster Session (Board #353), Fri, 8:00 AM-11:00 AM

Health plan expenditures young adults with newly-diagnosed Hodgkin lymphoma (HL) by care at NCI-designated comprehensive cancer centers (CCC) vs. other treatment sites (non-CCC). *First Author: Julie Anna Wolfson, City of Hope, Duarte, CA*

Background: Patients diagnosed with HL between 22-39y have worse outcomes than younger patients ($\leq$21y); we previously reported that treatment at a CCC mitigates these disparities [Wolfson, Leukemia 2017]. While there is general consensus that CCC care is expensive, expenditures for managing young adults with HL in CCC vs. non-CCC are not known. **Methods:** Cancer-related expenditures were examined in HL patients diagnosed between 2001-2014 at age 22-39y and treated at CCC and non-CCC sites using commercial insurance claims data (OptumLabs Data Warehouse). Multivariable generalized linear models with log link modeled average monthly health plan paid expenditures, adjusting for sociodemographics, stage, adverse events, pre-existing comorbidities, and diagnostic era. **Results:** Of the 1501 HL patients, 33% (n = 489) were treated at a CCC. Patients treated at CCC vs. non-CCC did not differ with respect to race, sex, income, diagnostic era or comorbidities ($p\geq0.3$). Mean duration of enrollment was longer in CCC than non-CCC (25 vs. 23 mos; $p < 0.001$) patients. *During the first year after HL diagnosis*, total average monthly expenditures were higher in CCC ($9,111) than non-CCC ($7,834, p = 0.001), including those related to inpatient (CCC: $1,790 vs. non-CCC: $1,011; p = 0.001) and outpatient (CCC: $6,971 vs. non-CCC: $6,487; p = 0.001) expenditures. The higher CCC expenditures were associated with higher monthly rates of inpatient admissions (IRR = 1.3, p = 0.001) and outpatient visits (IRR = 1.1, p = 0.02) at CCC. Rates of chemotherapy-related inpatient admissions were higher (IRR = 2.3, p = 0.001) in CCC than non-CCC patients, while outpatient chemotherapy visit rates were lower (IRR = 0.9, p = 0.001) in CCC. *During Years 2-3*, total average monthly expenditures were higher in CCC ($19,259) than non-CCC ($4,145, p = 0.002) patients. Outpatient expenditures were higher in CCC ($10,164) vs. non-CCC ($2,901, p = 0.001), with higher monthly outpatient visit rates (IRR = 1.7, p = 0.001) at CCC. **Conclusions:** Inpatient and outpatient cancer-related expenditures in young adults with HL were higher at CCC than non-CCCs. Higher outpatient expenditures at CCC were associated with only higher monthly visit rates. Higher inpatient expenditures were in the setting of higher admission rates, including those related to chemotherapy. Additional work is necessary to understand whether these higher expenditures at CCC are related to supportive care and/or differences in facility structure and billing practices. Research Sponsor: Stand Up to Cancer, Other Foundation.

7082 Poster Session (Board #354), Fri, 8:00 AM-11:00 AM

Patient-reported out-of-pocket costs and financial toxicity during early-phase oncology clinical trials. *First Author: Ryan Huey, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Clinical trials are an important therapeutic option for cancer patients (pts). Although financial burden in cancer treatment is well-documented, the financial burden associated with clinical trials is not well understood, especially for pts with lower income. **Methods:** We conducted a survey regarding economic burden and financial toxicity in cancer pts who had been on Phase I clinical trials for ≥1 month. Financial Toxicity Score (FTS) was assessed using the validated COmprehensive Score for Financial Toxicity (COST) survey (scale 0-44, lower scores indicate worse toxicity). Pts also reported monthly out-of-pocket (OOP) medical and non-medical expenses. We applied multivariable logistic regression to analyze risk of financial toxicity, and unanticipated expenses. **Results:** Early-phase clinical trial pts (N = 213, median age = 59y; 59% female; 74% White, 45% w/ annual income ≤$60K; 50% lived > 300 miles from the clinic; 40% required air travel; 37% had Medicare, 54% had employer sponsored insurance) had a median FTS of 20, with interquartile range of 12. Median monthly OOP costs for non-medical expenses was $1075, and for medical expenses was $475. Median total monthly OOP costs was $1750. 55% and 64% of pts reported that actual medical and non-medical expenses were higher than expected, respectively. Worse financial toxicity (≤ median FTS) in pts was associated with yearly household income < $60K (OR: 2.7, P = 0.008), having medical costs higher than expected (OR: 3.2, P = 0.024), participation on ≥1 Phase I clinical trial prior to their current trial (OR: 2.2, P = 0.028), and living > 100 miles away from the clinical trials hospital (OR: 2.3, P = 0.043). However, 34% of pts who lived > 100 miles away received partial/full reimbursement of clinical trial-related travel costs from study sponsor/other/insurance. Racial/ethnic minority (OR: 2.6, P = 0.008) and pts who were unemployed or not working outside the home (OR: 2.4, P = 0.023) were more likely to report that actual medical costs were much higher than expected. 53% of pts used savings and 18% retirement accounts to pay for treatment. **Conclusions:** Among cancer pts participating on clinical trials, economic burden is high, and most of pts' OOP costs were on non-medical expenses. Financial toxicity is disproportionally higher in pts with lower income. OOP costs can be substantial and are often unexpected for pts. Furthermore, prior participation in ≥1 Phase I clinical trial and living far away from the clinical trials hospital seem to increase risk of financial toxicity. Research Sponsor: Institutional Funds, Conquer Cancer Foundation of the American Society of Clinical Oncology.

7083 Poster Session (Board #355), Fri, 8:00 AM-11:00 AM

Financial burden of discarded weight-based cancer drugs to payers and patients in private insurance market. *First Author: Ya-Chen T. Shih, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Studies assessing wastage of discarded weight (WT)-based cancer drugs (can-RX) derived their estimates from Medicare Average Sales Prices + 6% mark-up. With higher mark-ups, financial impact of discarded can-RX can be much higher in private insurance market. In addition, no study has examined the financial burden for patients(pts) even though they are subject to out-of-pocket payment (OOP) of the discarded RX. This study fills in these important knowledge gaps. **Methods:** We obtained the list of WT-based can-RX from the 2017 Centers for Medicare and Medicaid Services Part B Discarded Drug Units Report and gathered information on package size and recommended dose from IBM Micromedex. We identified pts who received WT-based can-RX from 2017 MarketScan data and linked to MarketScan Health Risk Assessment to obtain WT and height for a subset of pts. For each claim, we derived the recommended dose based on pt's RX and his/her WT or body surface area (calculated from WT and height) and estimated the % of discarded dose. We quantified OOP as the sum of deductible, copayment, and coinsurance, and classified pts' insurance by their enrollment to high-deductible (HD) plans. For claim-level analysis, we applied beta regression (for fractional outcomes) to determine factors associated with % discarded while accounting for within pts correlations. Covariates were age group (grp) (< 50, 50-59, > = 60), WT grp (< 150, 150-199, > = 200lb), HD plan (yes/no), region, cancer type, and can-RX. For pt-level analysis, we calculated the amount payers and pts spent on all and discarded can-RX in 2017 and compared OOP b/t pts in HD and non-HD plans. **Results:** Of 27,883 claims of WT-based can-RX, the median discarded % was 0.10 (mean 0.19, SD = 0.21). In addition to can-RX and cancer type, significantly higher discarded % was found in the lowest WT grp (0.03, P < 0.001, vs. WT > = 200lb) and significantly lower % was found in the middle age grp (-0.01, P = 0.02 vs. age < 50). Of 1963 pts, 778 (40%) had HD plans. Payments by payers (NETPAY) and pts (OOP) for total and discarded can-RX and the comparison b/t HD and non-HD plans are shown in Table. **Conclusions:** Payers incurred substantial financial burden from discarded can-RX. While OOP costs were modest for most privately insured pts, 5.3% of pts (~8% in HD plans) paid > $400 for discarded RX. Research Sponsor: U.S. National Institutes of Health.

	Total	HD	non-HD	P value
Total				
median NETPAY	$12620	$13185	$12240	.7
mean OOP*	517	700	397	< .01
Discarded				
median NETPAY	1839	2087	1737	.1
mean OOP*	73	98	57	< .01
OOP: 90th percentile	218	331	177	< .01
OOP: 90th percentile	407	509	302	< .01
OOP > = $400	5.3%	7.7%	3.6%	< .01

* median OOP = 0

7084 Poster Session (Board #356), Fri, 8:00 AM-11:00 AM

Cost implications of clinical trial (CT) participation in metastatic non-small cell lung cancer (NSCLC). *First Author: Cristina Merkhofer, University of Washington, Seattle, WA*

Background: To assess the value of CTs in advanced NSCLC from the payer perspective, we compared insurance-related total direct medical costs for NSCLC patients who enrolled in CTs vs. those who did not. **Methods:** After linking electronic health records with tumor registry and claims data, we identified 101 patients with metastatic NSCLC diagnosed between 1/1/2007 and 12/31/2015 and treated at the Seattle Cancer Care Alliance. Eligibility criteria included 60-day minimum survival, claims for ≥ 1 anti-cancer drug within 180 days of diagnosis and insurance enrollment for the first 12 months after diagnosis. We abstracted patient sociodemographic, disease and treatment data, and obtained death dates from the Washington State Cancer Registry, censoring patients alive on 3/7/2019.We used the Kaplan-Meier sample-average (KMSA) estimator with bootstrapped 95% confidence intervals to describe direct medical costs and compared costs in CT enrollees vs. non-enrollees by applying a generalized linear model (Gamma distribution, log link) adjusted for confounding covariates. **Results:** Of 101 patients, 39 (39%) enrolled in CTs. Compared with non-enrollees, CT enrollees were younger (mean age 61.6 vs. 66.5 years), female (67% vs. 47%), Asian (18% vs. 11%), never smokers (41% vs.32%), had commercial insurance (44% vs. 35%), resided in metropolitan areas (90% vs. 79%) and had a higher median income ($81,149 vs. $76,844). Table shows KMSA estimates of total direct medical costs and adjusted mean lifetime total direct medical costs by CT participation. After adjusting for sex, smoking status, residence, income, insurance payer, ECOG and mutation status, CT enrollment was associated with an increase in lifetime total direct medical costs compared with no enrollment (adjusted cost ratio=1.39; 95% CI: 1.01, 1.90; p=0.043). **Conclusions:** CT participation is associated with increased total direct medical costs in patients with metastatic NSCLC. Our results may inform partnerships between trial sponsors, oncology centers and payers to sustain treatment innovation through CTs. Research Sponsor: Seattle Cancer Care Alliance Thoracic Oncology Research Donation Funds.

Total direct medical costs by CT participation.

Time after diagnosis	Non-CT participant KMSA estimates (95% CI)	CT participant KMSA estimates (95% CI)
0-12 months	$97,441 ($87,920, $105,823)	$113,425 ($103,243, $123,657)
> 12 months	$79,215 ($73,127, $84,931)	$175,685 ($162,688, $188,450)
	Non-CT participant adjusted mean total direct medical costs (95% CI)	**CT participant adjusted mean total direct medical costs (95% CI)**
Lifetime	$223,433 ($178,479, $268,387)	$309,629 ($231,891, $387,367)

7085 Poster Session (Board #357), Fri, 8:00 AM-11:00 AM

Cost-effectiveness analysis of stereotactic ablative radiotherapy in patients with oligometastatic cancer. *First Author: Abhishek Kumar, UC San Diego Health System, La Jolla, CA*

Background: The SABR-COMET randomized clinical trial found that stereotactic ablative radiotherapy (SABR) improved outcomes among cancer patients with oligometastatic disease. Yet, the cost of SABR along with the large number of patients with oligometastatic disease raises the important question of value. This study sought to evaluate the cost-effectiveness of SABR compared to standard therapy among cancer patients with oligometastatic disease. **Methods:** We constructed a Markov model to simulate treatment with stereotactic ablative radiotherapy or standard therapy among patients with oligometastatic cancers. The model derived transition probabilities from clinical trial data to estimate risks of toxicity, disease progression and survival. Healthcare costs and health utilities were estimated from the literature. Cost-effectiveness was estimated with an incremental cost-effectiveness ratio (ICER) defined as dollars per quality-adjusted life year (QALY), with an ICER less than $100,000/QALY considered cost-effective. One-way and probabilistic sensitivity analyses were used to examine model uncertainty. **Results:** The addition of SABR increased total costs by $54,279 and improved effectiveness by 1.20 QALYs compared with standard therapy, leading to an ICER of $45,162/QALY. The model was sensitive to assumptions about tumor progression, though the model was not sensitive to assumptions about survival or cost of treatment. The cost of SABR would need to increase approximately six-fold from $12,241 to $78,151 before SABR becomes cost-ineffective. Probabilistic sensitivity analyses demonstrated that SABR was the cost-effective treatment option 97.2% of the time. **Conclusions:** The addition of SABR increased costs and improved quality adjusted survival, overall leading to a cost-effective treatment strategy for patients with oligometastatic cancer. Research Sponsor: U.S. National Institutes of Health.

TPS7086 Poster Session (Board #358), Fri, 8:00 AM-11:00 AM

Open-label, randomized, multicenter, phase IV trial comparing parenteral nutrition using multi-chamber bags (Eurotubes) versus traditional 2/3-chamber bags in subjects with metastatic or locally advanced inoperable cancer requiring parenteral nutrition: The PEKANNUSS trial of the AIO. *First Author: Georg Martin Haag, Department of Medical Oncology, National Center for Tumor Diseases, University Hospital Heidelberg, Heidelberg, Germany*

Background: Approximately 50% of all cancer subjects suffer from cancer anorexia-cachexia syndrome accompanied by an inadequate food intake and predicting mortality, poor therapeutic response, diminished functional capacity, and reduced QoL. Especially in the advanced stages, parenteral nutrition (PN) is often required and accompanied by an increased risk of blood stream infections associated with increased mortality and other serious medical conditions such as sepsis. Furthermore, the switch from oral food intake to PN changes the patient's everyday life leading to reduced autonomy and flexibility (e.g. due to dependency on home nursing services). This study aims at evaluating the incidence of catheter-related infections (CRI) and the frequency of self-administered parenteral nutrition at home (HPN) in patients receiving standard PN via A) traditional two- or three-chamber bags (often requiring addition of vitamins and/or medications by home care service) or B). the multi-chamber bags Eurotubes (minimizing additional supplements and enabling self-administration by patients at home). In addition, one group of patients will receive low glucose HPN via Eurotubes to investigate a possible benefit on clinical outcome. **Methods:** This is an open-label, randomized, multicenter, investigator-initiated, phase IV trial. Overall, 350 patients with inoperable metastatic or locally advanced solid tumors who have an indication for parenteral nutrition will be enrolled. Patients will be randomized 1:1:1 ratio to Arm A (Standard PN using Eurotubes) or Arm B (Standard PN using 2/3-chamber bags), or to Arm A-1 (low glucose using Eurotubes). Patients will be assessed (physical exam, ECOG, weight, QoL, lab tests, AEs, HPN documentation) every 4 weeks during the 12 months HPN treatment period. Co-primary endpoints are incidence of CRI and patient autonomy (rate of self-administered PN at home). Secondary endpoints comprise weight change, change in albumin and CRP levels, overall survival, QoL, and safety. Recruitment has just started; first patient in was on February 5th, 2020. Clinical trial information: NCT04105777. Research Sponsor: Eurozyto Holding GmbH.

TPS7087 Poster Session (Board #359), Fri, 8:00 AM-11:00 AM

Head-to-head comparison of the non-G-CSF small molecule single agent (SA) plinabulin with SA pegfilgrastim for the prevention of docetaxel chemotherapy (chemo)-induced neutropenia (CIN) in the protective-1 trial. *First Author: Douglas W. Blayney, Stanford University, Stanford, CA*

Background: Plinabulin (Plin) is a small molecule with anti-cancer activity and CIN effects. The Phase (Ph) 2 clinical trial NPI-2358-101 (NCT00630110) evaluated Plin at 20 or 30 mg/m2 on Day (D) 1 and D8) plus D1 Docetaxel (Doc) 75 mg/m2 combination versus D1 Doc alone in patients (pts) with non-small cell lung cancer(NSCLC). In a large ($>$ 70%) subset of pts with a measurable lung lesion in the lung (per RECIST 1.1) receiving 30 mg/m2 Plin + Doc (n = 38), mOS was 4.6 months longer vs Doc alone (n = 38) (Mohanlal ASCO-SITC 2018). An unexpected post-hoc finding was a CIN benefit with adding at 20 or 30 mg/m2 Plin to Doc: 33% of pts in the Doc arm had grade 4 neutropenia, whereas in the Plin +Doc group 4% of pts ($P < 0.0003$) (Blayney ASH 2018). Plin boost the number the number of hematopoietic/progenitor cells in bone marrow. We subsequently initiated two global Ph3 programs with Plin: 1. A Ph 3 trial confirming its anticancer activity in NSCLC (study BPI-2358-103; NCT02504489; this trial is ongoing) and 2. An evaluation of Plin for CIN prevention through studies BPI-2358-105 (NCT03102606; PROTECTIVE-1), and study 106 (NCT03294577; PROTECTIVE-2). We previously reported from the Ph 2 portion of study 105, that SA Plin and Pegfigrastim (Peg) had comparable protection against CIN induced by Doc, however in contrast to Peg, Plin did not cause bone pain or thrombocytopenia (Blayney IASLC 2018, ESMO 2018). Plin is given by 30 min IV infusion on the same day of Chemo, 30 min after Chemo. The Ph3 portion of Study 105 in ongoing. **Methods:** In the Ph 3 portion of PROTECTIVE-1, pts with NSCLC, HRPC or BC are randomized (1:1) to either Plin 40 mg (over 30 minutes on D1; n = 75) or Peg 6mg (on D2, n = 75), and the primary endpoint is Duration of Severe Neutropenia (DSN). Plin 20 mg/m2 is similar to a 40 mg fixed dose. Absolute neutrophil counts (ANC) is determined on D 0, 1,2,3,6,8,9,10, 15 in Cycle 1 The trial aims to demonstrate non-inferiority of Plin vs Peg. Non-inferiority will be declared if the non-inferiority margin (NIM) of 0.65 day will be met, which NIM is more conservative than the 1 day NIM, typically employed for G-CSG biosimilar trials. Pts should have at least 1 risk factor as per NCCN guidelines.The trial is double-blinded to enable reliable PRO, Bone Pain and QoL assessments through validated questionnaires (EQ-5D-5L; EORTC QLQ-C30; Wang Baker Faces Pain Rating Scale). Following an Interim Analysis, the trial will continue without modifications. Clinical trial information: NCT03102606. Research Sponsor: BeyondSpring Pharmaceuticals Inc.

TPS7088 Poster Session (Board #360), Fri, 8:00 AM-11:00 AM

The FLEX real-world data platform explores new gene expression profiles and investigator-initiated protocols in early stage breast cancer. *First Author: Nina D'Abreo, NYU Winthrop Hospital, Mineola, NY*

Background: Genomic expression profiles have enabled the classification of breast cancers into molecular sub-types and provide prognostic information about the metastatic potential of the tumor, both of which have implications for the personalized treatment of breast cancer beyond clinical and pathological features. However, to precisely stratify tumors into actionable subgroups, full genome expression data should be combined with comprehensive clinical information. The FLEX Registry aims to aggregate a large, real-world dataset, which will enable discovery of novel genomic profiles, particularly for patient subsets that are underrepresented in traditional clinical trials and will contribute to improved precision in the management of breast cancer. **Methods:** The FLEX Registry (NCT03053193) is a multicenter, prospective, observational trial for patients with Stage I, II, and III breast cancer. Patients with stage I-III breast cancer who receive the 70-gene signature risk of recurrence test, with or without the 80-gene signature molecular sub-typing test, on a primary tumor are eligible for enrollment. The primary objective of FLEX is to create a large scale, population-based registry that links complete clinical data with full genome expression data to elucidate new prognostic and/or predictive gene associations in a real-world setting. The FLEX Registry employs a shared study infrastructure to develop and investigate hypotheses for targeted subset analyses and/or clinical trials based on full genome expression data. The adaptable protocol is designed to be amended with the inclusion of targeted sub-studies. Patients enrolled in the initial study are eligible for inclusion in sub-studies for which they meet all eligibility criteria and additional consent is not required. Data will be collected on patients from diagnosis through 10 years of follow-up and any necessary additional clinical data will be collected as specified in the appendix protocols. Target enrollment is a minimum of 10,000 patients; $>$4,000 patients have enrolled since April 2017 at more than 80 sites, including seven National Cancer Institute-designated comprehensive cancer centers. The FLEX collaborative platform enables participating investigators the opportunity to author their own sub-study protocols, as approved by the FLEX Steering Committee. Fifteen sub-studies have been approved for investigation within the FLEX Registry. Clinical trial information: NCT03053193. Research Sponsor: Agendia, Iinc.

7500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase Ib/II study of the IDH1-mutant inhibitor ivosidenib with the BCL2 inhibitor venetoclax +/- azacitidine in IDH1-mutated hematologic malignancies. *First Author: Curtis Andrew Lachowiez, M.D. Anderson Cancer Center, Houston, TX*

Background: Mutations in the isocitrate dehydrogenase-1 gene (*IDH1*) result in myeloid differentiation arrest and accumulation of the oncometabolite 2-hydroxyglutarate (2-HG), promoting leukemogenesis. We report a primary safety and efficacy analysis of the IDH1 inhibitor ivosidenib (IVO; 500 mg PO daily D15-continous) combined with venetoclax (VEN; D1-14 per 28-day cycle), with and without azacitidine (AZA; 75mg/m^2 D1-7). **Methods:** Eligible patients age ≥18 with *IDH1* mutated myeloid malignancies (high-risk MDS and AML) enrolled into one of three successive cohorts (Cohort 1: IVO+VEN 400 mg, Cohort 2: IVO+VEN 800 mg, Cohort 3: IVO+VEN 400 mg+AZA). Primary endpoints include safety and tolerability and overall response rate (ORR) by revised IWG criteria. Key secondary endpoints include survival endpoints and PK correlates. **Results:** 19 patients (median age 68) enrolled, 17 with AML: 9 relapsed/refractory AML (R/R; median 1 prior line of therapy), 5 treatment naïve AML, and 3 HMA-failure MDS with secondary AML. Two patients had high-risk MDS. ELN risk was favorable, intermediate, and adverse risk in 37%, 15%, and 47%. Co-mutations included *NPM1* (37%), chromatin-spliceosome (32%), methylation (16%), and RAS pathway (21%). Adverse events of special interest included IDH differentiation syndrome (n=4, grade > 3 in 1) and tumor lysis syndrome (TLS; n=2), including one grade 3 TLS event in a *NPM1*$^+$ patient (successfully managed without hemodialysis). In evaluable patients (n=18), composite complete remission (CRc: CR+CR$_i$+CR$_h$) rates were 78% overall (treatment naive: 100%, R/R: 75%), and 67%, 100%, and 67% by cohort (median time to best response: 2 months). 7 (50%) patients achieving CRc were also MRD negative by flow cytometry. 1 patient had HI without CR/CR$_i$ and 1 had a MLFS. 9 (50%) patients remain on study, 3 (17%) proceeded to SCT in CR, 2 were non-responders, and 5 (22%) experienced progressive disease following CR$_c$ occurring after a median of 3 months. After a median follow up of 3.5 months, median OS was not reached in treatment naïve patients, and 9.7 months in R/R patients. **Conclusions:** IVO+VEN +AZA therapy is well tolerated and highly effective for patients with *IDH1* mutated AML. Follow up and accrual is ongoing to better define duration and biomarkers of response. Clinical trial information: NCT03471260. Research Sponsor: Agios, AbbVie, Other Foundation.

Treatment outcomes.

Response	Cohort #1 (n=6)	Cohort #2 (n=6)	Cohort #3 (n=6)	Total (n=18)
Overall Response Rate	4	6	6	16 (89%)
CRc (CR+CRi+CRh)	4	6	4	14 (78%)
CR	3	3	1	7 (39%)
CRh	-	2	1	3(17%)
CRi	1	1	2	4 (22%)
MLFS	0	0	1	1(5.5%)
HR	0	0	1	1 (5.5%)
NR	2	0	0	2 (11%)

7501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Effect of enasidenib (ENA) plus azacitidine (AZA) on complete remission and overall response versus AZA monotherapy in mutant-*IDH2* (*mIDH2*) newly diagnosed acute myeloid leukemia (ND-AML). *First Author: Courtney Denton Dinardo, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: ENA and AZA each induce overall response rates (ORR) of ~30% and complete remission (CR) rates of ~20% in ND-AML. *In vitro*, combining ENA + AZA enhances cell differentiation. We report results of the phase II portion of an open-label, randomized phase I/II study of ENA + AZA (E+A) vs. AZA monotherapy (A) in patients (pts) with m*IDH2* ND-AML (NCT02677922). **Methods:** Pts age ≥ 18 years ineligible for intensive chemotherapy, with ECOG PS ≤ 2 and intermediate- or poor-risk cytogenetics, were randomized 2:1 to E+A or A in 28-day (d) cycles. All pts received SC AZA 75 mg/m^2/d x 7 d/cycle; pts randomized to E+A also received ENA 100 mg QD. The primary endpoint was ORR (CR, CR with incomplete recovery, partial remission, morphologic leukemia-free state). Other endpoints include duration of response (DOR), overall and event-free survival (OS, EFS), safety, and m*IDH2* VAF. **Results:** 101 pts received E+A (n = 68) or A (n = 33). Median age was 75 years (5785); most pts (83%) had intermediate-risk cytogenetics. 21 pts in the E+A arm and 1 in the A arm were ongoing at data cutoff (Aug 2019). Most common reason for discontinuation was disease progression (E+A 31%, A 52%). Median number Tx cycles was 10 (126) in the E+A arm and 6 (128) in the A arm. 7 pts (21%) in the A arm received subsequent Tx with ENA. ORR, CR rate and DOR were significantly improved with E+A *vs.* A (Table). Median OS was 22 mo in both arms (HR 0.99 [95%CI 0.52, 1.87]; $P = 0.97$). Median EFS was 17.2 and 10.8 mo in the E+A and A arms, respectively (HR 0.59 [95%CI 0.30, 1.17]; $P = 0.13$). Maximal m*IDH2* VAF change from BL was 83.4% with E+A *vs.* 17.7% with A ($P < 0.01$). No baseline co-mutation predicted primary resistance. Common Tx-related grade 34 AEs in the E+A arm were thrombocytopenia (37%), neutropenia (35%), anemia (19%), and febrile neutropenia (15%); these occurred in 19%, 22%, 22%, and 16% in the A arm. Grade 34 infections occurred in 18% of E+A pts and 31% of A pts. IDH differentiation syndrome occurred in 12 pts (18%) in the E+A arm. 5 E+A pts (7%) and 1 A pt (3%) died in the first 60 d. **Conclusions:** Combining ENA + AZA resulted in significantly improved response rates and durations, and was generally well-tolerated in older patients with m*IDH2* ND-AML. The impact of subsequent Tx on OS/EFS and new translational data will be presented at the meeting. Clinical trial information: NCT02677922. Research Sponsor: BMS.

Response.

	ENA + AZA n = 68	AZA Only n = 33	
ORR, n (%)	48 (71)	14 (42)	$P < 0.01$
DOR, mo, median [95%CI]	24.1 [11.1, NR]	12.1 [2.8, 14.6]	$P = 0.05$
CR, n (%)	36 (53)	4 (12)	$P < 0.01$
Stable disease, n (%)	13 (19)	13 (39)	

7502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Interim analysis (IA) of OPTIC: A dose-ranging study of three ponatinib (PON) starting doses. *First Author: Jorge E. Cortes, Georgia Cancer Center, Augusta, GA*

Background: In PACE (NCT01207440) heavily pretreated patients (pts) with chronic-phase CML (CP-CML) had deep, lasting responses to PON; long-term follow-up showed increasing rates of arterial occlusive events (AOEs). We present IA results from OPTIC (NCT02467270), evaluating the association between PON exposure, efficacy, and safety, and response-based dose reduction in pts with CP-CML. **Methods:** This ongoing, multicenter, randomized phase 2 trial enrolled pts with CP-CML resistant or intolerant to ≥2 TKIs or with a T315I mutation to receive PON at a starting dose of 45 mg (cohort A), 30 mg (B), and 15 mg (C) qd. Doses were reduced to 15 mg qd on achievement of ≤1% BCR-ABL1^{IS} in A/B. Primary endpoint: 12 mo ≤1% BCR-ABL1^{IS}; secondary endpoints include cytogenetic and molecular response and AOE, VTE, and TEAE rates. Results are descriptive at this IA and will be inferential by adjusting multiplicity across 3 cohorts at final analysis. **Results:** 283 pts were randomized (A/B/C: n = 94/95/94); median age 48 y (18–81 y). 26% had hypertension history; 2/43/55% received 1/2/≥3 TKIs; 40% had ≥1 baseline (BL) mutations, with 23% T315I. At IA data cutoff (20 Jul 2019), 162 pts (57%; n = 57/51/54) remained on study treatment. Among 282 pts in the safety population, median duration of exposure was ≈1 y (A/B/C, 12.9/11.2/11.0 mo). At 12 mo, 39% (95% CI, 27.6, 50.6), 27% (17.6, 39.1), and 26% (16.5, 38.6) in A, B, and C, respectively, achieved ≤1% BCR-ABL1^{IS}. Additional efficacy in Table. Dose reductions due to efficacy (A/B): 35/21%. Most common TEAEs (any grade/≥3): thrombocytopenia 39/27%, neutropenia 25/17%. AOEs/serious AOEs were reported by (A, B, C) 5%/2%, 4%/3%, and 1%/0%. Dose reductions due to TEAEs: (A/B/C): 44/31/28%; discontinuations due to TEAEs: 18/15/14%. There were 4 (1.4%) on-study deaths; A, sudden death, n = 2; C, pneumonia, n = 2; no deaths were due to AOEs. Clinical trial information: NCT01207440. **Conclusions:** OPTIC IA shows a trend toward dose-dependent efficacy and safety and may provide a refined understanding of the PON benefit:risk profile and its relation to dose. Data from longer follow-up may support an alternate dosing regimen for pts with CP-CML. Research Sponsor: ARIAD Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

Month 12 BCR-ABL1^{IS},[a] n (%)	45 mg n = 75	30 mg n = 73	15 mg n = 68
≤10%	38 (50.7)	31 (42.5)	30 (44.1)
≤1%	29 (38.7)	20 (27.4)	18 (26.5)
≤0.1% (MMR)	11 (14.7)	13 (17.8)	13 (19.1)

MMR, major molecular response.
[a]Includes all pts who are randomized and with measurable BCR-ABL1^{IS} at BL. Those still on treatment who have not reached 12 mo were excluded. As the primary endpoint was ≤1% BCR-ABL1^{IS} at 12 mo, pts who were already ≤1% BCR-ABL1^{IS} at BL (n = 3 pts; A, 2; C, 1) were not considered responders.

7503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Development and validation of a pediatric disease risk index for allogeneic hematopoietic cell transplantation. *First Author: Muna Qayed, Emory University, Atlanta, GA*

Background: Characteristics such as disease, disease status and cytogenetic abnormalities impact relapse and survival after transplantation for acute myeloid (AML) and acute lymphoblastic (ALL) leukemia. In adults, these attributes were used to derive the disease risk index for survival. Thus, the current analysis sought to develop and validate a pediatric disease risk index (p-DRI). **Methods:** Eligible were patients aged <18 years with AML (n=1135) and ALL (n=1228) transplanted between 2008 and 2017 in the United States. Separate analyses were performed for AML and ALL. Patients were randomly assigned (1:1) to a training and validation cohort. Cox proportional hazards model with stepwise selection was used to select significant variables (2-sided p<0.05). The primary outcome was leukemia-free survival (LFS; relapse or death were events). Based on the magnitude of log(HR), a weighted score was assigned to each characteristic that met the level of significance and risk groups were created. **Results:** Four risk groups were identified for AML and three risk groups for ALL (Table). The 5-year probabilities of LFS for AML were 81% (68-91), 56% (51-61), 44% (39-49) and 21% (15-28) for good, intermediate, high and very high-risk groups, respectively. The 5-year probabilities of LFS for ALL were 68% (63-72), 50% (45-54) and 15% (3-34) for good, intermediate, high risk groups, respectively. **Conclusions:** This validated p-DRI successfully stratified children with AML and ALL for prognostication undergoing allogeneic transplantation. Research Sponsor: U.S. National Institutes of Health.

p-DRI	Age	Disease status	Cytogenetic risk	Training Cohort	Validation cohort
Acute myeloid leukemia					Brier score 0.169
Good	≥3	1st/2nd CR MRD (-)	favorable	HR 1.00	HR 1.00
Score 0	years			P<0.0001	P<0.0001
Intermediate	≥3	1st/2nd CR MRD (-)	Intermediate/poor	HR 2.47	HR 3.09
Score 1-4	years	1st/2nd CR MRD (+)	favorable	P=0.048	P=0.027
	<3 years	1st/2nd CR MRD (-) 1st CR MRD (+)	favorable		
High	≥3	Relapse	favorable	HR 3.68	HR 4.78
Score 5-7	years			P=0.005	P=0.002
	<3 years	2nd CR MRD (+) Relapse	favorable		
		1st/2nd CR MRD (-)	Intermediate/poor		
Very high	<3 years	2nd CR MRD (+)	Intermediate/poor	HR 8.45,	HR 8.09
Score ≥8		Relapse		p<0.0001	P<0.0001
Acute lymphoblastic leukemia					Brier score 0.158
Good	≥2	1st CR MRD (-)	Any cytogenetic	HR 1.00	HR 1.00
Score 0	years	1st CR MRD (+)	risk	P<0.0001	P<0.0001
Intermediate	≥2	2nd CR MRD (-)		HR 1.51	HR 2.03
Score 2-4	years	2nd CR MRD (+) Relapse		P=0.004	P<0.0001
	<2 years	1st CR MRD (-) 1st CR MRD (+)			
High	<2 years	2nd CR MRD (-)		HR 5.22	HR 6.65
Score ≥5		2nd CR MRD (+) Relapse		P<0.0001	P<0.0001

7505 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Post-traumatic stress symptoms in hematopoietic stem cell transplant (HCT) recipients. *First Author: Sarah Griffith, Massachusetts General Hospital, Boston, MA*

Background: Patients admitted for HCT, an intensive and potentially curative therapy for hematologic malignancies, experience a prolonged, isolating hospitalization and endure substantial physical and psychological symptom burden. However, data are limited regarding long-term post-traumatic stress (PTSD) in HCT survivors and its risk factors. **Methods:** We conducted a secondary analysis examining longitudinal data from 250 patients who underwent autologous and allogenic HCT. We used the Post-Traumatic Stress Checklist (PTSD-CL) to assess for PTSD symptoms at six months post-HCT. We used the Functional Assessment of Cancer Therapy—Bone Marrow Transplant (FACT-BMT), and the Hospital Anxiety and Depression Scale to assess quality of life (QOL), depression, and anxiety symptoms at the time of admission for HCT, at week-2 during hospitalization, and at six months post-HCT. We used multivariate regression models to assess factors associated with PTSD symptoms, modeling QOL, depression, and anxiety symptoms separately given their collinearity. **Results:** The mean age was 56.3 (SD = 13.3). The rate of clinically significant PTSD symptoms at six months post-HCT was 18.9% and these patients experienced hypervigilance (92.3%), avoidance (92.3%), and intrusion (76.9%) symptoms. Among patients without clinically significant PTSD symptoms, 24.5% and 13.7% had clinically significant hypervigilance and avoidance symptoms, respectively. Lower QOL at time of HCT admission (B = -0.04, P = 0.004), and being single (B = -3.35, P = 0.027) were associated with higher PTSD symptoms at six months post-HCT. Higher anxiety at time of HCT admission (B = 1.34, P $<$ 0.001), change in anxiety during HCT hospitalization (B = 0.59, P = 0.006), and being single (B = -3.50, P = 0.017), were associated with higher PTSD symptoms at six months. In a separate model, younger age (B = -0.13, P = 0.017), being single (B = -3.58, P = 0.018), and higher baseline depression symptoms were also associated with higher PTSD symptoms at six months (B = 0.97, P $<$ 0.001). **Conclusions:** Approximately one fifth of patients undergoing HCT experienced clinically significant PTSD symptoms at six months post-transplant. Patients' baseline QOL and psychological symptoms emerged as important predictors of their risk for PTSD at six months post-HCT. Thus, interventions to prevent and treat PTSD symptoms in HCT recipients are clearly warranted. Research Sponsor: Lymphoma and Leukemia Society.

7506 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Phase II study of pevonedistat (P) + azacitidine (A) versus A in patients (pts) with higher-risk myelodysplastic syndromes (MDS)/chronic myelomonocytic leukemia (CMML), or low-blast acute myelogenous leukemia (LB AML) (NCT02610777). *First Author: Lionel Ades, Hôpital Saint-Louis, Paris, France*

Background: P, the first and only small-molecule inhibitor of the NEDD8-activating enzyme, disrupts proteasomal degradation of select proteins and has shown promising clinical activity and good tolerability in combination with A in AML. **Methods:** 120 pts with higher-risk (Revised International Prognostic Scoring System risk $>$ 3) MDS/CMML or LB AML naïve to hypomethylating agents were randomized 1:1 to receive P 20 mg/m^2 intravenously (IV) on days (d) 1, 3, 5 + A 75 mg/m^2 (IV/subcutaneously) on d 1–5, 8, 9 (n = 58), or A alone (n = 62), in 28-d cycles until unacceptable toxicity, relapse, transformation to AML, or progression. The primary endpoint was overall survival (OS), although the study was underpowered for OS. **Results:** Baseline characteristics were generally balanced between arms. Pts received a median of 13.0 vs 8.5 cycles of P+A vs A. Median OS in the intent-to-treat (ITT) population with P+A vs A (n = 120) was 21.8 vs 19.0 mos (hazard ratio [HR] 0.80; 95% CI 0.51–1.26; *P* = .334; median follow-up 21.4 vs 19.0 mos). Subanalyses showed median OS with P+A vs A in higher-risk MDS (n = 67) of 23.9 vs 19.1 mos (HR 0.70; 95% CI 0.39–1.27; *P* = .240) and in LB AML (n = 36) of 23.6 vs 16.0 mos; HR 0.49; 95% CI 0.22–1.11; *P* = .081). Event-free survival (EFS – time from randomization to death/transformation to AML) with P+A vs A trended longer in the ITT population (median 21.0 vs 16.6 mos; HR 0.65; 95% CI 0.41–1.02; *P* = .060) and was significantly longer in higher-risk MDS (median 20.2 vs 14.8 mos; HR 0.54; 95% CI 0.29–1.00; *P* = .045). In response-evaluable pts, overall response rate was 71% (n = 39/55; 46% complete remission [CR] + CR with incomplete blood count recovery [CRi], 5% partial response [PR], 20% hematologic improvement [HI]) with P+A vs 60% (n = 32/53; 38% CR+CRi, 8% PR, 15% HI) with A. In higher-risk MDS, CR rate was 52% vs 27% (*P* = .050) with P+A vs A. Median A dose intensity was 97% vs 98% with P+A vs A. Rates of grade ≥3 adverse events were 90% vs 87% with P+A vs A; the most common were 31% vs 27% neutropenia, 26% vs 29% febrile neutropenia, 19% vs 27% anemia, and 19% vs 23% thrombocytopenia. On-study deaths occurred in 9% of P+A pts and 16% of A pts. **Conclusions:** P+A had a comparable safety profile to A alone, did not increase myelosuppression, and maintained A dose intensity. Although not statistically significant, P+A increased OS, EFS, and response rates vs A, particularly in pts with higher-risk MDS. Further evaluation of P+A vs A is ongoing in a randomized phase. Clinical trial information: NCT02610777. Research Sponsor: Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

7507 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Tolerability and efficacy of the first-in-class anti-CD47 antibody magrolimab combined with azacitidine in MDS and AML patients: Phase Ib results. *First Author: David Andrew Sallman, Moffitt Cancer Center, Tampa, FL*

Background: Magrolimab (Hu5F9-G4) is an antibody blocking CD47, a macrophage immune checkpoint and don't eat me signal on cancers. It induces tumor phagocytosis and eliminates leukemia stem cells. Azacitidine (AZA) synergizes with magrolimab by inducing eat me signals on leukemic cells, enhancing phagocytosis. We report Ph1b data including a potential MDS registration cohort. **Methods:** Magrolimab+AZA was given to untreated intermediate to very high risk IPSS-R MDS and intensive chemo unfit AML patients. A magrolimab priming/intrapatient dose escalation regimen (1-30 mg/kg QW, Q2W Cycle 3+) was used. AZA was dosed 75mg/m^2 days 1-7. Efficacy was assessed by IWG 2006 (MDS) and ELN 2017 (AML) criteria. **Results:** 68 patients (39 MDS, 29 AML) with a median age of 72 were treated with magrolimab+AZA. 19% were intermediate cytogenetic risk with 68% poor risk (13% unknown). 27% were *TP53* mutant. The combo was well-tolerated with safety similar to AZA alone. Common treatment-related AEs were anemia (38%), fatigue (21%), neutropenia (19%), thrombocytopenia (18%) and infusion reaction (16%). Treatment-related febrile neutropenia was 1.5%. Only 1 patient (1.5%) discontinued due to an AE. In RBC transfusion dependent patients, 58% of MDS and 64% of AML patients became transfusion independent. 30/33 (91%) efficacy evaluable MDS patients had an objective response (42% CR, 24% marrow CR (4/8 also with HI), 3% PR, 21% HI alone, 9% SD). MDS patient responses deepened on study, with a 56% CR rate in patients with ≥ 6 mo follow-up. In AML, 16/25 (64%) responded (40% CR, 16% CRi, 4% PR, 4% MFLS, 32% SD, 4% PD). In 12 *TP53* mutant AML patients, 75% had a CR+CRi (42% CR, 33% CRi, 17% SD, 8% PD). Cytogenetic CR was seen in 35% and 50% of responding MDS and AML patients. 22% of MDS and 50% of AML patients with CR/CRi/marrow CR were MRD negative by flow cytometry. Median duration of response is not reached in either MDS or AML, including *TP53* mutant AML, with a median follow-up of 5.8, 8.8 and 9.4 mos, respectively (range: 1.9 – 16.8 mos). 91% of MDS and 100% of AML responding patients are in response at 6 mos. The 6 mo overall survival estimate is 100% in MDS and 91% in TP53 mutant AML patients. **Conclusions:** Magrolimab is a macrophage targeting immunotherapy that with AZA is well tolerated with durable efficacy in MDS, AML, particularly *TP53* mutant, a poor prognostic group. A potential registration single arm MDS cohort is ongoing (NCT03248479). ENHANCE, a randomized Ph3 MDS trial is planned. Additional patients/analyses will be reported. Funded by Forty Seven and CIRM. Clinical trial information: NCT03248479. Research Sponsor: Forty Seven, Inc., Other Government Agency

7508 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Updated results from phase I dose-escalation study of AMG 330, a bispecific T-cell engager molecule, in patients with relapsed/refractory acute myeloid leukemia (R/R AML). *First Author: Farhad Ravandi, Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: In this open label phase 1 dose escalation study, safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of AMG 330 were evaluated in patients (pts) with R/R AML (NCT#02520427). **Methods:** AMG 330 was evaluated as a continuous IV (cIV) infusion using a 3+3 design. Response was assessed per revised IWG criteria. Each cycle (2–4 weeks duration) was followed by an infusion-free interval. Eligible pts were ≥18 y/o with $>$ 5% blasts in bone marrow and ≥1 line/s of prior therapy. **Results:** As of December 10, 2019, 55 pts (median age, 58.0 [18.0–80.0] years) were enrolled in 16 cohorts. AMG 330 was administered on 4 schedules (0–3 dose steps) prior to the target dose (TD, 0.5–720 μg/day). Dose steps were implemented in the dose schedule design based on the adverse event (AE) profile. Across all schedules, 55 (100%) pts reported treatment-emergent AEs (any grade). AMG 330–related AEs reported in 49/55 (89%) pts included cytokine release syndrome (CRS; 67%; ≥ grade 3 in 13%), (60%) and nausea (20%) as the most frequent AEs. CRS was reversible and occurred in a dose/schedule-dependent manner mostly within the first 24 hours of administration of triggering AMG 330 dose. The frequency and severity of CRS correlated with the dose level and leukemic burden at baseline. AMG 330 exhibited dose-dependent increase in steady state exposures over the studied dose range with clinical PK profile consistent with cIV administration. Eight of 42 evaluable pts responded: 3 complete remissions (CR; including 1 CR with negative measurable residual disease reported after data snapshot), 4 CR with incomplete hematologic recovery, and 1 morphologic leukemia free state. Seven responders who achieved CR/CRi received a TD equal or above the minimal efficacious dose of 120 μg/day. Among analyzed CR/CRi responders, 4/6 (67%) had adverse cytogenetic risk profile, 3/6 (50%) had ≥4 lines of prior therapy and all had relapsed disease. Responders had higher AMG 330 exposures and 3 responders treated with ≥600 μg/day TD remain in CR/CRi: 1 patient for $>$ 5 months after cycle 1, 1 patient bridged to hematopoietic stem cell transplant after cycle 4 and 1 patient is in cycle 3. Preliminary response assessment showed a correlation with lower tumor burden at baseline with a trend towards higher CD8+ lymphocyte count and E:T ratio. **Conclusions:** AMG 330 dosed up to 720 μg/day provided early evidence of acceptable safety profile, drug tolerability and anti-leukemic activity, and supports further dose escalation. Clinical trial information: NCT02520427. Research Sponsor: Amgen Inc.

7509 Poster Discussion Session; Displayed in Poster Session (Board #282), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Glasdegib (GLAS) plus low-dose cytarabine (LDAC) in AML or MDS: BRIGHT AML 1003 final report and four-year overall survival (OS) follow-up. *First Author: Michael Heuser, Department of Hematology, Hemostasis, Oncology and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany*

Background: In newly diagnosed AML or high-risk MDS, primary analysis of the randomized phase 2 BRIGHT AML 1003 trial (data cutoff Jan 2017) showed superior OS for GLAS+LDAC vs LDAC alone. The trial then continued to predefined completion 4 years from randomization of all patients (pts), reached in Mar 2019 and presented herein. **Methods:** Pts with newly diagnosed AML or high-risk MDS and unsuitable for intensive chemotherapy were randomized 2:1 to GLAS+LDAC (n=88) or LDAC alone (n=44). For these groups, median (range) treatment duration was 83 (3-1575) and 47 (6-239) days; median follow-up for survival 47.6 and 48.1 months; 4 (4.5%) and 1 pt (2.3%) completed ≥4 years' follow-up. **Results:** Consistent with the primary findings (OS HR 0.51; 80% CI 0.39, 0.67 p=0.0004), GLAS+LDAC prolonged OS vs LDAC alone (table). Results were consistent in AML pts and cytogenetic risk/disease history subgroups (table), as were analyses by pt characteristics and baseline risk factors (not shown). Survival probability was 39.5% vs 9.5% at 1 year and 18.0% vs 2.4% at 2 years. GLAS+LDAC induced higher complete remission (CR) rates overall (16/88 vs 1/44; RR 8.12, 95% CI 1.05, 62.78, p=0.010) and across subgroups. Notably, fewer pts discontinued GLAS+LDAC due to AEs (38.1% and 46.3%) and there was no increased sepsis or bleeding vs LDAC alone despite longer glasdegib treatment. With GLAS+LDAC, SMO-inhibitor-associated AEs included dysgeusia (25.0%), muscle spasms (22.6%) and alopecia (10.7%), with only 1 pt discontinuing due to dysgeusia. **Conclusions:** Consistent with primary analyses, GLAS+LDAC continued to have an acceptable safety profile and improved OS vs LDAC alone. HRs were consistent across cytogenetic risk subgroups and support use of GLAS+LDAC in de novo and secondary AML. Clinical trial information: NCT01546038. Research Sponsor: Pfizer.

OS	GLAS+LDAC, n/N	mOS, mo (95% CI)	LDAC alone, n/N	mOS, mo (95% CI)	HR (95% CI)	p
All pts	80/88	8.8 (5.0, 11.7)	41/44	4.9 (2.9, 6.5)	0.53 (0.35, 0.80)	0.001
AML	71/78	8.3 (4.7, 12.2)	35/38	4.3 (1.9, 5.7)	0.53 (0.35, 0.80)	0.001
Good / int CGR	47/53	12.2 (6.9, 16.5)	19/22	5.3 (3.5, 8.7)	0.54 (0.31, 0.93)	0.011
Poor CGR	24/25	4.4 (2.6, 7.4)	16/16	2.1 (1.0, 4.9)	0.51 (0.26, 1.00)	0.023
De novo	34/38	6.6 (3.7, 12.4)	16/18	4.3 (1.3, 10.7)	0.75 (0.41, 1.36)	0.168
Secondary	37/40	9.1 (4.4, 16.5)	19/20	4.1 (1.5, 6.4)	0.29 (0.15, 0.55)	<0.001

1-sided p value. CGR=cytogenetic risk (good/intermediate = favorable, intermediate-I and -II risk; poor = adverse risk).

7510 Poster Discussion Session; Displayed in Poster Session (Board #283), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Five-year final results of a phase III study of CPX-351 versus 7+3 in older adults with newly diagnosed high-risk/secondary AML. *First Author: Jeffrey E. Lancet, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL*

Background: CPX-351 (Vyxeos; daunorubicin and cytarabine liposome for injection), a dual-drug liposomal encapsulation of cytarabine [C] and daunorubicin [D], is approved by the FDA and EMA for the treatment of adults with newly diagnosed therapy-related AML or AML with myelodysplasia-related changes. Primary analysis of the pivotal phase 3 study (NCT01696084) that formed the basis for these approvals evaluated patients (pts) aged 60-75 y with newly diagnosed high-risk/secondary AML and found that CPX-351 significantly improved median overall survival (OS) vs conventional 7+3, with a comparable safety profile. Here, we report the prospectively planned final 5-y follow-up results from this phase 3 study. **Methods:** Pts were randomized 1:1 to receive ≤2 induction cycles of CPX-351 (100 units/m^2 [C 100 mg/m^2 + D 44 mg/m^2] as a 90-min infusion on Days 1, 3, 5 [2nd induction: Days 1, 3]) or 7+3 (C 100 mg/m^2/d continuously for 7 d + D 60 mg/m^2 on Days 1-3 [2nd induction: 5+2]). Pts achieving complete remission (CR) or CR with incomplete platelet or neutrophil recovery could receive up to 2 consolidation cycles. Pts could receive a hematopoietic cell transplant (HCT) at the physician's discretion. Pts were followed until death or up to 5 y following randomization. **Results:** In total, 309 pts were randomized to CPX-351 (n = 153) or 7+3 (n = 156). The survival rate at 5 y was higher for CPX-351 vs 7+3 (18% vs 8%; Table). Among pts who died, the most common primary cause of death was progressive leukemia in both arms (CPX-351: 56%; 7+3: 53%). After a median follow-up of 60.65 mo, improved median OS with CPX-351 vs 7+3 was maintained: 9.33 vs 5.95 mo; Kaplan-Meier (KM) OS curves plateaued at ~30 mo. HCT was received by 53 (35%) vs 39 (25%) pts after CPX-351 vs 7+3; among these pts, the survival rate at 5 y was higher for CPX-351 vs 7+3 (52% vs 23%), and median OS landmarked from the HCT date was not reached for CPX-351 vs 10.25 mo for 7+3 (Table). **Conclusions:** After 5 y of follow-up, improved OS was maintained in this phase 3 study, supporting that CPX-351 has the ability to produce or contribute to long-term remission and survival in older pts with newly diagnosed high-risk/secondary AML. Clinical trial information: NCT01696084. Research Sponsor: Jazz Pharmaceuticals.

	CPX-351 (n = 153)	7+3 (n = 156)
Median follow-up (10th-90th percentiles),[a] mo	60.91 (58.84-63.97)	59.89 (58.22-63.90)
Median OS, mo	9.33	5.95
HR (95% CI)	0.70 (0.55-0.91)	
3-y survival rate,[a] %	21	9
5-y survival rate,[a] %	18	8
HCT rate	35	25
Median OS landmarked from HCT date, mo	Not reached	10.25
HR (95% CI)	0.51 (0.28-0.90)	
3-y survival rate in pts with HCT,[a] %	56	23
5-y survival rate in pts with HCT,[a] %	52	23

[a]KM estimated.

7511 Poster Discussion Session; Displayed in Poster Session (Board #284), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase III study of venetoclax plus low-dose cytarabine in previously untreated older patients with acute myeloid leukemia (VIALE-C): A six-month update. *First Author: Andrew H. Wei, The Alfred Hospital and Monash Universtiy, Melbourne, VIC, Australia*

Background: VIALE-C was designed to compare the safety and efficacy of the BCL-2 inhibitor venetoclax (VEN) or placebo (PBO) plus low-dose cytarabine (LDAC) in previously untreated patient (pts) with acute myeloid leukemia (AML; ≥75 yr or ≥18 yr with comorbidities precluding intensive chemotherapy). The primary overall survival (OS) analysis showed a clinically meaningful improvement with VEN+LDAC, although the primary endpoint was not met. Herein, we present a 6-mo update after primary analysis, with a focus on OS. **Methods:** This double-blind, PBO-controlled phase 3 study (NCT03069352) randomized pts 2:1 to VEN (600 mg orally QD, days [d]1–28) with 4-d ramp-up in first cycle or PBO in 28-d cycles, plus LDAC (20 mg/m^2 subcutaneously QD, d1–10). The primary endpoint was OS; secondary endpoints included response, transfusion independence (TI; red blood cells [RBC] or platelets), and event-free survival (EFS). OS and EFS were analyzed by the Kaplan-Meier method and compared between arms using the log-rank test stratified by AML status (de novo vs secondary) and age (18 to < 74 vs ≥75). The planned sample size was 210 pts (n = 140, VEN; n = 70, PBO) to detect a hazard ratio (HR) of 0.545 in OS with 2-sided alpha of 5% and power of 90%. **Results:** As of 15 Aug 2019, 211 pts were randomized (n = 143, VEN; n = 68, PBO); median age: 76 yr in both arms (range: 36–93); secondary AML: 38% (88% post-MDS/CMML); prior hypomethylating agent: 20%. With a median follow-up of 17.5 mo (range: 0.1–23.5), median OS was 8.4 mo vs 4.1 mo in the VEN+LDAC and PBO+LDAC arms (HR 0.70; 95% CI 0.50–0.99; *P*= .04), representing a 30% reduction in the risk of death. Complete remission (CR)/CRi and CR/CRh (CR with partial hematologic recovery) rates were both 48% for the VEN+LDAC arm, and 13% and 15%, respectively, for PBO+LDAC. RBC/platelets TI rates were 43%/49% vs 19%/32% for VEN+LDAC and PBO+LDAC. Median EFS was 4.9 mo vs 2.1 mo in the VEN+LDAC and PBO+LDAC arms (HR 0.61; 95% CI 0.44–0.84; *P*= .003). Grade ≥3 adverse events (AEs [> 30%]; VEN+LDAC/PBO+LDAC) included neutropenia (49%/18%), thrombocytopenia (45%/38%), and febrile neutropenia (32%/29%); serious AEs (> 10%) were febrile neutropenia (17%/18%) and pneumonia (14%/10%); tumor lysis syndrome occurred in 5.6%/0%. **Conclusions:** VEN+LDAC demonstrates a clinically meaningful improvement in OS compared with PBO+LDAC, with a tolerable and manageable safety profile. These data support VEN+LDAC as a frontline treatment option for older pts with AML, as well as those considered unfit for intensive chemotherapy. Clinical trial information: NCT03069352. Research Sponsor: AbbVie, Inc.

7512 Poster Discussion Session; Displayed in Poster Session (Board #285), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Inotuzumab ozogamicin (INO) plus bosutinib (BOS) in R/R PH+ ALL or CML in lymphoid blast phase (CML LBP). *First Author: Nitin Jain, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Pts with R/R Ph+ ALL and CML LBP have poor outcomes. INO is an anti-CD22 antibody drug conjugate approved for R/R ALL. BOS is a 2nd generation BCR-ABL TKI approved for CML. **Methods:** This was a phase I/II study of INO + BOS for R/R Ph+ ALL and CML LBP. Primary objective was to determine safety and the maximum tolerated dose (MTD) of the combination. Secondary objective was to assess efficacy. Pts with T315I mutation were excluded. Pts needed to have adequate organ function (Cr ≤2 gm/dL, total bilirubin ≤2 mg/dL, ALT & AST ≤3xULN). BOS was dosed once daily starting on cycle 1 day 1, and 3 dose levels were evaluated (300, 400, 500 mg) in a standard 3+3 design. INO was given IV weekly during cycle 1 (0.8 mg/m^2 day 1; 0.5 mg/m^2 day 8; 0.5 mg/m^2 day 15). In responding pts, INO was subsequently administered at 1 mg/m^2 once every 4 weeks for a total of 6 cycles. **Results:** Between June 2015 and December 2019 we enrolled 18 R/R pts (16 Ph+ ALL, 2 CML LBP). The median age was 62 yrs (range 19-74), median no. of prior therapies was 1 (range 1-5) and 9 pts had ABL kinase domain mutations at screening. There were no early deaths (<30 days). 3 pts were treated at BOS dose level 1; 6 pts at dose level 2; 9 pts at dose level 3. 1 pt had a DLT at dose level 2 - G3 skin rash, and 2 pts had a DLT at dose level 3 - both G3 skin rash. First 3 pts at dose level 3 did not receive ≥80% BOS doses during cycle 1 due to issues unrelated to adverse events (AE). As 2/6 DLT evaluable pts at dose level 3 had DLTs thus exceeding the MTD, the dose level 2 was identified as the MTD. Most frequent AE were diarrhea in 50%, rash in 50%, and nausea in 39%. Grade 3 AEs were rash (3), reversible ALT elevation (1) and hyponatremia (1). No pts had veno-occlusive disease. Pts have received a median of 3 cycles (range 1-8) with a median of 1 cycle to response (range 1-2). Responses are shown in Table. Median time to response was 1 months (mo, range 0.8-2.1), median time to negative MRD by flow cytometry (FCM) was 6.9 mo (range 3.4-18) and median time to complete molecular response (CMR) was 9.1 mo (range 3.4-18). After a median follow-up of 32 mo, the median overall survival was 15.4 mo and median event-free survival censored at stem-cell transplantation (SCT) was 6.1 mo. 6 pts underwent SCT, 8 pts relapsed, 10 pts are alive and 2 pts continue therapy. **Conclusions:** INO + BOS was well tolerated and showed promising activity in R/R Ph+ ALL and CML LBP. Clinical trial information: NCT02311998. Research Sponsor: U.S. National Institutes of Health.

Responses with INO + BOS in R/R Ph+ ALL and CML LBP.

Response	n/N (%)
Overall response rate	15/18 (83)
CR	11/18 (61)
CRi	4/18 (22)
Complete cytogenetic response	11/11 (100)
MRD negative by FCM	10/15 (67)
Major molecular response	13/15 (87)
CMR	8/15 (53)

7513 Poster Discussion Session; Displayed in Poster Session (Board #286), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Escalated dosing schedules of CC-486 for patients experiencing first acute myeloid leukemia (AML) relapse: Results from the phase III QUAZAR AML-001 maintenance trial. *First Author: Hartmut Dohner, Universitätsklinikum Ulm, Ulm, Germany*

Background: A goal of AML maintenance therapy is to decrease the risk of relapse by suppressing growth of residual leukemic cells post-induction. CC-486 is an oral hypomethylating agent that allows for extended dosing schedules (>7 days [d]/28d cycle) to sustain therapeutic activity. In the QUAZAR AML-001 trial (NCT01757535), CC-486 maintenance treatment (Tx) significantly prolonged overall (OS) and relapse-free survival vs. placebo (PBO) in pts with AML in first remission following induction chemotherapy (IC), who were not candidates for hematopoietic stem cell transplant (HSCT). Pts initially received CC-486 or PBO for 14d/cycle, but pts who relapsed with 5–15% blasts could receive escalated 21d/cycle dosing. We review outcomes of pts who received 21d dosing in QUAZAR AML-001. **Methods:** Pts were aged ≥ 55 years, with intermediate- or poor-risk cytogenetics and ECOG PS ≤ 3, and had achieved first CR/CRi after IC ± consolidation. Within 4 mo of CR/CRi, pts were randomized 1:1 to CC-486 300 mg or PBO QD on d 1–14 of 28d Tx cycles. CR/CRi status was assessed every 3 cycles. Pts relapsing with 5%–15% blasts in blood or bone marrow could receive study drug for 21d/cycle at the investigator's discretion. Tx could continue until > 15% blasts, unacceptable toxicity, or HSCT. **Results:** 91 patients (CC-486, 51/238 [21%]; PBO, 40/234 [17%]) were assigned to ≥ 1 21d/cycle dosing schedule. Median time to dose escalation was 9.2 mo (range 1.0-52.7) for CC-486 and 6.0 mo (0.5-19.3) for PBO. Median number of 21d dosing cycles was 2.0 (range 1-45) in the CC-486 arm and 2.0 (1-16) in the PBO arm; 43% and 18% of pts, respectively, received > 3 cycles of 21d dosing. Among 78 evaluable pts, 10/43 (23%) CC-486 pts and 4/35 (11%) PBO pts regained CR/CRi (central review) during dose escalation. Median OS from randomization was 22.8 mo *vs.* 14.6 mo with CC-486 *vs.* PBO, respectively (HR 0.66 [95%CI 0.42, 1.0]; $P = 0.073$), and 1-year survival rates were 80.4% *vs.* 59.5% (+20.9% [95%CI 2.1%, 39.7%]). The most common AEs with first onset during 21d dosing were febrile neutropenia (CC-486 24%, PBO 3%), thrombocytopenia (22%, 23%), anemia (22%, 20%), and neutropenia (20%, 10%). **Conclusions:** Escalated 21d CC-486 dosing was well tolerated and resulted in prolongation of OS and restoration of remission in approximately one-fourth of pts. Hematologic AEs first reported during escalated dosing in both Tx arms may be due in part to disease relapse. A 21d dosing schedule should be considered for pts receiving CC-486 who experience relapse with 5–15% blasts. Clinical trial information: NCT01757535. Research Sponsor: BMS.

7514 Poster Discussion Session; Displayed in Poster Session (Board #287), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Long-term survivors and gilteritinib safety beyond one year in *FLT3*-mutated R/R AML: ADMIRAL trial follow-up. *First Author: Alexander E. Perl, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA*

Background: The phase 3 ADMIRAL trial showed that gilteritinib was superior to salvage chemotherapy (SC; median overall survival [OS]: 9.3 vs 5.6 mo, respectively) in $FLT3^{mut+}$ R/R AML patients (pts; Perl, et al. *N Engl J Med.* 2019). This follow up (FU) of the ADMIRAL trial assessed long-term (LT) survivors and gilteritinib safety beyond 1 year. **Methods:** A data cut was performed 1 year after the primary analysis. Response outcomes in LT survivors (OS ≥18 mo) in the gilteritinib arm, and safety during and after 12 mo of gilteritinib therapy were assessed. **Results:** At 1 year after the primary analysis, median FU for OS was 29.2 mo. Median OS remained longer with gilteritinib (9.3 mo) than with SC (5.6 mo; HR=0.679 [95% CI: 0.527, 0.875], nominal *P*=0.0026); 18-mo OS rates were 27% and 15%, respectively (Table). Of 49 censored pts in the gilteritinib arm, 20 continued treatment; 13 of these 20 pts underwent transplantation (HSCT) and received gilteritinib post-HSCT. Median gilteritinib exposure was 4.1 mo (IQR, 2.1-8.2) and median average dose was 120 mg/day (range, 43.8-192.3); 12% (n=30/246) of pts had ≥18 mo and 7% (n=17/246) had ≥24 mo of drug exposure. A total of 63 gilteritinib-treated pts had OS ≥18 mo (median exposure, 17.6 mo [IQR, 3.1-25.7 mo]). A high proportion of these LT survivors achieved remission pre-HSCT (Table); median durations of complete remission (CR) or CR with partial hematologic recovery (CRh) have not been reached. After a median of 3.5 mo, 35 of 63 (56%) LT survivors underwent HSCT; 25 of these 35 pts (71%) received post-HSCT gilteritinib therapy. Of 28 pts who did not undergo HSCT, 15 (54%) received gilteritinib for ≥18 mo. Most common grade ≥3 adverse events (AEs) during the first 12 mo of gilteritinib therapy were febrile neutropenia (45%), anemia (40%), and thrombocytopenia (23%); rates of these grade ≥3 AEs decreased to 8%, 10%, and 0, respectively, after 12 mo of treatment. Most common fatal AEs during the first 12 mo of gilteritinib therapy were AML (11%), infections (11%), and cardiac disorders (3%); after 12 mo of treatment, rates of these fatal AEs were 6%, 8%, and 2%, respectively. **Conclusions:** Results from this ADMIRAL trial FU suggest LT survival in pts receiving gilteritinib is related to ongoing remission, subsequent HSCT, or post-HSCT gilteritinib therapy. The safety profile of gilteritinib beyond 1 year was stable. Clinical trial information: NCT02421939. Research Sponsor: Astellas Pharma, Inc.

	Gilteritinib (n=247)	SC (n=124)
Deaths, n (%)	198 (80%)	94 (76%)
OS Rates (%)		
12-mo	37	19
18-mo	27	15
24-mo	20	14
Pre-HSCT Remission Rates in Gilteritinib LT Survivors (n=63), n (%)		
CR	20 (32)	
CRi/CRp	25 (40)	
CRc	45 (71)	
CRh	10 (16)	
CR/CRh	30 (48)	

7515 Poster Discussion Session; Displayed in Poster Session (Board #288), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Type of prior genotoxic insult determines the genomic characteristics of therapy-related acute myeloid leukemia. *First Author: Michael Ozga, The Ohio State University Wexner Medical Center, Columbus, OH*

Background: Therapy-related AML (tAML) is a long-term complication of cytotoxic cancer therapy. It is characterized by adverse genetics and inferior survival outcomes when compared to de novo AML. A proposed mechanism in tAML pathogenesis includes treatment-induced selection of clones harboring pre-existing mutations (i.e. clonal hematopoiesis, CH). We hypothesize that genotoxic therapies used to treat prior malignancy drive leukemogenesis through different mechanisms leading to unique clonal compositions. **Methods:** AML patients (pts) treated at The Ohio State University between 2015-2018 were included. Genetic profiling was performed using Miseq Illumina platform with a 49-gene targeted sequencing panel at our clinical laboratory. **Results:** We studied 337 AML pts (Table), of whom 53% had smoking history. Mutations involving *ASXL1* were more common in smokers vs non-smokers (14% vs 5.8%, p= .001), while *JAK2* mutations were more common in non-smokers (8% vs 1.2%, p= .003). Regarding specific genotoxic therapies and mutations in tAML, we investigated common CH-associated mutations including *DNMT3A*, *TET2*, and *ASXL1* (DTA mutations). In tAML pts, those exposed to radiotherapy experienced a higher frequency of DTA (52% vs 27%, p= .05), *NPM1* (21% vs 0%, p= .002), and *SRSF2* (15% vs 0%, p= .01) mutations, and conversely, a lower incidence of *TP53* mutations (21% vs 46%, p= .04). Pts with history of cytotoxic chemotherapy had a lower incidence of DTA mutations, including those who received platinum agents (8% vs 49%, p= .005) and taxanes (7% vs 52%, p< .001), but had a higher incidence of *TP53* mutations (75% vs 25%, p< .001 for platinum; 53% vs 25%, p= .04 for taxanes). Similarly, alkylators and anthracyclines were associated with lower incidence of *DNMT3A* (0% vs 20%, p= .009) and *ASXL1* (0% vs 12.5%, p= .04) mutations. **Conclusions:** Different genotoxic agents demonstrate unique effects in leukemia development. Our data suggest that CH clones with DTA mutations may be enriched with smoking and radiotherapy, while cytotoxic chemotherapy may confer a higher incidence of *TP53* mutations. Given the adverse prognosis of *TP53* mutated AML, identification of pre-existing CH clones might influence treatment selection in solid tumor pts receiving anticancer therapy. Research Sponsor: None.

	tAML (n= 59)	sAML (n= 99)	dnAML (n= 179)
Median age	68	69	65
ELN17 risk, n (%)			
Favorable	7 (11)	6 (9)	23 (17)
Intermediate	15 (25)	16 (23)	39 (30)
Adverse	37 (63)	46 (68)	70 (53)
Therapies, n (%)			
Radiation	33 (56)		
Alkylators	19 (32)		
Anthracyclines	15 (25)	–	–
Taxanes	15 (25)		
Platinum agents	12 (20)		

7516 Poster Discussion Session; Displayed in Poster Session (Board #289), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Evolving risk of therapy-related myelodysplastic syndromes and acute myeloid leukemia (tMDS/AML) following modern cancer therapies. *First Author: Abhay Singh, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: Data describing risks of tMDS/AML after targeted and immunotherapy (IO) agents are lacking. Melanoma (Mel) and renal cell carcinoma (RCC) are considered chemotherapy insensitive and have been treated with IO (interferon and interleukin) since the 1990s. In 2004, use of tyrosine kinase inhibitors (TKIs) began in non-small cell lung cancer (NSCLC) and expanded to RCC in 2005 and Mel trials in 2011. Checkpoint inhibitor (CPI) use began in 2011 for Mel, 2012 for NSCLC in trials and later for RCC. For multiple myeloma (MM), use of lenalidomide has been increasing since 2007. All these modern therapies have well described immunomodulatory functions. **Methods:** Using 17 population-based SEER cancer registries, we studied 565,149 patients diagnosed from 2000-2015 with Mel, RCC, NSCLC, or MM who survived ≥1 year and assessed risk of tMDS/AML across periods P1 (2000-2005), P2 (2006-2010) and P3 (2011-2015). Censoring occurred at 5 years of follow up to limit bias and assess risk alteration across approval and utilization periods of these modern therapies. **Results:** tMDS/AML risk was significantly elevated after RCC in P1 [standardized incidence ratio *(SIR): 1.61*, possibly from chemo exposure that was still prevalent to some extent in P1 period] and a downtrend noted in P2 *(SIR: 1.11)* and P3 *(SIR: 0.60)*. tMDS/AML risk after Mel showed similar downtrend, not statistically significant. In contrast, risk for tMDS/AML after MM increased across all periods (*SIRs 4.51 > 5.05 > 5.23*), and risk after NSCLC increased from P1 to P2 but decreased thereafter, pattern most pronounced in stage I-III NSCLC (*1.64 > 3.15 > 1.92*). **Conclusions:** Periods when TKI and CPI use became standard in Mel and RCC, we observed a decrease in tMDS/AML risk. Similar decrease in the most recent period for stage I-III NSCLC was observed, possibly due to progression of these earlier staged cancers resulting in receipt of TKIs and CPI for stage IV disease. tMDS/AML risk after MM increased contradicting the decline in risk previously reported in the literature. Discordance may be due to survival bias as MM patients are now living longer (SEER 5-yr survival in '00 was 35% and 53% in '15) with more time to develop tMDS/AML. Overall, aside from better efficacy and/or tolerability of modern therapies, another observed benefit was lower tMDS/AML risk. This risk was lower than general population in Mel/RCC, suggesting a possible protective effect of these therapies. SIR tables/graphs with updated SEER data (available 04/2020) with follow up through 2018 will be presented. Research Sponsor: None.

7517 Poster Discussion Session; Displayed in Poster Session (Board #290), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Clonal hematopoiesis in the bone marrow and blood of healthy volunteers. *First Author: Pierre Hirsch, Sorbonne Université, UMRS 938, APHP, Hôpital Saint-Antoine, Paris, France*

Background: Clonal hematopoiesis of indeterminate potential (CHIP) has been described in blood samples from large series of patients. Its prevalence and consequences remain questioned because sequencing methods vary and because most studies were performed in cohorts of individuals suffering from non-hematological diseases (solid cancers, diabetes, cardiovascular or psychiatric diseases). CHIP has been described as a risk factor for blood cancer. However, the diagnosis of most blood cancers relies on morphologic and genetic examination of the bone marrow, and clonal hematopoiesis has never been evaluated in bone marrow samples from healthy individuals. Hence, it is not clear whether the current definition of CHIP is clinically relevant. To address this issue, we studied clonal hematopoiesis in paired peripheral blood and bone marrow samples from an unprecedented cohort of rigorously selected healthy volunteers. **Methods:** Here, we investigated the frequency of clonal hematopoiesis in 82 paired bone marrow and blood samples from carefully selected healthy adult volunteers (HEALTHOX clinical trial, ClinicalTrials.gov Identifier: NCT02789839). This study was approved by the ethics committees (CPP Tours and AFSSAPS identifier ID-RCB: 2011-A00262-39; CPP Ile-de-France III: 2753). Forty-one genes known to be mutated in myeloid malignancies were sequenced with a 1% threshold of detection. All variants were checked using IGV software v2.3. Statistical analyses were performed using Mann-Whitney, chi-squared, Fisher's exact, Wilcoxon matched-pairs tests or Spearman correlation using GraphPad Prism 6. **Results:** In bone marrow samples, clones were found in almost 40 % of healthy volunteers over 50 years-old (yo). The most frequent mutations were found in *DNMT3A* (48%) and *TET2* (28%) and the other mutations were found in *ASXL1* (8%), *JAK2* (8%), *RAD21* (4%) and *SRSF2* (4%) with one individual carrying three variants. Blood parameters and bone marrow smears were normal with the exception of two individuals with mild macrocytosis or thrombocytosis. Clonal hematopoiesis cases differed from others by age (62.8 vs. 38.6 years, $P < .0001$) and platelet count (294 vs. 241 G/L, $P < .0208$). **Conclusions:** These results confirm that clonal hematopoiesis is a very common condition in healthy adults over 50 years old. Consequently, the detection of driver myeloid mutations should be interpreted with caution in the absence of cytologic abnormalities in the blood and/or in the bone marrow. Research Sponsor: INCa - Institut National du Cancer, Paris, France.

7518 Poster Discussion Session; Displayed in Poster Session (Board #291), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Longer-term RBC transfusion reduction in the phase III MEDALIST study of luspatercept in patients (pts) with lower-risk MDS with ring sideroblasts (RS). *First Author: Rami S. Komrokji, Moffitt Cancer Center, Tampa, FL*

Background: MEDALIST (NCT02631070) is a randomized, placebo (PBO)-controlled, phase 3 trial evaluating the efficacy and safety of luspatercept, a first-in-class erythroid maturation agent, in pts with anemia due to lower-risk MDS (LR-MDS) with RS (Fenaux & Platzbecker et al. *NEJM.* 2020;382:140-51). **Methods:** Pts were aged ≥ 18 years; had IPSS-R-defined Very low-, Low-, or Intermediate-risk MDS with RS; were refractory, intolerant, or unlikely to respond to ESAs; and required RBC transfusions (≥ 2 units/8 weeks in the 16 weeks prior to randomization). 229 pts were randomized 2:1 to luspatercept (1.0 mg/kg, titration to 1.75 mg/kg) or PBO subcutaneously every 3 weeks. This analysis evaluates long-term transfusion burden reduction with luspatercept in all pts in the MEDALIST trial. **Results:** As of July 1, 2019, 77/153 (50.3%) and 11/76 (14.5%) pts in the luspatercept and PBO arms, respectively, achieved ≥ 50% RBC transfusion burden reduction for ≥ 24 weeks ($P <$ 0.0001). The median longest single response episode was 131.6 weeks with luspatercept, and not estimable with PBO due to pts stopping treatment. In Weeks 9–24, mean change from baseline in RBC units transfused was −3.0 (95% CI −3.9, −2.1) vs +0.4 (95% CI −0.6, 1.4) in the luspatercept vs PBO arms. In Weeks 33–48, mean change in RBC units transfused in the luspatercept arm was −4.9 (95% CI −5.9, −3.9). In Weeks 1–24, mean number of transfusion visits was 5.9 vs 9.5 in the luspatercept vs PBO arms. Risk of recurrent transfusion visits in Weeks 1–24 for luspatercept vs PBO was 0.699 (95% CI 0.597, 0.819; $P <$ 0.0001). Mean number (least squares [LS] mean) of RBC units transfused/48 weeks during Weeks 1–48 was 22.89 (23.28) vs 35.98 (35.20) in luspatercept vs PBO arms (LS mean difference −11.92 [95% CI −15.55, −8.28]; $P <$ 0.0001). The mean number (LS mean) of RBC transfusion events over 48 weeks was 12.95 (13.14) vs 19.54 (19.15) in the luspatercept vs PBO arms (LS mean difference −6.00 [95% CI −8.16, −3.85]; $P <$ 0.0001). LS mean change from baseline in serum ferritin was −2.7 μg/L vs +226.5 μg/L in luspatercept vs PBO (LS mean difference −229.1 μg/L; $P =$ 0.0024) in Weeks 9–24; and −72.0 μg/L vs +247.4 μg/L in Weeks 33–48 (LS mean difference −319.5 μg/L; $P =$ 0.0294). In Weeks 1–24, 38/127 (29.9%) vs 5/65 (7.7%) pts ($P =$ 0.0005) achieved major HI-E response per IWG 2018 criteria in luspatercept vs PBO arms, respectively. **Conclusions:** Luspatercept demonstrated clinical efficacy in pts with LR-MDS with RS and was associated with significant reductions in RBC transfusions (≥ 50%) and serum ferritin. Clinical trial information: NCT02631070. Research Sponsor: Bristol-Myers Squibb in collaboration with Acceleron Pharma.

7519 Poster Discussion Session; Displayed in Poster Session (Board #292), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Ten-day decitabine with venetoclax (DEC10-VEN) in AML and high-risk (HR) MDS. *First Author: Abhishek Maiti, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: VEN-based low intensity regimens have shown promise in older pts with newly diagnosed (ND) AML. We hypothesized that adding VEN to 10-day (d) DEC may improve outcomes in AML and HR MDS. **Methods:** Pts received VEN 400 mg daily or equivalent with DEC 20 mg/m^2 for 10d every 4-8 weeks for induction and DEC 5d with VEN for consolidation after CR/CRi. If cycle 1 day 21 bone marrow showed ≤5% blasts, VEN was held to enable count recovery. VEN duration could be further reduced for myelosuppression. FLT3 and IDH inhibitors were allowed for applicable pts. All pts received tumor lysis syndrome (TLS) prophylaxis. Primary objective was overall response rate (ORR). Secondary objectives were safety and overall survival (OS). Data cut-off date was February 6, 2020. **Results:** Between January 2018 and December 2019 we enrolled 184 pts with ND AML (>60 yrs), untreated secondary AML (sAML), treated sAML, relapsed/refractory (R/R) AML and HR MDS (Table). 58% pts were ≥70 yrs, 30% pts had ECOG PS ≥2, 67% pts had ELN adverse risk AML. Previously treated pts (n=96) had received a median of 1 prior therapy (range 1-8) including HMA (62), intensive chemotherapy (49) and stem cell transplantation (SCT, 27). 30d mortality was 3.3% and 60d mortality was 7.6%. 30d mortality in ND AML was 1.4%. Most common G3/4 adverse events were infections with G3/4 neutropenia (46%), febrile neutropenia (28%), infections with ANC ≥1x10^9/L (6%) and TLS (3%). Outcomes are shown in Table. 25 pts (14%) proceeded to SCT including treatment naive AML (ND+ untreated sAML, 12), previously treated AML (treated sAML + R/R, 11) and HR MDS (2). 100d post-SCT mortality was 4%. Median OS in treatment naïve AML pts undergoing SCT was not reached (1yr OS 100%) and for previously treated AML pts was 22.1 months (mo). After a median follow up of 15 mos, 25% PTS continue therapy. Additional analyses by molecular subgroups will be presented. **Conclusions:** DEC10-VEN is safe and highly effective in ND AML and can serve as an effective bridge to SCT in previously treated pts. Trial continues to accrue (NCT03404193). Clinical trial information: NCT03404193. Research Sponsor: U.S. National Institutes of Health.

Outcomes with DEC10-VEN in AML and MDS.

Outcome	ND AML N=70	Untreated sAML N=15	Treated sAML N=28	R/R AML N=55	R/R MDS N=13
	n (%) / median [range]				
ORR	62 (89)	12 (80)	17 (61)	34 (62)	8 (62)
CR + CRi or mCR	60 (86)	10 (67)	11 (39)	23 (42)	3 (23)
MRD negative (flow cytometry)	35/52 (67)	4/10 (40)	7/15 (47)	14/26 (57)	0/1 (0)
No. of cycles to response	1 [1-8]	1 [1-2]	1 [1-3]	2 [1-4]	2 [1-7]
Median OS, mos	18.1	7.8	6.0	7.8	8.9

3 more pts with untreated HR MDS achieved marrow CR (mCR) ongoing for a median of 5 mo
ORR = CR+CRi+MLFS+PR for AML and CR+mCR+PR+stable disease for MDS per IWG criteria

7520 Poster Discussion Session; Displayed in Poster Session (Board #293), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A fork in the road: A mixed methods study exploring why older adults with acute myeloid leukemia choose different treatment paths. *First Author: Thomas William LeBlanc, Duke University Medical Center, Durham, NC*

Background: Current treatment options for acute myeloid leukemia (AML) are diverse, including intensive chemotherapy (IC), low intensity therapy, best supportive care (BSC), and hospice care. Despite continued development of new therapies, recent data suggest that approximately 60% of older US patients remain untreated, but reasons for this are not well understood. By gathering insights from physicians, patients, and their family members, this study aims to better understand the factors that influence treatment decisions for adults with AML. **Methods:** Physicians in the US (n=4), UK (n=3) and Canada (n=3), and 15 US AML patient-family member dyads took part in one-on-one, 60-minute semi-structured interviews. Each participant rated a series of factors on a scale from 0 (not at all important) to 3 (very important) to determine their importance in treatment decision-making. Among the 15 adults with AML (>65 years, not taking IC) interviewed thus far, 13 had not received any treatment. Additional interviews are scheduled in the UK and Canada with patients having varied treatment experiences (data will be available for presentation). **Results:** To date, findings highlight the key role perceptions of side effects and patient health play in treatment decision making. A fear of treatment side effects was the primary reason patients (n=9/13) opted not to receive treatment. For the 2/15 study patients who had received treatment, side effects were considered the worst part of their treatment experience. Physicians also stated patients on BSC would be more willing to take low intensity treatments if risks (e.g., side effects) were minimized. Patients (n=11/15), their family members (n=11/15), and physicians (n=10/10) agreed that patients' health (including age and comorbidities) influenced if treatment was pursued. Additionally, US physicians suggested that some patients have little desire to pursue treatment, with patients' perception of low intensity therapy having poor efficacy and proximity of care influencing their choice for BSC or hospice care. Further analysis will explore other factors influencing patients' treatment decisions and differences among patients who receive treatment versus those who do not. **Conclusions:** The treatment decision-making process for older adults with AML is complex and multifactorial. Understanding factors that influence treatment decisions is important if drug developers and prescribers are to ensure the availability of therapies that better align with individual patients' needs. Research Sponsor: Pfizer.

7521 Poster Session (Board #294), Fri, 8:00 AM-11:00 AM

Ivosidenib (IVO) prior to hematopoietic cell transplant for patients with *IDH1*-mutant relapsed or refractory acute myeloid leukemia (R/R AML). *First Author: Courtney Denton Dinardo, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Allogeneic hematopoietic cell transplantation (HCT) provides a potentially curative option for patients (pts) with R/R AML. Disease status at the time of transplant is a major determinant of long-term prognosis, with pts typically receiving salvage chemotherapy prior to HCT to induce a remission. However, older and/or heavily pre-treated pts frequently cannot tolerate intensive chemotherapy (IC) or do not obtain adequate disease control to permit an HCT. IVO is an oral, potent, targeted inhibitor of mutant IDH1 (mIDH1) approved for the treatment of adults with newly diagnosed AML ≥75 y of age or ineligible for IC, and those with R/R AML. We assessed HCT outcomes in pts with m*IDH1* R/R AML who proceeded to HCT after treatment with IVO in a phase I study (NCT02074839). **Methods:** Baseline characteristics, clinical response (including CR, CRi/CRp, MLFS), and overall survival (OS) for the subgroup of pts with m*IDH1* R/R AML who received IVO 500 mg QD, responded to treatment and then underwent HCT are reported. m*IDH1* variant allele frequency (VAF) from bone marrow mononuclear cells was assessed using BEAMing digital PCR (0.02–0.04% VAF detection limit). **Results:** Among 179 pts with R/R AML treated with IVO, 18 proceeded to HCT: median age, 61.5 y (range 36–68); 56% male; 16.7% had secondary AML; 27.8% had ≥3 prior regimens; 11.1% had a prior HCT. The median duration of IVO treatment prior to HCT was 3.9 mo (range 2.1–15.2). The last reported response prior to HCT was 50.0% CR. Six- and 12-mo post-HCT survival rates were 77.8% and 50.0%; median relapse-free survival post HCT was 7.3 mo (range 2.6–NE). Median OS from start of IVO was 16.8 mo (95% CI 9.2, NE) for HCT pts vs 9.0 mo (95% CI 7.1, 10.2) in the entire study cohort; median follow-up time, 33.2 mo (range 3.2–41.9). Eight HCT pts were censored for OS: 5 are in remission, 2 relapsed and are in survival follow-up, and 1 was lost to follow-up. Median OS was not estimable (95% CI 9.1, NE) for the 12 HCT pts who achieved CR after IVO therapy and was 20.5 mo (95% CI 16.4, NE) for the 31 CR pts who did not undergo HCT. m*IDH1* was undetectable in 1/18 (6%) pts; 4/18 (22%) pts had reduction below 1% VAF in ≥1 at the last assessment prior to HCT. **Conclusions:** IVO monotherapy is a putative treatment option to induce remissions prior to HCT for m*IDH1* R/R AML pts who are not considered candidates for intensive salvage therapy. Post-transplant survival rates are encouraging and warrant further investigation of IVO monotherapy or combination salvage therapies prior to HCT. Clinical trial information: NCT02074839. Research Sponsor: Agios Pharmaceuticals, Inc.

7522 Poster Session (Board #295), Fri, 8:00 AM-11:00 AM

Activity of decitabine as maintenance therapy in core binding factor acute myeloid leukemia. *First Author: Mahran Shoukier, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Real-time quantitative (RTPCR) based minimal residual disease (MRD) monitoring provides prognostic information in core binding factor acute myeloid leukemia (CBF-AML). Earlier we reported on the activity of decitabine (DAC) as maintenance therapy in a smaller cohort of patients with CBF AML. **Methods:** We have summarized the results in patients (pts) with CBF who received DAC maintenance for persistent RTPCR positivity or because of inability to complete all planned consolidation in a fludarabine, GCSF, cytarabine (FLAG) based regimen. The planned number of DAC cycles was 12 but could be adjusted at the discretion of the treating physician based on RTPCR response. Serial RTPCR was obtained approximately every 2-3 months. **Results:** Thirty-four pts with CBF-AML [t(8;21)=14 and inv(16)=20] received DAC as maintenance. Eighteen pts (53%) completed a full course (7 cycles) of FLAG based regimen before DAC for persistent PCR positivity (group 1). Sixteen pts (47%) were switched to DAC as they did not complete planned consolidation (group 2). In group 2, 9 pts (56%) had negative PCR (group 2A) and 7 pts (46%) had positive PCR (group 2B) prior to starting DAC. Patient characteristics are summarized in table. The median follow up was 59.2 [15.4-107.2] and 32.47 [8.5-86.3] months for group 1 and 2, respectively. In Group 1 and group 2A only 1 patient each had relapse, while 5 pts (72%) from group 2B had relapse. All the patients in group 2B with relapse were at suboptimal RTPCR response (>0.1%). **Conclusions:** Our study shows DAC is an effective maintenance for CBF-AML pts who have persistent PCR positively after FLAG based induction consolidation and those unable to tolerate a full course, but have negative PCR. However patients with high levels of MRD persistence should be considered for stem cell transplant. Research Sponsor: None.

Patient characteristics and outcome.

Characteristics	Group 1 (N=18)	Group 2A (N=9) N (%) / Median [range]	Group 2B (N=7)
Age	50 [29 – 75]	61 [29 - 72]	58 [34-78]
Female	8 (44)	7 (78)	4 (57)
Inv 16	11 (61)	5 (56)	4 (57)
Mutations			
KIT	3 (16)	1 (6)	1 (20)
FLT3	6 (32)	4 (25)	2 (40)
RAS	7 (36)	3 (19)	1 (20)
Others	3 (16)	8 (50)	1 (20)
Treatments/PCR			
FLAG cycles	7	4 [3-6]	4 [1-6]
PCR at start of FLAG-IDA	100 [87-100]	100 [81-100]	20 [2-100]
PCR at start of DAC	0.03 [0.01-0.47]	0	0.27 [0.04-19.53]
DAC Cycles	12 [1-17]	5 [2-15]	3 [2-7]
Response			
Negative PCR after DAC	14 (78)	8 (89)	1 (14)
Positive PCR after DAC	3 (16)	0	1 (14)
PCR value	0.01 [0.01-0.03]		0.03
Relapse after DAC	1 (6)	1 (11)	5 (72)

7523 Poster Session (Board #296), Fri, 8:00 AM-11:00 AM

Comparative study of therapy-related (tALL) and de novo adult acute lymphoblastic leukemia (dnALL): Contemporary Mayo Clinic ALL cohort. *First Author: Zaid Abdel Rahman, Mayo Clinic, Jacksonville, FL*

Background: tALL is a recently appreciated but poorly defined clinical entity. We define tALL as any prior exposure to cytotoxic chemotherapy and/or radiation for another malignancy, and we report a comparative analysis of characteristics, cytogenetics and outcomes for this subset among a modern unselected ALL cohort from the Mayo Clinic Cancer Center (MCCC). **Methods:** We performed a systematic search in the 3-site MCCC registry and included all patients (pts) diagnosed and received at least 1 cycle of ALL-directed therapy and/or underwent allogeneic transplantation (AlloHCT) between 2008-2018. Comparisons of characteristics between tALL and dnALL were made using a Wilcoxon rank sum test (continuous variables) and Fisher's exact test (categorical variables). Time-to-event variables were compared using unadjusted Cox proportional hazards regression models. **Results:** 431 ALL pts were identified during the study period, including n = 69 (16%) classified as tALL. Median follow-up from diagnosis was 2.3 years (range 0-18 years). The most common prior malignancies among tALL pts were Breast (24.6%), Lymphoma (15.9%), Myeloid (15.9%), GU/GYN (14.5%) and Myeloma (11.6%). In comparison to dnALL, pts with tALL were significantly older (63.2 vs 45.2 years, $P < 0.001$), more often female (65.2% vs 39.8%, $P < 0.001$), less frequently Hispanic (3.5% vs 13.1%, $P = 0.042$); more often of B-lineage (92.8% vs 81.8%, $P = 0.022$). On review of cytogenetics, tALL pts more often had hypodiploidy/near triploidy (Ho/Tr) (21.7% vs 4.1%, $P < 0.001$), more often had monosomal (MDS-like) (33.3% vs 12.4%, $P = 0.0047$) and complex karyotype (38% vs 17.3%, $P = 0.0069$). Importantly, incidence of BCR/ABL-positive (Ph+) ALL was not significantly different. Latency period between exposure to prior cancer therapy and development of tALL was significantly longer for Ph+ compared to Ph-negative ALL (median 9 vs. 4 years, $P = 0.007$). Patients with tALL had a 3-year OS after diagnosis of 37% [vs 59.7% for dnALL (HR death 1.86, 95% CI 1.31-2.65, $P < 0.001$)]. However, the two groups did not differ significantly regarding occurrence of AlloHCT (HR = 0.91, 95% CI 0.63-1.31, $P = 0.61$) or post-AlloHCT survival (HR = 1.29, 95% CI 0.75-2.23, $P = 0.35$). **Conclusions:** Therapy-related ALL represents an important & unique clinical entity with poor prognosis & adverse cytogenetic features. Ph+ tALL has a longer latency and similar frequency in both tALL and dnALL. AlloHCT appears to be an appropriate treatment strategy, possibly abrogating the poor prognosis of tALL. Research Sponsor: None.

7524 Poster Session (Board #297), Fri, 8:00 AM-11:00 AM

Clinicopathologic and molecular profile of Philadelphia like ALL in Hispanic population of Central Valley California. *First Author: Hugo Akabane, UCSF Fresno, Clovis, CA*

Background: Philadelphia-like Acute B-ALL(PHL) are Ph negative B-ALL(PHN) with molecular signatures that mirrors Ph + B ALL. Studies have shown worse prognosis in this subtype of leukemias, but few have reported outcomes with incorporation of novel agents. Our study seeks to describe clinical and molecular profile of a single center experience. **Methods:** This is a retrospective study of patients treated for PHL in community referral center in central valley of California from 1/2009 to 12/2019. Of the initial 71 patients, 34 met the inclusion and exclusion criteria. 16 of the 34 patients who had Next Generation Sequencing (NGS) by Foundation Medicine (14) or NeoGenomics (2). Data for 34 PHN and 8 with PHL patients were analyzed. **Results:** There are no differences in mean ages (36.7 x 36) and gender between the PHN and PHL subgroup. There is over representation of Hispanics in both groups (63% x 65%) with slightly male predominance in PHL group (62%). This ratio is slightly higher than reported by 2010 census of 46%. The BMI 38.4(27.5-48.4) vs. 29.1(26.6-39.1), mean WBC (71 vs. 58), bone marrow CD20+ by flow cytometry (90% vs. 63%) and abnormal cytogenetics (50% vs.15%) are all higher in PHL compared to PHN group. The prevalence rate of PHL signature in 16 tested patients is 8(50%). CRLF2 like subtype accounted for 6/8(75%), with 1 each of ABL-like and JAK-Stat subtype. All patients harbored multiple other mutational abnormalities in addition to those associated with Ph-like genetic signatures (Table). The median number of mutations was 4.55(3-7). The distribution of the 20 other mutation is as shown in table. 6 patients had morphological remission after induction chemotherapy of HyperCVAD (37%) and CALGB 10403 (25%) with measurable MRD in 5 of the patients. 7 patients were exposed to novel therapy; Blinatumomab; 2nd line (6 patients), Cart T cell; 3rd line (2 patients), Inotuzumab; 3rd line (3 patients) and ASCT; (3 Patients post second- or third-line remission). 2 patients died at the time of data cut off, 1 from infection and other from refractory leukemia. **Conclusions:** Our data shows high incidence of PHL signatures in the cohort. The mutational heterogeneity between and within patients, may represent sub-clonal population vs. passenger and hence poor clinical outcomes. Research Sponsor: None.

Distribution of 20 mutations in 8 patients with PHL signatures.

	CRLF2	PAX5-ZCCHC7	RPTOR	FBXW7	Jak1	JAK2	ETV6	IKZF1	FLT3	CHD2	DDX3X	PDGFRB	CDKN2A/B	PI3KR1	TP53	NRAS	Kras	MII2	Ros1	ZRSR2	N
1	X	x	x																		3
2	X			x		x	x	x													5
3	X								x	x	x										4
4												x	x	x	x		x				5
5	X						x									x				x	4
6					x	x							x								3
7	X					x	x						x					x	X	x	7
8	x		x	x																	3

7525 Poster Session (Board #298), Fri, 8:00 AM-11:00 AM

Effect of early blood counts on overall survival (OS) following glasdegib + LDAC in newly diagnosed AML: BRIGHT AML 1003 post hoc analysis. *First Author: Eunice S. Wang, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: Addition of glasdegib (GLAS) to LDAC approximately doubled OS without significant worsening of myelosuppression-related complications, ostensibly by targeting leukemic stem cells dependent on the hedgehog pathway, which is not involved in normal adult hematopoiesis. We assessed potential association of early blood counts and OS. **Methods:** In BRIGHT AML 1003, patients (pts) with newly diagnosed AML were randomized to GLAS + LDAC (n = 78) or LDAC alone (n = 38). GLAS was given once daily continuously and LDAC on days 1–10 of a 28-day cycle. We evaluated peripheral blood counts measured early in the study (cycle 2 day 1 [C2D1]), approximately 1 month before the first bone marrow assessments. OS was compared for GLAS+LDAC vs LDAC alone subgroups meeting thresholds of absolute neutrophil count (ANC; ≥1000 or 500/μL), hemoglobin (Hb; ≥10 or 9 g/dL) or platelets (≥100,000 or 50,000/μL). Data cut-off was Apr 2019. **Results:** Among all pts regardless of baseline values, achievement of ANC, Hb and platelet thresholds at C2D1 was associated with improved OS with GLAS+LDAC (table, left side). Notably, in pts who did not meet ANC, Hb or platelet thresholds (table, right side), OS benefit with GLAS+LDAC was also observed (table, all p≤0.05). Among pts below threshold at baseline, C2D1 recovery of platelets ≥50,000 or 100,000 and Hb ≥9 or 10 was associated with improved OS (not shown). Clinical trial information: NCT01546038. **Conclusions:** In pts with newly diagnosed AML, improved OS was associated with various blood count thresholds after 1 cycle of GLAS+LDAC vs LDAC alone. In pts with baseline measurements below threshold, recovery of specific thresholds was associated with improved OS. These exploratory results are consistent with the hematopoiesis-sparing mechanism of GLAS, and merit further evaluation. Research Sponsor: Pfizer.

Median OS (months [95% CI]) by C2D1 cytopenic thresholds, all comparisons of GLAS+LDAC vs LDAC alone.

Thresholds	Met threshold at C2D1 (all p< 0.05)				Did not meet threshold at C2D1 (all p< 0.05)			
ANC (/μL)	n	GLAS+LDAC	n	LDAC alone	n	GLAS+LDAC	n	LDAC alone
500	38	9.0 [6.5, 14.5]	14	4.9 [1.8, 8.1]	19	13.6 [4.0, 18.5]	8	4.6 [1.5, 5.3]
1000	24	7.4 [3.6, 14.5]	10	3.8 [1.3, 6.4]	33	12.5 [6.5, 19.5]	12	4.8 [1.9, 7.2]
Hb (g/dL)								
9	28	12.4 [6.5, 19.5]	13	4.9 [2.3, 8.1]	32	8.8 [4.0, 14.7]	11	4.8 [1.8, 6.4]
10	14	8.7 [3.4, 24.4]	8	3.0 [1.3, 8.1]	46	11.1 [5.0, 14.9]	16	5.1 [3.5, 6.5]
Platelets (/μL)								
50,000	33	14.9 [8.3, 19.6]	10	4.7 [1.3, 6.4]	27	6.5 [3.6, 12.2]*	14	5.0 [1.9, 7.2]
100,000	24	18.5 [9.1, 24.2]	6	4.3 [1.8, 12.9]	36	6.5 [3.7, 12.2]	18	5.1 [2.3, 6.9]

n: pts with assessments at C2D1; *p = 0.05

7526 Poster Session (Board #299), Fri, 8:00 AM-11:00 AM

Glasdegib in combination with azacitidine (AZA) in patients (pts) with untreated higher-risk myelodysplastic syndromes (MDS), acute myeloid leukemia (AML) and chronic myelomonocytic leukemia (CMML): Effects on marrow recovery and transfusion independence. *First Author: Amer Methqal Zeidan, Yale University School of Medicine and Yale Cancer Center, New Haven, CT*

Background: Glasdegib, an oral inhibitor of the Hedgehog signaling pathway, is approved in the USA in combination with low-dose cytarabine to treat pts with newly diagnosed AML unable to receive intensive chemotherapy due to comorbidities or age (≥75 years). Glasdegib + AZA showed promising remission rates and overall survival with a generally well-tolerated and manageable safety profile in an analysis of BRIGHT MDS & AML 1012 in pts with MDS, AML and CMML. Here we evaluate early hematopoietic recovery and transfusion independence with glasdegib + AZA in this ongoing Phase Ib study. **Methods:** Untreated pts with MDS, AML and CMML ineligible for intensive chemotherapy received glasdegib (100 mg QD) + AZA (75 mg/m^2/D on D1–7 q28D). Data cutoff: Sept 11, 2019. **Results:** Among pts with MDS (n=30; including 3 with CMML), median duration of treatment was 5.0 months (range, 0.4–15.5). Recovery of absolute neutrophil count (ANC), hemoglobin (Hb) and platelets at 2 thresholds started in cycle (Cyc) 1 (Table). Early platelet recovery correlated with response to treatment; 54% (7/13) of pts with platelets ≥100,000/μL at Cyc 2, D1 achieved complete or partial remission vs 0% (0/13) of pts with <100,000/μL, *P*=0.002. Start of Cyc 2 was delayed due to AEs in 8% (2/26) of pts. 54% (7/13) of evaluable pts transfusion dependent at baseline (BL) became transfusion independent. Among pts with AML (n=30), median duration of treatment was 5.0 months (range, 0.3–14.9). ANC, Hb and platelet recoveries started in Cyc 1 (Table). 9% (2/23) of pts had Cyc 2 dose delays due to AEs. 64% (9/14) of evaluable pts transfusion dependent at BL became transfusion independent. Clinical trial information: NCT02367456. **Conclusions:** Glasdegib + AZA shows promising rates of survival with early marrow recovery in the up-front treatment of pts with MDS, AML and CMML ineligible for intensive chemotherapy. The association between early hematopoietic recovery and efficacy in the MDS cohort merits further study. Research Sponsor: Pfizer.

Recovery in Cyc 1, n/N (%)	AML		MDS*	
ANC	≥1000/μL	≥500/μL	≥1000/μL	≥500/μL
All pts	17/30 (57)	21/30 (70)	16/28 (57)	21/28 (75)
BL <threshold	3/14 (21)	3/10 (30)	3/15 (20)	1/7 (14)
Hb	≥10 g/dL	≥9 g/dL	≥10 g/dL	≥9 g/dL
All pts	7/30 (23)	21/30 (70)	9/29 (31)	18/29 (62)
BL <threshold	4/25 (16)	11/19 (58)	3/22 (14)	6/15 (40)
Platelets	≥100,000/μL	≥50,000/μL	≥100,000/μL	≥50,000/μL
All pts	11/30 (37)	17/30 (57)	17/29 (59)	24/29 (83)
BL <threshold	7/25 (28)	3/16 (19)	9/21 (43)	4/7 (57)

* Included CMML pts

7527 Poster Session (Board #300), Fri, 8:00 AM-11:00 AM

Health-related quality of life (HRQoL) in patients with untreated higher-risk myelodysplastic syndromes (MDS), acute myeloid leukemia (AML), and chronic myelomonocytic leukemia (CMML) receiving glasdegib + azacitidine (AZA). *First Author: Eunice S. Wang, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: Glasdegib + AZA showed promising remission rates and overall survival in an analysis of BRIGHT MDS & AML 1012 in patients (pts) with MDS, AML and CMML. Here we assess the impact of glasdegib + AZA on HRQoL in this ongoing Phase Ib study. **Methods:** Untreated pts with MDS, AML and CMML ineligible for intensive chemotherapy received glasdegib (100 mg QD) + AZA (75 mg/m^2/D on D1–7 q28D). Pt-reported outcomes (PRO) that characterize HRQoL were measured using the MD Anderson Symptom Inventory (MDASI)-AML/MDS, Pt Global Impression of Severity (PGI-S), and Pt Global Impression of Change (PGIC) tools. PRO were assessed at baseline (BL; except the PGIC), D7 and D15 of cycle (Cyc) 1, D1 of each subsequent Cyc and at end of treatment. Data cutoff: Sept 11, 2019. **Results:** For the MDS (n=30, including 3 with CMML) and AML (n=30) cohorts, median (range) number of Cyc started was 5 (1–14) and 5 (1–15), respectively. HRQoL over time, as determined by MDASI-AML/MDS, is shown in the Table, with mean scores indicating low symptom burden over time. For the PGI-S, both cohorts showed similar trends in pt's impression of current leukemia symptoms remaining constant over time (i.e. absent to mild). For the PGIC, pt's impression of change of leukemia symptoms since starting study medication remained constant over time (i.e. no to minimal change) for the MDS cohort and showed improvement in the AML cohort (i.e. minimal change to much improved). **Conclusions:** Glasdegib + AZA is a promising first-line treatment option that does not negatively impact the HRQoL of pts with MDS, AML and CMML ineligible for intensive chemotherapy. Clinical trial information: NCT02367456. Research Sponsor: Pfizer.

Mean scores over time.

	AML Cohort					MDS Cohort				
	BL n=29	Cyc 1, D15 n=28	Cyc 3 n=19	Cyc 6 n=14	Cyc 12 n=4	BL n=30	Cyc 1, D15 n=21	Cyc 3 n=22	Cyc 6 n=11	Cyc 11 n=5
MDASI-AML/MDS (scale 1–10)*										
Core cancer symptoms	1.8	2.6	1.9	2.8	1.7	1.6	1.8	2.0	1.4	1.8
AML/MDS symptoms	2.0	2.7	1.5	2.5	1.3	1.3	1.8	2.1	0.8	1.7
Total symptom severity	1.8	2.6	1.8	2.8	1.6	1.5	1.8	2.0	1.4	1.8
Six areas of interference†	3.0	3.5	2.8	3.2	1.9	2.4	2.3	2.7	1.4	2.0
PGI-S (scale 1–4)*	2.0	2.5	1.9	2.1	1.5	1.9	2.2	2.1	1.8	2.0
PGIC (scale 1–7) ‡	–	3.8	3.2	3.1	1.5	–	4.3	3.5	3.4	3.4

Note: Ns may vary for each endpoint due to pts not completing the survey * Higher scores indicate worse symptoms † General activity, mood, work, relations, walking, and enjoyment of life ‡ A score of 4 indicates pts felt symptoms did not change; lower scores indicate improvement and higher scores indicate worse symptoms

7528 Poster Session (Board #301), Fri, 8:00 AM-11:00 AM

Stability of rare TP53 co-mutations in AML patients. *First Author: Kenneth Joel Bloom, Clarient Diagnostic Services, Inc., Aliso Viejo, CA*

Background: Acute Myeloid Leukemia (AML) is a devastating disease with poor overall survival. Access to precision medicines, is revolutionizing AML care and is driving an increase in Next Generation Sequencing (NGS) utilization to determine the genomic profile of patients with AML. Advanced analysis into the interplay between mutational status for multiple genes is granting access to new targeted and precision medicine treatment options with improved outcomes. **Methods:** Rate of NGS adoption and TP53 mutation status were determined for a cohort of 984 AML patients tested by NGS from the Diaceutics Diagnostic Index between 2017 and 2019. Mutation rate of other genes on the same NGS panel used to determine if TP53 status was determined and compared using the z-score test for two population proportions. The stability of TP53 and co-mutation status at time of diagnosis and relapse/refractory was also analyzed. **Results:** We have seen a 2-fold increase in the average routine clinical practice uptake of NGS in a representative real-world patient cohort (Q3 2017, n = 144; Q3 2019, n = 290). In a cohort of 984 AML patients tested by NGS 151 (15.3%) had a TP53 mutation (Exon 4-9). Of those that had a TP53 mutation, significant negative associations were observed with mutations in seven other genes (ASXL1 p = 0.00308, CEBPA p = 0.0027, FLT3 p < 0.00001, IDH1 p = 0.04338, NRAS p = 0.0012, RUNX1 p = 0.01878 and TET2 p = 0.0251). There were no statistically significant differences in TP53 mutation and other gene mutation rates between diagnosis and relapse/refractory timepoints. **Conclusions:** This data suggests that TP53 and other gene co-mutants may act in similar activation pathways resulting in rare detection. One possibility is that double mutants result in synthetic lethality leading to a low clonal population. Second, when co-mutated clones escape immune surveillance and regulation, it results in particularly aggressive leukemias with lower overall survival. The stability of TP53 and co-mutation is relatively stable, which has implications for testing algorithms and clinical utility as a marker of MRD. Although a clinical trial may be difficult due to low numbers of patients, a TP53 antagonist and targeted therapy may be a valuable treatment option in rare cases where co-mutation does exist. Research Sponsor: Diaceutics (data analytics and implementation service provider in diagnostic commercialization).

	TP53 mutation detected		TP53 WT		
	Total patients	Percent mutated	Total patients	Percent mutated	z-test p-value
ASXL1	164	9.1%	1018	15.7%	0.00308
CEBPA	150	0.7%	923	7.0%	0.0027
FLT3	150	1.3%	948	17.5%	< 0.00001
IDH1	144	4.2%	798	9.3%	0.04338
NRAS	149	4.0%	884	13.3%	0.0012
RUNX1	155	5.2%	965	11.4%	0.01878
TET2	161	7.5%	996	13.9%	0.0251

7529 Poster Session (Board #302), Fri, 8:00 AM-11:00 AM

Post-remission clonal hematopoiesis; Practical implications for measurable residual disease assessment in acute myeloid leukemia (AML). *First Author: Sanam Loghavi, Department of Hematopathology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Clonal Hematopoiesis may persist following complete remission (CR) in patients with acute myeloid leukemia (AML) but does not necessarily indicate residual AML and may represent persistence of pre-leukemic stem cells. Post-remission CH identified by NGS has not been systemically studied in parallel with measurable residual disease (MRD) detection by flow cytometric immunophenotyping (FCI). **Methods:** We studied bone marrow sample from AML patients at baseline and CR by targeted deep NGS of 295 genes (median 403x depth) and compared the results to FCI. Measurable residual disease (MRD) detection by FCI was performed by comparing the phenotype at CR to baseline and by detection of leukemia associated immunophenotype (LAIP) and derivation from normal (DFN) (sensitivity: 0.1%). Post-CR CH was defined as presence of mutations originally detected in AML with variant allele frequency > 2.5%. FCI results were categorized into 4 groups: a) AML MRD negative by LAIP or DFN b) AML MRD+ (similar to baseline) c) AML MRD+ (different from baseline), d) Negative for AML MRD, but aberrant phenotype suggestive of pre-leukemic cells. We correlated FCI and NGS results. **Results:** 101 patients were included in the study. 45 (45%) had persistent post-CR clonal hematopoiesis; 23 (51%) had phenotypic alterations detected by FCI including AML MRD+ in 18 (40%) and pre-leukemic cells in 5 (10%). Among patient with no detectable mutations by NGS (n = 56; 55%), 14 (25%) had FCI aberrancies including AML MRD+ in 4 (7%) and pre-leukemic cells in 10 (18%). CH was significantly more common in samples with residual phenotypic aberrancies detected by FCI (p = 0.004). There was no significant correlation between FCI group d and persistent CH (p = 0.4). Persistent *ASXL1* (p = 0.024, OR = 7.2) and *RUNX1* (p = 0.016; OR = 17.3) mutations were significantly associated with FCI abnormalities. The correlation coefficient between FCI abnormalities and *RUNX1* mutations inferred from a Bayesian network structure was 0.66. **Conclusions:** NGS and FCI are complementary in evaluating post treatment disease status in AML. Post CR-CH is associated with phenotypic abnormalities that either represent residual AML or pre-leukemic cells. The latter may not have the same prognostic implications as AML MRD; however, the association with outcome needs to be elucidated. Single cell DNA sequencing technologies may be helpful in more accurately deciphering the association of individual gene mutations and their contribution to phenotypic aberrations. Research Sponsor: None.

7530 Poster Session (Board #303), Fri, 8:00 AM-11:00 AM

CC-486 is safe and well-tolerated as maintenance therapy in elderly patients (≥75 years) with acute myeloid leukemia (AML) in first remission following induction chemotherapy: Results from the phase III QUAZAR AML-001 trial. *First Author: Farhad Ravandi, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: About 40-50% of older patients (pts) with AML attain complete remission (CR) with induction chemotherapy (IC) but relapse is common.Effective, well-tolerated maintenance treatment (Tx) is needed for older pts in remission who are not eligible for hematopoietic stem cell transplant (HSCT). CC-486 is an oral hypomethylating agent that allows for extended dosing schedules (>7 days [d]/cycle) to sustain therapeutic activity. In the phase III placebo (PBO)-controlled QUAZAR AML-001 trial (NCT01757535), CC-486 maintenance therapy in pts with AML in first remission following IC produced significant improvements in overall and relapse-free survival. Here we report safety and tolerability findings among pt subgroups defined by age at study entry. **Methods:** Eligible pts were ≥ 55 yrs of age, with *de novo* or secondary AML, intermediate or poor risk cytogenetics, and ECOG PS ≤ 3; had achieved first CR or CRi after IC ± consolidation; and were not candidates for HSCT. Within 4 mo of CR/CRi, pts were randomized 1:1 to CC-486 300 mg or PBO QD on d 114 of repeated 28d Tx cycles. Safety was assessed across 3 age subgroups (≥ 55 to < 65, ≥ 65 to < 75, and ≥ 75 yrs) in pts who received ≥ 1 dose of study drug. Adverse events (AEs) were coded using MedDRA v. 22.0 and graded by NCI-CTCAE v. 4.0. **Results:** 469 pts (>99% of all enrolled pts) were evaluable for safety (CC-486 n = 236; PBO n = 233). Median age was 68 yrs (range 55-86). Age distribution was similar between the two Tx arms (Table). Between Tx arms, AE rates within each age stratum were similar to rates in the overall study population. The most common AEs (any grade) with CC-486 were GI events, which were more frequent than in the PBO arm across age groups. Within the CC-486 arm, AE rates were generally consistent across age groups, except for constipation, which was > 20% more frequent in pts aged ≥ 75 yrs, and thrombocytopenia, which was ≥ 20% less frequent in this group (Table). Overall, 13% and 4% of pts in the CC-486 and PBO groups discontinued Tx due to AEs. **Conclusions:** In QUAZAR AML-001, CC-486 was generally well tolerated in all age groups, including elderly pts aged ≥ 75 yrs. Clinical trial information: NCT01757535. Research Sponsor: BMS.

Table. Common AEs (> 20% of all pts; any grade) by pt age category

	CC-486			PBO		
	55 to < 65 n = 65 (28%)	65 to < 75 n = 143 (61%)	≥ 75 n = 28 (12%)%	55 to < 65 n = 68 (29%)	65 to < 75 n = 142 (61%)	≥ 75 n = 23 (10%)
Nausea	60	67	64	35	19	17
Vomiting	57	60	64	13	9	4
Diarrhea	55	46	61	28	18	26
Constipation	37	35	61	25	23	30
Neutropenia	45	44	46	28	28	13
Thrombocytopenia	34	37	14	29	25	30
Fatigue	29	29	36	19	20	17

7531 Poster Session (Board #304), Fri, 8:00 AM-11:00 AM

Timing of response to venetoclax combination treatment in older patients with acute myeloid leukemia. *First Author: Brian Andrew Jonas, University of California Davis Comprehensive Cancer Center, Sacramento, CA*

Background: Venetoclax (Ven) has synergistic activity with hypomethylating agents (eg, azacitidine [Aza] or decitabine [Dec]) or low-dose cytarabine (LDAC). These Ven-based combinations have demonstrated rapid median response times. This analysis describes the rapidity and likelihood of response to Ven treatments, and its associated characteristics, in older patients with newly diagnosed acute myeloid leukemia (AML). **Methods:** Included are data from two open-label trials of Ven, at label recommended doses, in combination with Aza, Dec (NCT02203773; phase 1b), or low-dose cytarabine (NCT02287233; phase 1/2) in newly diagnosed patients with AML. Patients were classified based on CR/CRi timing: within 2 cycles of therapy, after 2 cycles, or never achieving CR/CRi. Within each group, baseline and post-baseline characteristics were evaluated to determine impact on response timing. The percentage of patients in each category and duration of response (DOR) in each category were also evaluated. **Results:** Data cutoff was August 2018. Of 197 patients, 42% (n = 83) had CR/CRi in ≤2 cycles, 22% (n = 44) had CR/CRi in > 2 cycles, and 36% (n = 70) did not achieve CR/CRi. Median DOR was 21.2 mos. (95% CI 14.1-NR) for ≤2 cycle responders and 8.1 mos. (95% CI 5.3-14.9) for > 2 cycle responders. Baseline characteristics are shown in the Table. Patients with baseline *IDH1/2* mutation were more likely to have CR/CRi in ≤2 cycles, while those with secondary AML and no response by the end of cycle 2 were more likely to never achieve CR/CRi. Of the patients who achieved CR/CRi after 2 cycles of therapy, 43% (19/44) achieved MLFS within the first two cycles. Of those who never achieved CR/CRi, 17% (12/70) of patients achieved MLFS within 2 cycles. In depth regression analyses of factors predictive of response, including analysis of biomarkers, will be available upon presentation. **Conclusions:** Over 1/3rd of patients that achieved CR/CRi on Ven combination therapy within these two studies required more than 2 cycles of treatment. Therefore, prior to discontinuing therapy for nonresponders, it is critical to assess key predictive patient characteristics. Clinical trial information: NCT02203773 and NCT02287233. Research Sponsor: AbbVie and Genentech.

	≤2 Cycles n = 83	> 2 Cycles n = 44	No CR/CRi n = 70
Male, n (%)	52 (63)	26 (59)	41 (59)
Age, median yrs. (range)	74 (63-90)	74 (61-85)	74 (63-89)
Cytogenetic risk*, n (%)			
Intermediate	53 (64)	27 (61)	35 (50)
Poor	29 (35)	16 (36)	29 (41)
Secondary AML, n (%)	21 (25)	12 (27)	37 (53)
Genetic mutations, n (%)			
FLT3	10 (12)	6 (14)	14 (20)
IDH1/2	29 (35)	7 (16)	7 (10)
TP53	13 (16)	9 (21)	15 (21)
NPM1	16 (19)	6 (14)	4 (6)

* No mitosis detected in n = 1, 1, and 6 patients respectively

7532 Poster Session (Board #305), Fri, 8:00 AM-11:00 AM

FACT physical wellbeing to independently predict overall survival in patients with acute myeloid leukemia. *First Author: John Peipert, Northwestern University Feinberg School of Medicine, Chicago, IL*

Background: Patient-reported outcomes (PROs) predict overall survival (OS) in solid cancer populations, but little evidence exists around the prognostic value of PROs in patients with hematologic malignancies. We investigated whether scales from the Functional Assessment of Cancer Therapy – Leukemia (FACT-Leu) predicted OS beyond established prognostic factors. **Methods:** Data were from 317 AML patients unfit for intensive therapy from a clinical trial comparing Dacogen (decitabine) plus Talacotuzumab versus Dacogen (decitabine) alone (AML2002; NCT02472145). We used ridge-penalized Cox models to determine whether baseline (1st cycle) FACT-Leu scales predicted OS. FACT-Leu scales significant in these models and factors from a validated prognostic model, the AML composite model (AML-CL; covariates listed in Table), were entered into Cox proportional hazard models. Lastly, model selection procedures were run with 1000 bootstrapped samples using all variables. The inclusion frequency of each FACT-Leu scale in the final models was examined to evaluate prognostic value for OS (i.e., higher the % of inclusion, higher importance of the variable). **Results:** In the ridge-penalized Cox models, the Physical Wellbeing Scale (PWB), Trial Outcome Index (TOI), and FACT-Leu Total scales were significant predictors of OS. After adjusting for the AML-CL factors, an important difference (2 pts) in PWB score was associated with a 9% decline in OS. (Table) Model validity was evidenced as the PWB scale appeared in a large majority of selected models (90%-97%), while the TOI (45%-73%) and FACT-Leu Total (41%-71%) appeared less often. **Conclusions:** FACT-Leu scales, especially the PWB, were significant prognostic factors for OS among AML patients not suitable for intensive therapy. These results may indicate PROs' value as stratification factors in trials with AML patients and underscore the need to more systematically collect PRO data in routine care practice with AML patients. Clinical trial information: NCT02472145. Research Sponsor: None.

FACT-Leu Scales	Hazard Ratio (95%)	p-value
PWB per 2 point change	0.91 (0.86-0.97)	0.002
TOI per 4 point change	0.96 (0.93-0.99)	0.03
FACT-Leu Total Score per 5 point change	0.96 (0.92-0.99)	0.02

Separate models for each FACT-Leu scale.
Each adjusted for AML-CL factors: arrhythmia, cardiac comorbidity, IBD, diabetes, cerebrovascular disease, psychiatric disturbance, obesity, infection, rheumatologic comorbidity, peptic ulcer, renal comorbidity, prior solid tumor, heart valve disease, pulmonary comorbidity, hepatic comorbidity, cytogenetic/molecular risk, LDH level, and age.

7533 Poster Session (Board #306), Fri, 8:00 AM-11:00 AM

Health-related quality of life (HRQoL) in the phase III QUAZAR-AML-001 trial of CC-486 as maintenance therapy for patients with acute myeloid leukemia (AML) in first remission following induction chemotherapy (IC). *First Author: Gail J. Roboz, Weill Cornell Medical College and New York Presbyterian Hospital, New York, NY*

Background: Effective AML maintenance treatment (Tx) should decrease the risk of relapse and prolong survival without compromising HRQoL. In the placebo (PBO)-controlled phase III QUAZAR AML-001 trial (NCT01757535), CC-486, an oral hypomethylating agent, provided significant improvements in overall (OS) and relapse-free survival (RFS) in patients (pts) with AML in first remission following IC. Here we present pt-reported HRQoL outcomes from that study. **Methods:** Eligible pts were ≥ 55 yrs of age with intermediate- or poor-risk cytogenetics and ECOG PS ≤ 3, and in CR/CRi after IC ± consolidation. Pts were randomized 1:1 to CC-486 300 mg or PBO QD on days (d) 1–14 of 28d Tx cycles. HRQoL was assessed by FACIT-Fatigue scale and EQ-5D-3L health utility index, completed on d1 of each cycle and at end of Tx (EOT). Endpoints include Tx differences in mean changes from baseline (BL), and proportions of pts with clinically meaningful change from BL (improvement, no change, deterioration). Evaluable pts had an HRQoL assessment at BL and ≥ 1 post-BL visit. Stratified ANCOVA models included Tx and BL scores as covariates. **Results:** In all, 225/238 pts (95%) in the CC-486 arm were evaluable for FACIT-Fatigue and EQ-5D-3L, and 219/234 pts (94%) in the PBO arm were evaluable for FACIT-Fatigue and 217 (93%) for EQ-5D-3L. Pt characteristics were comparable between Tx arms. Most pts (61%) were 65-74 yrs of age. Median number of CC-486 Tx cycles was 12 and PBO cycles was 7. Compliance rates were > 95% at BL and remained high (> 85%) at all post-BL visits except for EOT. At BL, pts in both Tx arms had comparable low levels of fatigue and generally good HRQoL relative to an age-matched general population. There were no meaningful differences between CC-486 and PBO in mean changes from BL in FACIT-Fatigue or EQ-5D-3L scores at any post-BL visit. There was no statistically significant difference between Tx arms in proportion of pts with a clinically meaningful deterioration in FACIT-Fatigue score at any post-BL visit except at cycle 29 (likely due to chance; no adjustment made for multiple testing), or in EQ-5D-3L at any visit. Median time to deterioration was not significantly different between CC-486 and PBO on the FACIT-Fatigue scale (41 vs 44 weeks, respectively; $P = 0.70$) or the EQ-5D-3L (200 vs 164 weeks; $P = 0.63$). **Conclusions:** HRQoL and low levels of fatigue were preserved with CC-486 maintenance Tx. CC-486 significantly improved OS and RFS while maintaining HRQoL comparable to PBO. Clinical trial information: NCT01757535. Research Sponsor: BMS.

7534 Poster Session (Board #307), Fri, 8:00 AM-11:00 AM

Molecular dissection of normal karyotype acute myeloid leukemia. *First Author: Jacob Tyler Shreve, Indiana University School of Medicine, Indianapolis, IN*

Background: Conventional cytogenetics remain one of the most important prognostic factors in acute myeloid leukemia (AML), though 50-60% of patients (pts) have normal karyotype (NK), conventionally classified as intermediate-risk, and have very heterogeneous outcomes. A fraction of mutations such as *NPM1*, *FLT3-ITD,* and *CEBPa* can improve risk stratification for some pts but underestimate the molecular complexity and interactions between these genes and others. **Methods:** Genomic and clinical data of 2,793 primary AML (pAML) pts were analyzed. A panel of 35 genes that are commonly mutated in AML and myeloid malignancies and have shown to impact OS was included. Correlation of each mutation with others and their impact on OS were evaluated. OS was calculated from the date of diagnosis to date of death or last follow-up. **Results:** Of 2,793 pts with pAML, 1,352 (48%) had NK and were included in the final analysis. The median age was 55 years (range, 18-93). The median number of mutations/sample was 3 (range, 0-7). The most commonly mutated genes were: *NPM1* (49%), *DNMT3A* (37%), *FLT3-ITD* (24%), *CEBPa* (19%), *TET2* (17%), *IDH2* (17%), and *RUNX1* (15%). In univariate Cox regression analysis, mutations in *NPM1* (HR 0.81, p =0.008), and *CEBPa* (single mutant, HR 0.8, double mutant, HR 0.69, $p< 0.001$, respectively) were associated with longer OS, while mutations in *DNMT3a* (HR 1.26, p =0.003), *FLT3-ITD* (HR 1.49, $p<$ 0.001), *TET2* (HR 1.26, p =0.02), *RUNX1* (HR 1.36, p =0.003), *SRSF2* (HR 1.58, p <0.001), *IDH1* (HR 1.29, p <0.001), and *ASXL1* (HR 1.89, p <0.001) were associated with shorter OS. A total of 67% of pts had *NPM1, DNMT3A,* and *FLT3-ITD* mutated alone or in combination with each other. The median OS for pts with $NMP1^{Mut}/DNMT3A^{WT}/FLT3\text{-}ITD^{WT}$ was 99.1 months(m), $NMP1^{Mut}/DNMT3A^{Mut}/FLT3\text{-}ITD^{WT}$ 54.8m, $NMP1^{Mut}/DNMT3A^{WT}/FLT3\text{-}ITD^{Mut}$ 42.3m, $NMP1^{Mut}/DNMT3A^{Mut}/FLT3\text{-}ITD^{Mut}$ 13.4m, $NMP1^{WT}/DNMT3A^{Mut}/FLT3\text{-}ITD^{Mut}$ 13.1m, and $NMP1^{WT}/DNMT3A^{WT}/FLT3\text{-}ITD^{WT}$ (triple negative) 32.7m. The median OS for pts with 0-2 mutations/sample was 59.3m, compared to 34.1m for pts with 3-4 mutations, and 16.1m for pts with > 5 mutations ($p<$ 0.001). **Conclusions:** We propose a simplified and robust approach to risk stratify AML pts with NK based on the mutational status of *NPM1*, *DNMT3A*, *FLT3-ITD* (alone or in combination with each other), *CEBPa*, and the number of mutations/sample. Research Sponsor: None.

7535 Poster Session (Board #308), Fri, 8:00 AM-11:00 AM

Relation between measurable residual disease and morphologic relapse in AML. *First Author: Lauren Shih, University of Washington, Seattle, WA*

Background: Measurable residual disease (MRD) in AML portends a poor prognosis. The outcomes and treatments of MRD after an initial MRD negative complete remission (MRD- CR) are unclear. **Methods:** We retrospectively identified 432 patients ≥ 18 years of age treated for AML or high grade myeloid neoplasm (10-19% blasts in blood and/or marrow) at University of Washington/Seattle Cancer Care Alliance from 2008-2017 who achieved MRD- CR after initial treatment. Next disease recurrence was recorded, with patients either developing MRD (< 5% blasts via multiparameter flow cytometry; n = 44) or developing morphologic relapse (≥5% blasts; n = 100). The remaining patients remained in MRD- CR (n = 288, median follow up time 3.7 years). A landmark analysis at one year was performed to compare overall survival (OS). **Results:** Patients who developed MRD tended to be older (p = 0.009), but baseline characteristics were otherwise similar. Therapies for MRD included allogeneic transplant, low intensity chemotherapy, and high intensity chemotherapy; no significant associations were found between type MRD directed therapy and survival. Landmark OS at 1 year after MRD- CR was significantly different for patients without relapse at 1 year compared to those with MRD or morphologic relapse (median OS was 8.5 years for no relapse, 2.2 years for MRD, and 1.0 years for morphologic relapse). A multivariable Cox regression model among patients alive at 1 year showed patients without relapse had significantly improved OS compared to those with morphologic relapse [HR 0.18 (95% CI 0.1-0.31)]. Although there was a trend towards improved OS, we did not identify a significant difference between patients with MRD relapse compared to morphologic relapse [HR 0.54 (95% CI 0.27-1.11)]. There were no significant differences in patient characteristics for patients with MRD vs morphologic relapse matched by time of relapse (days 30-90, 90-150, 150-210). **Conclusions:** Following MRD- CR, development of either MRD or morphologic relapse were both associated with decreased OS. Notably, no significant differences in terms of survival were seen between patients who presented with MRD as opposed to morphologic relapse. No clear predictors were identified for MRD vs morphologic relapse. In this cohort, development of MRD carried a poor OS prognosis, similar to the prognosis of developing morphologic relapse. Future clinical trials should focus on MRD directed therapies, as no consensus exists about optimal treatment of MRD. Research Sponsor: None.

7536 Poster Session (Board #309), Fri, 8:00 AM-11:00 AM

Characterization of clinical pharmacokinetics and exposure-response relationships of AMG 330, a bispecific CD33 T-cell engager antibody construct, in patients with relapsed/refractory AML. *First Author: Suresh K Agarwal, Amgen Inc., South San Francisco, CA*

Background: AMG 330 binds both CD33 and CD3 and redirects T cells toward $CD33^+$ cells leading to T-cell–mediated cytotoxicity against AML blasts. An ongoing open label phase I dose-escalation study (NCT02520427) has shown preliminary activity and acceptable safety in relapsed or refractory (R/R) acute myeloid leukemia (AML) patients (pts) (Ravandi et al. ASH 2018). Pharmacokinetics and exposure-response (E-R) relationships of AMG 330 were characterized in this trial. **Methods:** A continuous IV infusion of AMG 330 was evaluated at escalating target doses (range from 0.5 to 720 μg/day) using a 3+3 design with pts receiving step dose/s prior to reaching target doses of ≥ 30 μg/day. Population pharmacokinetics (popPK) using non-linear mixed effects modeling and E-R analyses were conducted to characterize relationships between AMG 330 exposure (steady-state concentration [Css]) at target dose, the baseline tumor burden, clinical response per revised IWG criteria and incidence of cytokine release syndrome (CRS). **Results:** As of Dec 10, 2019, 55 patients (males, 56.4%; median age, 58.0 [18.0–80.0] years) were enrolled in 16 cohorts. AMG 330 PK was best described by a one-compartment linear PK model. Dose dependent increases were observed in AMG 330 Css exposures. Responders typically showed higher AMG 330 Css than non-responders. Preliminary exploratory analysis indicated that higher AMG 330 exposures, lower baseline leukemic burden in bone marrow and CD33+ AML cells in peripheral blood, and higher baseline Effector:Target cell ratio may be associated with clinical response. Additionally, a positive relationship was observed for AMG 330 exposures and baseline leukemic burden ($p < 0.05$) with probability of CRS occurrence and severity. Based on the model, at a baseline leukemic burden of 20%, a 240 μg/day target dose is predicted to result in a 28% and 4% probability of developing CRS of grade ≥ 2 and ≥ 3, respectively. **Conclusions:** Clinical pharmacokinetic profile and E-R relationships of AMG 330 were characterized to identify optimal AMG 330 dosing regimens that minimize the risk for CRS in ongoing and planned clinical investigations. Clinical trial information: NCT02520427. Research Sponsor: Amgen Inc.

7537 Poster Session (Board #310), Fri, 8:00 AM-11:00 AM

Outcomes in older patients with high-risk/secondary AML who achieved remission with CPX-351 versus 7+3 but did not undergo transplant: Phase 3 exploratory analysis. *First Author: Tara L. Lin, University of Kansas Medical Center, Kansas City, KS*

Background: CPX-351 (Vyxeos; daunorubicin [D] and cytarabine [C] liposome for injection) is approved by the FDA and EMA for the treatment of adults with newly diagnosed therapy-related AML or AML with myelodysplasia-related changes. In a phase 3 study (NCT01696084) in patients (pts) aged 60-75 y with newly diagnosed high-risk/secondary AML, CPX-351 demonstrated significantly longer overall survival (OS) and higher rates of remission and hematopoietic cell transplant (HCT) vs conventional 7+3, with a comparable safety profile. To better understand the impact of treatment on outcomes in pts who did not undergo HCT, this exploratory analysis evaluated outcomes in the subgroup who achieved complete remission (CR) or CR with incomplete neutrophil or platelet recovery (CRi) with CPX-351 vs 7+3 but did not undergo HCT. **Methods:** Pts were randomized 1:1 to receive ≤2 induction cycles of CPX-351 (100 units/m^2 [C 100 mg/m^2 + D 44 mg/m^2] as a 90-min infusion on Days 1, 3, 5 [2nd induction: Days 1, 3]) or 7+3 (C 100 mg/m^2/d continuously for 7 d + D 60 mg/m^2 on Days 1-3 [2nd induction: 5+2]). Pts achieving CR or CRi could receive up to 2 consolidation cycles. Pts could receive HCT at the physician s discretion. **Results:** CR+CRi was achieved by 73/153 (48%) pts with CPX-351 vs 52/156 (33%) with 7+3; of these pts, 33/73 (45%) vs 28/52 (54%) did not subsequently undergo HCT. The baseline characteristics of these pts were generally balanced between arms; however, the CPX-351 arm had more male pts vs 7+3 (64% vs 43%) and pts with ECOG PS of 1 (82% vs 54%), and fewer pts with antecedent MDS and HMA exposure (21% vs 39%). Median OS was longer with CPX-351 vs 7+3 (14.72 vs 7.59 mo; HR = 0.57 [95% CI: 0.31-1.03]; Table). There was no early mortality by Day 60 in either arm (see Table for additional data). **Conclusions:** CPX-351 improved median OS vs 7+3 in pts who achieved CR+CRi but did not undergo HCT, suggesting a treatment benefit with CPX-351 even among pts who do not undergo HCT. The CPX-351 safety profile in this subgroup was consistent with the overall study population and known profile of 7+3. Clinical trial information: NCT01696084. Research Sponsor: Jazz Pharmaceuticals.

	CPX-351 (n = 33)	7+3 (n = 28)
Median OS in pts with CR+CRi, mo	14.72	7.59
HR (95% CI)	0.57 (0.31-1.03)	
Median OS in pts with CR,[a] mo	19.15	8.41
Grade 3/4 AEs, n (%)	31 (94)	20 (71)
Serious AEs, n (%)	25 (76)	15 (54)
Febrile neutropenia	5 (15)	4 (14)
Acute respiratory failure	4 (12)	1 (4)
Pneumonia	1 (3)	3 (11)
Grade 5 AEs, n (%)	2 (6)	5 (18)
Median (range) days to recovery		
Neutrophils ≥500/μL	35 (21-63)	29 (21-43)
Platelets ≥50,000/μL	36 (14-106)	28.5 (21-144)

[a]CPX-351: n = 27; 7+3: n = 21.

7538 Poster Session (Board #311), Fri, 8:00 AM-11:00 AM

STAG2-mutated AML patients: ASXL1 cohesin binding motif status and mutation landscape. *First Author: Frank J Scarpa, NeoGenomics Laboratories, Aliso Viejo, CA*

Background: *ASXL1* and the cohesin complex (*STAG2*, *RAD21*, *SMC1A*, and *SMC3*) are commonly mutated chromatin regulators with significant clinical implications in AML. The ASXL1-cohesin interactome regulates gene expression through chromatin accessibility via *ASXL1*'s cohesin binding motif (CBM). *ASXL1* variants are most commonly located in the ASXM1 domain and onwards, and characteristically lead to loss of the PHD domain. Gain-of-functions in truncated *ASXL1* are suggested to increase catalytic activity of *BAP1,* which binds the ASXH domain at AA 351, and to gain an interaction with *BRD4,* which binds somewhere between the ASXN and ASXH domains, to drive H3K4Me3 and H2AK119Ub. **Methods:** 2463 suspected AML patient bone marrow, peripheral blood, or FFPE tissue samples were evaluated using an all exon amplicon-based 27 gene NGS panel. Patients with a VAF <10% in *ASXL1* were excluded to avoid reporting artifacts, particularly in variant c. 1934dup. Statistics were performed using Fisher's exact test. **Results:** Mutations in *STAG2*-mutated patients were enriched for sAML, as evidenced by the higher number of mutations in *ASXL1, SRSF2,* and *BCOR* (associated with sAML) compared to *NPM1, DNMT3A,* and *PTPN11* (pAML). *STAG2* mutations were found in 173 samples representing 93.5% of cohesin mutations. Of all *ASXL1* mutations (VAF 10.1– 54.5%; median 32.2%) 4.0% occurred in the CBM. While 23.5% of samples with mutations outside *ASXL1* CBM had concomitant mutations in *STAG2*, none of the 18 samples with CBM mutations (VAF 11.3 – 51.7%; median 42.5%) had any cohesin gene mutation (P = 0.0174). The proportion of *BCOR* (27.8% vs 9.2%; P = 0.024) and *CEBPA* (27.8% vs 8.2%; p = 0.016) mutated patients in the CBM+ group was significantly higher than the CBM- group. *JAK2* (16.7% vs 5.4%), *KRAS* (22.2% vs 13.6%), *EZH2* (22.2% vs 13.6%), and *RUNX1* (38.9% vs 27.7%) mutations were also higher though not significantly in this group. Mutations throughout all of *ASXL1*, the 13 amino acids after the CBM, and hotspot variants all had *STAG2* mutations at a frequency of 20.9-44.4%, further suggesting mutual exclusivity. **Conclusions:** STAG2 mutations and mutations in the CBM were mutually exclusive events and harbored different co-mutation frequencies. In compromised ASXL1 CBM cases, *BCOR* and *CEBPA* transcriptional regulators are significantly more mutated, but in cases of ASXL1 mutation outside the CBM, cohesin mutations are preferred, suggesting alternative chromatin accessibility mechanisms driving leukemogenesis. This observation has not been previously reported in the literature to our knowledge. Research Sponsor: None.

7539 Poster Session (Board #312), Fri, 8:00 AM-11:00 AM

Venetoclax (Ven) added to intensive chemo with cladribine, idarubicin, and AraC (CLIA) achieves high rates of durable complete remission with low rates of measurable residual disease (MRD) in pts with newly diagnosed acute myeloid leukemia (AML). *First Author: Tapan M. Kadia, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Ven is a BCL2 inhibitor that is approved in combination with lower intensity therapy for pts with newly diagnosed AML who are ineligible for intensive chemo. We previously reported the safety and efficacy of cladribine and araC with idarubicin in young and fit pts with AML. Here, we studied the combination of ven with the intensive CLIA regimen in newly diagnosed AML. **Methods:** Pts < 65 yrs with newly diagnosed FLT3-wildtype AML were enrolled. Induction was cladribine 5 mg/m^2 IV on D 1-5, followed by ara-C 1.5 g/m^2 IV on D 1-5, idarubicin 10 mg/m^2 IV D 1-3, and ven at an effective dose of 400mg PO on D2-8. There was no ramp up for ven and dose modifications for CYP3A4 inhibitors were made. Consolidation consisted of up to 5 more cycles of CLIA+Ven. All pts underwent baseline next generation sequencing and MRD testing by multiparameter flow cytometry at the time of response. **Results:** 18 pts are enrolled, with a median age of 50 yrs (range, 18-64). Baseline pt characteristics are in Table. 16 pts were evaluable for response and 2 are too early. 14 of 16 pts (88%) achieved a remission, including 10 (63%) complete remission (CR) and 4 (25%) CR with incomplete count recovery (CRi). The median time to response was 1 cycle and the median number of cycles given was 2 (1-5). 10 of the 14 responders (71%) had undetectable MRD at the time of remission. Both nonresponding pts had a complex karyotype and 1 had a TP53 mutation. With a median follow up of 4.5 months (0.2 – 11.2), none of the responding pts have relapsed. 8 of the 14 responders (57%) have received allogeneic stem cell transplant. The median survival has not been reached; the 6-month OS and RFS are 90% and 100%, respectively. Treatment was well tolerated, with 0% 4-week mortality. The median days to ANC ≥ 1 and Platelets ≥ 100 were 30 (19-49) and 26 (18-39), respectively. Tumor lysis syndrome was not seen. The most common adverse events were neutropenic fever, pneumonia, nausea, and liver transaminitis. **Conclusions:** The addition of ven to CLIA was safe and effective in newly diagnosed pts with AML. The combination was not associated with early mortality or prolonged myelosuppression, but did result in high rates of durable MRD negative remissions. Clinical trial information: NCT02115295. Research Sponsor: Internal Departmental Funds.

Characteristics	N = 18 Pts Median [Range] or N (%)
Age (yr)	50 [18-64]
Diploid Karyotype	11 (61%)
Intermediate	1 (6%)
Adverse	6 (33%)
Marrow Blast %	56 [8 – 81]
WBC [x10^9/L]	4.9 [0.8 – 41.2]
Peripheral Blast %	10 [0-67]
Platelet [x10^9/L]	34 [10-218]

7540 Poster Session (Board #313), Fri, 8:00 AM-11:00 AM

Meta-analysis of case-control studies to examine the relationship between occupational pesticide exposure and risk of acute myeloid leukemia. *First Author: Nicolas Vallet, Tours University Hospital and ERL7001 LNOX, EA 3549, Tours, France*

Background: Occupational pesticide exposure (OPE) is associated with the risk of developing lymphoid malignancies, but less information is available on large cohorts about the risk of occurrence of acute myeloid leukemia (AML). To answer this question, we performed a meta-analysis including relevant adult case-control studies which reported OPE. **Methods:** Following PRISMA and MOOSE guidelines, two investigators performed a systematic search in PubMed and Cochrane databases for case-control studies evaluating the association between OPE and AML between 1946 and August 28, 2018. In order to identify the maximum number of studies, keywords related to demographical, pesticides and chemicals data exposures were used. Studies reporting AML diagnosis based only on death certificates, controls from cancer databases and pediatric cases (<15 years-old) were not included. Statistical analyses were performed with R software and the 'mefafor' package. **Results:** Fifteen studies which included 4,068 AML patients and 250,975 control subjects were included. Using a random effects model, the overall analysis showed a significant adverse association between OPE and AML with OR=1.49 (95%CI: 1.10-2.01), and a significant heterogeneity between studies (I^2=0.73, p<0.001). The robustness was checked after sequential exclusion of one study at a time which did not influence the overall OR estimate. A publication bias underestimating the OR was suggested by an asymmetrical funnel plot. Using trim-and-fill method, hypothetical missing studies were added studies in order to adjust the OR (OR=1.76 [95%CI: 1.30-2.38]. A stratified analysis showed that the association was significant in Asian populations (OR=1.74; 95%CI: 1.32-2.30) and upon exposure to insecticides (OR=1.45; 95%CI: 1.16-1.81), yet partly influenced by other factors, since most of the studies reported unadjusted results (n=8, 53%). Data on biological characteristics were unavailable to stratify patients according to AML molecular or cytogenetic characteristics. **Conclusions:** From this new extensive review and analysis, it clearly appears that AML should be considered as occupational illness in patients with demonstrated OPE. Further studies will have to focus on the biological effects of individual and pesticides cocktails in order to determine the pathogenesis mechanisms involved in leukemogenesis, and to improve individual protection. Research Sponsor: None.

7541 Poster Session (Board #314), Fri, 8:00 AM-11:00 AM

Antibacterial antibiotic exposures and cytomegalovirus reactivation after allogeneic hematopoietic stem cell transplantation. *First Author: Shijia Zhang, Division of Hematology, Oncology, and Transplantation, University of Minnesota, Minneapolis, MN*

Background: Cytomegalovirus seropositive (CMV+) recipients of CMV seronegative (CMV-) hematopoietic cell allografts are at the highest risk for CMV reactivation. Inspired by the recently described effect of antibiotic (abx)-induced dysbiosis on antiviral immunity, we retrospectively evaluated whether antibacterial abx exposures influence the risk of CMV reactivation after CMV- to CMV+ cord blood (CB) or matched sibling donor (MSD) transplantation, the serologic setting with highest risk of CMV reactivation. **Methods:** We identified 213 eligible patients (pts; 146 CB, 67 MSD, mean age 50, range 18-73). Exposures to fluoroquinolones (FQN), 3rd or higher generation cephalosporins (CPN3+), intravenous vancomycin (Vanc), piperacillin-tazobactam (Pip-Tazo), carbapenems, and metronidazole/clindamycin (Metro/Clinda) from day (D) -7 to D +14 (binary variables) or until CMV reactivation (or D +100, whichever occurred first; time-varying variables) were included in multivariable Fine-Gray regression models with competing risk for non-CMV death to estimate the risk of CMV reactivation by D +100. Other pre-defined covariates were ATG use during conditioning, anti-CMV abx exposure for other viruses, and acute GVHD. **Results:** 91% of pts received FQN, 67% CPN3+, 56% Vanc, 21% Pip-Tazo, 22% carbapenems, and 28% Metro/Clinda until D +14. These numbers increased to 94%, 81%, 76%, 31%, 38%, and 39% by D +100 (or CMV reactivation), respectively. 83 pts (39%: 66 CB, 17 MSD) had CMV reactivation by D +100. Vanc exposure by D +14 almost doubled the risk of CMV reactivation (HR 1.96, 95%CI 1.11-3.46, $P = 0.02$). With abx exposures up to D +100 modeled as time-varying covariates, Vanc exposure predicted a higher risk for CMV reactivation (HR 1.86, 95%CI 0.99-3.52, $P = 0.06$). The table below summarizes the results, excluding non-abx covariates for brevity. **Conclusions:** Our results suggest that vancomycin-sensitive bacteria may protect against CMV reactivation. Identifying the specific taxa and their location (intestinal vs. extraintestinal) requires more research. Microbiota considerations and abx exposure patterns can help personalize CMV prophylaxis. Research Sponsor: None.

Antibiotic	HR (95%CI), D +14, binary	P	HR (95%CI), D +100, time-varying	P
FQN	1.56 (0.70-3.46)	0.28	1.55 (0.61-3.88)	0.35
CPN3+	0.77 (0.43-1.38)	0.37	1.22 (0.62-2.38)	0.56
Vanc	1.96 (1.11-3.46)	0.02	1.86 (0.99-3.52)	0.06
Pip-Tazo	0.91 (0.51-1.62)	0.75	0.79 (0.47-1.33)	0.38
Carbapenem	1.26 (0.75-2.14)	0.38	1.33 (0.82-2.14)	0.25
Metro/Clinda	0.75 (0.45-1.26)	0.28	0.59 (0.36-0.97)	0.04

7542 Poster Session (Board #315), Fri, 8:00 AM-11:00 AM

Incidence of graft versus host disease in peri transplant hospitalization after *clostridium difficile* infection. *First Author: Drew Carl Drennan Murray, Division of Hematology and Medical Oncology, James Graham Brown Cancer Center, University of Louisville, Louisville, KY*

Background: Hyperacute graft versus host disease (GVHD) after allogenic stem cell transplantation (SCT) has adverse outcomes with increased rates of chronic GVHD and relapse. GVHD risks include mismatched related or matched unrelated donors, myeloablative conditioning, heavy pretreatment, and donor-recipient sex mismatch. *Clostridium difficile* infection (CDI) is a leading cause of diarrhea in immunocompromised patients. Proposed microbiome effect on immunity and GVHD in allogenic SCT recipients prompts concern of microbiome modulation from CDI and antibiotics inciting GVDH. **Methods:** National Inpatient Sample database 2014 for hospitalizations with allogeneic SCT in patients ≥18yo. Characteristics (age, sex, race, insurance, graft source, hospital type, region, comorbidities) were compared for hospitalizations with and without CDI. Primary outcome was the difference in the incidence of GVHD during the transplant hospitalization between the 2 groups. Other outcomes were mortality, length of stay and hospital charges. Chi-square, t-test, and multivariate logistic regression utilized. **Results:** Of 6210 patients with allogenic SCT, 745 (12%) had CDI during the transplant hospitalization. In transplanted patients without CDI the average age was 55yo, 43.9% female, 69.5% Caucasian (C), 7.1% African American (AA), 8.6% Hispanic (H), 32.1% had Medicare/Medicaid, 61.8% private insurance, 5.7% uninsured, 44.7% had hypertension, 13.7% had diabetes, graft source was 84.3% PBSC (peripheral blood stem cells), 11.3% bone marrow, and 4.4% cord blood. CDI group the average age was 52.5yo, 45.3% female, 73% C, 4.7% AA, 8.1% H, 25.7% had Medicare/Medicaid, 66.2% private insurance, 8.1% uninsured, 41.9% had hypertension, 10.1% had diabetes, graft source was 83.8% PBSC, 10.8% bone marrow, and 5.4% cord blood. 25.7% of patients with CDI developed GVHD during that hospitalization while 14.2% of patients without CDI developed GVHD during the hospital stay (OR 2.1, $p < 0.001$ multivariate analysis). GVHD during the hospitalization had no difference in length of stay ($p = 0.32$), total cost of stay ($p = 0.50$) or same hospitalization mortality ($p = 0.94$). **Conclusions:** Allogeneic SCT patients with CDI develop GVHD on the same hospitalization at significantly higher rates than patients without CDI. This is true after controlling for age, sex, race, insurance, comorbidities, graft source, hospital location, and type of institution. Despite known associations of early evidence of GVHD on relapse, overall mortality was not different between the two groups. Research Sponsor: None.

7543 Poster Session (Board #316), Fri, 8:00 AM-11:00 AM

Etanercept with extracorporeal photopheresis (ECP) for steroid-refractory acute graft versus host disease following allogeneic hematopoietic stem cell transplantation. *First Author: Sunny R K Singh, Henry Ford Health System, Detroit, MI*

Background: Acute graft versus host disease (aGVHD) is a well-described complication of allogeneic stem cell transplantation (allo-SCT). Complete response to steroids is achieved in 40-50% of cases, with steroid refractory GVHD requiring second line therapy. Currently, there is no accepted standard of care in this setting. In our study, we assessed the safety and efficacy of etanercept with ECP for steroid refractory aGVHD in a single center tertiary care hospital. **Methods:** Thirty adult patients who underwent peripheral blood allo-SCT and developed steroid-refractory aGVHD between January 2010 - July 2019 were retrospectively analyzed. Patients were planned to receive etanercept 25 mg subcutaneously twice weekly for at least 4 weeks. Safety was assessed by estimating infection related mortality. For efficacy, we analyzed the change in grade of aGVHD using the Wilcoxon signed-rank test. **Results:** Median age at the time of allo-SCT was 57.6 years and the most common indication for transplant was Myelodysplastic syndrome. Median time from allo-SCT to steroid initiation was 39.5 days (range 14-183 days). Median time from steroid initiation to etanercept was 6 days, with 7.5 median number of etanercept doses received. A total of 25 patients (83.3%) received ECP. As depicted in the table, there was a significant improvement in severity of aGVHD after etanercept therapy compared to that before its initiation. Overall response rate was 83.3%, while overall mortality was 86.7%. Median overall survival for responders was 306 days (range 59-2005 days) and for non-responders was 181 days (range 89-261 days). Death attributed to infection alone occurred in 28% (n=7), infection along with GVHD in 28% (n=7) and infection with relapsed disease in 1 patient. Active infection within 6 months of transplant occurred in 93.3% patients. **Conclusions:** The use of Etanercept with ECP resulted in improvement of steroid refractory aGVHD following allo-SCT, with responses noted in the majority of patients. High rates of infection related mortality were also noted and remain a cause of concern. Research Sponsor: None.

Response at Day 56 for aGVHD (from initiation of steroids)	Complete Response	Partial Response	No Response	Progression
Skin	3 (30%)	4 (40%)	3 (30%)	
Gut	3 (20%)	10 (66.7%)		2 (13.3%)
Liver	3 (42.9%)	2 (28.6%)		2 (28.6%)
aGvHD Severity	**Before Etanercept**	**After Etanercept**	**Z-score (for change in severity)**	**p - value**
Absent		7 (26.9%)	-2.9	0.003
Grade I	2 (6.7%)	3 (11.5%)		
Grade II	9 (30%)	8 (30.8%)		
Grade III	13 (43.3%)	3 (11.5%)		
Grade IV	6 (20%)	5 (19.2%)		

7544 Poster Session (Board #317), Fri, 8:00 AM-11:00 AM

Incidence of large granular lymphocytosis (LGL) in patients with late cytopenias after allogeneic blood or marrow transplantation (AlloBMT). *First Author: Marcus Messmer, Johns Hopkins University, Baltimore, MD*

Background: LGL - often called LGL leukemia - is a clonal disorder of T or NK cells often associated with cytopenias, autoimmunity, splenomegaly, and B symptoms. There are a limited number of studies of benign LGL expansion after alloBMT, some suggesting an association with improved transplant-related outcomes. In contrast, clinically significant LGL leukemia after alloBMT is only described in case reports. **Methods:** We cross referenced all patients receiving an alloBMT at Johns Hopkins since 2010 with patients who were evaluated for LGL expansion by peripheral blood (PB) flow cytometry (FC) since 2012. **Results:** There were 1930 alloBMTs from 1/1/10 to 7/1/19. PB FC for suspected LGL was sent on 153 unique patients after alloBMT, usually in the setting of cytopenias (97%). Median age was 59. 69 (45%) had LGL expansion (LGL+) at a median 194 days after alloBMT. Among LGL+, 53 (77%) had an absolute neutrophil count (ANC) < 1500. The majority of the alloBMTs were non-myeloablative (NMA) (97%), related (88%), and haploidentical (89%), consistent with our center's characteristics. Graft vs host disease (GVHD) prophylaxis was post-transplant cyclophosphamide (PTCy), mycophenolate mofetil, and tacrolimus or sirolimus. 64 (93%) cases were T cell LGL (T-LGL) and 5 were NK cell. Of those with T-LGL, 43 were assessed for T cell receptor clonality. 21% were clonal, 53% oligoclonal, 5% polyclonal, and 21% indeterminate. There were no significant demographic or transplant-related differences between LGL+ and LGL- in our 153 patient cohort. LGL+ were more likely to have had CMV viremia (75% vs 26%, $p < 0.0001$), but not acute or chronic GVHD. LGL+ had higher lymphocyte counts (1520/cu mm vs 495, $p < 0.0001$) and a trend toward more neutropenia (77% vs 63%, $p = 0.07$). There were no differences in overall survival, relapse, or non-relapse mortality. 29 (42%) of LGL+ received immunosuppressive therapy (IST) for cytopenias. First line treatment was corticosteroids for 24 (83%). 65% had normalization of ANC with first line treatment, compared to improvements in anemia in 15% and thrombocytopenia in 36%. 34% of those treated required ≥2 lines of treatment. **Conclusions:** In contrast to prior studies, where LGL after alloBMT was asymptomatic and associated with improved transplant outcomes, we identified a high rate of LGL with cytopenias and no improvement in transplant outcomes. Neutropenia was common in LGL+ and usually improved with IST. Research Sponsor: None.

7545 Poster Session (Board #318), Fri, 8:00 AM-11:00 AM

Toxicities after high dose post-transplant cyclophosphamide in haploidentical donor transplants: Risk factors and impact on survival. *First Author: Dipenkumar Modi, Karmanos Cancer Institute/Wayne State University, Detroit, MI*

Background: Post-transplant cyclophosphamide (pCY) when given at 50mg/kg on day +3 and +4 in haploidentical donor transplants (HIDT) leads to considerable morbidity. Information on its toxicity and impact on outcomes is limited. **Methods:** We analyzed 91 patients (pt) undergoing HIDT with pCY to estimate incidence and risk factors of mucositis, hemorrhagic cystitis, renal and cardiac toxicities during the first 6 months after transplant and its impact on overall survival (OS). We compared these complications with 91 pt who were matched for age, disease, disease status at transplant, conditioning regimen and received 8/8 HLA-matched transplants without pCY (non-pCY cohort). **Results:** Fourteen pt (15%) in non-pCY and 28 (31%) in pCY experienced hypoxia requiring oxygen ($p = 0.03$). Ten pt (11%) in non-pCY and 21 (23%) in pCY developed clinically significant hypotension ($p = 0.05$). Day +100 cumulative incidence rate (CIR) of mucositis was 59.3% for non-pCY and 84.6% for pCY ($p < 0.001$). Seven pt (13%) in non-pCY cohort and 39 (51%) in pCY developed grade 3-4 mucositis ($p < 0.001$). Two pt (2%) in non-pCY and 22 (24%) in pCY developed gross hematuria ($p = 0.05$). Day +180 CIR of hemorrhagic cystitis was 13.2% for non-pCY and 29.7% for pCY ($p = 0.005$). Hemorrhagic cystitis did not have an adverse impact on non-relapse mortality (NRM) and OS. Day +180 CIR of renal toxicities was 17.6% for non-pCY and 28.6% for pCY ($p = 0.10$). The CIR of cardiac toxicities at day +180 was 9.9% for non-pCY and 14.3% for pCY ($p = 0.34$). Congestive heart failure (59%) and atrial fibrillation (36%) were the most common cardio-toxicities. One-year NRM was 38.5% in pt developing cardio-toxicity in the pCY cohort compared to no cardio-toxicity (15.3% in non-pCY and 18.3% in pCY, $p = 0.004$). OS was inferior in pt with cardio-toxicity in non-pCY (HR 5.49, $p < 0.001$) and pCY (HR 2.3, $p = 0.03$) compared to pt without cardio-toxicity. In multivariable analysis, pCY was associated with an increased risk of mucositis (HR 1.48, $p = 0.03$), and hemorrhagic cystitis (HR 2.67, $p = 0.004$). The number of infused CD34 cells was associated an increased risk of cardiac toxicity (HR 1.13, $p = 0.005$). pCY was not associated with higher cardiac complications, and no impact of the number of infused CD34 cells, conditioning regimen and prior transplant was observed on hemorrhagic cystitis and mucositis. **Conclusions:** pCY was associated with significant morbidity compared to HLA-matched non-pCY cohort. Although cardio-toxicities were similar between both groups, it was associated with worse survival. Research Sponsor: None.

7546 Poster Session (Board #319), Fri, 8:00 AM-11:00 AM

Grade III-IV cytokine release syndrome is associated with inferior survival in patients undergoing haploidentical donor stem cell transplants. *First Author: Omar Albanyan, Karmanos Cancer Institute/Wayne State University, Detroit, MI*

Background: Haploidentical transplant (HIDT) with post-transplant cyclophosphamide (pCY) is being increasingly used because of the universal availability of donor and rapid graft acquisition time. Cytokine release syndrome (CRS) is one of the commonly occurring complications in this population. The information on the impact of CRS on the post-HIDT outcomes is limited. **Methods:** We retrospectively evaluated 91 patients who underwent HIDT between June 2012 and June 2019 for the onset and severity of CRS. CRS was graded per ASTCT guidelines. The primary objective was to compare RFS (relapse-free survival), NRM (non-relapse mortality), OS (overall survival) and GVHD in patients with no CRS, CRS grade 1-2 and 3-4. **Results:** All received peripheral blood stem cells and pCY/tacrolimus/mycophenolate as GVHD prophylaxis. Fifty-six (62%) received reduced intensity and 35 (38%) received full intensity conditioning regimen. Ten (10.9%) had no CRS, 74 (81.3%) developed grade 1-2 CRS and seven (7.7%) experienced grade 3-4 CRS. Median time to onset of CRS was one day post-transplant. The most common symptoms were fever (87%), fatigue (30%), nausea/vomiting (24%), rigors (24%), diarrhea (20%) and rash (11%). Fifteen (20%) with grade 1-2 and six (85%) with grade 3-4 CRS received tocilizumab. Day +100 cumulative incidence of grade III-IV acute GVHD for no CRS, grade 1-2 and grade 3-4 CRS was 0%, 2.7%, and 14.3%, respectively ($P = 0.36$). One-year cumulative incidence of chronic GVHD for no CRS, grade 1-2 and grade 3-4 CRS was 30%, 31.9% and 14.3%, respectively ($P = 0.70$). One-year NRM for no CRS, grade 1-2 and grade 3-4 CRS was 30%, 16.5%, and 57.1%, respectively ($P = 0.002$). One-year RFS for no CRS, grade 1-2 and grade 3-4 CRS was 48%, 63.4% and 28.6%, respectively ($p = 0.03$). OS at 1-year for no CRS, grade 1-2 and grade 3-4 CRS was 60%, 73.9%, and 28.6%, respectively ($P = 0.008$). Multivariable analysis revealed that grade 3-4 CRS was associated with significantly higher NRM (HR 5.54, $P = 0.002$), worse RFS (HR 3.41, $P = 0.011$) and worse OS (HR 4.91, $P = 0.001$). Conditioning regimen, degree of HLA match and disease risk index did not affect post-transplant outcomes and were not predictors for developing CRS. **Conclusions:** Our study showed that grade 3-4 CRS was associated with inferior post-transplant outcomes. However, no impact on acute or chronic GVHD was noted. Therefore, early recognition and prompt management of CRS may help improve outcomes. Research Sponsor: None.

7547 Poster Session (Board #320), Fri, 8:00 AM-11:00 AM

Pre-transplant molecular minimal residual disease (MMRD) is associated with inferior outcomes in patients with acute myeloid leukemia undergoing allogeneic stem cell transplantation. *First Author: Muhammad Husnain, University of Miami/Sylvester Cancer Center, Miami, FL*

Background: Allogeneic Stem Cell Transplant (alloSCT) continues to be the optimal consolidation strategy for many patients with AML; cytogenetic and molecular abnormalities are known predictors of post-transplant outcomes. There is increasing evidence that Molecular Minimal Residual Disease (MMRD) following induction has important prognostic implications and its value in the prediction of post-transplant relapse continues to be elucidated. We aim to evaluate the impact of genetics and pre-transplant MMRD on clinical outcomes following alloSCT. **Methods:** We retrospectively evaluated eighty-nine patients, ≥18 years with a diagnosis of AML in complete morphologic remission (i.e. < 5% BM blasts by morphologic assessment) who received alloSCT between 01/2012-05/2018 at the University of Miami and for whom cytogenetic and comprehensive molecular data was available prior to transplantation. Patients were stratified into favorable, intermediate and poor-risk categories based on 2017 ELN criteria. MMRD was defined as persistent leukemia-specific mutations prior to transplantation (i.e. NPM1, FLT3, CEBPA, IDH1-2, RUNX1 and TP53). Persistence of DTA mutations (DNMT3A, TET2 and ASXL1) was not considered MMRD, patients with unavailable cytogenetic/molecular data at diagnosis were excluded. **Results:** Seventy-four (83%) patients were transplanted in CR1, myeloablative conditioning was used in 72% of patients. Two-year OS and LFS were 69.4% and 78.2%, respectively. Stratification by ELN criteria resulted in prognostic separation for patients transplanted in CR1: 2-year OS for favorable (87%), intermediate (68%) and adverse risk (51%) patients ($p = 0.0417$). The presence of MMRD was the strongest predictor of post-transplant outcomes for the whole cohort with 2-year OS and LFS of 29.4% and 37.1% (HR 5.45 [95%CI 2.43-12.3] $p = 0.0001$; HR 12.4 [95%CI: 3.76 to 39.8] $p = 0.0001$); respectively. Subgroup analysis confirmed that MMRD was associated with significantly inferior LFS for IM/favorable and adverse risk patients (HR: 6.76 [95% CI 1.12 to 40.9], $p = 0.038$). **Conclusions:** Pre-transplant MMRD was the most important prognostic factor for relapse and survival in our cohort of AML patients undergoing alloSCT. Correlation of MMRD with other transplant variables such as conditioning intensity, MRD status by MFC and the impact of pre-emptive/therapeutic strategies in high-risk patients continues to be explored. Research Sponsor: None.

7548 Poster Session (Board #321), Fri, 8:00 AM-11:00 AM

Discontinuation of tyrosine kinase inhibitor (TKI) therapy in chronic myeloid leukemia in chronic phase (CML-CP) in US clinical practice after guideline updates. *First Author: Ehab L. Atallah, Hematologic Malignancies, Medical College of Wisconsin, Milwaukee, WI*

Background: NCCN CML practice guidelines were updated in 11/2016 and in 9/2019 to include considerations for discontinuation of TKI therapy in patients (pts) with CML-CP. This study characterized TKI discontinuation practices in the US after these updates and drew parallels with a similar study conducted prior to these guideline updates (Ritchie et al. *Leuk Lymphoma.* 2019). **Methods:** Pt charts of adult CML-CP pts with TKI discontinuation (1/2017-12/2018) outside a clinical trial after achieving an adequate response were abstracted (11/2019-12/2019) via an online case report form by US oncologists/hematologists. Physicians' assessment of adequate response (TKI duration, molecular response [MR], MR duration) and relapse were described. **Results:** 61 physicians (academic: 43%; community-based practices: 57%) contributed 153 pt charts. Most physicians were from large practices (57%), had > 10 years (y) experience since completing subspecialty training (59%), and treated a median of 30 CML pts in the last 2y; 56% did not have access to precise molecular response monitoring for BCR-ABL of ≥4.5 log when attempting TKI discontinuation. Pts with TKI discontinuation had mean age 56 years, were mostly male (60%), white (69%), and had TKI discontinued in first-line (96%). Most common reasons for TKI discontinuation were pt request (54%) and adverse events (18%), besides achieving an adequate response. Physicians' assessment of adequate response for TKI discontinuation are reported in the Table. 21% of pts (academic: 12%; community: 30%) relapsed after TKI discontinuation (treatment-free remission [TFR] failure; 66% relapsed within 1y). **Conclusions:** Although NCCN CML practice guidelines provide guidance for discontinuation of TKI therapy, there remains heterogeneity in US practice and TKI discontinuation is predominantly attempted in first-line (similar to Ritchie et al. 2019). TKI discontinuation is being practiced without adequate sensitive tools mandated by practice guidelines to monitor response. Broader application of practice guidelines for optimal TKI therapy discontinuation in CML-CP pts is needed, particularly in community-based practices, to improve long-term TFR rates. Research Sponsor: Novartis Pharmaceutical Corporation.

	Before TKI discontinuation	Overall (N = 153)	Academic (N = 77)	Community (N = 76)
TKI therapy duration	< 1y	20%	17%	17%
	1 - < 2y	15%	17%	13%
	2 - < 3y	14%	9%	20%
	≥3y	50%	57%	43%
PCR (BCR-ABL1/ABL1) MR	≤MR3	23%	21%	25%
	MR4	38%	31%	45%
	MR4.5	39%	48%	30%
MR duration	≤1y	48%	36%	61%
	2y	21%	25%	17%
	≥3y	31%	39%	22%

7549 Poster Session (Board #322), Fri, 8:00 AM-11:00 AM

Bosutinib (BOS) for chronic phase (CP) chronic myeloid leukemia (CML) after imatinib (IMA) failure: ≥8-y update of a phase I/II study. *First Author: Tim H. Brümmendorf, Universitätsklinikum RWTH Aachen, Aachen, Germany*

Background: BOS is approved for newly diagnosed CP CML and CML resistant/intolerant to prior therapy. In a phase I/II study, BOS showed durable efficacy and manageable toxicity in patients (pts) with CP CML after IMA failure. We report an ≥8-y update of this phase I/II and ongoing extension study. **Methods:** Pts with CP CML resistant/intolerant to IMA (CP2L) or IMA + dasatinib and/or nilotinib (CP3L) or with accelerated/blast phase (AP/BP) CML or Philadelphia chromosome+ acute lymphoblastic leukemia with prior tyrosine kinase inhibitor (TKI) therapy (ADV) received BOS starting at 500 mg/d. **Results:** 54/284 (19%) CP2L pts were still on BOS after ≥9 y and 8/119 (7%) CP3L and 5/167 (3%) ADV pts after ≥8 y; 61 CP2L pts discontinued BOS since y 5 and 21 CP3L and 12 ADV pts since y 4. Overall, the most common reason for discontinuation was disease progression/lack of efficacy in CP2L (27%), CP3L (42%) and ADV (50%) pts; last dose before discontinuation was ≥500 mg/d in 59 (21%), 28 (24%) and 46 (28%) pts, respectively. In CP2L pts, median (range) of follow-up was 54 (1–155) mo, treatment duration 26 (<1–155) mo and dose intensity 438 (87–599) mg/d; responses were durable (Table) and overall survival (OS) at 9 y was 74% vs 84% at 5 y. OS at 8 y was 69% in CP3L, 54% in AP CML and 23% in BP CML pts vs 78%, 59% and 23% at 4 y. 55 CP2L, 29 CP3L and 98 ADV pts died on study (10, 3 and 2 since the 4/5-y reports); 15, 5 and 3 had on-treatment transformations to AP/BP. Most common new treatment-emergent adverse events since y 5 in CP2L pts were pleural effusion (n=13), arthralgia (n=12) and increased blood creatinine (n=11). **Conclusions:** After ≥8 y, BOS continued to show durable efficacy and no new safety signals in pts with CP CML on long-term treatment, providing further support for BOS use after prior TKIs. Clinical trial information: NCT00261846 and NCT01903733. Research Sponsor: Pfizer Inc.

	IMA-resistant n=195	IMA-intolerant n=89	Total CP2L n=284
Cytogenetic response, n*	**182**	**80**	**262**
MCyR†, n (%)	109 (60)	49 (61)	158 (60)
9-y probability of maintaining MCyR‡, % (95% CI)	63 (52–72)	75 (57–87)	67 (58–74)
CCyR†, n (%)	88 (48)	42 (53)	130 (50)
9-y probability of maintaining CCyR‡, % (95% CI)	64 (52–74)	64 (44–78)	64 (54–72)
MMR, n*,§	**127**	**70**	**197**
MMR, n (%)	58 (46)	25 (36)	83 (42)
9-y probability of maintaining MMR‡, % (95% CI)	56 (41–68)	81 (57–93)	63 (50–73)

* Evaluable pts had a valid baseline assessment
† Maintained/newly attained; CCyR imputed from MMR in extension study
‡ Kaplan-Meier estimate for responders only
§ Molecular data not available for pts in China, Russia, South Africa and India
CCyR=complete cytogenetic response; MCyR=major cytogenetic response; MMR=major molecular response

7550 Poster Session (Board #323), Fri, 8:00 AM-11:00 AM

An independent review of arterial occlusive events (AOEs) in the ponatinib (PON) phase II PACE trial (NCT01207440) in patients (pts) with Ph+ leukemia. *First Author: James L Januzzi, Massachusetts General Hospital, Boston, MA*

Background: The final 5-year analysis of the PACE trial, which evaluated use of PON in pts with refractory chronic myeloid leukemia (CML) and Ph+ acute lymphoblastic leukemia, identified a 25% incidence of AOEs (Cortes, *Blood* 2018) from a search utilizing > 400 preferred terms (PTs) defined by MedDRA and related to vascular ischemia or thrombosis. We performed a retrospective review using an independent Endpoint Adjudication Committee (EAC) to better understand clinically relevant AOE rates in PACE. **Methods:** The EAC consisted of 3 cardiologists, 1 hematologist, and 1 neurologist to review AOEs (identified using > 500 terms) in PACE using American College of Cardiology/American Heart Association (ACC/AHA) definitions for major adverse cardiovascular events (MACE), and to review pt profiles including event, severity, concomitant medication, and hospitalization data. These results were compared with MedDRA PT search results. The EAC was blind to dose, dose modification, and investigator causality opinion. **Results:** The PACE review included 449 heavily pretreated pts with Ph+ leukemia (median age, 59 y; 47% female; 93% ≥2 tyrosine kinase inhibitors). With median follow-up 37.3 mo in all pts, AOEs were identified by MedDRA PT search in 25% of pts and EAC-verified in 17% (Table). In each category listed in the table, the EAC verification identified fewer AOEs and serious AOEs. Serious AOEs were identified by MedDRA PT search in 20% of pts and EAC-verified in 16%. Events that were not associated with a cardiovascular etiology or failed to meet the MACE definition set forth by the ACC/AHA were determined by the EAC not to be an AOE. **Conclusions:** The independent EAC review showed a lower rate of clinically relevant AOEs than was reported in PACE, suggesting an earlier possible overestimation that may not accurately reflect the risk of AOEs with PON. The ongoing PON dose-ranging OPTIC study will further evaluate the PON risk:benefit profile. Clinical trial information: NCT01207440. Research Sponsor: ARIAD Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

		CP-CML n = 270 AE	Serious AE	Total N = 449 AE	Serious AE
Any AOE, n (%)	PT	84 (31)	69 (26)	111 (25)	90 (20)
	EAC	57 (21)	54 (20)	78 (17)	74 (16)
Cardiovascular[a]	PT	42 (16)	33 (12)	59 (13)	44 (10)
	EAC	23 (9)	22 (8)	34 (8)	33 (7)
Cerebrovascular	PT	35 (13)	28 (10)	41 (9)	33 (7)
	EAC	19 (7)	17 (6)	22 (5)	20 (4)
Peripheral vascular	PT	38 (14)	31 (11)	48 (11)	38 (8)
	EAC	29 (11)	24 (9)	37 (8)	30 (7)
Exposure-adjusted incidence, no. pts with events/100 pt-y	PT	11.3	9.3	13.8	10.6
	EAC	8.7	8.1	8.9	8.4

CP-CML, chronic-phase CML; EAC, EAC-verified AOE; PT, AOE identified by broad PT search. [a]Excludes hypertension AEs.

7551 Poster Session (Board #324), Fri, 8:00 AM-11:00 AM

Bosutinib in patients with chronic phase chronic myeloid leukemia intolerant to prior tyrosine kinase inhibitors: Analyses from the BYOND study. *First Author: Susanne Saussele, University Hospital Mannheim, Heidelberg University, Mannheim, Germany*

Background: Bosutinib (BOS) is approved for patients (pts) with Philadelphia chromosome (Ph)+ chronic myeloid leukemia (CML) resistant/intolerant to prior therapy and in newly diagnosed pts in chronic phase (CP). **Methods:** The ongoing phase 4 BYOND study is further evaluating efficacy and safety of BOS (starting dose 500 mg/d) for CML resistant/intolerant to prior tyrosine kinase inhibitors (TKIs). We report findings in pts intolerant to all prior TKIs. Data are reported ≥1 y after the last enrolled pt (~85% TKI-intolerant pts had ≥2 y follow-up). **Results:** Of 163 pts who received BOS, 156 had Ph+ CP CML. 73 pts entered the study due to intolerance; 29, 26 and 18 had 1 (CP2L), 2 (CP3L) and 3 (CP4L) prior TKIs, respectively. After a median follow-up of 30.4 mo, median treatment duration across all 3 cohorts (CP2L, CP3L, CP4L, respectively) was 25.3 mo (29.2, 24.6, 17.6) and median dose intensity was 292.0 mg/d (304.5, 284.8, 272.1). Across CP CML cohorts (CP2L, CP3L, CP4L, respectively), 84.9% of patients (82.8%, 88.5%, 83.3%) had ≥1 dose reduction and 83.6% (79.3%, 84.6%, 88.9%) had ≥1 dose interruption due to adverse events (AEs). At the data cutoff, 53.4% (CP2L 65.5%, CP3L 42.3%, CP4L 50.0%) were still receiving BOS. The most common reason for discontinuation was AEs (28.8%). The most common (> 40%) treatment-emergent AEs (TEAEs) were diarrhea (87.7%) and nausea (43.8%). Grade 3/4 TEAEs in > 10% of pts were diarrhea (16.4%), increased alanine aminotransferase (19.2%) and increased lipase (12.3%). Most pts with a valid baseline assessment achieved major molecular responses (MMR) across therapy lines (Table). Deaths occurred in 4 pts (CP2L 1, CP3L 3, CP4L 0); none were related to BOS or CML. Overall survival rate (95% CI) at 2 y in TKI-intolerant pts was 97.2% (89.2–99.3); rates were 96.4% (77.2–99.5), 96.0% (74.8–99.4) and 100% (100–100) in CP2L, CP3L and CP4L pts, respectively. **Conclusions:** A long duration of treatment and high response rate were observed in TKI-intolerant pts treated with BOS. Despite being intolerant to all prior therapies, ≥50% of pts in the overall intolerant cohort remained on BOS treatment at the data cutoff and > 80% achieved/maintained MMR. These results further support BOS use in pts with Ph+ CP CML and intolerance to all prior TKIs. Clinical trial information: NCT02228382. Research Sponsor: Pfizer Inc.

Cumulative response, n/N (%)	CP2L	CP3L	CP4L	Total
MMR	26/29 (89.7)	22/26 (84.6)	12/18 (66.7)	60/73 (82.2)
Excluding pts with baseline MMR	10/11 (90.9)	9/11 (81.8)	6/9 (66.7)	25/31 (80.6)

7552 Poster Session (Board #325), Fri, 8:00 AM-11:00 AM

Myelodysplastic syndrome survival and secondary AML trends in the United States. *First Author: Wade T. Swenson, University of North Dakota School of Medicine and Health Sciences, Grand Forks, ND*

Background: Myelodysplastic syndrome (MDS) is a rare heterogeneous group of hematologic stem cell disorders. The most recent FDA therapies approved for the treatment of MDS were decitabine (May 2006), lenalidomide (June 2005), and azacitidine (November 2004). This analysis utilized a population-based cancer registry to identify changes in survival rates and secondary AML rates among patients with MDS. **Methods:** SEER 18 regions database (November 2017 submission) was accessed to obtain data on survival and secondary malignancies using SEER*Stat 8.3.6. ICD-O-3 codes were used to identify patients with refractory anemia (RA), refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, refractory cytopenia with multilineage dysplasia, MDS with 5q deletion, therapy-related MDS, and MDS, not otherwise specified. An observed survival analysis was conducted using a cohort diagnosed between 2001 and 2004 and another diagnosed between 2009 and 2012. Secondary AML risk was calculated using multiple primary - standardized incidence ratios (MP-SIR) to obtain observed/expected (O/E) ratio. **Results:** Three-year observed survival rates for patients diagnosed between 2001 and 2004 was 53.2% (50.4%, 55.9%) and was 61.2% (57.9%, 64.3%) for patients diagnosed between 2009 and 2012. There was no observed survival difference among other MDS subtypes. O/E ratio for development of AML among patients with RA was 2.77 (0.57, 8.11) for patients diagnosed between 2001 and 2004, and 49.49 (33.39, 70.65) for patients diagnosed between 2009 and 2012. **Conclusions:** Survival among patients diagnosed with RA has improved in recent years, whereas survival among other subtypes of MDS has not changed. Secondary AML rates have increased among RA patients identified in the population-based cancer registry. Research Sponsor: None.

7553 Poster Session (Board #326), Fri, 8:00 AM-11:00 AM

Molecular diagnostic testing patterns in patients (pts) with myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) in the Connect MDS/AML Registry. *First Author: Tracy George, University of Utah and ARUP Laboratories, Salt Lake City, UT*

Background: MDS and AML diagnosis requires an integrated approach including morphologic, cytogenetic and molecular testing. The WHO classification criteria for MDS and AML diagnosis were updated in 2016; however, the impact on clinical practice is unclear. We investigated molecular testing patterns for pts with MDS or AML treated in academic (AC) or community/government (CO/GOV)-based centers in the Connect MDS/AML Registry. **Methods:** The Connect MDS/AML Disease Registry (NCT01688011) is a large ongoing, US, multicenter, prospective observational cohort study of pts with MDS (aged ≥ 18 yrs) or AML (aged ≥ 55 yrs). Patient data were collected for this analysis upon enrollment from 12 Dec 2013 to 13 Dec 2019, the analysis cut-off. Differences in molecular testing between MDS and AML pts were evaluated and logistic regression used to assess factors associated with increased molecular testing. **Results:** As of 13 Dec 2019, 800 MDS pts and 626 AML pts were enrolled; median age was 74 vs 71 yrs, 66.3% vs 61.5% were male, and 73.5% vs 60.2% were insured by Medicare/Medicaid. A greater proportion of AML pts (77.5%) had molecular testing vs MDS pts (29.1%). Of 380 MDS pts enrolled before 2017 (< 2017), 16.8% had molecular testing, increasing to 40.2% in 420 MDS pts enrolled from 2017 onward (≥ 2017). Of 289 AML pts enrolled < 2017, 68.9% had molecular testing, increasing to 84.9% in 337 AML pts enrolled ≥ 2017. Mean number of mutations tested increased between < 2017 and ≥ 2017 from 6.9 to 12.7 in MDS pts and from 6.1 to 10.4 in AML pts. Of the 11 mutations most frequently tested ≥ 2017 in MDS and AML pts, 0% and 36%, respectively, have FDA-approved targeted therapies. Gene mutations tested differed between MDS and AML pts; *ASXL1* was most frequently tested in MDS pts (68.2%) and *FLT3-ITD* in AML pts (89.7%). Testing rates increased between < 2017 and ≥ 2017 for *ASXL1* from 48.4% to 75.7% in MDS pts and for *FLT3-ITD* from 84.4% to 93.4% in AML pts. Factors associated with increased testing were age < 75 (vs ≥ 75) yrs, ELN score ≥ 2 (vs 1) and enrollment at AC site (vs CO/GOV) (all $P < 0.01$) in AML pts and age < 80 (vs ≥ 80 yrs; $P < 0.01$), AC site (vs CO/GOV; $P < 0.01$), and geographic region outside the Midwest ($P = 0.015$) in MDS pts. **Conclusions:** While molecular testing rates have increased since the publication of the WHO 2016 criteria, molecular testing rates for MDS pts remain lower than those for AML pts in real-world clinical practice. Elderly pts and pts enrolled in CO/GOV sites were found to have lower rates of molecular testing in both MDS and AML patient cohorts. Research Sponsor: Bristol-Myers Squibb.

7554 Poster Session (Board #327), Fri, 8:00 AM-11:00 AM

Clinical benefit of luspatercept in patients (pts) with lower-risk MDS (LR-MDS) and high transfusion burden in the phase III MEDALIST study. *First Author: Amer Methqal Zeidan, Department of Internal Medicine, Yale School of Medicine and Yale Cancer Center, Yale University, New Haven, CT*

Background: Anemic pts with LR-MDS and high baseline RBC transfusion burden (HTB) have very few treatment options and constitute a pt population with significant clinical unmet need. In this secondary analysis of the MEDALIST trial (NCT02631070), we sought to evaluate the clinical benefit of luspatercept in this pt population. **Methods:** MEDALIST is a randomized, placebo (PBO)-controlled, phase 3 study evaluating the efficacy and safety of luspatercept in pts with anemia due to LR-MDS with ring sideroblasts (RS) (Fenaux & Platzbecker et al. *NEJM.* 2020;382:140-51). Pts were aged ≥ 18 years; had IPSS-R-defined Very low-, Low-, or Intermediate-risk MDS with RS; were refractory, intolerant, or unlikely to respond to erythropoiesis-stimulating agents (serum erythropoietin > 200 U/L); and had anemia requiring regular RBC transfusions (≥ 2 units/8 weeks in the 16 weeks prior to randomization). 229 pts were randomized 2:1 to luspatercept (starting dose 1.0 mg/kg; titration up to 1.75 mg/kg allowed) or PBO subcutaneously every 3 weeks. HTB was defined as ≥ 6 RBC units transfused/8 weeks. **Results:** 153 pts were randomized to luspatercept and 76 to PBO. As of July 1, 2019, 23/66 (34.8%) and 12/66 (18.2%) HTB pts receiving luspatercept achieved a ≥ 50% and ≥ 75% reduction from baseline in RBC transfusion burden over ≥ 24 weeks, respectively, vs 3/33 (9.1%; $P = 0.0063$) and 1/33 (3.0%; $P = 0.0363$) pts receiving PBO. 6/66 (9.1%) luspatercept-treated HTB pts and 1/33 (3.0%) PBO-treated HTB pt achieved RBC-transfusion independence (TI) ≥ 8 weeks in Weeks 1–24 ($P = 0.2699$). The median (range) time to achieve RBC-TI with luspatercept was 50.0 days (1.0–100.0) and median (range) duration of RBC-TI in the luspatercept arm was 42.6 weeks (8.4–81.1). Mean number of transfusion events in Weeks 1–24 was 9.2 in the luspatercept arm vs 12.4 in the PBO arm (hazard ratio [95% confidence interval] 0.794 [0.660–0.956]). 65/66 (98.5%) luspatercept- and 29/33 (87.9%) PBO-treated HTB pts reported ≥ 1 treatment-emergent adverse event (TEAE); 11/66 (16.7%) and 3/33 (9.1%) pts, respectively, reported ≥ 1 TEAE leading to discontinuation. 28/66 (42.4%) luspatercept- and 15/33 (45.5%) PBO-treated pts reported ≥ 1 serious AE. Incidence of grade 3–4 TEAEs in HTB pts was similar between arms (53.0% luspatercept vs 54.5% PBO). **Conclusions:** Luspatercept treatment resulted in clinically significant reductions in transfusion burden and reduced number of transfusion events in HTB pts with LR-MDS with RS, with an acceptable safety profile consistent with the overall population. Clinical trial information: NCT02631070. Research Sponsor: Bristol-Myers Squibb in collaboration with Acceleron Pharma.

7555 Poster Session (Board #328), Fri, 8:00 AM-11:00 AM

Disparities in receipt of complete diagnostic evaluation to confirm myelodysplastic syndromes. *First Author: Sudipto Mukherjee, Leukemia Program, Department of Hematology and Medical Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH*

Background: A complete diagnostic evaluation (CDE), including bone marrow (BM) biopsy, cytogenic testing, FISH panel, and/or flow cytometry, is widely accepted as a prerequisite for histopathologic confirmation of MDS. Earlier reports have raised concerns regarding accuracy of MDS diagnosis in population registries that do not require confirmatory tests for disease reporting. We queried Medicare files to analyze the extent of use of, and factors associated with CDE for diagnosing MDS. **Methods:** The study population included Medicare patients with at least one inpatient or two outpatient claims for MDS within a 12-month period during the years 2012 and 2013. Variables included age, sex, race, morphologic MDS categories, cytopenias (isolated or any combination), transfusion burden, comorbididities, as well as county-level characteristics (income, educational attainment, rurality, and availability of internal medicine subspecialists). Classification and regression tree (CART) and multivariable logistic regression analysis were used to identify combinations of factors associated with receipt of CDE. **Results:** Our study population included 45,067 MDS patients, of whom only 68.6% received CDE that included BM biopsy and/or chromosomal studies. The percent of patients undergoing CDE was significantly lower among those 85 years of age or older (56.1%); women (63.7%); Blacks (64.2%); patients with isolated anemia (60.3%); and those who were transfusion independent ($p < 0.001$ for all comparisons). On the other hand, CDE was significantly higher among patients with the category of MDS with excess blasts (89.4%); those presenting with pancytopenia (92.2%); and those with high transfusion burden (80%). There was little variation by comorbidity burden, county level characteristics, or availability of subspecialists. In CART analysis, 80% of patients presenting with any two or more cytopenias received CDE. In multivariable analysis, advanced age, female sex, Black race, higher comorbidity burden and availability of subspecialists were associated with a lower likelihood to receive CDE, while patients with MDS with excess blasts, and with any > 2 cytopenias were more likely to receive CDE ($P < .0001$). **Conclusions:** Nearly one third (31%) of MDS patients in the Medicare database lack CDE especially BM biopsy. Disparities in CDE can be corrected through proper physician education and stringent registry reporting to avoid such high diagnostic inaccuracies, leading to potential missed treatment opportunities. Research Sponsor: Celgene Corporation.

7556 Poster Session (Board #329), Fri, 8:00 AM-11:00 AM

Phase II study of lower-dose pracinostat plus azacitidine safety and efficacy in patients with high/very high-risk myelodysplastic syndromes. *First Author: Ehab L. Atallah, Hematologic Malignancies, Medical College of Wisconsin, Milwaukee, WI*

Background: Hypomethylating agents (HMA), such as azacitidine (AZA), are the standard of care for patients (pts) with higher-risk myelodysplastic syndromes (MDS). However, overall response rate (ORR=CR+PR) with HMA alone is approximately 30%, with a 2-year overall survival (OS) rate of 50.8%. Preclinical studies show that pracinostat (PRAN), an oral histone deacetylase inhibitor, synergizes with HMA. A study in pts with untreated IPSS intermediate-2/high-risk MDS receiving 60 mg PRAN plus AZA resulted in early discontinuations, mainly due to adverse events (AE), potentially leading to diminished clinical benefit. This follow-up phase II study evaluates a lower dose of PRAN (25% reduction) in combination with AZA in order to reduce toxicity, decrease early discontinuations, and improve outcomes. An interim analysis showed low discontinuation rate and promising efficacy, allowing trial expansion. Herein, we report preliminary safety and efficacy in the overall population. **Methods:** Open-label, II-stage, phase II trial (NCT03151304) in pts (≥18 years) naive to HMA therapy and with IPSS-R of high/very high-risk MDS. Planned enrollment was 60 pts. Pts received 45 mg PRAN 3 days/week for 3 consecutive weeks plus standard AZA dose for 7 days of each 28-day cycle. Primary objectives were to define the safety/tolerability of the combination and to assess the ORR (CR+PR). OS was a secondary endpoint. **Results:** Sixty-four pts were enrolled and received ≥1 dose of treatment. Most pts were male (67%), median age was 68 years (range 47–89), and the proportion of pts with high/very high-risk MDS was similar. After 17.6 months' median follow-up, 31% of pts remain on treatment; 69% of pts discontinued treatment due to stem cell transplant (25%), disease progression (17%), AEs (11%), consent withdrawal (3%), pt noncompliance (3%), death (3%), lost to follow-up (2%), and other (5%). Most common nonhematologic AEs were constipation (55%), nausea (52%), fatigue (45%), decreased appetite (39%), peripheral edema (36%), diarrhea, and dyspnea (31% each). Frequent hematologic AEs were decreased neutrophil count (50%), anemia (39%), decreased platelet count (38%), febrile neutropenia (36%), and thrombocytopenia (30%). ORR was 33% (95% CI 22-46), with 33% achieving CR; 34% of pts had marrow CR. Median OS was 23.5 months (95% CI 16.4-nc), with an estimated 1-year OS of 77%. **Conclusions:** In pts with high/very high-risk MDS, a lower dose of pracinostat in combination with AZA demonstrated a tolerable safety profile and promising efficacy. Clinical trial information: NCT03151304. Research Sponsor: Helsinn Healthcare SA and MEI Pharma, Inc.

7557 Poster Session (Board #330), Fri, 8:00 AM-11:00 AM

Expression of CD47 and CALR in myeloproliferative neoplasms and myelodysplastic syndrome: Potential new therapeutical targets. *First Author: Ciro Roberto Rinaldi, University of Lincoln, Lincoln, United Kingdom*

Background: Myelodysplastic neoplasms (MPN) and myelodysplastic syndrome (MDS) are myeloid malignancies tendency to evolve into acute myeloid leukaemia. We investigate the expression and cellular localisation of pro-phagocytic CALR and anti-phagocytic CD47 in untreated and treated patients with essential thrombocythemia (ET), polycythemia vera (PV) myelofibrosis (MF), and in MDS patients in comparison with healthy controls. **Methods:** Mononuclear cells were collected by Ficoll separation, from peripheral blood of 27 MPN (8 PV, 16 ET, 3 MF); 14 MPN patients received cyto-reductive therapies (Hydroxyurea, Anagrelide or Ruxolitinib); 10 MDS patients and 4 controls. Cells were fractionised into 4 compartments: membrane, cytoplasm, cytosol and nucleus. Proteins were extracted using TRIzol, with CALR and CD47 protein expression analysed by western blotting. **Results:** CD47 showed higher expression of its overall protein on MPN cell membranes when compared with CALR (22% vs 13.9%). We observed a significant reduction of CALR expression in all MPN subtypes when patients were treated with cyto-reductive agents (ET- untreated 43.3% vs treated 2%, PV- 3.6% vs 2.2%, ET- 21% vs 11%). Interestingly we have observed a significant increase in CD47 cell membrane expression after treatment in MF and PV (CD47 in MF- untreated 11.8% vs treated 34.3%, PV-11.4% vs 35.9%). In MDS cells CD47 is overexpressed compared with controls (CD47- 11.31 vs 2.2 fold, respectively) and it mainly located to the membrane. Interestingly the degree of CD47 expression correlated to patients IPSS-R, increasing from low risk to high risk (low – 15.7%, intermediate 1 – 41.3%, intermediate 2 – 53.9% and high – 67.6%). CALR expression is also reduced in MDS cells comparing with controls when split by IPSS-R risk score (low – 9%, intermediate 1 – 11.9%, intermediate 2 – 17%, high – 17.9% Vs control - 29.1%). **Conclusions:** CD47, but not CALR, is overexpressed on the membrane of patients with MPN and MDS. In MDS, we observed a progressive increase in CD47 expression as the MDS evolve in accordance to the IPSS-R risk score. In MPN patients we observed a significant difference in CD47 expression across different MPN subtypes. The use of anti-CD47 antibodies could represent a new strategy to enhance the pro-phagocytic signal via increasing the CALR expression, and in combination with standard cyto-reduction therapy, might represent a new therapeutical strategy in both MPN and MDS. Research Sponsor: Celgene.

7558 Poster Session (Board #331), Fri, 8:00 AM-11:00 AM

Comparative analysis of characteristics, survival trends, and associated malignancies of B-cell and T-cell prolymphocytic leukemia: A surveillance, epidemiology, and end results (SEER) based study1998 to 2016. *First Author: Doaa Attia, Alexandria University, Alexandria, Egypt*

Background: Prolymphocytic leukemia (PLL) compromises two subsets; B-cell and T-cell, accounting for less than 2% of mature lymphocytic leukemia. Both of them are rare lymphoid neoplasms with a very aggressive clinical course and poor prognosis. **Methods:** We used SEER program dataset between 1998 and 2016. We divided the patients into 2 groups: B-PLL and T-PLL and identified them using 'ICD-O-3 histology recode: 9833/3 and 9834/3 respectively. We used SPSS software (version 26, IBM, NY, USA) to calculate overall survival using Kaplan-Meier methods and compare the survival between the two subtypes using the log-rank test. We also used multivariable covariate-adjust cox models to determine the impact of age, sex, race, cause of death, and associated primary malignancies on survival in both types. **Results:** A retrospective cohort study of 783 patients (295 B-PLL and 488 T-PLL) with overall survival rate of 22.5% (30.2% B-PLL and 18% T-PLL). The overall median survival for PLL was 16 months (95 CI, 13.745-18.255). The median survival of B-PLL (25 months, 95%CI, 15.733-34.267) was much better than T-PLL (14 months, 95%CI, 11.922-16.078). The mean age was 68.7 ± 15.3. Patient age was an independent factor in determining the survival and inversely associated with survival time in both types ($p < 0.0001$). The survival rate was worst) among age groups older than 79, between 70-79 years (8.9%, 18.9%) respectively. Although white male patients were more affected in both types, neither sex nor race significantly affected survival (P 0.554, 0.062 respectively). 64.7% of PLL patients died due to cancer. Patients with cancer-related death had significantly shorter survival time in both T-PLL group (HR = 0.351, 95% CI 0.241-0.512) and B-PLL group (HR = 0.682, 95% CI 0.491-0.945). We also found that 24.4% of B-PLL and 19% of T-PLL patients have another associated primary malignancy. Among hematological malignancies, non-hodgkin lymphoma was the commonest. Although associated solid tumors were less common, Prostate cancer and breast cancer were the commonest for both types and lung/bronchus malignancies were more associated with T-PLL. **Conclusions:** T-PLL subtype has worse prognosis. Age is the most important independent predictor of survival in both types. Although most of affected patients were white males, race and gender have no impact on survival. Non-hodgkin lymphoma is the commonest primary associated malignancy followed by breast and prostate cancer in both types. Research Sponsor: None.

7559 Poster Session (Board #332), Fri, 8:00 AM-11:00 AM

Chronic myelomonocytic leukemia genomic signature correlates with the degree of bone marrow fibrosis: A single-institutional retrospective study. *First Author: Feras Ally, City of Hope National Medical Center, Duarte, CA*

Background: Chronic myelomonocytic leukemia (CMML) has features of both a myeloproliferative neoplasm and a myelodysplastic syndrome. The median overall survival (OS) in most series is 20-40 months. CMML is a relatively rare entity, and there is limited understanding of prognostic molecular markers. CMML associated with bone marrow fibrosis grade 1, appear to have shorter progression free survival. In this study we investigated the correlation of mutations with bone marrow reticulin fibrosis in patients with CMML. **Methods:** We investigated a cohort of 41 consecutive patients diagnosed with CMML 0, 1, 2, and CMML-AML from 2014 to 2019 at our institute. The median age of 41 patients was 68 years (range, 34-82). 27% were females and 73% were males. This cohort consists of 8 (20%) patients with CMML0, 19 (46%) with CMML1, 8 (20%) with CMML2 and 6 (15%) with CMML-AML. Genomic DNA was extracted from the bone marrow aspirates and targeted mutation NGS libraries were prepared from 200 ng of genomic DNA using the SureSelect target enrichment system (Agilent Technologies Inc.). The gene panel consists of 73 genes focused on myeloid neoplasms. The data were curated on the basis of our molecular pathology and national databases. Additionally, clinical data and bone marrow (BM) reticulin fibrosis grades (n = 27 available) were retrieved from the patient's medical record. **Results:** The mutational profile frequency in our cohort showed that the most common mutations were *TET2* (31%), *ASXL1* (31%), and *SRSF2* (23%), with frequencies very similar to those reported in the literature. Of the 27 cases with an available reticulin stain, only low grade fibrosis (MF-0, n = 18. MF-1, n = 9) were identified in our cohort. The frequencies of mutations in *ASXL1*, *U2AF1*, *TP53*, *JAK2* and *RUNX1*, positively correlated with low grade fibrosis (MF-1). Additionally, patients with higher frequencies of *SRSF2*, *TET2*, and *SETBP1* mutations showed no fibrosis (MF-0). **Conclusions:** This study is the first to correlate the degree of fibrosis with the frequency of mutations in CMML. We found similar mutations spectrum reported in the literature in patients with CMML. The mutational profile associated with CMML cases appears to affect the degree of the bone marrow fibrosis at the time of diagnosis. Research Sponsor: None.

7560 Poster Session (Board #333), Fri, 8:00 AM-11:00 AM

Long-term outcome of 117 patients with Erdheim-Chester disease and mixed histiocytosis receiving targeted therapies (BRAF and MEK inhibitors): A monocentric experience. *First Author: Fleur Cohen-Aubart, Department of Internal Medicine and French reference Center for Rare Auto-immune and Systemic Diseases, Institut E3M, Assistance Publique-Hôpitaux de Paris (AP-HP), Pitié-Salpêtrière Hospital, & Université Pierre et Marie Curie, UPMC, Paris, France*

Background: Erdheim–Chester disease (ECD), an inflammatory myeloid neoplasm from the L group, is an histiocytosis associated with multisystem infiltration. Around 1500 cases have been reported worldwide since 1930. In 15% of cases, ECD is associated with another histiocytosis corresponding to mixed histiocytosis. Before 2004, 60% of patients died within 3 years after diagnosis. The targetable $BRAF^{V600E}$mutation is present in as much as 70% of all ECD cases. Targeted therapies (BRAF inhibitors in April 2012, followed by MEK inhibitors after 2015) have revolutionized the therapeutic options and prognosis of refractory ECD and mixed histiocytosis. **Methods:** This retrospective study was conducted between April 2012 and December 2019 on 117 ECD patients who received targeted therapies in the French National Referral Center for Histiocytosis at Pitié-Salpêtrière Hospital in Paris, France. 28 patients (pts) (24%) had a mixed histiocytosis. **Results:** 43 (36.7%) pts were female and 95/116 exploitable pts (81.9%) had a $BRAF^{V600E}$ mutation. 12 (10.3%) pts had a co-ocurring hemopathy (myeloproliferative neoplasm or myelodysplastic syndrom). Age at diagnosis was 57.2 yr (+/- 13.8). The main sites of involvement were: vascular ("coated aorta") in 85 pts (73%), heart in 83 pts (71%), xanthelasma in 30 pts (26%), central nervous system in 56 pts (48%) and peri-renal ("hairy kidney") in 84 pts (72%). 34 pts (29%) had previously received corticosteroids, and 63 pts (54%) interferon alpha regimen (mainly PEG interferon). 86 (74%) pts received the BRAF inhibitor vemurafenib, and 42 (36%) pts the MEK inhibitor cobimetinib (some patients receiving both). 25 pts died during follow-up. The median survival of patients with targeted therapies in december 2019 was undefined, whereas the patients with no targeted therapies had a median survival of 133 months (HR 0.64 (0.42-0.99); p = 0.04). Among the 117 pts, only 2 had a progression of VAF of mutations within genes frequently mutated in myeloid neoplasms. The most serious adverse events were cutaneous (squamous cell carcinoma, basocellular carcinoma, DRESS) and acute pancreatitis with BRAF inhibitors, whereas chorioretinitis and left ventricular dysfunction were seen with MEK inhibitors. None of the patients receiving targeted therapies progressed. **Conclusions:** Targeted therapies (BRAF and/or MEK inhibitors) were found dramatically efficacious in 117 patients with severe and refractory ECD and mixed histiocytosis, improving survival of patients. Research Sponsor: None.

TPS7561 **Poster Session (Board #334), Fri, 8:00 AM-11:00 AM**

A phase II study of BP1001 (liposomal Grb2 antisense oligonucleotide) in patients with hematologic malignancies. *First Author: Maro Ohanian, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: The growth factor receptor bound protein-2 (Grb2) is vital to oncogene signaling and tumor progression. BP1001 is a liposome-incorporated Grb2 antisense oligonucleotide that inhibits Grb2 expression. Grb2 inhibition suppresses cancer growth and survival. A Phase I/Ib single center study in patients with refractory/relapsed leukemias demonstrated the safety of BP1001 up to 90 mg/m^2 dose and the efficacy of BP1001 in combination with low dose cytarabine (LDAC) in refractory/relapsed acute myeloid leukemia (AML) patients (Ohanian, Lancet Haematol 2018). Based on pharmacokinetic (PK) considerations, the recommended Phase II dose was 60 mg/m^2. A phase II study was initiated to explore the clinical impact of BP1001 in combination with LDAC in untreated AML patients. Interim safety and efficacy of BP1001 + LDAC in untreated AML patients was presented at the 2018 Annual ASH Meeting. BP1001 was safely administered to 25 patients with untreated AML, who were considered unfit for standard chemotherapy. Efficacy data compared favorably to what has been reported with available options for unfit patients largely with secondary AML or adverse-risk AML. Since the Interim Data presentation, the study was amended to investigate BP1001 + decitabine combination and include myelodysplastic syndrome (MDS) patients. This is because BP1001 enhanced decitabine anti-leukemic effects in preclinical studies. **Methods:** This is a multi-center, open-label study with 2 parallel cohorts of BP1001 + decitabine treatment in untreated AML/high risk MDS patients and refractory/relapsed AML/high risk MDS patients who are considered by the investigator unsuitable for or refused intensive chemotherapy. BP1001 is given intravenously (IV) at 60 mg/m^2 twice weekly. Decitabine is given 20 mg/m^2 IV daily for 5 consecutive days. Each cycle is 28 days. Each cohort can enroll 19 patients, with a decision to stop or proceed to 54 patients. The primary objective of this study is to assess whether BP1001 + decitabine provides higher complete remission rates than decitabine alone (by historical comparison) in AML/high risk MDS patients. The secondary objectives of this study are to assess: Safety of BP1001 + decitabine; partial remissions and blast count reductions; overall survival, time to response and duration of response; minimal residual disease status in patients who achieve complete remission; and plasma PK profile of BP1001. The exploratory objective of this study is to evaluate the association of treatment response with cytogenetic and molecular characteristics. Clinical trial information: NCT02781883. Research Sponsor: Bio-Path Holdings, Inc.

TPS7562 **Poster Session (Board #335), Fri, 8:00 AM-11:00 AM**

A phase I clinical trial testing the safety of IL-21-expanded, off-the-shelf, natural killer cells for relapsed/refractory acute myeloid leukemia and myelodysplastic syndrome. *First Author: Sumithira Vasu, The Ohio State University, Columbus, OH*

Background: Allogeneic transplantation (Allo-HCT) demonstrates the enduring and potent role of the immune system in the control and eradication of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). However, patients with relapsed, refractory (R/R) disease or comorbidities are not eligible for Allo-HCT. We sought to develop an allogeneic Natural killer (NK) cell-based immunotherapy approach to induce remission for these patients. The efficacy of haploidentical NK cells expanded ex vivo using a K562 feeder-cell line transfected with IL-21 and 41BBL has been established in R/R AML patients. However, haploidentical donor-derived NK cell manufacturing exceeds three weeks with the possibility of fulminant malignancy rendering patients ineligible for cellular therapy. To address this limitation we established a third-party NK cell bank derived from KIR and HLA-mismatched 'ideal' donors that allows scalable, affordable mass-production of large numbers of NK cells suitable for banking and immediate 'off-the-shelf' (OTS) administration to a broad population of recipients. **Methods:** This phase I study follows a 3+3 design to investigate the safety of mIL-21-expanded, third-party, OTS NK cells for treatment of R/R AML and MDS patients. Patients aged $\geq$18 or $\leq$80 years are enrolled into two cohorts: those $<$60 years and able to tolerate intensive chemo will receive Fludarabine 30mg/m^2/day (days -6 to -2) and Cytarabine 2g/m^2/day (days -6 to -2). Patients $>$60 years or $<$60 years and unable/unwilling to tolerate intensive chemo will receive Fludarabine 30mg/m^2/day (days -5 to -2) and Decitabine 20mg/m^2/day (days -6 to -2). All patients subsequently receive a total of 6 infusions of NK cells administered thrice weekly for two weeks (between days 0-21) and will be followed up to day 56 from first NK cell infusion. Three NK cell dose-levels: 1x10^7, 3x10^7 and 1x10^8 cells/kg/dose will be explored to determine maximum tolerated dose (MTD). 3-18 patients/cohort/dose may be enrolled for MTD determination plus an additional 10 patients/dose in an expansion phase (maximum 28/cohort = 56 total subjects). Primary objective is to determine safety and feasibility of NK cell infusions. Secondary objectives will explore rates of remission PFS, overall survival and measurable residual disease negativity, cell counts, infectious complications, and patients proceeding to transplant. Enrollment in dose level 1 has started. Clinical trial information: NCT04220684. Research Sponsor: None.

TPS7563 **Poster Session (Board #336), Fri, 8:00 AM-11:00 AM**

A phase I/II study of IMGN632, a novel CD123-targeting antibody-drug conjugate, in patients with relapsed/refractory acute myeloid leukemia, blastic plasmacytoid dendritic cell neoplasm, and other CD123-positive hematologic malignancies. *First Author: Naval Guastad Daver, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Overexpression of CD123 occurs in multiple hematological malignancies, including acute myeloid leukemia (AML), blastic plasmacytoid dendritic cell neoplasm (BPDCN), acute lymphoblastic leukemia (ALL) and others, thus making this antigen an attractive target for the development of new therapeutics. IMGN632 is a CD123-targeting antibody-drug conjugate (ADC) comprising a novel anti-CD123 antibody coupled, via a peptide linker, to a unique DNA-alkylating cytotoxic payload of the recently developed IGN (indolinobenzodiazepine pseudodimer) class. Preclinically, IMGN632 has demonstrated potent activity against AML, BPDCN and ALL models, with a wide therapeutic index in animal models, as well as a 150-fold differential cytotoxicity in AML patient samples compared to normal hematopoietic progenitors (PMIDs: 29661755, 30361418). Remarkable sensitivity of BPDCN patient derived xenografts to IMGN632 has been demonstrated (Blood 2018 132:3956). **Methods:** This Phase I/II study comprises a dose escalation phase designed to establish the recommended phase II dose (RP2D) for IMGN632, as well as dose expansion cohorts to further explore the safety and preliminary anti-leukemia activity of IMGN632. Expansion cohorts were designed to evaluate the following patient populations: adult patients with relapsed or refractory BPDCN or patients with untreated BPDCN who are inappropriate for available therapies, patients with relapsed or refractory AML, or with other CD123+ relapsed or refractory hematologic malignancies including ALL. Inclusion criteria include up to four prior lines of therapy which may include transplant. Patients with active central nervous system disease, history of veno-occlusive disease of the liver, or history of grade IV capillary leak syndrome or non-cardiac grade IV edema are ineligible. Expansion cohorts for unfit frontline and relapsed/refractory BPDCN, and relapsed/refractory ALL continue to enroll at the RP2D (0.045 mg/kg Q3W). Clinical trial information: NCT03386513. Research Sponsor: ImmunoGen, Inc.

TPS7564 **Poster Session (Board #337), Fri, 8:00 AM-11:00 AM**

A phase Ib/II study of the CD123-targeting antibody-drug conjugate IMGN632 as monotherapy or in combination with venetoclax and/or azacitidine for patients with CD123-positive acute myeloid leukemia. *First Author: Naval Guastad Daver, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Overexpression of CD123 is characteristic of a number of hematological malignancies, including acute myeloid leukemia (AML) and blastic plasmacytoid dendritic cell neoplasm (BPDCN). IMGN632 is a CD123-targeting antibody-drug conjugate (ADC) with a novel anti-CD123 antibody coupled to a unique DNA-alkylating payload of the recently developed IGN (indolinobenzodiazepine pseudodimer) class of payloads. In preclinical models of AML, IMGN632 exhibited potent anti-leukemia activity, with a wide therapeutic index. Confirming preclinical expectations, encouraging single-agent activity and favorable tolerability have emerged for IMGN632 in the ongoing Phase I trial in patients with CD123-positive AML (ASH 2019, NCT03386513). Preclinical data from AML xenograft models have demonstrated synergy in IMGN632 combinations with azacitidine and venetoclax (EHA 2019), supporting the exploration of these combinations in AML patients. **Methods:** This Phase Ib/II study is designed to determine the safety, tolerability, and preliminary anti-leukemia activity of IMGN632 when administered in combination with azacitidine and/or venetoclax to patients with relapsed and frontline CD123-positive AML, and the single-agent activity of IMGN632 in patients with minimal residual disease (MRD)-positive AML after frontline treatment. Study Design: Adult patients with CD123-positive relapsed or refractory AML, who are deemed appropriate for experimental therapy, are eligible to enroll as part of the dose escalation phase. Key exclusion criteria for all regimens include active central nervous system disease, and history of sinusoidal obstruction syndrome/venous occlusive disease of the liver. Three combination regimens are being evaluated: Regimen A, IMGN632 plus azacitidine (632+AZA); Regimen B, IMGN632 plus venetoclax (632+VEN); and Regimen C, IMGN632 plus azacitidine and venetoclax (632+AZA+VEN). For each regimen, a Phase Ib dose escalation cohort will determine the recommended Phase II dose (RP2D) of IMGN632 for the specific combination. This will be followed by a Phase II dose expansion stage to further characterize the safety profile and assess antileukemia activity in frontline or relapsed AML patients, depending on combination regimen. In addition, IMGN632 monotherapy is being explored in expansion cohorts of MRD-positive patients to assess conversion rate from MRD+ to MRD-, in fit and unfit AML subpopulations. Clinical trial information: NCT04086264. Research Sponsor: ImmunoGen, Inc.

TPS7565 Poster Session (Board #338), Fri, 8:00 AM-11:00 AM

CULMINATE: A phase II study of cusatuzumab + azacitidine in patients with newly diagnosed AML, ineligible for intensive chemotherapy. *First Author: Geralyn Carol Trudel, Janssen Research & Development, LLC, Raritan, NJ*

Background: AML, the most common acute leukemia in adults, is a heterogeneous malignancy characterized by uncontrolled clonal expansion of hematopoietic progenitor cells. Median diagnosis age is ~67 yrs. Despite current therapies prognosis is poor with 5-yr OS ~25% for patients (pts) ≥65 yrs. For pts unable to receive intensive chemotherapy, survival rates are worse, indicating a critical need to develop better treatments. CD70 is expressed on >95% of AML blasts harvested from newly diagnosed AML pts but not on normal hematopoietic stem cells nor most normal tissues. Cusatuzumab is a first-in-class, high-affinity anti-CD70 monoclonal antibody with multiple mechanisms of action, including Fc-mediated cytotoxicity with enhanced ADCC and inhibition of CD70/CD27 signaling, resulting in leukemia blast and stem cell cytotoxicity. As cusatuzumab and azacitidine target distinct pathways of myeloblast propagation, a combination may have a synergistic therapeutic effect and overcome treatment resistance. Initial data from a Phase I study (NCT03030612) with cusatuzumab (1–20 mg/kg) + standard dose azacitidine in AML pts ineligible for intensive chemotherapy showed no dose-limiting toxicity and a CR/CRi (CR with partial/incomplete hematologic recovery) in 10 of 12 pts (ASH 2019, Abs #234). This abstract describes a follow-on Phase II study (NCT04023526). **Methods:** CULMINATE is a 2-part study of cusatuzumab + azacitidine to determine the optimal dose of cusatuzumab (Table). Inclusion criteria: ≥18 yrs with *de novo* or secondary AML unfit for intensive therapy (≥75 or <75 yrs with a comorbidity [i.e. ≥1 of: ECOG 2, severe cardiac/pulmonary or moderate hepatic impairment]). In Part 1, pts are randomized 1:1 to cusatuzumab 10 or 20 mg/kg (IV, on Days 3 and 17 of each 28-day cycle) + azacitidine (75 mg/m^2 SC or IV on Days 1–7). Data will be reviewed after 15, 30 and 50 pts are enrolled into each arm to select the cusatuzumab dose for the Part 2 expansion cohort in which efficacy and safety will be further evaluated. Follow-up continues until death, loss to follow-up or study end. The primary objective is to determine CR rate. Secondary objectives include rate of CRi/CRh, rate of MRD-negativity, ORR, time to and duration of response, pharmacokinetics, immunogenicity, transfusion independence and safety. Enrollment began in Sept 2019 and is currently two-thirds complete. Clinical trial information: NCT04023526. Research Sponsor: Janssen R&D.

		Cusatuzumab dose + azacitidine 75 mg/m^2	
	No. of pts	10 mg/kg	20 mg/kg
Part 1 Dose selection	Stage 1	15	15
	Stage 2	30	30
	Stage 3	50	50
Part 2Expansion phase	Interim analysis	80	
	Final analysis	100	

TPS7566 Poster Session (Board #339), Fri, 8:00 AM-11:00 AM

Safety and efficacy of gemtuzumab ozogamicin and venetoclax in patients with relapsed or refractory CD33+ acute myeloid leukemia: A phase Ib study. *First Author: Saad Arain, UIC, Chicago, IL*

Background: AML is predominantly a disease of the elderly, yet outcomes remain dismal, especially for relapsed/refractory (R/R) AML patients (pts). Gemtuzumab Ozogamicin (GO) is a monoclonal antibody targeting CD33–commonly expressed on AML blasts, and, critically, AML stem cells (LSC)–that is linked to the cytotoxin calicheamicin. Recognized mechanisms of GO resistance include decreased (or aberrant) blast CD33 expression, upregulation of p-glycoprotein (re-exports calicheamicin), and decreased mitochondrial apoptosis. GO-induced apoptosis depends on pro-apoptotic Bax and Bak and is inhibited by overexpression of anti-apoptotic BCL-2 and BCL-XL. Venetoclax (VEN) is a BH3 mimetic, binding BCL-2, dislodging its binding to Bak/Bax, thus facilitating apoptosis. LSC uniquely overexpress BCL-2, however VEN resistance develops rapidly. Hypothesis: VEN targeting of BCL-2 proteins that protect LSC from GO-induced apoptosis will synergistically increase GO efficacy. Correlative studies include pre-treatment AML blast BH3 profiling and CD33 expression (& sequencing for isoforms), MRD measurement at post-therapy timepoints using digital drop PCR technology, and quality of life assessments (EORTC QLQ-C30, FACT-Fatigue). **Methods:** Single arm, open-label, multi-center (BTCRC), dose-escalation phase Ib study of combination of VEN and GO in R/R AML pts (18-75y), using a 3+3 design. Major eligibility: ECOG 0-2, adequate organ function, CD33+ in ≥ 20% AML blasts, ≤2 lines of prior therapy, no prior use of GO or VEN, no previous VOD, no BMT within 2 months, no CNS disease, and no history of HIV. Induction: 3-day VEN ramp-up to the target dose of 200 (cohort i), 400 (ii), or 600 (iii) mg daily x 28 d, with GO 3mg/m^2 infused d 1, 4, and 7. If CR/CRi achieved, pts proceed to BMT if applicable, otherwise, if in CR/CRi (provided ANC > 1000, plts 100K) or PR (regardless of counts), they are consolidated with VEN at the prescribed dose x 28d and GO 3mg/m^2 on days 1 and 4 (Cycle 2). If BMT not applicable, and then in CR/CRi or PR (as above), proceed to VEN alone as Maintenance in cycles 3+ until progression or toxicity. The primary endpoint is MTD of VEN with GO. Secondary endpoints include ORR, anti-leukemic activity, characterization of AEs, and estimates of RFS, EFS, and OS. This study is currently open and has to date enrolled 2 pts. Clinical trial information: NCT04070768. Research Sponsor: AbbVie, Pfizer.

TPS7567 Poster Session (Board #340), Fri, 8:00 AM-11:00 AM

Phase Ib study of CPX-351 lower-intensity therapy (LIT) plus venetoclax as first-line treatment for patients with AML who are unfit for intensive chemotherapy (IC). *First Author: Tara L. Lin, University of Kansas Medical Center, Kansas City, KS*

Background: CPX-351 (Vyxeos; daunorubicin and cytarabine liposome for injection) is approved by the FDA and EMA for the treatment of adults with newly diagnosed therapy-related AML or AML with myelodysplasia-related changes. In a phase 3 study in patients (pts) aged 60-75 y with newly diagnosed high-risk/secondary AML who were fit for IC, CPX-351 significantly improved median survival versus 7+3 cytarabine/daunorubicin and had a comparable safety profile. However, it may not be appropriate to administer CPX-351 at the label dosage in pts unfit for IC. Venetoclax, a BCL-2 inhibitor, has clinical efficacy in combination with low-dose cytarabine in AML pts unfit for IC, and preclinical data suggest a rationale for combining CPX-351 and venetoclax. This study thus evaluates CPX-351 LIT in combination with venetoclax in AML pts unfit for IC. **Methods:** This is an open-label, multicenter, 2-part, phase 1b study (NCT04038437) to determine the maximum tolerated dose (MTD) and evaluate the safety, efficacy, and pharmacokinetics of CPX-351 LIT plus venetoclax. Key eligibility criteria are shown in the Table. In the dose-escalation phase (3+3 design), up to 24 pts will receive CPX-351 (dose levels: 20, 40, 60, and 75 units/m^2) on Days 1 and 3 plus venetoclax 400 mg on Days 2-21 of each cycle to determine the MTD, with each dose escalation confirmed by a safety assessment committee. Pts who achieve complete or partial remission after 1 or 2 cycles may receive up to 4 similar cycles of CPX-351 plus venetoclax. In the expansion phase, an additional 20 pts will be treated at the MTD. All pts are assessed for response by morphology and minimal residual disease testing, and are monitored for safety (until 1 month after end of treatment) and survival (up to 1 year after start of treatment). The study is ongoing and actively enrolling pts. Clinical trial information: NCT04038437. Research Sponsor: Jazz Pharmaceuticals.

Key eligibility criteria.

- ≥18 y
- Histologically confirmed (per WHO criteria) newly diagnosed AML
- Considered unfit for IC
  - o ≥75 y
  - OR
  - o 18-74 y and ≥1 of the following criteria:
- ECOG PS 2-3
- History of congestive heart failure requiring treatment or LVEF ≤50%
- Diffusing capacity of the lung for carbon monoxide ≤65% or forced expiratory volume in 1 sec ≤65%
- Creatinine clearance ≥30 to < 45 mL/min
- Moderate hepatic impairment with total bilirubin > 1.5 to ≤3.0 × upper limit of normal
- Other comorbidity incompatible with conventional IC
- No CNS involvement
- No antecedent myeloproliferative neoplasms
- No favorable-risk cytogenetics (per NCCN guidelines)
- No prior AML treatment except hydroxyurea

TPS7568 Poster Session (Board #341), Fri, 8:00 AM-11:00 AM

A phase II/III study of JZP-458 in patients with acute lymphoblastic leukemia (ALL)/lymphoblastic lymphoma (LBL) who are hypersensitive to E. coli-derived asparaginases. *First Author: Luke Maese, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT*

Background: L-asparaginase is an important component of ALL therapy and the inability to receive asparaginase secondary to hypersensitivity has been associated with poor patient (pt) outcomes. Alternative options for pts after hypersensitivity reactions are needed. JZP-458 is a recombinant *Erwinia* asparaginase produced using a novel *Pseudomonas fluorescens* expression platform that yields an enzyme with no immunologic cross-reactivity to *E. coli*derived asparaginases. In a phase 1 study, JZP-458 was well tolerated and maintained adequate (≥0.1 IU/mL) serum asparaginase activity (SAA), a surrogate marker for asparagine depletion, for up to 72 hrs in healthy adults. **Methods:** This is a pivotal, open-label, multicenter, dose confirmation, and pharmacokinetic (PK) study (NCT04145531) of JZP-458 in pts with ALL/LBL who develop hypersensitivity reactions to a long-acting *E. coli*derived asparaginase and have ≥1 course of asparaginase remaining in their treatment plan (Table); 6 doses of JZP-458 will be substituted for each remaining course. Treatment duration will depend on the number of asparaginase courses remaining in the treatment plan. The study has 2 sequential parts: Part A will determine the dose of intramuscular (IM) JZP-458 and confirm safety/efficacy; Part B will explore the dose/schedule of intravenous (IV) JZP-458. Blood samples will be collected to determine SAA levels and pts will be monitored for adverse events. Immunogenicity of JZP-458 will be assessed. Primary objectives are to determine (1) the efficacy of IM JZP-458 measured by the last 72-hr nadir SAA (NSAA) level (≥0.1 IU/mL) during the first treatment course, and (2) the safety/tolerability of IM JZP-458. Secondary objectives are to determine the efficacy (measured by the last 48-hr NSAA level [≥0.1 IU/mL] and the last 48- and 72-hr NSAA levels [≥0.4 IU/mL]), PK, and immunogenicity of IM JZP-458. Exploratory objectives include efficacy, safety, PK, and immunogenicity of IV JZP-458. The trial is active and enrolling. Clinical trial information: NCT04145531. Research Sponsor: Jazz Pharmaceuticals.

Eligibility criteria.

Pediatric and adult pts with ALL/LBL (excluding relapsed ALL/LBL)
≥1 course of *E. coli*derived asparaginase remaining in treatment plan
Full recovery from prior allergic reaction to long-acting *E. coli*derived asparaginase or silent inactivation with undetectable SAA levels (≤0.02 IU/mL), except for pts receiving < 10% *E. coli*derived asparaginase IV before the reaction
Adequate liver function
No prior exposure to asparaginase *Erwinia chrysanthemi* or JZP-458

8000 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Is autologous transplantation (autoHCT) in relapsed diffuse large B-cell lymphoma (DLBCL) patients achieving only a PET/CT positive partial remission (PR) appropriate in the CAR-T cell era? *First Author: Nirav Niranjan Shah, Medical College of Wisconsin, Milwaukee, WI*

Background: In relapsed, chemosensitive DLBCL patients (pts), autoHCT consolidation is a standard therapy option. With the approval of anti-CD19 CAR T-cells in 2017, relapsed DLBCL pts with residual PET/CT avid disease after salvage therapies are increasingly being offered CAR T-cells in lieu of autoHCT. According to Center for International Blood and Marrow Transplant Research (CIBMTR) data in 2018, the number of autoHCT for DLBCL in the U.S. decreased by ~45% from prior years, likely due to application of CAR T-cells for both chemorefractory DLBCL and chemosensitive DLBCL pts not achieving a complete remission. Using the CIBMTR database, we report outcomes of autoHCT in relapsed chemosensitive DLBCL pts achieving only a PET/CT+ PR prior to HCT. **Methods:** 249 relapsed DLBCL pts undergoing an autoHCT from 2003-13 with a PET/CT+ PR prior to transplant were identified. The study cohort was divided into two groups: (a) early chemo-immunotherapy failure (ECF) defined as pts with primary refractory disease (PRefD) or relapse within 12 months of diagnosis, (b) late chemoimmunotherapy failure (LCF) defined as pts relapsing ≥12 months. Primary outcome was overall survival (OS). Secondary outcomes included progression-free survival (PFS) and relapse. **Results:** 182 pts had ECF and 67 pts had LCF. The median age of ECF pts was 57 years versus (vs) 63 years for LCF ($p < 0.01$). ECF pts more frequently had stage III-IV at diagnosis (74% vs 54%, $p = < 0.01$). 79% of ECF pts had PRefD. The most common conditioning regimen was BEAM in both cohorts. The adjusted 5-year probabilities for PFS and OS (ECF vs LCF) was not different between the 2 cohorts: 41% vs 41% ($p = 0.93$) and 51% vs 63% ($p = 0.09$), respectively. Cumulative incidence of relapse at 5 years in similar order was 48% vs 57%, $p = 0.27$. On multivariate analysis compared to the LCF, pts with ECF had an increased risk of death (HR = 1.61, 95%CI 1.05-2.46, $p = 0.03$) but no increased risk in PFS or relapse. **Conclusions:** Using the CIBMTR registry, we report outcomes of relapsed DLBCL pts in a PR with residual PET/CT avid disease at time of autoHCT. While OS favored LCF pts, the adjusted 5-year PFS (41%) was comparable in both cohorts. This 5 year PFS is comparable to results reported in historical trials of auto-HCT for DLBCL. With no randomized data demonstrating superiority of CAR T-cell therapy in chemosensitive PR patients, these findings strongly support that autoHCT should remain the current standard of care for this patient population. Research Sponsor: None.

8001 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Phase I Alexander study of AUTO3, the first CD19/22 dual targeting CAR T cell therapy, with pembrolizumab in patients with relapsed/refractory (r/r) DLBCL. *First Author: Wendy Osborne, Newcastle, Newcastle, United Kingdom*

Background: CD19 directed CAR T cells are effective in patients with r/r DLBCL, however relapses due to CD19 loss or PDL1 upregulation are common. In this study, we evaluate the safety and efficacy of AUTO3, a CAR T targeting CD19/22 with limited duration of PD-1 blockade. **Methods:** We constructed a bicistronic retroviral vector encoding both an anti-CD19 (OX40 co-stim) and an anti-CD22 (41BB co-stim) CAR with humanized binders. The cell product was manufactured in a semi-automated and closed process using CliniMACS Prodigy. Patients (≥ 18 years) with r/r DLBCL (NOS) or transformed (tDLBCL); ECOG <2, adequate organ function are eligible. Lymphodepletion was Flu/Cy prior to AUTO3. Bridging therapy was allowed. The three dose levels explored are 50, 150, and 450 x 10^6 CAR T cells. Patients received AUTO3 alone, or with 3 doses of pembrolizumab (pem) 200 mg q 3 wks starting on D14 (regimen A), or with a single dose of pem 200 mg on D-1 (regimen B). The primary endpoint is frequency of DLTs and grade (G) 3-5 adverse events (AE) and secondary endpoints included ORR, CRR, and biomarkers. **Results:** As of Jan 21, 2020, 28 patients underwent leukapheresis, 27 successfully manufactured, 1 being manufactured, and 19 patients treated with AUTO3. The median age was 57 (28 - 71) and median number of prior therapies was 3 (2 - 10). 89% had refractory disease, 74% were DLBCL NOS, and 26% were tDLBCL. Dose escalation from 50 to 450 x 10^6 cells with pem regimen A and B have been completed without DLTs. G > 3 treatment emergent AEs that occurred > 15% were neutropenia (89%), thrombocytopenia (58%), anemia (47%), febrile neutropenia (16%), and hypophosphataemia (16%). Across all dose levels, there were 0% sCRS with primary infusion and 5% severe neurotoxicity (sNT) (1/19), which resolved. There were no cases of sCRS and no neurotoxicity of any grade at > 50 x 10^6 cells. Eighteen patients were evaluable for efficacy. Among the 11 treated at dose > 50 x 10^6, the ORR and CRR were 64% and 55%, and all CRs are ongoing (1-12 mth). Two out of 3 patients achieved CR at 450 x 10^6 cells on pem regimen B. Additional patients and longer follow up, as well as biomarkers, will be presented. **Conclusions:** AUTO3 at > 50 x 10^6 CAR T cells with pembrolizumab induces CRs without severe CRS or neurotoxicities of any grade. Clinical trial information: NCT03287817. Research Sponsor: Autolus Therapeutics.

8002 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

First-in-human data of ALLO-501 and ALLO-647 in relapsed/refractory large cell or follicular lymphoma (R/R LBCL/FL): ALPHA study. *First Author: Sattva Swarup Neelapu, The University of Texas MD Anderson Cancer Center, Department of Lymphoma/Myeloma, Houston, TX*

Background: Allogeneic (off the shelf) chimeric antigen receptor (CAR) T cell therapy addresses the logistical challenges and variable product quality of autologous CAR T therapy. ALLO-501 is a genetically modified anti-CD19 CAR T cell product in which the *TCR alpha constant* gene is disrupted to reduce the risk of graft-versus-host disease (GvHD) and the *CD52* gene is disrupted to permit the use of ALLO-647, an anti-CD52 mAb, for selective and prolonged host lymphodepletion. **Methods:** This is an open-label, Phase 1 trial (NCT03939026) in adults with R/R LBCL/FL who have received ≥ 2 prior lines of therapy; prior anti-CD19 cell therapy is allowed. Patients (pts) receive fludarabine (flu) 90 mg/m^2, cyclophosphamide (cy) 900 mg/m^2, and ALLO-647 39 or 90 mg followed by ALLO-501 at 1 of 3 dose levels (DL) in a 3+3 design: 40, 120, and 360 × 10^6 CAR+ T cells. **Results:** As of 20 January 2020, 12 pts were enrolled: 9 received ALLO-501 at 3 DLs (4, 4 & 1 pts in DL1, DL2 and DL3 respectively), 1 pt discontinued due to kidney injury prior to lymphodepletion and 2 are starting treatment. Of the 9 treated pts aged 42 to 70 years: 5 had LBCL, 2 were female, 3 had primary refractory disease, and 3 had prior autologous stem cell transplants. The median number of prior lines of therapies was 3 (range 2 to 4). All treated pts received 39 mg of ALLO-647. No DLTs or GvHD have been observed to date. Most common Grade (Gr) ≥ 3 adverse events were neutropenia (55.6%), leukopenia (33.3%) and anemia (22.2%). Two pts (22.2%) developed cytokine release syndrome (1 Gr1 and 1 Gr2) that resolved within 72 hrs without steroids or tocilizumab. One pt developed Gr1 neurotoxicity that resolved without treatment. Infections included upper respiratory tract infection (Gr2), CMV (Gr3) and EBV viremia (Gr1), all reported in a single pt and resolved. One pt had a Gr2 infusion reaction to ALLO-647 which resolved with antihistamines. The overall response rate is 78% (95% exact CI: 40%, 97%): 3 complete and 4 partial responses. With a median follow up of 2.7 mos, 4 pts have ongoing responses and 3 pts progressed at 2, 4 and 6 mos. ALLO-501 cell expansion by qPCR was observed in 4 of 6 pts in varying degrees. **Conclusions:** These early data suggest that ALLO-501 and ALLO-647 have a manageable safety profile. ALLO-647 may be an effective and selective lymphodepleting agent with CD52 gene editing, and ALLO-501 shows evidence of clinical activity in pts with advanced NHL. Enrollment is ongoing, and updated safety, efficacy, PK/PD data will be presented including pts treated with increasing doses of ALLO-647. Clinical trial information: NCT03939026. Research Sponsor: Allogene Therapeutics.

8003 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Phase I study of the Bcl-2 inhibitor venetoclax with DA-EPOCH-R as initial therapy for aggressive B-cell lymphomas. *First Author: Sarah C. Rutherford, Weill Cornell Medicine, New York, NY*

Background: Dose-adjusted (DA) EPOCH-R is a frontline treatment for aggressive B-cell lymphomas. Bcl-2 is associated with chemoresistance due to BCL2 gene rearrangement or protein overexpression in lymphomas and is antagonized by BH3 mimetic venetoclax (ven). We conducted a phase I study combining ven with DA-EPOCH-R in aggressive B-cell lymphomas. **Methods:** This phase 1 study used Bayesian optimal interval design with dose expansion. Eligible patients (pts) were 18 years with newly diagnosed diffuse large B-cell (DLBCL), primary mediastinal, and high grade B-cell lymphoma (HGBCL) with double hit (DHL) or not otherwise specified (NOS). Ven was dosed at 400 mg (DL1), 600 mg (DL2), and 800 mg (DL3) daily for 10 days with 6 cycles of DA-EPOCH-R. A subsequent cohort received ven 600 mg daily for 5 days (DL2B). Toxicities were graded by CTCAE v4.0 and response assessed by Lugano criteria. Dose limiting toxicity (DLT) period was cycle 1 and primarily included grade (gr) ≥3 neutropenia on cycle 2 day 1, gr ≥4 febrile neutropenia/thrombocytopenia, and gr ≥3 nausea, vomiting, diarrhea despite supportive care. **Results:** 30 pts enrolled with median age 64 (24-79), and 50% female. Ann Arbor stage was III-IV in 23. IPI was high risk in > 50%. Diagnosis was DHL (15), DLBCL NOS (13), and HGBCL NOS (2). 18 had *MYC* and 14 had *BCL2* rearrangements. Bcl-2 was expressed ≥50% by IHC in 21/26 with data. There were no DLTs in DL1 (3 pts) or DL2 (9 pts). 1/6 had DLT in DL3 (gr 4 thrombocytopenia). Ven dose reductions occurred in subsequent cycles in 4 (2 in DL2; 2 in DL3). Of 18 in DL1-3, EPOCH was escalated above level 1 in 1 and de-escalated below level 1 in 7. Because of delays and ven dose reductions in DL2-3 due in part to cytopenias, infections and GI toxicities, we accrued DL2B. In DL2B, 0/12 pts had DLTs or ven dose reductions. EPOCH was escalated above level 1 in 4 and de-escalated below level 1 in 3. 1 died of sepsis during cycle 3. Most common gr 3-4 toxicities across all dose levels were cytopenias; febrile neutropenia occurred in 57%. Most common non-hematologic toxicities of all grades were hypocalcemia, nausea, diarrhea, hypokalemia and fatigue. ORR (N = 30) ITT was 97% with 27 (90%) complete and 2 (7%) partial responses; 1 was not evaluable. Follow up is ongoing. Of 15 DHL, ORR and CRR were 93% and 80%. **Conclusions:** We identified ven 600 mg for 5 days per cycle as RP2D with DA-EPOCH-R. DL2B was well tolerated and required no ven dose reductions. Further efficacy and safety is being evaluated in Alliance 51701, DA-EPOCH-R/R-CHOP in DH/double expressor lymphomas, using the dosing regimen defined by this study. Clinical trial information: NCT03036904. Research Sponsor: Genentech.

8004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A multicenter phase II study of venetoclax plus dose-adjusted R-EPOCH (VR-EPOCH) for Richter's syndrome. *First Author: Matthew Steven Davids, Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA*

Background: While therapeutic options for CLL have improved, patients (pts) who develop Richter's Syndrome (RS) still have a poor prognosis. Chemoimmunotherapy regimens such as R-EPOCH lead to CR in about 20% of RS pts, but PFS/OS is typically < 6 mo. The oral Bcl-2 inhibitor venetoclax (ven) had a 43% single agent response rate in RS. Here, we report the results of a phase 2 study of VR-EPOCH in RS. **Methods:** This is a single-arm, phase 2, IST of VR-EPOCH for RS (NCT03054896) at 3 US sites. CLL pts with biopsy-confirmed DLBCL were treated with R-EPOCH for 1 cycle, then after count recovery underwent accelerated inpatient ven daily ramp-up (20/50/100/200/400 mg), then ven + R-EPOCH for up to 5 more 21d cycles (ven 400 mg qd, d1-10 each cycle). Responders went to alloHCT or to continuous daily ven 400 mg maintenance. Response evaluation by Lugano criteria with PET/CT. **Results:** As of the data cut on 2/3/2020, the study is fully enrolled with 27 pts. Median age: 63 yrs (range 49-77). CLL features: 26% del(17p); 44% complex karyotype; 48% *IGHV* unmutated; 41% *TP53* and 15% *NOTCH1* mutation. Median prior CLL treatments: 2 (range 0-5, prior ibrutinib [n = 8], ven [n = 2], and PI3Ki [n = 2]) with 6 untreated CLL pts. Median # ven + R-EPOCH cycles: 4 (range 0-6). 5 pts had dose de-escalation of R-EPOCH, 1 pt had dose escalation. ≥Gr 3 heme tox: neutropenia (58%), anemia (50%), thrombocytopenia (50%). ≥Gr 3 non-heme tox in > 15% of pts: febrile neutropenia (38%) and hypophosphatemia (23% each). No pts had TLS with daily ven ramp-up. Infections: pneumonia (n = 4), sepsis during C1 of R-EPOCH prior to starting ven (n = 3), enterocolitis (n = 3), sinusitis (n = 2), and 1 pt each with influenza A and norovirus. 10 pts have died, including 7 due to disease progression (2 during C1 before ven), and 1 each due to sepsis, sudden death, and GVHD post-alloHCT. In ITT analysis, 16 responded (ORR 59%); 13/27 (48%) had CR as best response, all with undetectable bone marrow MRD for CLL. Six pts were not evaluable for efficacy of the combo (5 had toxicity in C1 and never started ven, 1 withdrew after C1). In the 21 pts who started combo therapy, the ORR was 76%, CR rate 62%. Only 1 pt with CR has progressed. The pt on longest ven maintenance is in CR 2 years post chemo. 8 pts went to alloHCT, with pts still in CR now up to 2.5 yrs post-alloHCT. With a median follow-up of 9.3 mo (range 0.6-30), median PFS and OS are both 16.3 mo. **Conclusions:** VR-EPOCH is active for RS. Expected toxicities from intensive chemoimmunotherapy and ven were seen, but daily ven ramp-up was feasible. The 48% CR rate and median PFS of 16.3 mo are favorable in the context of historical results. Clinical trial information: NCT03054896. Research Sponsor: Genentech, Other Foundation.

8005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

KEYNOTE-204: Randomized, open-label, phase III study of pembrolizumab (pembro) versus brentuximab vedotin (BV) in relapsed or refractory classic Hodgkin lymphoma (R/R cHL). *First Author: John Kuruvilla, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: PD-1 blockade via pembro monotherapy showed antitumor activity in R/R cHL. KEYNOTE-204 (NCT02684292) was a randomized, international, open-label, phase III study of pembro vs BV in R/R cHL. **Methods:** Patients (pts) were aged ≥18 y, were post−autologous stem cell transplant (auto-SCT) or ineligible for auto-SCT, and had measurable disease and ECOG PS 0 or 1. BV-naive and BV-exposed pts were eligible. Pts were randomized 1:1 to pembro 200 mg IV Q3W or BV 1.8 mg/kg IV Q3W and stratified by prior auto-SCT (yes vs no) and status after 1L therapy (primary refractory vs relapsed <12 mo vs relapsed ≥12 mo after end of 1L therapy). Primary end points: PFS by blinded independent central review (BICR) per International Working Group (IWG) criteria including clinical and imaging data after auto-SCT or allogeneic SCT (allo-SCT) and OS. Key secondary end points: PFS excluding clinical and imaging data after auto-SCT or allo-SCT (PFS-secondary), and ORR by BICR per IWG, PFS by investigator review per IWG, and safety. Exploratory end point: DOR by BICR per IWG. **Results:** 304 pts were randomized and 300 were treated (148, pembro; 152, BV); 256 discontinued. Median (range) follow-up: 24.7 (0.6-42.3) mo. 15 pts were BV exposed. Median (range) time on treatment was 305.0 (1-814) and 146.5 (1-794) days with pembro and BV, respectively. Statistically significant improvement was observed with pembro vs BV for primary PFS analysis (HR 0.65 [95% CI 0.48-0.88; P =0.00271]; median 13.2 vs 8.3 mo); 12-mo PFS rates were 53.9% vs 35.6%, respectively. Benefit was observed in all subgroups tested, including pts with no auto-SCT (HR=0.61), primary refractory disease (HR=0.52), prior BV (HR=0.34) and BV naive (HR=0.67). Significant improvement in PFS-secondary was observed with pembro vs BV (HR 0.62 [95% CI 0.46-0.85]; median 12.6 vs 8.2 mo). Per investigator assessment, PFS was longer with pembro vs BV (HR 0.49 [95% CI 0.36-0.67]; median 19.2 vs 8.2 mo). ORR was 65.6% for pembro and 54.2% for BV; CR rates were 24.5% and 24.2%, respectively. Median (range) DOR was 20.7 mo (0.0+ to 33.2+) for pembro and 13.8 mo (0.0+ to 33.9+) for BV. Grade 3-5 TRAEs: 19.6% of pts with pembro and 25.0% with BV. One death due to TRAE occurred with pembro (pneumonia). **Conclusions:** In pts with R/R cHL, pembro was superior to BV and demonstrated statistically significant and clinically meaningful improvement in PFS across all subgroups, with safety consistent with previous reports. Pembro monotherapy should be standard of care for this pt population with R/R/cHL. Clinical trial information: NCT02684292. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

8006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Initial results of a multicenter, investigator initiated study of MRD driven time limited therapy with zanubrutinib, obinutuzumab, and venetoclax. *First Author: Jacob Drobnyk Soumerai, Massachusetts General Hospital Cancer Center; Harvard Medical School, Boston, MA*

Background: Venetoclax (Ven)-Obinutuzumab (O) is approved for chronic lymphocytic leukemia (CLL) achieving frequent undetectable minimum residual disease (uMRD; Fischer NEJM 2019). Ven-Ibrutinib is synergistic with frequent uMRD but with grade >3 neutropenia in 33-48% patients (pts; Tam ASH 2019; Jain NEJM 2019). Zanubrutinib (B) is a highly specific BTK inhibitor that demonstrated 100% occupancy in lymphoid tissues, so may be preferred to combine with OVen. We hypothesize that treatment (tx) with BOVen using an MRD driven discontinuation strategy will achieve frequent uMRD and durable responses. **Methods:** In this multicenter, investigator initiated phase 2 trial (NCT03824483), eligible pts had previously untreated CLL requiring tx per iwCLL, ECOG PS <2, ANC >1, PLT >75 (ANC >0, PLT >20 if due to CLL). BOVen was administered in 28D cycles: B 160 mg PO BID starting D1; O 1000 mg IV D1 or split D1-2, 8, 15 of C1, D1 of C2-8; Ven ramp up initiated C3D1 (target 400 mg QD). Tx duration was determined by a prespecified uMRD endpoint (min 8 cycles). MRD was assessed in peripheral blood (PB; flow cytometry, sensitivity $>10^{-4}$) starting C7D1 then every 2 cycles. Once PB uMRD was determined and confirmed in bone marrow (BM), tx continued 2 additional cycles. Adverse events (AE) were assessed per CTCAE v5. Median (med) time to uMRD (primary endpoint) was estimated using the Kaplan-Meier method. **Results:** The study accrued 39 pts (3-10/19): med age 59 years (23-73), 3:1 male, CLL IPI >4 26/39 (67%), unmutated IGHV 28/39 (72%), 17p del/*TP53* mutated 4/39 (10%), all pts were evaluable for toxicity with 37 evaluable for efficacy. At a med follow up of 8 months (mo; 3-10), 25/37 (68%) pts achieved PB uMRD. Med time to PB uMRD is 6 mo (4-8+). Another 8/37 (22%) had PB MRD < 0.1%. Of 25 with PB uMRD, 19 had BM uMRD with 10/19 completing 2 additional cycles and discontinued; 3 had BM MRD (all <0.02%); 3 pending. The most common tx emergent AEs were neutropenia (49%), infusion related reaction (41%), bruising (39%), and diarrhea (39%). Grade ≥3 AEs in ≥5% pts were neutropenia (13%), thrombocytopenia (5%), rash (5%), and pneumonia (5%). Of 17 pts at high risk for TLS on C1D1, 2 cycles of BO reduced TLS risk to low/medium at Ven initiation in 15 (88%). No pts had laboratory/clinical TLS (Howard). **Conclusions:** BOVen is well tolerated and achieves rapid uMRD: currently 68% PB uMRD and 51% BM uMRD with limited follow up (to be updated on presentation). Ten (27%) have discontinued treatment thus far. The value of MRD directed treatment duration will be evaluated with continued follow up. Clinical trial information: NCT03824483. Research Sponsor: BeiGene; Genentech/Roche, Other Foundation, Lymphoma Research Fund (Andrew Zelenetz)).

8007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

ASPEN: Results of a phase III randomized trial of zanubrutinib versus ibrutinib for patients with Waldenström macroglobulinemia (WM). *First Author: Constantine S. Tam, Peter MacCallum Cancer Centre, Melbourne, St Vincent's Hospital, Fitzroy, University of Melbourne, Parkville and Royal Melbourne Hospital, Parkville, Victoria, Australia*

Background: Bruton tyrosine kinase (BTK) inhibition is an emerging standard of care for WM. ASPEN is a randomized phase 3 study comparing zanubrutinib (ZANU), a potent and selective BTK inhibitor, versus ibrutinib (IBR), a first generation BTK inhibitor, in WM patients. **Methods:** Patients with WM and *MYD88* mutation were randomly assigned 1:1 to receive ZANU (160 mg twice daily) or IBR (420 mg once daily). Patients without *MYD88* mutations were assigned to a separate cohort, received ZANU, and are reported separately. Randomization was stratified by CXCR4 mutational status and the number of lines of prior therapy (0 vs 1-3 vs >3). The primary end point was the proportion of patients achieving a complete response or very good partial response (CR+VGPR). Sample size was calculated to provide 81% power to detect a difference in CR+VGPR rate of 35% vs 15% in the subset of patients with relapsed or refractory (R/R) WM. Primary analysis was planned to occur at ~12 months after last patient enrolled. **Results:** In total, 201 patients were randomized from Jan 2017 to Jul 2018. The treatment groups were well balanced for important baseline factors, except in the ZANU arm there were more elderly patients (aged >75 years, 33.3% vs 22.2%) and more anemia (hemoglobin ≤110 g/L, 65.7% vs 53.5%). At a median follow-up of 19.4 months, the rate of CR+VGPR was 28.4% vs 19.2% with ZANU vs IBR, respectively (2-sided P=0.09). Rates of atrial fibrillation, contusion, diarrhea, edema peripheral, hemorrhage, muscle spasms, pneumonia, and adverse events (AEs) leading to discontinuation or death were lower with ZANU. The rate of neutropenia was higher with ZANU (Table); however, grade ≥ 3 infection rates were similar (17.8% vs 19.4%). **Conclusions:** ASPEN is the largest phase 3 trial of BTK inhibitors in WM and the first head-to-head comparison of BTK inhibitors in any disease. Although not statistically significant, ZANU was associated with a higher CR+VGPR response rate, and demonstrated clinically meaningful advantages in safety and tolerability compared to IBR. Clinical trial information: NCT03053440. Research Sponsor: BeiGene.

Assessment, %	ZANU (n=102)	IBR (n=99)
CR+VGPR Rate	28.4	19.2
12-mo PFS/OS – overall population	89.7/97.0	87.2/93.9
12-mo PFS/OS – R/R population (n=83 vs 81)	92.4/98.8	85.9/92.5
AEs ≥Grade 3 / Grade 5	58.4 /1.0	63.3/4.1
AEs leading to discontinuation	4.0	9.2
Atrial fibrillation/flutter	2.0	15.3
Hypertension	10.9	17.3
Major bleeding[a]	5.9	9.2
Neutropenia	29.7	13.3

PFS/OS, progression-free survival/overall survival.
[a]Includes grade ≥3 hemorrhage and central nervous system bleeding of any grade.

8008 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Interim analysis of ZUMA-5: A phase II study of axicabtagene ciloleucel (axi-cel) in patients (pts) with relapsed/refractory indolent non-Hodgkin lymphoma (R/R iNHL). *First Author: Caron A. Jacobson, Dana-Farber Cancer Institute, Boston, MA*

Background: Advanced stage iNHL, including follicular lymphoma (FL) and marginal zone lymphoma (MZL), is considered incurable as most pts experience multiple relapses (Wang, et al. *Ther Adv Hematol*. 2017), highlighting a need for novel therapies. Here, we present interim results from ZUMA-5, a Phase 2, multicenter study of axi-cel, an autologous anti-CD19 chimeric antigen receptor (CAR) T cell therapy, in pts with R/R iNHL. **Methods:** Adults with R/R FL (Grades 1-3a) or MZL (nodal or extranodal) after ≥ 2 lines of therapy (including an anti-CD20 monoclonal antibody [mAb] with an alkylating agent), and an ECOG of 0 – 1 were eligible. Pts were leukapheresed and received conditioning chemotherapy followed by axi-cel infusion at 2×10^6 CAR T cells/kg. The primary endpoint was objective response rate (ORR) by central review (Cheson, et al. *J Clin Oncol*. 2014). Secondary endpoints included duration of response (DOR), progression-free survival (PFS), overall survival (OS), safety, and blood levels of cytokines and CAR T cells. **Results:** As of 8/20/19, 94 pts (80 FL; 14 MZL) received axi-cel with a median follow-up of 11.5 mo (range, 4.2 – 24.9). Median age was 63 y (range, 34 – 79), 47% of pts were male, 52% had stage IV disease, 51% had ≥ 3 FLIPI, and 59% had high tumor bulk (GELF). Pts had a median 3 prior lines of therapy, 66% progressed < 2 y after initial anti-CD20 mAb-containing therapy (POD24), and 73% were refractory to the last prior treatment. Of 87 pts evaluable for efficacy, ORR was 94% (79% complete response [CR] rate). Pts with FL (n = 80) had an ORR of 95% (80% CR rate). Pts with MZL (n = 7) had an ORR of 86% (71% CR rate). Overall, 68% of pts had ongoing responses as of the data cutoff. Updated data, including DOR, PFS, and OS with longer follow-up, will be included in the presentation. Of 94 pts evaluable for safety, 83% experienced Grade ≥ 3 adverse events (AEs), most commonly neutropenia (33%) and anemia (28%). Grade ≥ 3 cytokine release syndrome (CRS; per Lee et al, *Blood* 2014) and neurologic events (NEs; per CTCAE v4.03) occurred in 11% and 19% of pts, respectively. Median times to onset of CRS and NEs were 4 and 7 d, with median durations of 6 and 14.5 d. There were 2 Grade 5 AEs: multisystem organ failure in the context of CRS (related to axi-cel) and aortic dissection (unrelated to axi-cel). Median peak and $AUC_{0\text{-}28}$ CAR T cell levels were 44 cells/μL and 490 cells/μL × d, respectively. **Conclusions:** Axi-cel demonstrated significant and durable clinical benefit, with high rates of ORR and CR, and a manageable safety profile in pts with R/R iNHL. Clinical trial information: NCT03105336. Research Sponsor: Kite, a Gilead Company.

8009 Poster Discussion Session; Displayed in Poster Session (Board #342), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Epcoritamab (GEN3013; DuoBody-CD3×CD20) to induce complete response in patients with relapsed/refractory B-cell non-Hodgkin lymphoma (B-NHL): Complete dose escalation data and efficacy results from a phase I/II trial. *First Author: Martin Hutchings, Rigshospitalet, Copenhagen, Denmark*

Background: CD3×CD20 bispecific antibodies (bsAbs) have demonstrated promising results for the treatment of pts with R/R B-NHL. Epcoritamab is a novel subcutaneously administered bsAb with a favorable safety profile and encouraging preliminary anti-tumor activity at low doses in both aggressive and indolent B-NHL. Here we present updated safety and efficacy data from the ongoing trial (NCT03625037). **Methods:** Adults with R/R CD20+ B-NHL received a single SC injection of flat-dose epcoritamab in 28-day cycles (q1w: cycle 1–2; q2w: cycle 3–6; q4w thereafter) until disease progression or unacceptable toxicity. Primary objectives are determination of maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D). Secondary objectives include anti-tumor activity. **Results:** As of 8 Jan 2020, 41 pts with median age of 66 (range: 21–82) were enrolled. Most pts had DLBCL/HGBCL (73%) or FL (20%) and received a median (range) of 3 (1–6) and 5 (2–18) prior lines of treatment. No DLTs were observed (median follow-up: 4.7 mo; range: 3.7– 5.6). MTD has not been reached. Most common TEAEs (>35%) were pyrexia (71%), fatigue (46%), and injection site reaction (39%; all Gr 1). AEs of special interest included cytokine release syndrome (59%; all Gr 1/2; all resolved) and cytokine release-related decreased CARTOX-10 score (n=1). There was no clinical tumor lysis syndrome or treatment-related deaths. Treatment is ongoing in 13 pts. Anti-tumor activity was observed at minimal efficacy threshold (based on PK modelling) for DLBCL/HGBCL and FL (Table). Complete dose escalation data and RP2D will be presented. **Conclusions:** SC epcoritamab continues to demonstrate a favorable safety profile across all doses with no ≥Gr 3 CRS and no DLTs. Dose escalation data show improved efficacy as doses reach above the modeled predicted exposure threshold, inducing CRs in heavily pretreated DLBCL pts. All pts achieving CRs remain in remission. Clinical trial information: NCT03625037. Research Sponsor: Genmab.

Anti-tumor activity in R/R B-NHL.

	DLBCL/HGBCL ≥6 mg (n=12)	FL ≥0.76 mg (n=7)
Evaluable pts	9	6
ORR, n(%) CR	5 (56%) 4 (44%)	6 (100%) 0
PR	1 (11%)	6 (100%)
SD	2 (22%)	0
PD	2 (22%)	0
Data snapshot 02112020		

8010 Poster Discussion Session; Displayed in Poster Session (Board #343), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Durable responses to REGN1979, a human CD20 x CD3 bispecific antibody (bsAb), in patients (pts) with relapsed/refractory B-cell non-Hodgkin lymphoma (R/R B-NHL) including with or without (w/wo) prior chimeric antigen receptor T-cell therapy (CAR T). *First Author: Rajat Bannerji, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ*

Background: REGN1979 is a human CD20 x CD3 IgG4 bsAb targeting CD20+ tumor cells via T cell-mediated cytotoxicity. We report extended follow-up of a global Phase 1 study (NCT02290951) of REGN1979 monotherapy in R/R B-NHL. **Methods:** Primary objectives were to assess safety, tolerability, and occurrence of dose limiting toxicities (DLTs) in R/R B-NHL pts after prior CD20 Ab therapy. REGN1979 (0.03–320 mg) dose regimen evolved over time to QW×12 with initial, intermediate, and step-up dosing in first weeks, followed by Q2W×12 (36 weeks total). **Results:** As of 1/7/2020, 116 pts with R/R B-NHL were enrolled; diffuse large B-cell lymphoma (DLBCL; 65), follicular lymphoma Gr 1–3a (FL; 31), mantle cell lymphoma (MCL; 11), marginal zone lymphoma (6), or other B-NHL (3). Pts had received a median (med) of 3 (range: 1–11) prior lines of therapy; 25 pts received prior CAR T (DLBCL: 21; FL: 2; MCL: 2). Med follow-up was 4.2 (0.4–25.4) months (mo). Most common treatment-emergent adverse events (TEAEs) were pyrexia (93 pts) and cytokine release syndrome (CRS; 70 pts). Gr 3/4 CRS occurred in 8 pts; all events were transient and no Gr 5 CRS was observed. No DLTs occurred during DE. Seven pts discontinued due to treatment-related AEs. Seventeen pts died during the study, 10 with progressive disease (PD), 6 due to TEAEs (5 related to treatment) and 1 due to fungal pneumonia unrelated to treatment. **Conclusions:** REGN1979 continues to show acceptable tolerability in pts with R/R B-NHL. FL pts had the longest follow up, KM estimate of med PFS was 11.4 mo. Durable responses can be >20 mo in pts with FL and >12 mo in pts with DLBCL w/wo CAR T failure. Enrollment into disease-specific registration intent expansion cohorts is ongoing. Clinical trial information: NCT02290951. Research Sponsor: Regeneron Pharmaceuticals, Inc.

Efficacy in pts with opportunity for Week 12 assessment.*

Cohort:	FL at doses ≥5 mg (n=24)	All DLBCL at doses ≥80 mg w/ wo CAR T (n=28)	DLBCL without prior CAR T at doses ≥80 mg (n=10)	DLBCL at doses ≥80 mg post CAR T failure (n=18)
ORR (CR/partial response [PR]), n (%)	23 (95.8)	14 (50.0)	6 (60.0)	8 (44.4)
CR	20 (83.3)	11 (39.3)	6 (60.0)	5 (27.8)
PR	3 (12.5)	3 (10.7)	0	3 (16.7)
Stable disease	1 (4.2)	4 (14.3)	2 (20.0)	2 (11.1)
PD	0	6 (21.4)	2 (20.0)	4 (22.2)
Not evaluable	0	4 (14.3)	0	4 (22.2)
Med observed DoR (range), mo	6.5 (1.3–22.9)	2.8 (0–12.4)	4.41 (1.5–11.1)	1.9 (0–12.4)
Ongoing responses as of data cut-off, n (%)	14 (60.9)	11 (78.6)	5 (83.3)	6 (75.0)
Med PFS (95% CI), mo; KM estimate	11.4 (7.1, NE)	5.1 (1.1, NE)	NR	2.6 (0.7, NE)

*Data cut-off: Jan 7, 2020.

8011 Poster Discussion Session; Displayed in Poster Session (Board #344), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Prognostic impact of dose, duration, and timing of corticosteroid therapy in patients with large B-cell lymphoma treated with standard of care axicabtagene ciloleucel (Axi-cel). *First Author: Paolo Strati, The University of Texas MD Anderson Cancer Center, Department of Lymphoma/Myeloma, Houston, TX*

Background: Corticosteroids are commonly used for management of severe toxicities associated with chimeric antigen receptor (CAR) T-cell therapy. However, it remains unclear whether the dose, duration, and timing of corticosteroid therapy may impact clinical efficacy of CAR T-cell therapy. **Methods:** This is a retrospective analysis of patients with relapsed or refractory LBCL treated with standard of care axi-cel at MD Anderson Cancer Center, Houston, Texas between 01/2018 and 05/2019 (data cut-off 12/21/2019). Progression-free survival (PFS) was defined as time from axi-cel infusion to progression/death or last follow-up, and the Breslow test was used for comparisons between subgroups. **Results:** One hundred patients with relapsed or refractory LBCL were included in the study, and 60 (60%) received corticosteroids for management of toxicities after axi-cel infusion. There was no significant difference in baseline tumor burden, disease stage or international prognostic index between the 2 groups. The median cumulative dexamethasone-equivalent dose was 186 mg (range, 8-1803 mg) and the median duration of corticosteroid treatment was 9 days (range 1-30); 45 (45%) patients started corticosteroid treatment between day 0 and 7, and 15 (15%) beyond day 7. After a median follow-up of 10 months (95% CI 8-10 months), median PFS was 8 months (95% CI, 3-13 months), and use of corticosteroids (any dose) showed a trend for association with shorter PFS (6 vs 9 months, p = 0.13). Use of high-dose corticosteroids (Quartiles (Q) 3-4, 195-1803 mg) significantly associated with shorter PFS (2 vs 9 months, p = 0.005). A trend for shorter PFS was observed among patients receiving corticosteroids for a prolonged time (Q3-Q4, 10-30 days) (5 vs 8 months, p = 0.12) and among patients starting corticosteroids within the first 7 days after axi-cel infusion (6 vs 11 months, p = 0.07). At most recent follow-up, 36 patients died, 28 of progression. Median overall survival has not been reached, and was significantly shorter among patients who received corticosteroids (13 vs not reached, p = 0.006). **Conclusions:** Early and prolonged use of high-dose corticosteroids is associated with early progression and death in patients with LBCL treated with axi-cel. Additional evaluation is needed to understand the mechanism underlying this association. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

8012 Poster Discussion Session; Displayed in Poster Session (Board #345), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Retreatment (reTx) of patients (pts) with refractory large B-cell lymphoma with axicabtagene ciloleucel (axi-cel) in ZUMA-1. *First Author: Frederick Lundry Locke, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL*

Background: Axi-cel, an autologous anti-CD19 chimeric antigen receptor (CAR) T cell therapy, is approved in the US and EU for pts with relapsed/refractory large B cell lymphoma after ≥ 2 prior therapies. In the ZUMA-1 pivotal study (NCT02348216), the objective response rate (ORR) was 83% (58% complete response [CR] rate; Locke et al. *Lancet Oncol.* 2019). While axi-cel has demonstrated durable responses in a subset of pts, approximately half of all responders relapsed, and little is known on the viability of reTx with CAR T cell therapy. Here we report outcomes of pts retreated with axi-cel in ZUMA-1. **Methods:** Pts with progressive disease (PD) were eligible for reTx if there was no evidence of CD19 loss by local review, and if during 1st Tx they did not experience any dose-limiting toxicities, as defined in Phase 1, or comparable toxicities in Phase 2. Pts received the same regimen at reTx as at 1st Tx: 2×10^6 CAR T cells/kg after conditioning chemotherapy. **Results:** Thirteen pts in Cohorts 1 – 4 received axi-cel reTx. Prior to 1st Tx, most pts (69%) had an IPI score 3-4, 85% had disease stage 3-4, and the median number of prior regimens was 3 (range, 2 – 6). At first Tx, 6 pts achieved a CR, 6 achieved partial response (PR), and 1 pt had stable disease (SD) prior to PD. Median duration of first response was 96 days (range, 56 – 274). There was no Grade ≥ 3 cytokine release syndrome (CRS; 6 pts each had Grade 1 and 2). There were no Grade 4 or 5 neurologic events (NEs; 2 pts had Grade 1, 1 had Grade 2, and 7 had Grade 3). Upon reTx, 54% of pts achieved response (4 CR, 3 PR). Response to reTx was more common among pts who achieved CR at 1st Tx (83%; 4/6 CR, 1 PR, 1 SD) than in pts who achieved PR at 1st Tx (33%; 2/6 PR, 1 SD, 3 PD), and no response was observed in the pt with SD at 1st Tx. Median duration of response at reTx was 81 days (range, 1 – 225+). Response with reTx was longer than that with 1st Tx for 2 pts. One pt remains in response 255 days post-reTx. Comparable rates of CRS were observed with reTx as with 1st Tx. Compared with 1st Tx, fewer pts experienced NEs with reTx, and those that did occur were of lower grade: 23% (3 of 13 pts) had Grade 3; 23% (3 of 13 pts) had Grade 1, and 8% (1 of 13 pts) had Grade 2. Peak CAR T cell expansion was lower upon reTx vs 1st Tx (median, 4.3 vs 66.1 CAR gene-marked cells/μL blood). **Conclusions:** Based on this limited sample size, reTx with axi-cel may have clinical efficacy, although transient, in some pts, especially those who achieve CR with 1st Tx. CAR T cell expansion and severe CRS and NEs may be attenuated at reTx. Further studies with additional pts are needed to confirm these results. Clinical trial information: NCT02348216. Research Sponsor: Kite, a Gilead Company.

8013 Poster Discussion Session; Displayed in Poster Session (Board #346), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Nivolumab and brentuximab vedotin (BV)-based, response-adapted treatment in children, adolescents, and young adults (CAYA) with standard-risk relapsed/refractory classical Hodgkin lymphoma (R/R cHL): Primary analysis. *First Author: Peter D. Cole, Rutger's Cancer Institute of New Jersey, New Brunswick, NJ*

Background: Outcomes for younger patients (pts) with R/R cHL are poor, particularly for those without complete metabolic response (CMR) before autologous transplant (auto-HCT). Nivolumab + BV has shown 67% CMR and a high 2-y PFS rate as first salvage in adults with R/R cHL. CheckMate 744 (NCT02927769) is an ongoing phase 2 study for CAYA with R/R cHL, evaluating a risk-stratified, response-adapted approach using nivolumab + BV and, for pts without CMR, BV + bendamustine. In the initial analysis of the standard-risk cohort (R2), the regimen was well tolerated with high CMR rates before consolidation with high-dose chemotherapy plus auto-HCT. We report data from the primary analysis. **Methods:** Pts were aged 5–30 y and had first-line treatment (tx) without auto-HCT. Risk stratification has been described previously (Harker-Murray, ASH 2018). Pts received 4 induction cycles of nivolumab + BV; pts without CMR by blinded independent central review (BICR) received BV + bendamustine intensification. Pts with CMR at any time could proceed to consolidation off study. Response was per Lugano 2014 criteria. Primary endpoint: CMR rate (Deauville ≤3) per BICR any time before consolidation. **Results:** At database lock, 44 pts were treated in R2 (median follow up: 20.9 mo); 43 received 4 induction cycles and 11 received intensification. Median age was 16 y (range 9–30); 24 (55%) pts had primary refractory cHL and 20 had relapsed cHL. CMR rates and ORR any time before consolidation and after induction are shown in Table. 1-y PFS rate by BICR was 91% (90% CI 77–96). During induction, 8 (18%) pts experienced grade (G) 3–4 tx-related adverse events (TRAEs); the most common any grade TRAEs were nausea and hypersensitivity (20% each). 1 TRAE led to discontinuation (G3 anaphylaxis). Most tx-related immune-mediated AEs were G1–2 (1 pt had 2 G3 infusion-related reactions). **Conclusions:** This risk-stratified, response-adapted approach offers a well-tolerated salvage strategy with high CMR rates and no new safety signals for CAYA with R/R cHL. Most pts avoided alkylator exposure prior to consolidation. Further follow up may confirm durability of disease control. Clinical trial information: NCT02927769. Research Sponsor: Bristol-Myers Squibb.

CMR and ORR per BICR and investigator (INV) in response-evaluable pts.

	BICR	INV
Any time before consolidation		
n	43	44
CMR, n (% [90% CI])	38 (88 [77–95])	39 (89 [78–95])
ORR, n (%)	42 (98)	43 (98)
After 4 cycles nivolumab + BV induction		
n	44	44
CMR, n (%)	26 (59)	29 (66)
ORR, n (% [90% CI])	36 (82 [70–91])	39 (89 [78–95])

8014 Poster Discussion Session; Displayed in Poster Session (Board #347), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II, multicenter trial of nivolumab (Nivo) and brentuximab vedotin (BV) in patients (Pts) with untreated Hodgkin lymphoma (HL) over the age of 60 years or unable to receive standard ABVD chemotherapy: Results of a study of Academic and Community Cancer Research United (ACCRU) RU051505I. *First Author: Bruce D. Cheson, Georgetown University Hospital, Washington, DC*

Background: HL is highly curable with > 90% of pts with limited and > 80% with advanced stage disease experiencing long-term disease-free survival. HL typically occurs in younger pts, yet 15-35% are > 60 yrs and experience a lower response rate, shorter survival, and greater toxicity. BV and checkpoint inhibitors have impressive activity in pts with relapsed and refractory HL. Thus, we initiated a phase II trial of BV-nivo in untreated pts with HL >60 yrs of age or considered unsuitable for standard ABVD therapy. **Methods:** Inclusion criteria: previously untreated pts with classical HL > 60 yrs or < 60 yrs but considered unsuitable for standard chemotherapy because of a cardiac ejection fraction of < 50%, diffusion capacity < 80%, or creatinine clearance > 30 but < 60 mL/min, or refused chemotherapy; ECOG PS 0-2, ANC >1500/mm^3, platelets > 100,000/mm^3, hemoglobin > 9 g/dl, bilirubin <1.5 x upper limits of normal (ULN), aspartate/alanine transaminases < 2.5 x ULN, amylase and/or lipase < 1.5 x ULN, and serum creatinine < 2.0 mg/dl. Pts received BV at 1.8 mg/kg (cap at 180 mg) and nivo 3 mg/kg every 21 days for 8 cycles. Response was assessed per the Lugano Classification. **Results:** The study accrued 46 pts between May 13, 2016-January 30, 2019. Median age of 71.5 yrs, 69.5% had ECOG PS 1 or 2; 64% stage III or IV; 39.1% with B symptoms; 4.3% were < 60 years. Median follow-up was 21.2 months (range 2.9, 38.5), and 35 pts (76.1%) completed all 8 cycles of therapy. At the interim analysis (1st 25 pts) ORR was 64% (52% mCR, 12% pMR) which was lower than the projected 80%. In all 46 pts, 45.7% achieved mCR and 15.2% mPR (ORR 60.9%); in evaluable pts, best ORR was 95% with 68% mCR. No clinical factors predicted response. Neither median duration of response nor median survival has been reached. Median PFS is 21.8 months (17.8, Not reached). 22 pts experienced 33 treatment delays, primarily due to BV. 22 pts experienced peripheral neuropathy (5 grade 3). Grade 4 toxicities included increased transaminases (n = 1), increased lipase and/or amylase (n = 2), pancreatitis (1). One pt died from cardiac arrest, possibly treatment-related. **Conclusions:** BV-nivo is active in untreated older HL pts with comorbidities. However, efficacy and response durability did not meet pre-specified criteria. Future trials based on these drugs, selecting pts most likely to benefit, may lead to a chemo-free approach for pts with HL. Clinical trial information: NCT02758717. Research Sponsor: Seattle Genetics, Bristol Myers Squibb.

8015 Poster Discussion Session; Displayed in Poster Session (Board #348), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Acalabrutinib (Acala) versus idelalisib plus rituximab (IdR) or bendamustine plus rituximab (BR) in relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL): ASCEND final results. *First Author: Paolo Ghia, Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milan, Italy*

Background: Acala is a next-generation, highly selective, covalent Bruton tyrosine kinase inhibitor approved for patients (pts) with CLL including those with R/R CLL. The efficacy and safety of acala alone vs IdR or BR were shown in R/R CLL pts in a preplanned interim analysis of ASCEND; final results are reported herein. **Methods:** In this randomized, multicenter, phase 3, open-label study (NCT02970318), R/R CLL pts were randomized 1:1 to receive oral (PO) acala 100 mg BID or investigator's (INV) choice of IdR (Id: 150 mg PO BID until progression or toxicity; R: 375 x1 then 500 mg/m^2 intravenously [IV] for 8 total infusions) or BR (B: 70 mg/m^2 IV and R: 375 x1 then 500 mg/m^2 IV for 6 total cycles) until progression or toxicity. Progression-free survival (PFS), overall survival (OS), overall response rate (ORR), and safety were assessed. **Results:** 310 pts (acala, n=155; IdR, n=119; BR, n=36) were enrolled (median age: 67 y; del(17p) 16%, del(11q) 27%, Rai stage 3/4 42%). At a median follow-up of 22.0 m, acala significantly prolonged INV-assessed PFS vs IdR/BR (median: not reached vs 16.8 m; hazard ratio: 0.27, P<0.0001); 18-m PFS rates were 82% for acala and 48% for IdR/BR. 18-m OS rate was 88% for both treatment regimens. ORR was 80% with acala vs 84% with IdR/BR (ORR + partial response with lymphocytosis: 92% vs 88%, respectively). Common adverse events (AEs) are listed in the Table. AEs led to drug discontinuation in 16% of acala, 56% of IdR, and 17% of BR pts. AEs of interest included atrial fibrillation (acala 6%, IdR/BR 3%), major hemorrhage (all grade; acala 3%, IdR/BR 3%), grade ≥3 infections (acala 20%, IdR/BR 25%), and second primary malignancies excluding non-melanoma skin cancer (acala 5%, IdR/BR 2%). **Conclusions:** Final ASCEND results with additional follow-up confirm earlier findings and support the favorable efficacy and safety of acala compared with standard-of-care regimens in R/R CLL pts. Clinical trial information: NCT02970318. Research Sponsor: Acerta Pharma, a member of the AstraZeneca group.

	Acala		IdR		BR	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Common AEs[a], n (%)						
Headache	34 (22)	1 (1)	7 (6)	0	0	0
Neutropenia	33 (21)	26 (17)	54 (46)	47 (40)	12 (34)	11 (31)
Diarrhea	30 (20)	3 (2)	58 (49)	29 (25)	5 (14)	0
Upper respiratory tract infection	30 (20)	3 (2)	19 (16)	4 (3)	4 (11)	1 (3)
Cough	25 (16)	0	18 (15)	1 (1)	2 (6)	0
Anemia	24 (16)	19 (12)	11 (9)	8 (7)	4 (11)	3 (9)
Pyrexia	21 (14)	1 (1)	22 (19)	8 (7)	6 (17)	1 (3)
Fatigue	17 (11)	2 (1)	10 (9)	1 (1)	8 (23)	1 (3)
Nausea	11 (7)	0	16 (14)	1 (1)	7 (20)	0
Infusion-related reaction	0	0	9 (8)	2 (2)	8 (23)	1 (3)

[a]Any grade in ≥15% of pts

8016 Poster Discussion Session; Displayed in Poster Session (Board #349), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Tolerability and durable respones of the PI3Kδ inhibitor ME-401 administered on an intermittent schedule in relapsed/refractory (R/R) follicular lymphoma (FL) and other B-cell malignancies. *First Author: Andrew David Zelenetz, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: ME-401, a potent, selective, and structurally differentiated oral PI3kδ inhibitor was evaluated in a dose escalation/expansion Phase 1b study, and previously demonstrated a high objective response rate (ORR) in FL and chronic lymphocytic leukemia (CLL)/small lymphocytic leukemia (SLL) when given on a continuous (CS) or an intermittent schedule (IS). IS appeared to significantly reduce the incidence of immune-mediated adverse events of special interest (AESI) associated with PI3kδ inhibitors (diarrhea, rash, transaminase elevation, pneumonitis). We report maturing data from patients treated on the IS in this study. **Methods:** Eligible patients (pts) had FL, CLL/SLL, marginal zone lymphoma (MZL) and diffuse large B-cell lymphoma (DLBCL), at least 1 prior therapy, adequate bone marrow and organs function, ECOG status ≤2, and no prior PI3K therapy. IS dosing: ME-401 at 60 mg/day for two 28-day cycles, followed by 7 days of therapy every 28-day cycle until disease progression or intolerance. Pts received ME-401 monotherapy (n = 21) or a combination with rituximab (n = 36) given at 375 mg/m^2 for 8 doses in Cycles 1-6. **Results:** Total of 57 pts treated with IS: 35 FL, 10 CLL/SLL, 4 MZL, and 8 DLBCL with 38 (67%) currently still ongoing. Median age: 66 years (range 38-94) and median prior therapies: 2 (range 1-8). As of January 2020, median follow-up = 9.7 mo (range 0.6-25.4+). Grade 3 AESI reported in 7 pts: 2 diarrhea (3.5%), 2 colitis (3.5%), 1 rash (2%), 1 ALT increased (2%), and 1 pneumonitis (2%). No Grade 3 AESI reported beyond Cycle 3. Discontinuation for AE in 3 pts (5%). There were no discernable safety differences between the monotherapy and rituximab combination groups. ORR was 83% in FL (76% in monotherapy group, 88% in combination group) and 89 % in CLL/SLL (100%, 83%), with median duration of response not reached. Median PFS was not reached in all patients with FL and CLL (combined analysis of both single agent and with rituximab). ORR was 100% (4/4) in MZL and 25 % (2/8) in DLBCL (in combination group only). **Conclusions:** ME-401 administered on an IS was well-tolerated, with a low-rate of Grade 3 class-related AESI and achieved a high-rate of durable objective responses in R/R indolent B-cell malignancies. These results may differentiate ME-401 and support further evaluation as a single-agent and in combination regimens. An ongoing global trial is evaluating ME-401 by IS in pts with FL after failure of ≥2 prior therapies (NCT03768505). Clinical trial information: NCT02914938. Research Sponsor: MEI Pharma, Inc.

8017 Poster Discussion Session; Displayed in Poster Session (Board #350), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Results of a completed phase I study of LAM-002 (apilimod dimesylate), a first-in-class phosphatidylinositol-3-phosphate 5 kinase (PIKfyve) inhibitor, administered as monotherapy or with rituximab or atezolizumab to patients with previously treated follicular lymphoma or other B-cell cancers. *First Author: Catherine S. Magid Diefenbach, Perlmutter Cancer Center at NYU Langone Health, New York, NY*

Background: LAM-002 is a selective inhibitor of PIKfyve that disrupts lysosomal homeostasis, inducing cytotoxicity in B-cell lymphoma models as monotherapy or with anti-CD20 or anti-PDL1 antibodies (Gayle et al., Blood 2017;129(13):1768). **Methods:** In this study, patients received LAM-002 orally 2-3 times per day (BID or TID) in a 3+3 escalation. Additional patients received LAM-002 125 mg BID as monotherapy; with rituximab 375 mg/m^2 intravenously (IV) and or subcutaneously weekly (Q1W) x 4 → Q8W x 4; or atezolizumab 1200 mg IV Q3W until disease progression or unacceptable toxicity. Pharmacokinetics (PK) were assessed for 8 hours postdose on Days 1 and 8. Efficacy was evaluated Q6-12W. **Results:** The study enrolled 62 patients (M:F n = 32/30); median [range] age = 69 [46-89] years; with diagnoses (n) of diffuse large B-cell lymphoma (25), follicular lymphoma (19), marginal zone lymphoma (8), mantle cell lymphoma (5), or chronic lymphocytic leukemia (5) to receive LAM-002 alone (n) at 50 mg BID (3), 100 mg BID (8), 150 mg BID (8), 75 mg TID (4), or 125 mg BID (20); LAM-002/rituximab (12); or LAM-002/atezolizumab (7). During LAM-002 dose-ranging (50 mg BID → 100 mg BID → 150 mg BID → 75 mg TID → 125 mg BID) transient, reversible nausea and/or diarrhea occurred at 150 mg BID and 75 mg TID, resulting in a LAM-002 recommended Phase 2 dosing regimen (RP2DR) of 125 mg BID. Among 39 patients receiving LAM-002, 125 mg BID, alone or in combination for up to 22 cycles (1.9 years), adverse events were typically low-grade. LAM-002 PK showed rapid absorption, dose proportionality, minimal accumulation, and no substantive changes with rituximab or atezolizumab coadministration. In patients with follicular lymphoma and median [range] prior therapies = 3 [1-9] treated with the RP2DR, objective response rates were 2/7 (29%; 1 complete response [CR], 1 partial response [PR]) with LAM-002, 5/8 (63%; 1 CR, 4 PRs) with LAM-002/rituximab, and 2/2 (100%; 2 PRs) with LAM-002/atezolizumab. **Conclusions:** LAM-002, the first clinical PIKfyve inhibitor, is safe alone or with full-dose anti-CD20 or anti-PD-L1 inhibition. LAM-002 does not cause the myelosuppressive or immune adverse events associated with lenalidomide or PI3K inhibitors. Promising efficacy supports registration-directed Phase 2/3 testing of LAM-002 monotherapy and combination therapy for patients with previously treated follicular lymphoma. Clinical trial information: NCT02594384. Research Sponsor: AI Therapeutics, Inc.

8018 Poster Discussion Session; Displayed in Poster Session (Board #351), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Outcomes of GDPT (gemcitabine, cisplatin, prednisone,thalidomide) versus CHOP in newly diagnosed peripheral T-cell lymphoma patients. *First Author: Ling Li, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China*

Background: Peripheral T-cell lymphoma(PTCL) is highly heterogeneous invasive NHL.There is no consensus standard treatment for it now. So outcomes of GDPT versus CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) in treating newly diagnosed PTCL were compared. **Methods:** An open-label prospective clinical trial with 153 newly diagnosed PTCL patients conducted between January 2010 and December 2018 was designed. Patients were randomly assigned to the GDPT group (77 cases) and CHOP group (76 cases). Patients in each group were further divided into four subgroups: PTCL-NOS, ALCL, AITL, and an other types, in accordance with pathological patterns. Based on expression of RRM1, TOP2A, TUBB3 and ERCC1, patients were divided into groups with high and low gene expression levels. Clinical characteristics, side effects, efficacy, PFS and OS were compared. **Results:** There were no significant differences in the basic clinical features or side effects between the GDPT and CHOP groups. The ORR of the GDPT group was better than that of the CHOP group (66.3%vs. 50.0%, *P*= 0.042), as was the CR rate (42.9% vs. 27.6%, *P*= 0.049). Patients in the GDPT group had a longer PFS and OS than the CHOP group. The 4-year PFS and OS rates in the GDPT group were both superior to those in the CHOP group (63.6% vs. 53.0% for PFS, *P*= 0.035; 66.8% vs. 53.6% for OS, *P*= 0.039).In the GDPT group, the difference in CR between the four subgroups was statistically significant (P = 0.046).In the CHOP group, differences in both CR and ORR among the four subgroups were statistically significant (*P*= < 0.001 and *P*= 0.005, respectively).There were also statistically significant differences in CR between patients treated with CHOP and GDPT in the PTCL-NOS subgroup, AITL subgroup, and the other types subgroup(*P*= 0.015;*P*= 0.003;*P*= 0.005, respectively).The data also showed a significant difference in OS among the four subgroups within the GDPT group (*P*= 0.001).The OS of AITL was shorter than that of the other three subgroups. Four subgroups of CHOP showed a significant difference in PFS (*P*= 0.019). There was no statistical association between responses and the gene expression levels of RRM1, ERCC1, TUBB3 and TOP2A. **Conclusions:** The GDPT group had better response rates and prolonged the patients' PFS and OS. As a promising new regimen, GDPT is expected to become the first-line therapy for PTCL. New agents should be applied to patients who do not achieve good responses with previous treatment, such as those diagnosed with angioimmunoblastic T cell lymphoma. Clinical trial information: NCT01664975. Research Sponsor: the National Natural Science Foundation of China, Provincial Medical Science and Technology Research Project in Henan.

8019 Poster Discussion Session; Displayed in Poster Session (Board #352), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Lenalidomide plus R-GDP (R2-GDP) in relapsed/refractory diffuse large B-cell lymphoma: Final results of the R2-GDP-GOTEL trial. *First Author: Luis de la Cruz Merino, Clinical Oncology Department, Hospital Universitario Virgen Macarena, Seville, Spain*

Background: Lenalidomide is an immunomodulatory drug that could reverse rituximab refractoriness in lymphoma patients (pts). We conducted an open label multicenter phase 2 trial testing the efficacy and toxicity of a combination of lenalidomide and rituximab (R2) plus GDP schedule (R2-GDP) in Relapsed/Refractory Diffuse Large B Cell Lymphoma (R/R DLBCL) pts, not suitable for autologous stem cell transplant (ASCT). **Methods:** Patients with R/R DLBCL previously treated with at least 1 prior line of immunochemotherapy including rituximab, and not candidates for ASCT, were eligible. After a run-in phase period, treatment consisted of an induction phase with lenalidomide (LEN) 10 mg po d1-14, rituximab 375 mg/m2 iv d1, cisplatin 60 mg/m2 iv d1, gemcitabine 750 mg/m2 iv d1 and d8 and dexamethasone 20 mg d1-3, up to a maximum of 6 cycles. Pts without disease progression (DP) entered into a maintenance phase with LEN 10 mg, or last LEN dose received in the induction phase, d1-21 in cycles every 28 days. Primary endpoint was overall response rate (ORR) by investigator assessment. Secondary endpoints included disease free survival (DFS), event free survival (EFS), overall survival (OS), safety and response by cell of origin (COO), type of DLBCL (double-triple hit) and other microenvironment and genomic biomarkers. **Results:** 79 pts were enrolled between April 2015 and September 2018. Median age was 70 years (range 23-86), 48,7% women. 78 pts were considered for efficacy and safety in the intention to treat (ITT) analysis. With a median follow-up of 13 months at the time of cut-off (November 2019), ORRwas 59.0%, with 32.1% complete responses (CR) and 26.9% partial responses (PR). In the primary refractory population (n = 33), ORR was 45.5%, with 21.2% CR and 24.3% PR. There were no statistically significant differences in ORR with respect to COO. In Double-Hit R/R DLBCL (n = 16), ORR was 37.5% with 25% CR. Median OS was 12.0 months (6.9-17.0). Most common grade 3/4 (G3/4) adverse events were thrombocytopenia (60.2%), neutropenia (60.2%) and anemia (26.9%). Febrile neutropenia occurred in 14.1% pts. Most frequent non-hematologic G3/4 events were asthenia (19.2%), infection (15.3%) and renal insufficiency (6.4%). There were 4 toxic deaths related to the R2-GDP schedule. **Conclusions:** LEN with Rituximab and GDP (R2-GDP) is feasible and active in R/R DLBCL. Results in the primary refractory DLBCL population are particularly promising. Analysis of COO did not revealed differences in response rates. Immune biomarkers results will be showed at the meeting. Clinical trial information: EudraCT 2014-001620-29. Research Sponsor: CELGENE.

8020 Poster Discussion Session; Displayed in Poster Session (Board #353), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

RE-MIND study: A propensity score-based 1:1 matched comparison of tafasitamab + lenalidomide (L-MIND) versus lenalidomide monotherapy (real-world data) in transplant-ineligible patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). *First Author: Grzegorz S. Nowakowski, Division of Hematology, Mayo Clinic, Rochester, MN*

Background: Patients with R/R DLBCL ineligible for autologous stem cell transplant (ASCT) have a poor prognosis. In these patients, tafasitamab (anti-CD19 antibody) plus lenalidomide (LEN) has shown encouraging results in the open-label, single-arm, phase II L-MIND study (n = 81; NCT02399085). To evaluate the contribution of tafasitamab to the activity of this doublet, we conducted a global, real-world study of patients treated with LEN monotherapy (RE-MIND; NCT04150328). Here we present the primary analysis of a 1:1 patient-level matched comparison between the L-MIND and RE-MIND cohorts. **Methods:** Patients treated with LEN monotherapy for R/R DLBCL were enrolled in the observational, retrospective RE-MIND cohort. As in L-MIND, patients had 1–3 prior systemic therapies, including ≥1 CD20-targeting regimen; were aged ≥18 years; and were not eligible for ASCT. A 1:1 estimated propensity score (ePS) matching methodology ensured balancing of nine pre-specified baseline covariates. The primary analysis set, Matched Analysis Set 25 (MAS25), included patients who received a LEN starting dose of 25 mg/day. The primary endpoint was investigator-assessed best objective response rate (ORR). Key secondary endpoints included overall survival (OS) and complete response (CR) rate. **Results:** 490 patients were enrolled in RE-MIND across 58 centers in the US and Europe, of which 140 fulfilled the ePS matching criteria. The MAS25 included 76 patients each from the two cohorts. Baseline characteristics between cohorts were comparable. The primary endpoint was met with a significantly better ORR of 67.1% (95% CI: 55.4–77.5) for the L-MIND cohort versus 34.2% (95% CI: 23.7–46.0) for the RE-MIND cohort (odds ratio 3.89; 95% CI: 1.90–8.14; $p < 0.0001$). The CR rate was 39.5% (95% CI: 28.4–51.4) in the L-MIND cohort and 13.2% (95% CI: 6.5–22.9) in the RE-MIND cohort. A significant difference in OS favored the L-MIND cohort (HR = 0.499; 95% CI: 0.317–0.785). ORR and CR outcomes in the RE-MIND cohort were similar to the published literature for LEN monotherapy in R/R DLBCL. **Conclusions:** Significantly better ORR, CR and OS indicate potential synergistic effects of the tafasitamab + LEN combination in ASCT-ineligible R/R DLBCL. ePS-based 1:1 matching allows robust estimation of the treatment effect of tafasitamab when added to LEN. RE-MIND demonstrates the utility of real-world data in interpreting non-randomized trials. Clinical trial information: NCT04150328. Research Sponsor: MorphoSys AG.

8021 Poster Session (Board #354), Fri, 8:00 AM-11:00 AM

Autologous stem cell transplantation for untreated transformed indolent B-cell lymphoma in first remission: An international, multicenter propensity matched study. *First Author: Collin K Chin, The University of Texas MD Anderson Cancer Center, Department of Lymphoma/Myeloma, Houston, TX*

Background: Transformation of untreated indolent B-cell lymphoma (Tr-iNHL) is associated with poor outcomes. Current practices are extrapolated from prospective studies of *de novo* large B-cell lymphoma (DLBCL) or small retrospective studies. High dose chemotherapy (HDC) and autologous stem cell transplantation (ASCT) is used as consolidation in first remission (CR1) in some centers but the evidence-base is weak. **Methods:** CLL/SLL, MCL as primary diseases and non-DLBCL transformations were excluded. Propensity score analysis (PSM) using the "greedy match" algorithm was used to match the baseline covariates to adjust for potential selection bias. Landmark analysis was performed with time zero at 3 months after completion of front line chemotherapy (FLC). Kaplan-Meier method and the Cox proportional hazards model were was used for time-to-event analysis including progression-free survival (PFS) and overall survival (OS). **Results:** 319 transplant eligible patients (age <75, LVEF >45%, no severe lung disease, CR by PET or CT >3 months after FLC) who received >/= standard RCHOP intensity FLC were identified across three centers in Australia & US. 283 (89%) patients had follicular lymphoma, 30 (9%) marginal zone lymphoma, 6 (2%) other subtypes. 49 patients underwent HDC and ASCT in CR1, a matched cohort of 98 pts based on age, stage, HGBL-DH and ECOG PS at diagnosis was generated with a 1:2 ratio using PSM. After a median follow-up of 3.6 (min: 0.1, max: 18.3) years, ASCT was associated with significantly superior PFS on multivariable analysis (MVA) (HR 0.51, 0.27-0.98; P=0.043). Univariate analysis demonstrated a trend towards inferior OS in the ASCT cohort (HR 2.36; 0.87-6.42; P=0.092) with more deaths in the ASCT arm due to PD (8% *v* 4%). Of the 40 patients (41%) with relapsed disease in the non-ASCT cohort–15 patients underwent salvage HDC & ASCT with 7/15 (47%) ongoing CR; 10 patients underwent CAR-T therapy (5 relapse post ASCT, 4 refractory disease, 1 relapse post FLC) with 6/10 (60%) ongoing CR; 3 patients underwent allogeneic SCT (2 relapse post ASCT, 1 relapse post FLC) with 2/3 (67%) ongoing CR. **Conclusions:** Although ASCT in CR1 may improve initial duration of disease control in *de novo* Tr-iNHL, the impact on OS is less clear with effective salvage therapies in the CAR-T era. Research Sponsor: None.

8022 Poster Session (Board #355), Fri, 8:00 AM-11:00 AM

Effect of adding ublituximab to ibrutinib on PFS, ORR, and MRD negativity in previously treated high-risk chronic lymphocytic leukemia: Final results of the GENUINE phase III study. *First Author: Jeff P. Sharman, Willamette Valley Cancer Institute and US Oncology Research Center, Eugene, OR*

Background: The BTK inhibitor ibrutinib (IB) has advanced the treatment for patients (pts) with CLL, however, among pts with high-risk CLL, disease control with IB is less durable. Ublituximab (UTX) is a glycoengineered mAb with enhanced ADCC. The GENUINE study evaluated the addition of UTX to IB vs. IB alone in high-risk rel/ref CLL. With a median follow up now 3.5+ yrs, we present the final results. **Methods:** Eligible pts having rel/ref CLL with centrally confirmed del17p, del11q, and/or a TP53 mutation, were randomized 1:1 to IB (420 mg QD) alone or with UTX (900 mg on D1, 8, 15 of Cy 1, D1 of Cy 2-6, and Q3 Cy thereafter). No limit on # of prior Tx; prior IB excluded. Primary endpoint was overall response rate (ORR) by iwCLL 2008 (excludes PR-L); secondary endpoints were CR rate, peripheral blood MRD negativity (analyzed centrally), PFS, and safety. Response was by blinded independent review. **Results:** 117 pts were treated (59 in UTX + IB arm; 58 in IB arm). Med age was 66 yrs and med # of prior Tx was 1 (range 1-5) for each arm. Baseline features were relatively balanced including ECOG, gender, and med time since diagnosis (6+ yrs). 17p del was greater in the IB arm (50% vs 44%); bulky disease was greater in UTX + IB arm (47% vs 28%); IGHV-unmut was 83% for both arms. At data-cutoff of Sep 1, 2019, AEs were comparable between the arms, except infusion reactions (UTX + IB: All G 53% / G 3/4 3%) and neutropenia (All G 36% vs 21%, G 3/4 19% vs. 12%) which were higher for UTX + IB. At a med follow up of 42 mos, all efficacy endpoints were in favor of UTX + IB (see Table). **Conclusions:** In contrast to prior studies adding rituximab to IB, GENUINE is the first randomized trial to demonstrate a PFS benefit with the addition of an anti-CD20 to IB. Increasing depth of response (CR rate, MRD-neg) post first year of Tx supports maintenance therapy with UTX. Clinical trial information: NCT02301156. Research Sponsor: TG Therapeutics, Inc.

Efficacy	UTX + IB	Ibrutinib	p-value
ORR (CR/CRi, PR)	53 (90%)	40 (69%)	$p < 0.01$
CR/CRi	12 (20%)	3 (5%)	$p < 0.05$
ORR (CR/CRi, PR, PR-L)	55 (93%)	45 (77.5%)	$p < 0.05$
MRD-neg	27 (46%)	4 (7%)	$p < 0.0001$
PFS (All pts; N = 117)	Med NR (NE, NE) HR 0.455 (95%CI: 0.239 0.865)	Med 35.9 mos (17, NE)	p = 0.016
PFS (17p del and/or p53; N = 63)	Med NR (NE, NE) HR 0.253 (95%CI: 0.099 0.646)	Med 18.9 mos (11.4, NE)	p = 0.004
OS	HR 0.532 (95%CI: 0.241 1.174)		p = 0.118

PFS was superior for UTX + IB vs. IB alone, driven primarily by pts with del17p/p53mut. No meaningful difference in PFS was observed for pts with del11q. Among pts treated with UTX + IB, MRD-neg was associated with significant improvement in PFS. OS at 4 yrs was 82% vs. 70% for UTX + IB vs. IB alone.

8023 Poster Session (Board #356), Fri, 8:00 AM-11:00 AM

Comparison of efficacy and safety with obinutuzumab plus chemotherapy versus rituximab plus chemotherapy in patients with previously untreated follicular lymphoma: Updated results from the phase III Gallium Study. *First Author: William Townsend, Cancer Research UK and UCL Cancer Trials Centre, London, United Kingdom*

Background: Immunochemotherapy is standard of care for patients (pts) with previously untreated advanced stage follicular lymphoma (FL). Four-year data from the Phase III GALLIUM study (NCT01332968) have previously demonstrated an improvement in the primary endpoint of investigator-assessed progression-free survival (PFS) for obinutuzumab (GA101, G) plus chemotherapy (G-chemo) versus rituximab plus chemotherapy (R-chemo) (Townsend et al. ASH 2018). Here, we report efficacy and safety results from an updated analysis. **Methods:** Eligibility criteria: ≥18 years; advanced stage, previously untreated grade 1–3a FL; requiring treatment according to Groupe d'Etude des Lymphomes Folliculaires criteria. Pts were randomized 1:1 to receive G 1000mg IV (day [D] 1, 8 and 15 of Cycle 1; D1 of each subsequent cycle) or R 375mg/m^2 IV (D1 of each cycle) with CHOP, CVP, or bendamustine for 6 or 8 cycles. Responders received maintenance therapy with the same monoclonal antibody every 2 months for 2 years. **Results:** 1202 pts (median age 59 years) were enrolled (n = 601 per treatment arm). Median duration of follow-up was 76.5 months. Pts receiving G- vs R-chemo demonstrated improved PFS (5-year PFS: hazard ratio [HR] 0.76; 95% CI: 0.62–0.92; p = 0.0043; 70.5% [95% CI: 66.4–74.1] vs 63.2% [95% CI: 59.0–67.1]). There was no notable difference in 5-year overall survival (OS), with few events in either arm (HR 0.87; 95% CI: 0.62–1.22; p = 0.41; G-chemo: 90.2% [95% CI: 87.5–92.4]; R-chemo: 89.4% [95% CI: 86.6–91.6]). Time-to-next-treatment (TTNT) was greater in the G- vs R-chemo arm (5-year TTNT rate: HR 0.72; 95% CI: 0.57–0.90; p = 0.0039; 79.7% [95% CI: 76.1–82.7] vs 72.9% [95% CI: 69.1–76.4]). Incidence of grade 3–5 adverse events was 79.3% in the G-chemo arm and 71.2% in the R-chemo arm, and consistent with those reported in the primary analysis (Marcus et al. N Engl J Med 2017). **Conclusions:** These data further demonstrate the clinically meaningful and durable benefit of treatment with G-chemo relative to R-chemo in previously untreated FL pts. Acknowledgement: GALLIUM was sponsored by F. Hoffmann-La Roche Ltd. Third-party medical writing assistance, under the direction of William Townsend, was provided by Louise Profit and Stephanie Lacey of Gardiner-Caldwell Communications, and was funded by F. Hoffmann-La Roche Ltd. Clinical trial information: NCT01332968. Research Sponsor: F. Hoffmann-La Roche Ltd.

8024 Poster Session (Board #357), Fri, 8:00 AM-11:00 AM

Acalabrutinib in treatment-naïve chronic lymphocytic leukemia: Mature results from phase II study demonstrating durable remissions and long-term tolerability. *First Author: John C. Byrd, The Ohio State University Comprehensive Cancer Center, Columbus, OH*

Background: The next-generation Bruton tyrosine kinase inhibitor acalabrutinib was approved in patients (pts) with treatment-naïve (TN) and relapsed/refractory chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) based on two complementary phase 3 studies, ELEVATE-TN and ASCEND. This report of ACE-CL-001 (NCT02029443), the first phase 2 study of acalabrutinib, provides the longest safety and efficacy follow-up to date in symptomatic TN CLL pts. **Methods:** Adults with TN CLL/SLL were eligible if they met iwCLL 2008 criteria for treatment, were inappropriate for/declined standard chemotherapy and had ECOG performance status 0–2. Pts received acalabrutinib 100 mg BID or 200 mg QD, later switching to 100 mg BID, until progressive disease (PD) or unacceptable toxicity. Primary endpoint was safety. Events of clinical interest (ECI) were based on combined AE terms for infections, bleeding events, hypertension, and second primary malignancies (SPM) excluding non-melanoma skin, and on a single AE term for atrial fibrillation. Additional endpoints included investigator-assessed overall response rate (ORR), duration of response (DOR), time to response (TTR), and event-free survival (EFS). **Results:** Ninety-nine pts (n = 62 100 mg BID; n = 37 200 mg QD), were treated [median age: 64 years, 47% Rai stage 3–4 disease, 10% del(17p), 62% unmutated IGHV]. At median follow-up of 53 months (range, 1–59), 85 (86%) pts remain on treatment; most discontinuations were due to AEs (n = 6) or PD (n = 3 [n = 1 Richter transformation]). Most common AEs (any grade) were diarrhea (52%), headache (45%), upper respiratory tract infection (44%), arthralgia (42%), and contusion (42%). All-grade and grade ≥3 ECIs included infection (84%, 15%), bleeding events (66%, 3%), and hypertension (22%, 11%). Atrial fibrillation (all grades) occurred in 5% of pts (incidence: 1% in years 1, 2, 4; 3% in year 3). SPMs excluding non-melanoma skin (all grades) occurred in 11%. Serious AEs were reported in 38% of pts; those in > 2 pts were pneumonia (n = 4) and sepsis (n = 3). ORR was 97% (7% complete response; 90% partial response). Median TTR was 3.7 months (range, 2–22). Response rates were similar across high-risk groups. Median DOR and median EFS were not reached; 48-month DOR rate was 97% (95% CI, 90%–99%), and 48-month EFS rate was 90% (95% CI, 82%–94%). **Conclusions:** Long-term data from ACE-CL-001 further support the favorable results with acalabrutinib in phase 3 studies and demonstrate durable responses with no new long-term safety issues. Clinical trial information: NCT02029443. Research Sponsor: Acerta Pharma, a member of the AstraZeneca group.

8025 Poster Session (Board #358), Fri, 8:00 AM-11:00 AM

First-line immunochemotherapy for follicular lymphoma in the GALLIUM study: Prognostic value of PET-CT status after long-term follow-up. *First Author: Tina Nielsen, F. Hoffmann-La Roche Ltd., Basel, Switzerland*

Background: The prognostic value of ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) response assessment following first-line immunochemotherapy for advanced-stage symptomatic follicular lymphoma (FL) was previously demonstrated for patients (pts) enrolled in the Phase III GALLIUM study (NCT01332968; Trotman et al. ICML 2017). Here, we evaluated the association between PET complete metabolic response (CMR) and survival after longer follow-up in this patient population. **Methods:** In the GALLIUM study, 1202 pts with previously untreated FL were randomized 1:1 to induction therapy of 1000mg obinutuzumab (G; Days 1, 8, 15 of Cycle 1 then Day 1 of subsequent cycles) or 375mg/m^2 rituximab (R; Day 1 of each cycle), in combination with chemotherapy (CHOP, CVP, or bendamustine) (Marcus et al. New Engl J Med 2017). PET-CT scans were mandatory, where available, at baseline and end-of-induction (EOI) for the first 170 pts enrolled, and optional thereafter. For this response analysis, the Lugano 2014 criteria were applied by an independent review committee (IRC) (Cheson et al. J Clin Oncol 2014). Associations between EOI PET complete metabolic response (PET-CMR) status and progression-free survival (PFS) and overall survival (OS) were evaluated, with hazard ratios (HR) stratified according to chemotherapy regimen and FL International Prognostic Index. **Results:** Of the 609 pts with a baseline PET scan, 595 (98%) had detectable lesions. Of these, 519 pts had an EOI PET evaluable by Lugano 2014 criteria. At EOI, per IRC assessment, 450/595 (76%) pts had achieved CMR. Pts with non-available scans were considered as non-responders and were excluded from the landmark (LM) analyses. Pts who died or progressed (CT-based progression assessment) before or at EOI were excluded from the PFS LM analysis; pts who died before EOI were excluded from the OS LM analysis. After a median follow-up of 76.5 months, EOI PET status was highly prognostic for both longer investigator-assessed PFS (non-CMR vs CMR: HR 3.40; 95% CI: 2.33–4.97; $p < 0.0001$) and longer OS (HR 3.34; 95% CI: 1.81–6.17; $p < 0.0001$). Six-year investigator-assessed PFS from EOI was 62.6% (95% CI: 57.0–67.6) for CMR pts compared with 23.4% (95% CI: 12.2–36.7) for non-CMR pts; the corresponding OS was 91.3% (95% CI: 88.1–93.6) vs 79.6% (95% CI: 68.0–87.4). **Conclusions:** With more than 6 years of follow-up, this analysis confirms that after first-line chemoimmunotherapy for FL, achieving CMR on PET-CT is an early and strong predictor of increased PFS and OS. Clinical trial information: NCT01332968. Research Sponsor: GALLIUM was sponsored by F. Hoffmann-La Roche Ltd. Third-party medical writing assistance, under the direction of Judith Trotman, was provided by Aisling Lynch and Katie Smith of Gardiner-Caldwell Communications, and was funded by F. Hoffmann-La Roche Ltd.

8026 Poster Session (Board #359), Fri, 8:00 AM-11:00 AM

Cause of death in patients with newly diagnosed chronic lymphocytic leukemia (CLL) stratified by the CLL-International Prognostic Index (CLL-IPI). *First Author: Yucai Wang, Mayo Clinic, Rochester, MN*

Background: CLL progression and CLL-related complications (infections and second malignancies) were the leading cause of death (COD) in a prospective cohort of CLL patients (Strati, BJH 2017). The CLL-IPI integrates major clinical and molecular prognostic factors and stratifies patients into 4 risk groups with distinct prognosis. It is unknown if COD differs according to CLL-IPI risk group in patients with newly diagnosed CLL. **Methods:** Patients diagnosed with CLL between 1/2000-12/2019 and seen within 1 year of diagnosis were identified from the Mayo Clinic CLL database. Cumulative incidences of cause-specific death were analyzed using Gray's test, with deaths from different causes treated as competing events and deaths from unknown causes excluded. **Results:** 1276 patients were included in this study. The median age at diagnosis was 63 years (range 24-92), and 880 (69%) were male. Based on CLL-IPI score, 449 (35%) had low risk disease, 443 (35%) had intermediate risk disease, and 384 (30%) had high/very high risk disease. Median follow-up time for the study was 6 years; 286 deaths occurred. The COD was CLL progression in 99 (35%), infection in 16 (6%), second malignancy in 47 (16%), CLL-unrelated in 59 (21%), and unknown in 65 (23%) patients. The rates of death due to CLL progression were higher (17.3% at 5 years; 30.3% at 10 years) than the rates due to CLL-related complications (5.7% at 5 years; 12.9% at 10 years) or due to CLL-unrelated causes (8.6% at 5 years; 16.9% at 10 years) in the CLL-IPI high/very high risk group, but not the CLL-IPI low or intermediate risk group (Table). A higher CLL-IPI risk group was associated with a higher rate of death due to CLL progression ($P < 0.001$), as well as a higher rate of death due to CLL-related complications ($P = 0.013$), and CLL-unrelated causes ($P < 0.001$). **Conclusions:** Causes of death in newly diagnosed CLL patients differ according to their CLL-IPI risk group. In patients with high/very high risk CLL, improving CLL disease control with novel agents seems justified. In patients with low/intermediate risk CLL, there should be increased efforts to reverse immune dysfunction to reduce infections and second malignancies. Research Sponsor: None.

	Cumulative Incidence of Death (%)								
	CLL progression			CLL-related complications (infection or second malignancy)			CLL-unrelated		
	5-yr	10-yr	*P* value	5-yr	10-yr	*P* value	5-yr	10-yr	*P* value
All patients	5.7	13.2		3.2	8.5		3.8	8.7	
CLL-IPI risk			< 0.001			0.013			< 0.001
Low	0.3	2.8		2.1	6.4		0.6	3.6	
Intermediate	2.0	10.4		2.5	7.0		3.1	7.4	
High/Very high	17.3	30.3		5.7	12.9		8.6	16.9	

8027 Poster Session (Board #360), Fri, 8:00 AM-11:00 AM

Fixed-duration venetoclax-obinutuzumab for previously untreated patients with chronic lymphocytic leukemia: Follow-up of efficacy and safety results from the multicenter, open-label, randomized, phase III CLL14 trial. *First Author: Othman Al-Sawaf, Department I of Internal Medicine and Center of Integrated Oncology Cologne-Bonn, German CLL Study Group, University of Cologne, Cologne, Germany*

Background: The CLL14 trial demonstrated significant improvement of progression-free survival (PFS) with fixed-duration venetoclax-obinutuzumab (VenG) as compared to chlorambucil-obinutuzumab (ClbG) in patients with previously untreated CLL and coexisting conditions. Here, we report follow-up data on safety and efficacy. **Methods:** Patients with previously untreated CLL and coexisting conditions were randomized 1:1 to receive 12 cycles of venetoclax with 6 cycles of obinutuzumab or 12 cycles of chlorambucil with 6 cycles of obinutuzumab. Primary endpoint was investigator-assessed progression-free survival. Key secondary endpoints were response rates, rates of minimal residual disease (measured every 6 months up to 5 years after last patient enrolment) and overall survival. Follow-up is ongoing but all patients are off study treatment. This trial was registered with ClinicalTrials.gov, number NCT02242942. **Results:** Of the 432 enrolled patients, 216 were randomly assigned to receive VenG and 216 to receive ClbG. After a median follow-up of 39.6 months (interquartile range 36.75 - 43.04), progression-free survival continued to be superior for VenG as compared to ClbG (median not reached vs 35.6 months; hazard ratio [HR] 0.31 [0.22-0.44], $p < 0.001$). At 3 years, the estimated progression-free survival rate was 81.9% in the VenG arm and 49.5% in the ClbG arm. This benefit was consistently observed across all clinical and biological risk groups, including patients with *TP53* mutation/deletion and unmutated IGHV status. Of note, PFS was also significantly longer for VenG treated patients with mutated IGHV status. Assessment of minimal residual disease 18 months after end of treatment showed that 47.2% of patients in the VenG arm had undetectable (u) uMRD ($< 10^{-4}$), 13% had low (L)-MRD ($\geq 10^{-4}$ and $< 10^{-2}$) and 7.9% high (H)-MRD ($\geq 10^{-2}$), compared to 7.4% uMRD, 17.1% L-MRD, 26.9% H-MRD in the ClbG arm. No difference has been observed (HR 1.027, 95% CI 0.602-1.753, p = 0.921) for overall survival; median overall survival has not been reached in either group. Second primary malignancies were reported in 36 (17%) patients in the VenG arm and 22 (10.3%) in the ClbG arm. No new safety signals were observed. **Conclusions:** The results suggest that the superior efficacy and deep remissions after fixed-duration VenG are maintained during extended follow-up, and show the long-term benefits of 12 cycles of VenG across all known risk categories. Clinical trial information: NCT02242942. Research Sponsor: F. Hoffmann–La Roche and AbbVie.

8028 Poster Session (Board #361), Fri, 8:00 AM-11:00 AM

Impact of premature venetoclax (Ven) discontinuation/interruption on outcomes in relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL): Phase III MURANO study results. *First Author: Anthony R. Mato, Center for CLL, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Ven + rituximab (VenR) has a manageable safety profile and improves survival in patients (pts) with R/R CLL, but discontinuation/interruption is frequent. We present new data from the Phase III MURANO study on the impact of Ven early discontinuation/interruption on outcomes in pts with R/R CLL. **Methods:** Time-dependent Cox proportional hazards regression models, stratified by 17p deletion and risk status, evaluated the impact of Ven discontinuation/interruption on investigator-assessed PFS and OS. Analyses were performed retrospectively (without type-1 error control) in intent-to-treat pts with R/R CLL from the fixed-duration VenR arm of MURANO (NCT02005471; data cut-off: May 8, 2019). **Results:** 140/194 pts (72%) in the VenR arm completed 2 years of therapy. Early discontinuation occurred in 54/194 (28%) pts (adverse events [AEs]: 29, disease progression [PD]: 12, withdrawal: 5, physician decision: 3, death: 2, other: 2, non-compliance: 1). Median Ven durations for pts discontinuing due to AEs and PD: 11.3 (0.5–24.6) and 17.1 (4.6–25.1) months, respectively ($p = 0.08$). Inferior PFS was observed in pts who discontinued Ven early for any reason except PD or due to AEs, versus those who completed therapy (Table). Greater cumulative Ven exposure significantly reduced risk of a PFS/OS event (PFS: HR 0.93, 95% CI 0.88–0.99, $p = 0.0168$; OS: HR 0.85, 95% CI 0.79–0.92, $p < 0.0001$). Treatment interruption for AEs occurred in 134/194 (69%) pts, most commonly due to neutropenia (84/194; 43%), per protocol requirements. Median duration of interruption: 9 (1–93) days. Treatment interruption, regardless of duration, had no impact on PFS or OS (Table). 36 (19%) pts with interruptions later discontinued Ven. **Conclusions:** In MURANO, early Ven discontinuation was associated with suboptimal outcomes; Ven interruption was not. These data highlight the importance of effective control of toxicity to realize the full benefit of VenR treatment. Clinical trial information: NCT02005471. Research Sponsor: Genentech and AbbVie provided financial support for the study. Third-party medical writing assistance, under the direction of authors was provided by Rachel Dobb of Gardiner-Caldwell Communications, and was funded by F. Hoffmann-La Roche Ltd.

Impact of early Ven discontinuation/interruption on PFS and OS.

Ven	PFS HR (95% CI)	p-value	OS HR (95% CI)	p-value
Early discontinuation				
Any* (n = 181)	5.98 (3.31–10.82)	< 0.0001	–	–
Due to AE (n = 174)	5.82 (2.39–11.57)	< 0.0001	–	–
Interruption†‡				
Any	0.67 (0.38–1.19)	0.17	0.97 (0.43–2.21)	0.95
≥8 days	1.01 (0.59–1.72)	0.97	1.35 (0.60–3.02)	0.46
≥14 days	0.92 (0.51–1.65)	0.77	1.47 (0.63–3.45)	0.37
≥21 days	0.82 (0.41–1.65)	0.58	1.31 (0.46–3.73)	0.62

*Except PD; †PFS n = 165, OS n = 194; ‡Consecutive days

8029 Poster Session (Board #362), Fri, 8:00 AM-11:00 AM

Brentuximab vedotin and bendamustine as first-line treatment of Hodgkin lymphoma in the elderly (HALO Trial). *First Author: Jean Marc Schiano de Colella, Institut Paoli-Calmettes, Marseille, France*

Background: Hodgkin Lymphoma (HL) treatment in the elderly is a challenge, as standard ABVD is able to cure no more than 60% of the patients (p.). Bendamustine (Be), and Brentuximab Vedotin (BV), are well-tolerated and effective drugs in relapsing HL, but only preliminary data exist in 1st line treatment of the elderly (Evens AM 2018). **Methods:** HALO is a prospective international multicenter open-label phase I/II study (NCT02467946) to assess the safety and efficacy of Be-BV in advanced-stage elderly HL p. Briefly, BV 1.2 mg/kg on D1, and Be 90 mg/m2 on D1-2 were administered Q3W for 6 cycles. The primary endpoint was the feasibility and the efficacy of Be-BV. **Results:** Between July 2015 and February 2019, 59/60 p. consecutive enrolled received at least 1 Be-BV cycle, and are valuable for primary endpoint. One p. was excluded because a histological review showing angioimmunoblastic T-Cell Lymphoma. The mean age was 70.32 (62-79), and M/F ratio 41/18. The Ann-Arbor stage was IIB in 12, III in 14 and IV in 33 patients, B-symptoms (y/n) 40/19. IPS was 0-2 in 19 and ≥ 3 in 40 p., P.S. (ECOG) was 0-1 in 53, 2 in 6 p., nonetheless most of them were frail, as ADL was ≥ 6 in 47 (79%) and IADL was ≥ 8 in 42 (71%) p. Most frequent co-morbidities were cardio-vascular disease (45) metabolism disorders (31) prostatic adenoma (11). 163 treatment-related adverse events (WHO 3-4) were recorded: neutropenia and lymphopenia, (134), infections (7), cutaneous reactions (5), liver toxicity (2). No case of grade > 2 peripheral neuropathy was recorded. Out of 59 p., 41 concluded and 18 interrupted the treatment for toxicity (8), progression (5), treatment failure (2), CMV reactivation (3). The latter was recorded in 17 p., 12/17 received valgancyclovir. 4 p. died with CMV viremia. After a mean follow-up of 20.6 (0.3-46.5) months, 37/59 (63%) were in CR, while 22 (37%) have progressed (5) or relapsed (17). The 2-y OS and PFS in ITT analysis were 83% (95% CI 71-96) and 54% (95% CI 41-72) and in PP 89% (95%CI 75-100) and 78% (95%CI 64-96), respectively. 22 p. had a PFS event: 5 progression (2 deaths), 17 relapse (8 deaths). 10 p. died for recurrent HL (5), sepsis (1), secondary malignancy (2), respiratory insufficiency (1) and unknown (1). **Conclusions:** The Be-BV combination, a novel anthracycline-free regiment for first line treatment of HL in elderly, proved effective in unselected, frail, poor-risk, HL p. aged more than 60 in daily hospital real life. The CMV reactivation is frequent and should be treated with preemptive antiviral therapy upon detection of CMV DNA in plasma. Clinical trial information: NCT02467946. Research Sponsor: TAKEDA MILLENIUM.

8030 Poster Session (Board #363), Fri, 8:00 AM-11:00 AM

Effect of antibiotic use prior to or concurrent with immune checkpoint inhibitors on outcomes in patients with Hodgkin lymphoma. *First Author: Steven R Hwang, Department of Internal Medicine, Mayo Clinic, Rochester, MN*

Background: There is growing interest in the identification of modifiable patient-specific factors that may predict response to immune checkpoint inhibitors (ICIs) in classical Hodgkin lymphoma (cHL). Recently, it has been proposed that antibiotic use could decrease the efficacy of ICIs in the treatment of advanced solid malignancies. The objective of our study is to assess whether antibiotic use prior to or concurrent with ICIs is associated with changes in outcomes in patients with cHL. **Methods:** Patients who received a PD-1 or CTLA-4 blocker for the treatment of cHL at Mayo Clinic Rochester between January 1, 2011 and October 20, 2018 were identified. We conducted a longitudinal retrospective chart review to identify those who received antibiotics within 30 or 90 days prior to initiation or concurrent with ICI therapy. Univariate cox regression analysis was used to assess for an association between antibiotic use and overall survival (OS) and progression-free survival (PFS) within these groups; a time-dependent variable was used for concurrent antibiotic use. **Results:** A total of sixty-two patients were identified (61% male, median age at ICI initiation 35 years [range: 19-87]). Median duration of follow up from ICI start was 38 months (range: 4-78). Twenty-one patients (34%) received antibiotics within 90 days of initiation of ICI, of which thirteen (21%) received antibiotics within 30 days. Thirty-five patients (57%) received antibiotics concurrently with ICI. Concurrent and prior antibiotic use within 90 days of ICI were both associated with inferior PFS (concurrent HR = 6.38 [95% CI 3.02-13.47]; 90-day HR = 2.21 [95% CI 1.10-4.47]) and OS (concurrent HR = 8.77 [95% CI 1.91-40.36]; 90-day HR = 2.96 [95% CI 1.09-8.04]). **Conclusions:** Antibiotic use is associated with inferior outcomes in patients with cHL treated with ICIs in this single institution cohort. This may reflect potential antibiotic effects on the gut microbiome (GMB) and immune system as has been suggested in prior studies. Further confirmatory studies and examination of potential confounding covariates are needed. Research Sponsor: U.S. National Institutes of Health.

8031 Poster Session (Board #364), Fri, 8:00 AM-11:00 AM

Outcome of elderly patients with classical Hodgkin lymphoma (HL) in British Columbia. *First Author: Phoebe Tsz Man Cheng, Department of Medicine, University of British Columbia, Vancouver, BC, Canada*

Background: Outcomes in elderly patients (pts) with Hodgkin lymphoma (HL) have traditionally been poor. We evaluated the survival of elderly pts (>60 years [y]) with classical HL in British Columbia (BC). **Methods:** All pts aged >60 y newly diagnosed with classical HL from 1961 to 2019 were identified in the BC Cancer Lymphoid Cancer Database. Limited stage was defined as non-bulky (<10 cm) stage 1A/1B or 2A (before 2000 1B = advanced stage), with the remainder considered advanced stage. **Results:** Following exclusions (HIV positive n=4, incomplete data n=21, prior or concurrent other lymphoproliferative disease n=67), 713 pts were identified. With a median follow up of 6.0 y (0.1 - 24.0 y) in living pts, there has been an improvement in 5 y DSS/OS (both p<.001) by decade comparison: 1960s (n=52) 25%/17%; 1970s (n=75) 38%/31%; 1980s (n=90) 51%/43%; 1990s (n=115) 53%/42%; 2000s (n=180) 66%/57%; 2010s (n=201) 63%/53%. To account for advances in diagnosis, staging, supportive care, and therapy in the modern era, we evaluated the outcome of pts diagnosed since 01/1995. A total of 368 pts were treated with curative intent (Table). Most pts received multi-agent chemotherapy (n=359, 98%: ABVD[like] n=351, alkylator-based n=7, CHOP n=1), 8 pts had radiotherapy (RT) alone, and 1 pt had surgery (primary CNS HL). The 5 y DSS, PFS, and OS were 74%, 57%, and 62%, respectively. Increasing age was associated with inferior outcomes (5 y DSS/PFS/OS): 61-70 y (81%/70%/74%), 71-80 y (69%/47%/52%), and >80 y (59%/27%/31%) (DSS p=.011; PFS p<.0001; OS p<.0001). Of 318 pts that received bleomycin, 60 (19%) developed pulmonary toxicity, including 22 cases that occurred after cycles 1 and 2. Overall, 24/368 pts (7%) died of acute treatment toxicity (pulmonary [bleomycin n=10, radiation n=1], infection n=10, cardiac n=3). There was no association between age and developing bleomycin (p=.80) or lethal treatment toxicities (p=.74). **Conclusions:** The outcome of elderly pts with HL has improved in recent decades. However, treatment related toxicity remains a concern and use of multi-agent chemotherapy, particularly bleomycin-containing regimens, should be undertaken with caution. Research Sponsor: None.

Clinical features of HL patients treated with curative intent in the modern era (1995 – present).

Clinical feature	Pts, n=368 (%)
Age, y	-
Median (range)	70 (61-92)
61-70	199 (54)
71-80	128 (35)
>80	41 (11)
Advanced stage	255/365 (70)
Male	212 (58)
ECOG PS >1	132/360 (37)
Mass >10 cm	32/339 (9)
Subtype	-
Nodular sclerosis	177 (48)
Not classifiable	90 (24)
Mixed cellularity	72 (20)
Lymphocyte rich	22 (6)
Lymphocyte depleted	7 (2)

8032 Poster Session (Board #365), Fri, 8:00 AM-11:00 AM

Frontline brentuximab vedotin as monotherapy or in combination for older Hodgkin lymphoma patients. *First Author: Christopher A. Yasenchak, Willamette Valley Cancer Institute and Research Center/US Oncology Research, Eugene, OR*

Background: Older patients with classical Hodgkin lymphoma (cHL) have poor outcomes relative to younger patients, often due to comorbidities and toxicities related to standard first-line (1L) chemotherapy (5-yr PFS: 30%–45% vs 75%–80%) (Evens 2008; Proctor 2009). Brentuximab vedotin (BV, ADCETRIS®), a CD30-directed antibody-drug conjugate, has robust activity in patients refractory to several lines of chemotherapy. **Methods:** This phase 2, open-label study, SGN35-015 (NCT01716806), evaluated efficacy and tolerability of BV alone or combined with single-agents in treatment-naive cHL patients ≥60 yr. The full-analysis set (FAS) includes all patients who received BV (1.8 mg/kg IV). Patients in Part A received BV monotherapy on Day 1 of every 3-week cycle (n = 26); Part B: BV+dacarbazine (DTIC; 375 mg/m^2; n = 19); Part C: BV+bendamustine (benda; 70 mg/m^2; n = 20); and Part D: BV+nivolumab (nivo; 3 mg/kg; n = 20). The efficacy evaluable (EE) set includes all patients who had at least 1 post-baseline response assessment (n = 25, 19, 17, 19). **Results:** Demographic characteristics were generally similar: median age 78, 69, 75, and 72 yr in Parts A, B, C, and D, respectively, and 62% of patients (range 45%–70%) reported impaired physical functioning at baseline. Most patients had disease stage III/IV (62%, 68%, 75%, 80%), were ECOG 0/1 (77%, 74%, 80%, 95%), and male (54%, 68%, 50%, 75%). Median time from diagnosis was 1.2 to 1.5 mo (FAS; 10 Jan 2019 data cutoff). ORR were high (92%, 100%, 100%, 95%) at a median follow-up of 59.4, 58.6, 51.3, and 19.4 mo in the EE data set. Median OS in the FAS set was 77.5 mo with monotherapy; 64.0, 46.9, and not reached in the combination parts. Treatment-related AE ≥ Grade 3 occurred in 50%, 37%, 70%, and 60% of patients; peripheral neuropathy (PN) was most common (35%, 26%, 20%, 35%). Treatment-related SAEs occurred in 12%, 11%, 40%, and 5% of patients. Part C enrollment (BV+benda) closed early due to multiple acute toxicities. There were no treatment-related deaths in any part of the study. The median treatment cycles per patient were 8.0, 12.0, 5.0, and 14.5. Treatment discontinuation due to related AEs occurred in 42%, 42%, 40%, and 30% of patients, most commonly due to PN (38%, 37%, 30%, 20%). **Conclusions:** Older patients with cHL and multiple comorbidities have very high response rates with BV as monotherapy or combined with other single agents and improved tolerability versus combination chemotherapy. Median overall survival exceeded 6 yr with BV monotherapy. BV+nivo or BV+DTIC appeared to be the most reasonable combination treatment options in this study. Clinical trial information: NCT01716806. Research Sponsor: Seattle Genetics.

8033 Poster Session (Board #366), Fri, 8:00 AM-11:00 AM

Gls-010, a novel anti-PD-1 mAb in Chinese patients with relapsed or refractory classical Hodgkin lymphoma: Preliminary impressive result of a phase II clinical trial. *First Author: Yuqin Song, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), the Department of Lymphoma, Peking University Cancer Hospital & Institute, Beijing, China*

Background: classical Hodgkin lymphoma (cHL) are characterized by genetic alterations at the 9p24·1 locus and PD-L1 ligand overexpression. GLS-010 is a novel fully human anti-PD-1 mAb and exhibited favorable result in previous Phase I study. This multi-center, single-arm Phase II clinical trial is aimed to further evaluate the safety and efficacy profile of GLS-010 in Chinese patients (pts) with relapsed or refractory cHL. **Methods:** All pts enrolled received GLS-010 240mg every 2 weeks until disease progression, death, unacceptable toxicity or withdraw from the study. The primary endpoint was objective response rate (ORR) by independent review committee (IRC) per Lugona 2014. Adverse events (AEs) were graded by NCI CTCAE v4.03. **Results:** 85 pts with relapsed or refractory cHL who had received at least 2 lines of prior systemic chemotherapies were enrolled and treated. As of August 2 2019, data cutoff, pts received a median of 8 treatment cycles (1 cycle include 2 injections), with 12 pts discontinued and 73 pts were still in treatment. At a median follow-up of 6.57 months, an ORR was reported in 78 of 85 patients (91.76%, 95%CI, 83.77-96.62), by an IRC assessment, including 30(35.3%) pts with a complete response (CR) and 48 pts (56.5%) with a partial response (PR). Median duration of response (DoR) and progression free survival (PFS) were not reached yet. Treatment-related adverse events (TRAEs) of any grade occurred in 77 (90.6%) of 85 patients, most of which were Grade 1-2.The most common TRAEs were fever (26/85, 30.6%), neutrophil count decreased (16/85, 18.82%), white blood cell count decreased (15/85, 17.65%). ≥ Grade 3 TRAEs occurred in 23 (27.06%) pts, most commonly, hepatic function abnormal (5/85, 5.88%), hyperuricaemia (4/85, 4.71%). **Conclusions:** GLS-010 showed impressive anti-tumor activity (ORR = 91.96%) and manageable safety profile in Chinese patients with relapsed or refractory cHL, which could be a new safe and effective treatment option in this setting. Clinical trial information: NCT03655483. Research Sponsor: Guangzhou Gloria Biosciences Co,. Ltd.

8034 Poster Session (Board #367), Fri, 8:00 AM-11:00 AM

Sintilimab for relapsed/refractory classical Hodgkin's lymphoma: Long-term follow-up on the multicenter, single-arm phase II ORIENT-1 study. *First Author: Hang Su, The Fifth Medical Center, Chinese PLA General Hospital, Beijing, China*

Background: Sintilimab, a programmed death-1 checkpoint inhibitor, has demonstrated efficacy in relapsed/refractory cHL after the primary analysis of the ORIENT-1 study. Here, we report the updated safety and efficacy profile after long-term follow-up. **Methods:** ORIENT-1 is a multicenter, single-arm, phase II study in China. Classical Hodgkin's lymphoma patients who had failed ≥2 lines of systemic therapy, including autologous hematopoietic stem cell transplantation (HSCT) were enrolled. Sintilimab, 200 mg IV was given every 3 weeks, until disease progression, death, unacceptable toxicity, or withdrawal from study. The primary endpoint objective response rate (ORR) by an independent radiological review committee (IRRC) per IWG 2007 has been reported before. The progression free survival (PFS) by IRRC follow-up data are reported herein. **Results:** 96 patients were treated. As of the data cutoff on 30 Sep, 2019, 57.3 % patients complete two-year treatment, with a median follow-up of 26.7 months. The median duration of treatment was 24.1 months (range: 0.7 to 24.8). Of 49 patients with progressive disease (PD) by investigator, 39/49 (79.6%) patients received treatment beyond PD, with a median treatment duration after PD of 8.0 months (range: 1.4 to 20.8). The median PFS was 18.6 months (95%CI: 14.4 to 22.3). Median overall survival has not been reached. Two-year OS rate was 96.3% (95%CI: 88.9% to 98.8%). The treatment-related adverse event (TRAE) was reported in 92/96 (95.8%) patients, most (71/96, 74.0%) of which were grade 1-2. The most common grade 3 or 4 TRAEs were pyrexia (3/96, 3.1%), lipase increased (3/96, 3.1%) and lymphocyte decreased (3/96, 3.1%). **Conclusions:** The results from long-term follow-up showed that, in addition to a high rate of response, sintilimab also demonstrated durable efficacy and favorable long-term safety profile. Considering the high rate (nearly 80%) of treatment beyond PD, IWG 2007 which was used to evaluate PFS may not be a suitable criteria for evaluating the efficacy of anti-PD-1 antibody in cHL. Further investigation and analysis are required. Clinical trial information: NCT03114683. Research Sponsor: Innovent Biologics, Inc., China National Major Project for New Drug Innovation (2017ZX09304015 and 2018ZX09301014009) and CAMS Innovation Fund for Medical Sciences (CIFMS) (2016-I2M-1-001)

8035 Poster Session (Board #368), Fri, 8:00 AM-11:00 AM

Mantle cell lymphoma: initial report from the North American Mantle Cell Lymphoma Consortium. *First Author: Kai Fu, University of Nebraska Medical Center, Omaha, NE*

Background: The goal of the North American Mantle Cell Lymphoma (MCL) Project is to evaluate the clinical, biological, and genomic markers that affect the outcome of patients with MCL. **Methods:** We have retrospectively studied the clinical and pathological features of 307/421 patients diagnosed with MCL between January 2000 to December 2012 from 23 institutions across North American. **Results:** The male to female ratio of MCL patients was 3.5:1, with a median age of 66 years (range: 24-106 years). Approximately 29% of patients (78/269) presented with B symptoms and 257 (257/307, 83.7%) patients had extranodal involvement at diagnosis. Median follow-up was 7.1 years (range, 0.03 to 16.6 years) with the five-year PFS and OS at 27.8%, and 54.4%, respectively. Univariate analysis revealed that the following factors were significantly associated with both inferior OS and PFS ($p< 0.05$): older age (≥60 years), presence of B symptoms, advanced Ann Arbor stage, elevated LDH, low platelets (≤100K/ml), blastoid/pleomorphic cytology, Ki67 proliferation ≥30%, circulating tumor cells, no transplantation (vs. transplantation), and allogeneic (vs. autologous) stem cell transplantation. In addition, large tumor size (maximal diameter > 3cm), high WBC ($> 10\times10^3$/ml), CD5 or CD23 positivity, and a complex karyotype were associated with inferior OS ($p< 0.05$). Multivariate Cox regression analysis showed age (≥ 60y; $p= 0.0028$, HR = 2.44, 95% CI: 1.36-4.38) and high LDH ($p= 0.0062$, HR = 2.19, 95% CI: 1.25-3.84) were the two factors predicting the clinical outcome. MIPI-c, a commonly used prognostic scoring system which includes Ki67, stratified the 100 MCL cases into four group with distinct clinical outcomes ($p< 0.001$). Using readily-available clinical and pathological variables, we developed a simple and robust scoring system, MIPI-P (pathology), which consisted of age (≥60 years), LDH (high), Ki67 index (≥30%), Ann Arbor stage (III/IV), and cytological type (blastoid/pleomorphic), each contributing one point. The MIPI-P system stratified 104 MCL cases into three distinct groups ($p< 0.001$). Median survival for the different groups were: low grade (0-1 points): 11.8 years; intermediate grade (2-3 points): 4.9 years; and high grade (4-5 points): 1.6 years. We further validated this system in an independent cohort of 33 MCL cases and confirmed that the modified MIPI-P provided robust prognostic predication ($p= 0.014$). **Conclusions:** The clinical and biologic characteristics of MCL can provide information assisting with the prognosis of patients with MCL. Research Sponsor: University of Nebraska Foundation.

8036 Poster Session (Board #369), Fri, 8:00 AM-11:00 AM

Clinical activity of cirmtuzumab, an anti-ROR1 antibody, in combination with ibrutinib: Interim results of a phase Ib/II study in mantle cell lymphoma (MCL) or chronic lymphocytic leukemia (CLL). *First Author: Hun Ju Lee, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: ROR1 is an onco-embryonic tyrosine kinase receptor that is re-expressed at high levels on many hematologic and solid cancers but not on normal adult tissues. ROR1 binds Wnt5a, resulting in increased tumor growth and survival, cancer cell stemness and epithelial mesenchymal transition. Cirmtuzumab (Cirm) is a humanized monoclonal antibody designed to inhibit the tumor promoting activity of ROR1. In this study, we examined the safety and efficacy of Cirm in combination with ibrutinib (Ibr) in MCL or CLL. **Methods:** As of Jan 29, 2020, 12 pts with relapsed refractory (RR) MCL were enrolled into Part 1 Dose Escalation (DE). All MCL pts had stage 3/ 4 at original diagnosis, 25% had bulky tumor at study entry, 58% had intermediate/high risk MIPI scores and the majority (83%) had ≥ 2 prior regimens. 34 pts with CLL [12 treatment naïve (TN) and 22 RR pts] enrolled into Part 1 DE (n = 18) or Part 2 Expansion (n = 16). At least 79% of CLL pts were high risk as determined by unmutated IGHV, 17p/p53 loss, and/or del 11q. DE pts received Cirm IV q2wks x 3-5 doses then q4wks plus Ibr (starting D28). Following DE, Cirm 600mg IV q2wks x3 then q4wks plus Ibr (420mg/day CLL or 560mg/day MCL) was chosen for Expansion. **Results:** *Safety:* only grade 1/ 2 AEs were reported as possibly related to Cirm alone, whereas the safety profile attributed to Ibr or Ibr / Cirm was similar to published data, with no new or unexpected events. *Efficacy for MCL:* 83% ORR, 33% (4) CR, 50% (6) PR, 17% (2) SD**.** CRs were achieved at a median of 3.6 mos in heavily pretreated pts, including 2 with bulky disease > 5cm. Prior therapy of the 4 CR pts: 2 pts failed R-Ibr (7-10 mos) and R-hyperCVAD, 1 pt, auto-SCT and allo-SCT, 1 pt, auto-SCT and CAR-T. *Efficacy for CLL:* 88% ORR (92% TN, 86% RR), 3% (1) CR, 85% (22) PR/ (7) PR-L, 12% (4) SD. In addition, 3 PR pts with CLL met criteria for "Clinical CR, bone marrow biopsy not performed". The pt achieving a CR had RR disease with del 11q; this pt remains in remission > 6 mos after stopping all therapy. At a median follow-up of 9.9 mos, 100% of CLL pts are free of disease progression and > 82% remain on study. **Conclusions:** Cirm in combination with Ibr is a well-tolerated and active regimen for RR MCL and TN or RR CLL. In this evaluation of 46 pts, the ORR and PFS continue to improve with longer follow-up and additional pts, supporting continued investigation of this regimen in ROR1 expressing tumors. This study is ongoing and enrolling an Expansion arm for MCL pts and an open-label randomized Phase 2 in CLL pts comparing Ibr alone to Cirm /Ibr. Clinical trial information: NCT03088878. Research Sponsor: California Institute for Regenerative Medicine (CIRM) grant, Pharmaceutical/Biotech Company.

8037 Poster Session (Board #370), Fri, 8:00 AM-11:00 AM

Outpatient treatment with lisocabtagene maraleucel (liso-cel) across a variety of clinical sites from three ongoing clinical studies in relapsed/refractory (R/R) large B-cell lymphoma (LBCL). *First Author: Carlos R. Bachier, Sarah Cannon Blood Cancer Network, Nashville, TN*

Background: Currently approved CAR T cell therapies are generally administered as inpatient (inpt) treatment at university medical centers due to concerns about frequency, onset, severity, and management of AEs, including cytokine release syndrome (CRS) and neurologic events (NEs). We sought to characterize whether patients (pts) could be safely monitored in the outpatient (outpt) setting after receiving liso-cel, an investigational, CD19-directed CAR T cell product administered at equal target doses of CD8+ and CD4+ CAR+ T cells, across university and non-university sites in TRANSCEND NHL 001 (NCT02631044), OUTREACH (NCT03744676), and PILOT (NCT03483103). **Methods:** Eligible pts had R/R LBCL after systemic chemoimmunotherapy; moderately impaired organ function was allowed. For outpt infusion of liso-cel, pts were required to receive safety monitoring education, have a caregiver and stay within 1 h travel to site of care for 30 d post-treatment. All study sites had a multidisciplinary CAR T cell team and standard operating procedures for toxicity monitoring and management. **Results:** At data cutoff, 53 pts had received liso-cel on Study Day 1 and were monitored as outpts (university, n = 33; non-university, n = 20), including pts ≥65 y of age (n = 23) and with high tumor burden (SPD ≥50 cm^2; n = 16). Any grade CRS and NEs were reported in 18 (34%) and 14 pts (26%), respectively. Severe CRS and/or NEs occurred in only 2 pts (4%) and were reversible. Median (range) time to onset of CRS and NEs was 5 (2–9) and 8.5 (3–22) d, respectively. Tocilizumab and/or corticosteroids for treatment of CRS and/or NEs were required in 8 pts (15%). Overall, 30 pts (57%) required hospitalization post-treatment, with a median (range) time to hospitalization post-treatment of 5.5 (2–22) d; 9 pts (17%) were hospitalized Study Day 4 or earlier. Two pts required ICU-level care. There were no grade 5 treatment-emergent AEs. Safety in pts monitored as outpts was comparable across types of sites. Overall response rate was 81% (95% CI, 68–91). Safety and efficacy were consistent with data from inpts across the 3 studies (N = 270). **Conclusions:** Pts with R/R LBCL were successfully treated with liso-cel and monitored for CAR T cell-related toxicity in the outpt setting across different types of sites. Incidences of severe CRS, NEs, and early hospitalization were low; 43% of pts did not require hospitalization. A larger dataset will be presented, including comparisons of outpts vs inpts and sites of care. Clinical trial information: NCT02631044 (TRANSCEND NHL 001), NCT03744676 (OUTREACH), NCT03483103 (PILOT). Research Sponsor: Juno Therapeutics, a Bristol-Myers Squibb Company.

8038 Poster Session (Board #371), Fri, 8:00 AM-11:00 AM

Relevance of bone marrow biopsies for response assessment in NCTN follicular lymphoma clinical trials. *First Author: Sarah C. Rutherford, Weill Cornell Medicine, New York, NY*

Background: Bone marrow biopsies (BMB) are performed pre/post therapy to confirm complete response (CR) in patients (pts) with lymphoma on clinical trials. We evaluated 2 prior data sets and concluded that BMB impact response assessment in a minority of pts with follicular lymphoma (FL) (Rutherford BJH 2017; Rutherford ASH abstract 1605, 2018). We sought to establish if BMB add value in assessing response or identify distinct progression free (PFS) or overall survival (OS) outcomes in a large, multicenter, multi-trial cohort. **Methods:** Data were pooled from 7 trials of 580 pts with untreated FL conducted through the Alliance for Clinical Trials in Oncology and SWOG from 2002-2016. The proportion of pts with positive (+) baseline BMB, CR on imaging after treatment, and (+) repeat BMB was calculated using total pts enrolled as the denominator. We tested against the null hypothesis that the proportion was = 10%, the threshold below which BMB would be considered irrelevant for response assessment, versus (vs) the alternative hypothesis that this proportion was < 10%, using 1-sided exact binomial test. Response criteria were CT-based. Imaging was not used to assess BM involvement. Because confirmatory BMB were not completed in all indicated pts, landmark survival analyses compared PFS/ OS of pts with CR on imaging and negative (-) BMB vs pts with CR on imaging without repeat BMB. Pts with CR on imaging were categorized as having (-) repeat BMB or no repeat BMB within 60 days of first CR on imaging. PFS and OS were calculated from time of first CR and estimated using Kaplan-Meier and Cox models adjusting for age, sex, stage, Follicular Lymphoma International Prognostic Index (FLIPI) score, and treatment type (targeted vs chemotherapy plus targeted therapy), and stratified by treatment arm. **Results:** Median age was 55 with 51% male, 96% stage III-IV, and 88% grade I-II. FLIPI scores were 113 low, 265 intermediate, and 199 high risk. 67% received chemotherapy-based regimens. Baseline BMB was (+) in 321 (55%). Only 5/580 (0.8%) had (+) baseline BMB, CR on imaging, and subsequent (+) BMB (p < 0.0001). Of pts with CR on imaging, PFS and OS were not different among pts with (-) BMB vs pts without repeat BMB (PFS: HR = 1.08, 95%CI 0.61-1.93, p = 0.783; OS: HR = 0.52, 95%CI 0.20-1.40, p = 0.199). **Conclusions:** BMB requirements may discourage pt participation in trials and add pain, expense and time without providing necessary information. We recommend eliminating BMB for response assessment from FL clinical trials. Clinical trial information: NCT00553501, NCT01145495, NCT01190449, NCT01286272, NCT01829568, NCT00822120, and NCT00770224. Research Sponsor: Alliance for Clinical Trials Foundation, https://acknowledgments.alliancefound.org, Pharmaceutical/Biotech Company, U.S. National Institutes of Health, U10CA180821, U10CA180882.

8039 Poster Session (Board #372), Fri, 8:00 AM-11:00 AM

Real-world outcomes of elderly patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) treated with chimeric antigen receptor T-cell (CAR-T) therapy. *First Author: Lindsey Fitzgerald, Huntsman Cancer Institute-University of Utah Health Care, Salt Lake City, UT*

Background: CAR-T has drastically improved outcomes for R/R DLBCL patients (pts). While CAR-T is now standard of care for the treatment of R/R DLBCL, little is known about its efficacy and toxicity in elderly pts. **Methods:** We conducted a multi-center retrospective analysis of pts age ≥ 70 years old with R/R DLBCL treated with either axicabtagene ciloleucel (axi-cel) or tisagenlecleucel (tisa-cel). Pt demographics, tumor characteristics, CAR-T data, survival and toxicity outcomes were collected at the time of T cell infusion and follow up. Comorbidities were measured using the cumulative illness rating score (CIRS) and hematopoietic cell transplantation-specific comorbidity index (HCT-CI). **Results:** A total of 77 pts were analyzed with a median age of 73 (range, 70-88); 30 (39%) pts were age ≥75. Most pts received axi-cel (n = 61, 79%). Unfavorable tumor characteristics included 27 (35%) pts with activated B-cell subtype and 12 (16%) with double/triple hit lymphomas. Median CIRS was 8 (range 0-25) and median HCT-CI was 2 (range 0-9) with significantly higher median CIRS and HCT-CI in pts age ≥75. With a median time to follow up of 5.2 months (m), median progression free survival (PFS) was 12m and median overall survival (OS) was 15.5m. There was no difference in PFS when comparing younger pts (age 70-74) to older pts (age ≥ 75), but median OS was significantly shorter for older pts (7.8m vs. not reached; hazard ratio [HR] 0.46, CI 0.21-0.98; p = 0.04). In a multivariate analysis (MVA) of PFS adjusting for baseline characteristics, HCT-CI > 2 (HR 0.23, CI 0.07-0.77; p = 0.02) and use of axi-cel (HR 0.07, CI 0.02-0.32; p = < 0.001) were associated with worse PFS. Grade 3/4 (Lee criteria) cytokine release syndrome (CRS) and CAR-related encephalopathy syndrome (CRES) were assessed in MVA adjusting for baseline characteristics. CRS was associated with CIRS ≥6 (odds ratio [OR] 3.92, CI 1.07-14.3; p = 0.002) and use of axi-cel (OR 44.9, CI 8.20-245.6; p = 0.006). CRES was associated with older age (OR 6.10, CI 1.86-20.0; p = 0.003), CIRS ≥6 (OR 3.92, CI 1.07-14.3; p = 0.04) and use of axi-cel (OR 44.9, CI 8.2-245.6; p = < 0.0001). **Conclusions:** Pts age ≥75 treated with CAR-T had worse OS, but comparable PFS as compared to younger pts. Validated frailty measurements (CIRS) predicted for increased CRS and CRES. Use of axi-cel was associated with worse PFS and increased toxicities in the elderly, but propensity matched scoring analysis will need to confirm this. Additional pts and longer follow up are required to validate these results. Research Sponsor: None.

8040 Poster Session (Board #373), Fri, 8:00 AM-11:00 AM

Lisocabtagene maraleucel (liso-cel) for treatment of second-line (2L) transplant noneligible (TNE) relapsed/refractory (R/R) aggressive large B-cell non-Hodgkin lymphoma (NHL): Updated results from the PILOT study. *First Author: Alison R. Sehgal, University of Pittsburgh Medical Center, Pittsburgh, PA*

Background: Patients (pts) with aggressive large B-cell NHL who are R/R after first-line immunochemotherapy and not eligible for high-dose chemotherapy and HSCT have a poor prognosis and no established standard of care. The ongoing, open-label phase 2 PILOT study is the first to assess the safety and efficacy of liso-cel, an investigational, CD19-directed, defined composition, 4-1BB CAR T cell product infused at equal target doses of CD8+ and CD4+ CAR+ T cells, as 2L therapy in TNE pts (NCT03483103). **Methods:** Eligible pts had aggressive R/R diffuse large B-cell lymphoma NOS (de novo or transformed follicular lymphoma [FL]), high-grade B-cell lymphoma, or FL grade 3B with 1 line of prior therapy containing an anthracycline and anti-CD20 agent. Pts were deemed TNE by meeting ≥1 criteria: age ≥70 y, ECOG PS 2, or impaired organ function (DLCO ≤60% [but SaO_2 ≥92% and CTCAE ≤1 dyspnea], LVEF ≥40% to < 50%, creatinine clearance > 30 to < 60 mL/min, or AST/ALT > 2 to ≤5 × ULN). Liso-cel (100×10^6 CAR+ T cells) was administered 2–7 days after lymphodepletion (LD) with fludarabine/cyclophosphamide. The primary endpoint is ORR; key secondary endpoints are AEs and CR rate. **Results:** At data cutoff, 25 pts had LD followed by liso-cel infusion. Pt characteristics are summarized in the Table. Overall, 48% (n = 12) had high tumor burden and 48% were primary refractory. 18/25 (72%) pts had grade ≥3 treatment-emergent AEs, 40% of which were cytopenias. No grade 5 AEs occurred within the first 30 days after liso-cel. Five pts (20%) had cytokine release syndrome (CRS) and 3 (12%) had neurological events (NEs). No grade 3/4 CRS was observed; 2 pts (8%) had grade 3/4 NEs. Five pts (20%) received tocilizumab and/or dexamethasone for CRS/NEs. At a median follow-up of 3.5 mo, the ORR was 80% (95% CI, 59–93; n = 20); 48% of pts (n = 12) achieved CR. **Conclusions:** These interim data suggest that elderly and/or comorbid pts with R/R aggressive large B-cell NHL, who are not eligible for high-dose chemotherapy and HSCT, can receive 2L liso-cel with similar safety and efficacy to 3L+ pts as previously reported (Abramson, ASH 2019 #241). Updated data with longer follow-up will be presented. Clinical trial information: NCT03483103. Research Sponsor: Juno Therapeutics, a Bristol-Myers Squibb company.

Pt characteristics, n (%)	Liso-cel–treated pts (n = 25)
Age, y	72 (53–85)
Male	16 (64)
TNE screening criteria	
Age ≥70 y	17 (68)
ECOG PS 2	7 (28)
Organ function	6 (24)
≥2 TNE criteria	6 (24)
R/R to last therapy	13 (52)/12 (48)
SPD ≥50 cm^2/LDH ≥500 U/L	10 (43.5)/5 (20)
HCT-CI score, median (range) (n = 24)	2.5 (0–9)

8041 Poster Session (Board #374), Fri, 8:00 AM-11:00 AM

Role of radiotherapy and dose-densification of R-CHOP in primary mediastinal B-cell lymphoma: A subgroup analysis of the unfolder trial of the German Lymphoma Alliance (GLA). *First Author: Gerhard Held, Department Internal Medicine I, Westpfalzklinikum Kaiserslautern, Kaiserslautern, Germany*

Background: Primary mediastinal B-cell lymphoma (PMBCL) is a distinct entity of aggressive lymphoma, which typically presents in young patients (pts) with a bulky mediastinal mass. Therapy is based on R-CHOP or similar regimens, but the role of treatment intensification and consolidative radiotherapy (RT) is controversial, because data from randomized trials are rare. **Methods:** The UNFOLDER trial included 18-60 year-old pts (aaIPI = 0 with Bulk [≥7.5 cm] or aaIPI = 1) qualifying for radiotherapy to Bulk or extralymphatic involvement (E). Pts were randomized in a 2 x 2 factorial design to 6xR-CHOP-14 or 6x-R-CHOP-21 without RT or with RT (39.6 Gy) to Bulk and E. Primary endpoint was event-free survival (EFS), secondary endpoints were progression-free (PFS) and overall survival (OS). Response was evaluated by the Internat Standardized Response Criteria, Cheson 1999. **Results:** 131 PMBCLs were included with a median age of 34 years, 54% were female, 79% had elevated LDH > UNV and 24% had E. 82 pts (R-CHOP-21: 43; R-CHOP-14: 39) were assigned to RT and 49 (R-CHOP-21: 27, R-CHOP-14: 22) to no-RT. 96% (79/82) received RT per protocol and 5 pts in the no-RT arm received unplanned RT (4 after PR and 1 after CR/CRu). Response RT vs no-RT were CR/Cru 94% vs 84%, PR 2% vs 10%, PD 2% vs 4%. 3-year EFS was superior in pts assigned to RT (94% vs. 78%; p = 0.007), mostly due to events caused by initiation of RT (n = 5) in the no-RT arm. In an as treated analysis the difference between the RT and the no-RT arm was not significant (p = 0.136). Regarding PFS and OS no difference between the RT vs no-RT arm was detected (PFS: 95% (95% CI: 90-100) vs 90% (95% CI: 81-98), p = 0.253; OS: 98% (95% CI: 94-100) vs 96% (95% CI: 90-100), p = 0.636). Dose-densification of R-CHOP-21 by R-CHOP-14 did not improve EFS, PFS nor OS. Only 4 pts died. **Conclusions:** To our knowledge, this is the largest series of PMBCLs so far, which have been treated in a prospective, randomized trial in the rituximab era. The results reveal no differences between R-CHOP-14 vs R-CHOP-21. Pts assigned to RT had a superior EFS mostly due to a higher PR rate in the no-RT arm triggering RT, with no differences in PFS and OS. The results suggest a benefit of RT only for pts, who are responding to R-CHOP with PR. Testing RT in PET-positive residual tumors in a randomized trial can solve the question, while RT in PET-negative pts is studied in the ongoing randomized IELSG 37 trial. Our results indicate a very favorable 3-year OS of 96% in PMBCL pts treated with R-CHOP. Supported by Deutsche Krebshilfe, Amgen and Roche. Clinical trial information: NCT00278408. Research Sponsor: Deutsche Krebshilfe (German Cancer Aid), Pharmaceutical/Biotech Company.

8042 Poster Session (Board #375), Fri, 8:00 AM-11:00 AM

Myeloablative versus non-myeloablative consolidative chemotherapy for newly diagnosed primary central nervous system lymphoma: Results of induction therapy in Alliance 51101. *First Author: Tracy Batchelor, Brigham and Women's Hospital, Boston, MA*

Background: Optimal consolidative therapy for primary central nervous system lymphoma (PCNSL) is not defined. Avoidance of whole brain radiation may reduce risk of neurotoxicity. Non-radiation consolidative options include myeloablative chemotherapy followed by autologous stem cell transplantation (HDT/ASCT) or non-myeloablative chemotherapy. **Methods:** This is a randomized phase 2, National Clinical Trials Network study of induction methotrexate (MTX) (8 g/m^2days 1, 15), temozolomide (TMZ) (150-200 mg/m^2 D7-11), and rituximab (RTX) (C1 D3, 10, 17, 24 and C2 D3, 10) in four 28-day cycles followed by one cycle of cytarabine (ARA-C) (2 g/m^2 BID, D1, 2) (MTRA). Following induction, patients (pts) received consolidation with thiotepa (5 mg/kg BID, D -5, -4) plus carmustine (400 mg/m^2, day -6) and ASCT (Arm A) or one cycle of ARA-C (2 g/m^2 BID, D1-4) plus infusional etoposide (40 mg/kg over 96h) (Arm B). The primary endpoint was median progression-free survival (PFS), designed to compare consolidation regimens. This report describes the results of the 5 cycles of induction therapy. **Results:** 113 pts (median age 61 years, range 33-75) were randomized (Arm A: 57, Arm B: 56) across 27 centers. 108 eligible pts who received induction therapy were evaluated. 36 pts (33.3%) did not proceed to consolidation, mainly due to disease progression (17), pt withdrawal (8), or adverse events including death (6). Grade 3 or 4 febrile neutropenia occurred in 12 pts (11.1%) during induction. Dose modifications of MTX were required in 75% of pts and 63.3% of cycles, mainly due to renal adjustments. Dose delays of MTX were required in 52.8% of pts and 22.2% of cycles. Overall response rate (CR, CRu, PR) at the end of induction was 65.7% (95% CI, 56%, 74.6%). **Conclusions:** While MTRA is feasible and active a significant proportion of pts did not receive consolidation, supporting the need to develop more effective induction strategies. Clinical trial information: NCT01511562. Research Sponsor: U.S. National Institutes of Health.

8043 Poster Session (Board #376), Fri, 8:00 AM-11:00 AM

Outcomes of Burkitt lymphoma (BL) managed in academic (Acad) or community (Comm) centers: real-world evidence (RWE) from 30 US sites. *First Author: Adam J. Olszewski, Rhode Island Hospital-The Warren Alpert Medical School of Brown University, Providence, RI*

Background: Prior analyses have suggested better overall survival (OS) of cancer patients (pts) treated in Acad rather than Comm hospitals, but these disparities may reflect different patient characteristics. We examined outcomes of pts with BL in a large RWE cohort from 30 US healthcare systems (Evens, *ASH* 2019) with a mix of Acad and affiliated Comm sites. **Methods:** We collected clinical data on adults with BL diagnosed in 2009-2018, individually assigned to Acad or Comm principal setting of care. We compared duration of chemotherapy (CTx, incl. standard CODOX-M/IVAC, hCVAD/MA, DA-EPOCH), rates of complete response (CR), progression-free survival (PFS), and OS adjusting for age, sex, HIV, performance status (PS), stage, LDH > 3x upper limit of normal (ULN), involvement of bone marrow or cerebrospinal fluid (CSF), reporting adjusted risk (RR) or hazard ratio (HR) with 95% CI. **Results:** Among 641 BL pts, 77 (12%) were managed in Comm setting. Comm pts had lower median age (45 vs 48 in Acad, *P*= .049), less frequent HIV (13% vs 23%, *P*= .039), less marrow (21% vs 36%, *P*= .009) or detected CSF involvement (8% vs 15%, *P*= .11), and less LDH > 3xULN (21% vs 41%, *P*= .013), with no significant differences in sex, PS, stage, hemoglobin, or receipt of CTx (97% vs 99%). Acad sites more often applied standard intensive CTx regimens (93% vs 85%, *P*= .03) and rituximab (92% vs 79%, *P*= .001), without significant difference in median time to CTx (*P*= .69) or treatment-related mortality (TRM, *P*= .16). Pts managed in Comm (vs Acad) sites were less likely to achieve CR (61% vs 75%, *P*= .03; RR = 0.79 [0.65-0.95]) and had worse 3-year PFS (46% vs 67%, log-rank *P*= .003; HR = 2.17 [1.51-3.14]) and OS (53% vs 72%, *P*= .006; HR = 2.20 [1.48-3.25]). There was no significant interaction with age, sex, HIV, PS, or CSF involvement. Excess mortality concentrated in the 1st year of follow-up. CR, PFS, and OS appeared similar between Acad and Comm settings for pts receiving hCVAD or DA-EPOCH, but outcomes were significantly worse in Comm setting for pts receiving CODOX-M/IVAC. Median number of cycles did not differ between Comm or Acad sites, but median duration of CODOX-M/IVAC delivery was significantly longer in Comm setting (113 vs 101 days, *P*= .023). **Conclusions:** In this large RWE analysis, superior outcomes of adults with BL in Acad setting were not explained by baseline patient characteristics or TRM. Differences in the use of standard CTx regimens, rituximab, duration of Ctx, and CR rates suggest need for further research on potential barriers to delivery of intensive CTx for BL in a broader Comm setting. Research Sponsor: None.

8044 Poster Session (Board #377), Fri, 8:00 AM-11:00 AM

Efficacy and safety of ABP 798 compared with rituximab: Results from the comparative clinical study in patients with non-Hodgkin's. *First Author: Dietger Niederwieser, University of Leipzig, Leipzig, Germany*

Background: ABP 798* is being developed as a biosimilar to rituximab, a CD20-directed cytolytic antibody. A randomized, double-blind, active-controlled study compared the efficacy, safety, and immunogenicity of ABP 798 with rituximab reference product (RP) in subjects with CD20-positive NHL; results of the final analysis are presented here. **Methods:** Adult subjects with grade 1, 2, or 3a follicular B-cell NHL and low tumor burden were randomized to receive intravenous ABP 798 or RP (375 mg/m^2) once weekly for 4 weeks, then at weeks 12 and 20. The primary endpoint was risk difference (RD) of overall response rate (ORR) by week 28. Secondary endpoints included RD of ORR at week 12, pharmacokinetics, pharmacodynamics, safety, and immunogenicity. **Results:** 254/256 randomized subjects were treated with at least one infusion of ABP 798 (n = 128) or RP (n = 126); ORR by week 28, based on independent central blinded assessment of the modified full analysis set, was comparable between the ABP 798 and RP groups (78% vs. 70%, respectively). The 2-sided 90% confidence interval of RD of ORR (-1.4%; 16.8%) was within the pre-specified margin (-15%; 35.5%) thereby establishing clinical equivalence between ABP 798 and RP. This result was supported by analyses of the secondary efficacy endpoint of RD of ORR at week 12. In the two groups, the geometric least squares means for serum concentrations over time (e.g., week 12, pre-dose: ABP 798, 21.89 vs. RP, 20.57; week 12 post-dose: ABP 798, 201.30 vs. RP, 203.52) and the extent of B-cell depletion from day 1 to day 8 (ABP 798, 98.3% vs. RP, 98.3%) were similar. Frequency, type, and severity of adverse events (AEs) were comparable between ABP 798 and RP groups; grade ≥3 AEs were reported in 10.9% and 10.3% of subjects and serious AEs in 3.9% and 4.0%, respectively. Most common AEs were headache, fatigue, and nausea; the most common AE of interest was infusion reactions. No new or unexpected safety signals were observed. Binding and neutralizing anti-drug antibodies were comparable between groups. **Conclusions:** Results of this study demonstrated clinical similarity between ABP 798 and rituximab RP in subjects with CD20-positive NHL. *At the time of this submission, ABP 798 had not been approved by the FDA or any relevant regulatory agency and the indications are yet undetermined. Please consult ABP 798's later approved label in the relevant country for information regarding the approved uses for ABP 798. Research Sponsor: Amgen.

8045 Poster Session (Board #378), Fri, 8:00 AM-11:00 AM

Treatment stratification in B-cell PTLD after solid organ transplantation (SOT) by international prognostic index (IPI) and response to rituximab: Interim results from the PTLD-2 trial. *First Author: Ralf Ulrich Trappe, Department of Hematology and Oncology, DIAKO Ev. Diakonie-Krankenhaus, Bremen, Germany*

Background: The PTLD-1 trials have established risk-stratified sequential treatment of B-cell PTLD. After rituximab induction, patients (pts) in complete remission (25 %) received rituximab consolidation, while all others received R-CHOP. The PTLD-2 trial tests modified risk-stratification including clinical risk factors. These are the results of the 2nd scheduled interim analysis (40/60 planned pts). **Methods:** The prospective, multicenter phase II PTLD-2 trial (NCT02042391) enrols treatment-naïve adult SOT recipients with CD20-positive PTLD. Key exclusion criteria are CNS involvement, ECOG > 2, pregnancy, and severe organ dysfunction or severe, active infection. Treatment consists of rituximab (1400 mg SC; first application 375 mg/m^2 IV) on days 1, 8, 15 and 22. After restaging, pts in CR as well as those in PR with ≤ 2 IPI risk factors at diagnosis (low-risk group) continue with four three-weekly courses of rituximab. Most other pts (high-risk group) receive 4 cycles of R-CHOP-21, while thoracic SOT recipients who progress under rituximab (very-high-risk group) receive six cycles of alternating R-CHOP-21 and R-DHAOx. The primary endpoint (event-free survival in the low-risk group) is not analyzed here. Secondary endpoints presented here are response and overall response (ORR) by computed tomography, overall survival (OS), time to progression (TTP) and treatment-related mortality (TRM) overall and by risk group. **Results:** 40 pts were recruited at 12 centers (2015 – 2019). 21/40 were kidney, 11 lung, 4 liver, 3 heart, and 1 liver/kidney transplant recipients. Median age was 54 years. 38/40 PTLD were monomorphic and 15/40 EBV-associated. 38 pts were evaluated for response at interim staging: 13 were allocated to the low-risk, 17 to the high-risk and 8 to the very-high-risk group. ORR was 28/30 (93 %, CR: 16/30 [53 %]). With a median follow-up of 1.9 years, the 1-year/3-year Kaplan-Meier (KM) estimates of TTP and OS in the intention-to-treat population (40 pts) were 85 %/80 % and 70 %/70 %, respectively. In the low-risk group, the 2-year KM estimate of OS was 100 %. The frequency of infections (all grades) was 50 %, and TRM occurred in 3/40 pts (8 %). **Conclusions:** One third of enrolled pts were treated in the low-risk group and the recruitment goal for evaluation of the primary endpoint will likely be reached. Interim efficacy and toxicity data with rituximab SC and modified risk-stratification are encouraging despite the inclusion of 35 % thoracic SOT recipients. Clinical trial information: NCT02042391. Research Sponsor: Roche.

8046 Poster Session (Board #379), Fri, 8:00 AM-11:00 AM

MAGNIFY phase IIIb interim analysis of induction R^2 followed by maintenance in relapsed/refractory indolent NHL. *First Author: David Jacob Andorsky, Rocky Mountain Cancer Centers/The US Oncology Network, Boulder, CO*

Background: Patients (pts) with relapsed iNHL have limited standard treatment options. The immunomodulatory agent lenalidomide shows enhanced activity with rituximab (ie, R^2), which recently reported 39.4-mo median PFS in R/R iNHL pts (AUGMENT; *J Clin Oncol*. 2019;37:1188). **Methods:** MAGNIFY is a multicenter, phase IIIb trial in pts with R/R FL gr1-3a, MZL, or MCL (NCT01996865) exploring optimal lenalidomide duration. Lenalidomide 20 mg/d, d1-21/28 + rituximab 375 mg/m^2/wk c1 and then q8wk c3+ (R^2) are given for 12c followed by 1:1 randomization in pts with SD, PR, or CR to R^2 vs rituximab maintenance for 18 mo. Data presented here focus on induction R^2 in efficacy-evaluable FL and MZL pts (MCL not included) receiving ≥ 1 treatment with baseline/post-baseline assessments to analyze the primary end point of ORR by 1999 IWG criteria. **Results:** As of June 16, 2019, 393 pts (81% FL gr1-3a; 19% MZL) were enrolled with a median follow up of 23.7 mo (range, 0.6-57.8) for censored pts (n = 335). Median age was 66 y (range, 35-91), 83% had stage III/IV disease, with a median of 2 prior therapies (95% prior rituximab-containing). ORR was 69% with 40% CR/CRu (Table). Median DOR was 39.0 mo, and median PFS was 40.1 mo. 199 pts (51%) have completed 12c of R^2, and 188 (48%) have been randomized and entered maintenance. 139 pts (35%) prematurely discontinued both lenalidomide and rituximab, primarily due to AEs (n = 52, 13%) or PD (n = 45, 11%). Most common all-grade AEs were 48% fatigue, 43% neutropenia, 36% diarrhea, 31% nausea, and 30% constipation. Grade 3/4 AE neutropenia was 36% (9 pts [2%] had febrile neutropenia); all other grade 3/4 AEs occurred in < 7% of pts. **Conclusions:** R^2 is active with a tolerable safety profile in pts with R/R FL and MZL, including rituximab-refractory, double-refractory, and early relapse pts. Clinical trial information: NCT01996865. Research Sponsor: Bristol-Myers Squibb, Summit, NJ.

Efficacy for induction R^2 in R/R iNHL.

	ORR, %	CR/CRu, %	DOR, median (95% CI), mo	PFS, median (95% CI), mo*
Overall	69	40	39.0 (36.8-NR)	40.1 (37.6-NR)
Histology FL	70	41	NR (36.8-NR)	39.4 (30.0-NR)
MZL	63	38	38.6 (29.4-NR)	41.2 (38.4-NR)
R-refractory Yes	60	36	35.8 (35.2-NR)	25.9 (18.1-41.6)
No	73	43	NR (38.4-NR)	41.2 (39.4-NR)
Double refractory Yes†	50	26	20.1 (14.6-NR)	17.7 (10.7-23.0)
No	73	44	39.0 (38.4-NR)	41.6 (39.4-NR)
Early relapse Yes‡	66	31	35.8 (22.4-NR)	26.5 (18.1-41.6)
No	70	45	NR (38.4-NR)	41.2 (39.4-NR)

*If pts in maintenance at cutoff, response assessments also contributed to PFS †Refractory to both rituximab (monotherapy or combo) and alkylating agent ‡Progressed or relapsed ≤ 2 y of initial diagnosis after 1L systemic treatment

8047 Poster Session (Board #380), Fri, 8:00 AM-11:00 AM

Machine learning prediction of survival in diffuse large B-cell lymphoma based on gene-expression profiling. *First Author: Selin Merdan, Value Analytics Labs, Alpharetta, GA*

Background: The current clinical risk stratification of Diffuse Large B-cell Lymphoma (DLBCL) relies on the International Prognostic Index (IPI) comprising a limited number of clinical variables but is imperfect in the identification of high-risk disease. Our study aimed to: (1) develop a risk prediction model based on the genetic and clinical features; and (2) evaluate the model's biological implications in association with the estimated profiles of immune infiltration. **Methods:** Gene-expression profiling was performed on 718 patients with DLBCL for which RNA sequencing data and clinical covariates were available by Reddy et al (2017). Unsupervised and supervised machine learning methods were used to discover and identify the best set of survival-associated gene signatures for prediction. A multivariate model of survival from these signatures was constructed in the training set and validated in an independent test set. The compositions of the tumor-infiltrating immune cells were enumerated using CIBERSORT for deconvolution analysis. **Results:** A four gene-signature-based score was developed that separated patients into high- and low-risk groups with a significant difference in survival in the training, validation and complete cohorts ($p < 0.001$), independently of the IPI. The combination of the gene-expression-based score with the IPI improved the discrimination on the validation and complete sets. The area-under-the-curve at 2 and 5 years increased from 0.71 and 0.69 to 0.75 and 0.74 in the validation set, respectively. **Conclusions:** By analyzing the gene-expression data with a systematic approach, we developed and validated a risk prediction model that outperforms existing risk assessment methods. Our study, which integrated the profiles of immune infiltration with prognostic prediction, unraveled important associations that have the potential to identify patients who could benefit from the various therapeutic interventions, as well as highlighting possible targets for new drugs. Research Sponsor: None.

8048 Poster Session (Board #381), Fri, 8:00 AM-11:00 AM

Immunohistochemical characterization of anaplastic large cell lymphoma using tissue microarray. *First Author: Poorvi Kirit Desai, University of South Florida, Tampa, FL*

Background: Anaplastic Large Cell Lymphoma (ALCL) is a subtype of mature T-cell lymphoma comprised of systemic (ALK+ or ALK-) and primary cutaneous (PCALCL) forms. ALK+, usually associated with *NPM1-ALK* gene, has a favorable prognosis. PCALCL is usually indolent. Despite worse prognosis for ALK-, pts with *DUSP22* rearrangement have favorable outcomes similar to ALK+ while those with *p63* aberration have poor outcomes. We hypothesize that other genetic alterations in ALCL could aid in diagnosis and prognosis. We compared protein expression levels of selected signaling molecules (JAK1, STAT3, DUSP22, ERBB4/HER4, PRDM1/BLIMP1 and SOCS3) among the subtypes and correlated to outcomes. **Methods:** Of 50 pts with ALCL at Moffitt (MCC) from 2000-2019, 27 tissue samples (6 ALK+, 10 ALK-, 8 PCALCL, 3 controls) met eligibility criteria. Tissue microarrays (TMAs) were constructed from formalin-fixed, paraffin-embedded lymph node biopsies. Up to 3 replicate cores were taken from each block. Immunohistochemistry was performed with antibodies to the selected proteins. Stained TMA slides were scanned using the Aperio™ ScanScope XT2 to determine % positive biomarker stain within each core per established algorithm. Statistics: ANOVA was used to compared protein expression levels, with pairwise tests when significant. T-test compared PCALCL to systemic ALCL. Boxplots were created for differences in protein expression levels and time to event outcomes (OS and RFS) using Log rank test and Cox proportional hazards models. Kaplan-Meier curves were used for clinical time-to-event outcomes and quartiles of the protein expression levels. **Results:** The 3 subgroups had a significant difference in SOCS3 expression with mean and std respectively: 42.4% (0.153), 17.4% (0.089), and 21.0% (0.155), p = 0.008. Among all pairs, ALK+ and PCALCL groups were statistically different (P = 0.011). Patients with high BLIMP1 (≥28.5%) across 3 ALCL subgroups were associated with better median OS (not reached) in comparison to pts with lower expression (27.3 mos) (Log rank test p = 0.014, HR = 0.17, 95% CI 0.034-0.829). The same was seen for median RFS (81.1 vs. 12.5 mos). (Log rank test p = 0.009, HR 0.23, 95% CI 0.069-0.755). **Conclusions:** High BLIMP1 suggests favorable prognosis in ALCL and could potentially be a positive prognostic marker. High SOCS3 appears more prevalent in PCALCL than systemic and could aid in differential. Larger samples should be used to validate results. Secondary markers like Bcl-2 can be considered in the future to correlate expression levels to targeted treatments like venetoclax. Research Sponsor: University of South Florida Graduate Medical Education Grant ($7500).

8049 Poster Session (Board #382), Fri, 8:00 AM-11:00 AM

The Integration of PD1 blockade with epigenetic therapy is highly active and safe in heavily treated patients with T-cell lymphoma (PTCL) and cutaneous T-cell lymphoma (CTCL). *First Author: Enrica Marchi, Center for Lymphoid Malignancies, Columbia University Medical Center, New York, NY*

Background: Our group has demonstrated that combinations of epigenetic modifiers produce potent synergy in pre-clinical models of PTCL and induce the expression of cancer testis antigen, suggesting a role in the addition of the immune-checkpoint inhibitor, pembrolizumab. **Methods:** This is a phase 1b study of pembrolizumab combined with pralatrexate alone (Arm A), with pralatrexate + decitabine (Arm B), or decitabine alone (Arm C) in patients with relapsed and refractory PTCL and CTCL. A standard 3+3 dose-escalation is applied in the triplet Arm (Arm B) while in the doublet Arms (A and C) de-escalation is applied in case of toxicity. Pharmacokinetic and pharmacodynamic studies are ongoing. **Results:** We treated a total of 12 patients with 4 patients in each Arm. All patients that received at least one dose of drug were evaluable for toxicity. There was a dose limiting toxicity (DLT) in each arm including prolonged grade 3 thrombocytopenia (Arm A), febrile neutropenia (Arm B), grade 3 hyponatremia, and rash (Arm C). There were no treatment-related deaths. Six patients out of 12 were evaluable for response at the time of this analysis. One patient achieved a complete remission, 2 had partial remission, 1 had stable disease, and 2 experienced progression of disease. Interestingly, all of the responses were seen in the triple combination of pralatrexate, decitabine, and pembrolizumab. Table summarizes the patient characteristics, toxicities, and response rates. **Conclusions:** These preliminary clinical data suggest that the integration of pembrolizumab on an epigenetic backbone is safe and demonstrates encouraging responses in patient with PTCL and CTCL. Clinical trial information: 03240211. Research Sponsor: Merck.

Patient characteristics, toxicities and responses (n = 12).

Median age, years (range)	65 (38 - 77)
Sex	
Male	6
Female	6
Race	
White/Non-Hispanic	6
White/Hispanic	1
Black	3
Asian	2
Histology	
PTCL, NOS	5
AITL	3
Mycosis Fungoides	2
ATLL	1
Sezary Syndrome	1
Stage at diagnosis	
I	1
II	1
III	4
IV	5
Tumor Stage	1
Median number of prior therapies (range)	2 (1-5)
Adverse Event, Grade 3/4, n (%)	
Thrombocytopenia	1
Neutropenia	2
Fatigue	1
Vomiting	1
Hyponatremia	1
Rash	1
	Evaluable/Total Patients (Best Response)
Arm A	2/4 (POD, POD)
Arm B	2/4 (CR, PR)
Arm C	1/4 (SD)

8050 Poster Session (Board #383), Fri, 8:00 AM-11:00 AM

Sintilimab for relapsed/refractory (r/r) extranodal NK/T cell lymphoma (ENKTL): Extended follow-up on the multicenter, single-arm phase II trail (ORIENT-4). *First Author: Jianyong Li, Jiangsu Province Hospital, Nanjing, China*

Background: Patients with r/r ENKTL have a poor prognosis after failing an asparaginase-based regimen. The overexpression of PD-L1 induced by EBV infection is a potential mechanism for ENKTL to avert immune surveillance. Sintilimab, a fully human anti-PD-1 monoclonal antibody, has demonstrated efficacy in r/r ENKTL after the primary analysis of the ORIENT-4 study. Here, we report the updated efficacy and safety results with extended follow-up. **Methods:** Patients with pathologically confirmed r/r ENKTL were enrolled. Sintilimab was given 200 mg IV Q3W, until PD, death, unacceptable toxicity, or withdrawal from the study. Treatment beyond PD is allowed. Tumor response evaluation was performed by both PET-CT and CT/MRI with contrast. The primary endpoint was objective response rate per Lugano 2014. Data cut-off date for this analysis was Jan 17, 2020. **Results:** A total of 28 patient were enrolled and treated. With a median follow-up of 26.9 months (range, 23.3 to 28.6), the median treatment duration was 24.15 months (range, 1.4 to 28.7). Of 20 patients with progressive disease (PD) by investigator per Lugano 2014 criteria, 19/20 (95%) patients received treatment beyond PD. The median OS has not been reached and 24-month OS rate was 78.6% (95% CI, 58.4% to 89.8%). ORR was 67.9% (95% CI, 47.6% to 84.1%), including 4 pts who experienced PD prior to having a response. DCR was 85.7%, including 5 pts who experienced PD before SD or response. Median duration of response was 4.1 months (range, 1.9 to 15.2+). After treatment, the mean EQ-5D-5L VAS Score (from 79.3 to 90.8), EQ-5D-5L Index Value (from 0.8 to 0.9) and EORTC QLQ-C30 (from 70.5 to 87.3) were all increased. The Treatment-related adverse events (TRAEs) of any grade occurred in 28 (100%) pts; grade 3 occurred in 11 (39.4%) pts, most commonly, decreased lymphocyte count (2 [7.1%]) and diabetes (2 [7.1%]); no grade 4-5 TRAE. **Conclusions:** In addition to an encourage response, sintilimab also demonstrated long-term clinical benefit, with 78.6% of 24-month OS rate, and favorable long-term safety profile after extended follow-up. Considering the high rate (95%) of treatment beyond PD, Lugano 2014 may not be a suitable criteria for evaluating the efficacy of anti-PD-1 antibody in r/r ENKTL. Clinical trial information: NCT03228836. Research Sponsor: Innovent Biologics, Inc.

8051 Poster Session (Board #384), Fri, 8:00 AM-11:00 AM

Three-year follow-up of treatment-naïve and previously treated patients with Waldenström macroglobulinemia (WM) receiving single-agent zanubrutinib. *First Author: Constantine S. Tam, Peter MacCallum Cancer Centre, Melbourne, St Vincent's Hospital, Fitzroy, University of Melbourne, Parkville and Royal Melbourne Hospital, Parkville, Victoria, Australia*

Background: Inhibitors of Bruton tyrosine kinase (BTK) have established therapeutic activity in patients with WM. Zanubrutinib, a potent and selective BTK inhibitor was evaluated in a phase 1/2 study in treatment-naïve (TN) and relapsed/refractory (R/R) patients with WM. **Methods:** Patients had TN or R/R WM and required treatment as per International Workshop on WM (IWWM) criteria. Treatment consisted of oral zanubrutinib at 160 mg twice daily (n = 50) or 320 mg once daily (n = 23) until disease progression or unacceptable toxicity. Efficacy endpoints included the proportion of patients achieving a complete response (CR) or very good partial response (VGPR) in accordance with IWWM-6 criteria. Efficacy analyses were conducted on the 73 patients evaluable (24 TN, 49 R/R). **Results:** Between September 2014 and August 2018, 77 patients with WM (24 TN and 53 R/R) began treatment with zanubrutinib (55% aged > 65 years; 21% aged > 75 years). At a median follow up of 32.7 months, 73% remain on treatment. Reasons for treatment discontinuation included adverse events (AE) in 13% (only one related), disease progression (10.4%), and other (3.9%). Results are presented for TN and R/R combined. The overall response rate was 96% and VGPR/CR rate was 45%. The rates of VGPR/CR increased over time; 22% at 6 mos, 33% at 12 months and 45% at 24 months. Three-year progression-free survival (PFS) was 81%, and overall survival (OS) was 85%. The most commonly reported AEs were upper respiratory tract infection (52%), contusion (33%, all grade 1) and cough (22%). AEs of interest include neutropenia (18.2%), major hemorrhage (4%), atrial fibrillation/flutter (5%), and grade 3 diarrhea (3%). **Conclusions:** Long-term follow up with continued zanubrutinib treatment demonstrated deep and durable responses in the majority of WM patients. The rates of VGPR/CR increased with prolonged therapy. Disease progression was uncommon. The safety profile of long-term zanubrutinib therapy in these patients was tolerable. Clinical trial information: NCT02343120. Research Sponsor: BeiGene.

Efficacy and safety outcomes.

Assessment	TN WM (n = 24), %	R/R WM (n = 53), %	Total (n = 77), %
VGPR/CR rate	33.3	51.0	45.2
36-mo PFS	91.5	76.2	80.5
36-mo OS	100.0	80.2	84.8
AEs leading to discontinuation	12.5	13.2	13.0
≥Grade 3 AEs	45.8	64.2	58.4
Grade 5 AEs	0	9.4	6.5
Atrial fibrillation/ flutter	4.2	5.7	5.2
Major hemorrhage	8.3	1.9	3.9
≥Grade 3 infections	8.3	35.9	27.3

8052 Poster Session (Board #385), Fri, 8:00 AM-11:00 AM

Prognostic relevance of CD4+ T-cells in the microenvironment of newly diagnosed follicular lymphoma (FL) patients is independent of the tumor gene expression profile. *First Author: Patrizia Mondello, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: A significant proportion of patients with FL experience an early relapse and a subsequent poor outcome. While several prognostic indices have been developed, none were designed to predict early failure. Recently, we established that lack of intrafollicular CD4+ T-cell expression predicted risk of early failure, and integrating this microenvironment biomarker with the Follicular Lymphoma International Prognostic Index, termed BioFLIPI, further improved identification of FL patients at risk of early failure (*Blood* 2019; 134(suppl1):121). However, the microenvironment may be influenced by the genetic composition of tumor. We investigated whether the CD4 biomarker and BioFLIPI were impacted by genetic features of the tumor as assessed by a 23-gene expression prognostic score (*Lancet Oncol* 2018;19:549-61). **Methods:** Of the 186 cases with FL grade 1-3A treated with immunochemotherapy (IC) in our prior study, 152 had digital expression quantification of 23 selected genes (23-GEP score), which used RNA from formalin-fixed, paraffin-embedded samples. Event-free survival (EFS) was defined as time from diagnosis to progression, relapse, retreatment, or death. Early failure was defined as failing to achieve EFS at 24 months. Risk of early failure was estimated using odds ratios (ORs) and 95% confidence intervals from logistic regression models. We also used Cox regression to assess associations with continuous EFS and overall survival (OS). **Results:** 28% of patients failed to achieve EFS24. Lack of CD4+ intrafollicular expression (38% of patients, OR = 2.33, p = 0.024) and high risk 23-GEP score (26% of patients, OR = 3.52, p = 0.001) each predicted early failure, and in a multivariable model that included FLIPI, both CD4+ (OR = 2.26, p = 0.046) and 23-GEP score (OR = 2.26, p = 0.0.057) remained predictors. Similarly, BioFLIPI modeled as a continuous score (1-4, OR per one point increase = 2.31, $p < 0.001$) predicted early failure, and the association remained (OR = 2.14, $p < 0.001$) when the high risk 23-GEP score (OR = 2.79, p = 0.013) was included in the model. When stratified on 23-GEP score, BioFLIPI was a stronger predictor of early failure in low risk (74%, OR = 2.51, p = 0.002) relative to high risk (26%, OR = 1.55, p = 0.27) patients. Similar patterns were observed for EFS and OS. **Conclusions:** CD4+ T-cell infiltrate and tumor gene expression appear to be independently predictive of early failure in newly diagnosed FL patients treated with IC. Future studies should integrate and validate these measures. Research Sponsor: U.S. National Institutes of Health.

8053 Poster Session (Board #386), Fri, 8:00 AM-11:00 AM

Atezolizumab + obinutuzumab + venetoclax in patients with relapsed or refractory diffuse large B-cell Lymphomas (R/R DLBCL): Primary analysis of a phase II trial from LYSA. *First Author: Charles Herbaux, Centre Hospitalier Régional Universitaire de Lille, Institute of Hematolog-Tranfusion, Lille, France*

Background: R/R DLBCL treatment remains challenging. Atezolizumab (ATE) and obinutuzumab (OBI) are monoclonal antibodies acting respectively to inhibit T-lymphocyte exhaustion or by inducing lymphoma cells cytotoxicity, whereas venetoclax (VEN) is a small molecule inhibiting BCL-2. Combining tumor-targeted therapies with agents that enhance anti-tumor immunity represents an attractive treatment paradigm. This LYSA sponsored multicenter phase 2 trial (NCT03276468) evaluate the combination of ATE, OBI and VEN in R/R B lymphomas, we present here primary efficacy and safety data fromthe DLBCL cohort. **Methods:** Patients ≥18 years with biopsy-confirmed R/R DLBCL who failed at least one line of therapy were eligible. OBI was given IV at the dose of 1 g on day (D) 1, 8 and 15 of cycle (C) 1 and on D1 from C2 to C8 every 3 weeks. ATE was given IV, 1.2 g every 3 weeks, started at D2 of C1, then administered at D2 of each cycle for 24 cycles. VEN was given orally at 800 mg/D at full dose, started on D8C1 for 24 cycles. The primary endpoint wasthe Overall Metabolic Response Rate (OMRR) by Lugano criteria at the end of induction (EOI) after 8 cycles of ATE, OBI and VEN (M6) or at premature treatment discontinuation. **Results:** At the time of the primary analysis (03 Jan 2020), 58 pts were enrolled and the median follow-up was 9 months [6.9-11.8]. Baseline characteristics were: median age, 70 years; male, 53.4%; Ann Arbor Stage IV, 84.5%; aaIPI (≥2), 63.2%; > 2 prior lines of therapy, 83.6%; and refractory to last line of prior regimen, 63.6%. The OMRR at EOI was measured at 23.6% [14.58%-34.93%], including 18% of CMR. To date, these responses seem durable with only 3 reported relapses. According to the highest diameter mass, OMRR was 38.5% versus 10.3%, < 5cm and > 5cm respectively; P = 0,02. All three treatments were stopped in 78% of patients, mostly for progressive disease. At the time of analysis, a median of 4 cycles [1-8] has been administered. A total of 48 (84.2%) pts experienced grade 3–4 adverse event (AE) and 6 (10.5%) had an AE that led to discontinuation of any drug.AE of grade 3 or more reported in at least 20% of patients were neutropenia (33.3%) and lymphopenia (35.1%). Of note, a grade 3 autoimmune colitis and a grade 1 hypothyroidism were reported during induction. **Conclusions:** The ATE, OBI and VEN combinationappears to be well tolerated. The OMRR rate at EOI is comparable with currently available treatment options in this population, with durable responses. The OMRR seems better in patients with a low tumor burden. Clinical trial information: NCT03276468. Research Sponsor: Roche and AbbVie.

8054 Poster Session (Board #387), Fri, 8:00 AM-11:00 AM

Identification of predicted neoantigen vaccine candidates in follicular lymphoma patients. *First Author: Cody Ramirez, McDonnell Genome Institute, Washington University School of Medicine in St. Louis, St. Louis, MO*

Background: Follicular lymphoma (FL) is incurable with conventional therapies and poorly responsive to immune checkpoint blockade. There is a need for new therapies without long-term complications of chemotherapy and with curative potential. We hypothesize that FL contains tumor-specific mutant antigens (TSMAs) that can be targeted by the immune system by vaccination. Recent reports have highlighted the potential for unique immunoglobulin peptides to elicit immune response in lymphomas. We utilized whole exome sequencing (WES) and RNA sequencing (RNA-Seq) of FL patient samples to infer HLA genotype, and predict TSMAs with the goal of designing a personalized cancer vaccine, supported by recent reports of this approach in solid cancers. **Methods:** DNA and RNA from 58 patients' FL biopsies underwent WES and RNA-Seq. pVACtools and MiXCR predicted potential somatic and B-cell clonotype neoantigens, which were filtered to identify high quality TSMAs. B-cell oligoclonality was determined by comparison to B-cell receptor (BCR) repertoire profiling of healthy individual lymph nodes. RNA-seq data allowed us to identify expressed TSMAs. Complementary *in silico* analysis based on mRNA-based peptide reconstruction and custom HLA affinity binding predictions were performed. **Results:** An average of 52 somatic mutations per patient (range: 2-172) were identified. At least one high quality TSMA was predicted for 57 of 58 patients. Five or more TSMA candidates were identified for 52 (90%) patients with a mean of 17 predicted peptides per patient (range: 0-45). 81% (813/1,004) of the total predicted TSMA peptides arose from missense mutations, 9% (94/1,004) from indels, and 10% (97/1,004) from BCR. 78% (45/58) of patients have both somatic and BCR vaccine candidates, while 21% (12/58) of patients had only somatic vaccine candidates. Predicted TSMAs were identified in multiple genes recurrently mutated in lymphoma (e.g., BCL2). There was a high prediction concordance with the orthogonal BostonGene Vaccine Module V1 pipeline. These pre-clinical results led to a first-in-human pilot trial of personalized TSMA vaccine combined with anti-PD-1 mAb for rel/ref FL patients (NCT03121677), with one response observed within 4 patients evaluable for response to date. **Conclusions:** TSMA peptides suitable for cancer vaccines were identified for most FL patients via next-generation sequencing, MiXCR and pVACtools. This pre-clinical study suggests that FL patients will be candidates for TSMA vaccine clinical trials and pilot clinical results provide proof of concept for this approach. Research Sponsor: Siteman Cancer Center, Other Foundation, The Jamie Erin Follicular Lymphoma Research Consortium.

8055 Poster Session (Board #388), Fri, 8:00 AM-11:00 AM

Multi-omics analysis of mantle cell lymphoma reveals an immune-cold tumor microenvironment associated with ibrutinib resistance. *First Author: Krystle Nomie, The University of Texas MD Anderson Cancer Center, Department of Lymphoma/Myeloma, Houston, TX*

Background: Mantle cell lymphoma (MCL) is an aggressive and incurable B-cell lymphoma. Although the role of the MCL tumor microenvironment (TME) in survival and therapeutic response has been studied, greater knowledge regarding the tumor-immune interaction is needed to develop MCL immunotherapeutic strategies. **Methods:** Whole exome sequencing (WES; n = 41) and RNA-seq (n = 93) were performed on fresh peripheral blood, apheresis, or biopsy MCL patient primary samples. Joint WES and RNA-seq mutation calling, expression analysis were performed by BostonGene. **Results:** Both tumor and TME molecular signatures were characterized based on ibrutinib response. Concurrent analysis of MCL biopsy samples with an additional previously published cohort (n = 122; Scott et al., *JCO*, 2017) identified 4 MCL microenvironment signatures (Nomie et al., *Blood*, 2019) in which the ibrutinib-resistant MCL samples primarily belonged to the "stroma-enriched" subtype (29%; 6/8 resistant, non-immune with increased stromal signature and tumor-promoting cytokines), whereas most of the ibrutinib-sensitive samples were assigned to the "immune-hot" subtype (53%, 9/9 sensitive; anti-tumor infiltration, high immune and checkpoint molecule expression with low stromal expression, Chi-square test p-value = 0.001). *NOTCH1* gain-of-function mutations (25%, 3/12 resistant) in the PEST domain were found exclusively in the ibrutinib-resistant cohort associated with the microenvironment-depleted subtype. Frequent recurring inactivating mutations in the epigenetic modifier *KMT2D* (30%) were identified in MCL cells associated with the 'immune-suppressed" subtype ($p < 0.05$). Loss-of-function mutations in epigenetic modifiers have been tied to immune evasion. PD-L1 was significantly downregulated in the ibrutinib-resistant MCL tumors (p = 0.03), indicating that targeting the PD-L1 and PD-1 immune checkpoint axis may not be beneficial. **Conclusions:** Ibrutinib sensitivity and resistance were defined by immune-hot and immune-cold TME portraits, respectively, suggesting that the TME has a prominent role in mediating ibrutinib response. Ibrutinib has been suggested to activate the immune TME through its off target inhibition of interleukin 2–inducible T-cell kinase (ITK). The immune activation by ibrutinib suggests that anti-tumor activity of ibrutinib may be better harnessed by combining ibrutinib with immunotherapy. Research Sponsor: None.

8056 Poster Session (Board #389), Fri, 8:00 AM-11:00 AM

Phase Ib trial combining rapid determination of drug-drug interaction (DDI) followed by a dose finding period to assess safety and preliminary efficacy of fimepinostat plus venetoclax in patients with aggressive B-cell lymphoma. *First Author: Tycel Jovelle Phillips, University of Michigan, Ann Arbor, MI*

Background: Fimepinostat (F), a dual inhibitor of PI3K (α, β, δ) and HDACs type 1/2, causes suppression of MYC levels (Shulman *et al.*, 2017). A pooled analysis of diffuse large B-cell lymphoma (DLBCL) pts treated with F in two Ph 1/2 trials revealed an objective response rate in evaluable/ITT MYC-altered DLBCL pts of 29%/23%, respectively (Landsburg *et al.*, 2018). Based on compelling preclinical activity of F in combination with venetoclax (V) (a Bcl2 inhibitor), we initiated a Ph 1b/2 study of F + V in pts with relapsed or refractory (R/R) DLBCL or high-grade B-cell lymphoma (HGBL), with or without MYC alteration. V is metabolized primarily by CYP3A, and preclinical studies showed that F may inhibit CYP3A4 (IC_{50} of 13.58 and 0.28 μM for midazolam and testosterone, respectively), suggesting F could cause DDI with V. **Methods:** Cohorts of patients received increasing dose levels of F administered on a 5-days-on/2-days-off (5/2) schedule in combination with daily V in 21-day cycles (Cohort 1: F 30 mg QD 5/2 + V 400 mg QD; Cohort 2: F 60 mg QD, 5/2 + V 400 mg QD; Cohort 3: F 60 mg QD 5/2 + V 800 mg QD). A potential DDI was assessed during Cycle 0 (Table), where PK for V (10 mg) monotherapy was compared to that for V (10 mg) in the presence of F. Patient PK samples were collected, analyzed and reviewed in < 10 days to determine the final ramp-up dose level of V. **Results:** As of 1-Feb-2020, 16 pts have been enrolled in 2 dose cohorts. Intensive PK analysis of 13 pts showed only mild (≤ 2-fold) to no increase in V exposure in the presence of F. In Cohort 1 (n = 6), the mean AUC increased 1.6-fold, and mean C_{max} by 1.5-fold. In Cohort 2 (n = 7), no increase in mean AUC (0.9-fold) or C_{max} (1.0-fold) was observed. Accordingly, all pts ramped up V to 100% of the target dose (400 mg) upon entering Cycle 1; rapid escalation of V was well tolerated. DLT was observed in 1 pt (Grade 3 diarrhea) in Cohort 2. Overall, 75% of TEAEs have been mild or moderate (Grade 1/2), and most were of limited duration. 11 pts (69%) experienced SAEs; 4 pts (25%) had SAEs considered related to either F or V. **Conclusions:** Real-time PK evaluation showed that F had only a mild to no DDI with V. F + V is well tolerated at clinically active dose levels, and evaluation of higher dose-level cohorts was ongoing. Enrollment in Cohort 2 remains on-going. Clinical trial information: NCT01742988. Research Sponsor: Curis, Inc.

Cycle:	Cycle 0													Cycle 1
Day:	1	2-5	6-7	8	9-10	11-14	15	16	17	18	19 - End of PK Evaluation Period			1-2
V (dose mg):	10			10		10	20	50	100	(100-200)	Continue to target dose			200-400
F:			X	X	X		X	X	X	X	X			X
PK:	X	X		X	X		X	X	X	X				X

8057 Poster Session (Board #390), Fri, 8:00 AM-11:00 AM

Haemophagocytic lymphohistiocytosis (HLH) in patients with large B-cell lymphoma treated with standard of care (SOC) axicabtagene ciloleucel (Axi-cel). *First Author: Sairah Ahmed, The University of Texas MD Anderson Cancer Center, Department of Lymphoma/Myeloma, Houston, TX*

Background: HLH is a rare but serious complication of chimeric antigen receptor (CAR) T cell therapy, characterized by severe immune activation, and immune mediated multi-organ failure. Diagnosis is difficult in the context of cytokine release syndrome (CRS) and optimal treatment and outcomes are unclear. **Methods:** Retrospective, descriptive analysis of patients with relapsed/refractory LBCL treated with SOC axi-cel at MD Anderson Cancer Center between 01/2018 - 10/2019 (data cut-off 12/21/2019). Progression-free survival (PFS) defined as time from axi-cel infusion to progression/death or last follow-up. Diagnosis of HLH per HLH-2004 and CART cell therapy toxicity guidelines (Neelapu, 2018) **Results:** One hundred and five patients with relapsed/refractory LBCL included, 6 diagnosed with HLH. No significant difference in baseline characteristics, disease stage, international prognostic index or inflammatory markers at baseline between groups, with exception of platelet count which was lower in HLH group 116 [37-129] versus 141 [9-391] (p = 0.07). Development of HLH was early after CART cell infusion at a median 11 days [7 – 78 days] with 3 patients having bone marrow hemophagocytosis; all 6 had abnormalities in liver function tests, fibrinogen, triglycerides, and at least 1 ferritin level > 10,000. CART toxicity in HLH cohort: 4 patients experienced grade 0-1 CRS, and 1 with grade 2 CRS while 3 HLH patients experienced grade 3-4 IEC-associated neurotoxicity syndrome (*ICANS*), and 2 patients had grade 0-1 ICANS. Five HLH patients treated with high dose steroids, and tocilizumab; anakinra administered in 2 patients. Four of 6 patients had resolution of HLH with treatment and didn't require escalation to HLH specific therapy however 1 patient was treated with steroids/etoposide. PFS and overall survival (OS) were significantly shorter in HLH group, PFS 1 months vs 8 months, respectively (p < 0.001) and median OS 2 months vs not reached, respectively (p = 0.001) follow up 10 months (95% CI 8-12 months). One patient died of acute respiratory failure, 2 patients died of HLH and multi-organ failure without progressive disease (PD). Of 3 remaining patients, all had radiographic PD at day 30, 2 of whom died of PD. **Conclusions:** HLH is likely an underreported complication of CART cell therapy, and patients with HLH have significantly worse outcomes. In this series the majority of patients died of PD, not the syndrome itself. More information is necessary to design treatment strategies that won't compromise CART outcomes. Research Sponsor: None.

8058 Poster Session (Board #391), Fri, 8:00 AM-11:00 AM

Safety and efficacy of TQ-B3525, a novel and selective oral PI3K α/δ inhibitor, in Chinese patients with advanced malignancies: A phase I dose-escalation and expansion trial. *First Author: Huaqing Wang, First People's Hospital of Tianjin, Tianjin, China*

Background: TQ-B3525 is a novel and selective oral PI3K α/δ inhibitor with activity 41 and 138 folds higher than Buparlisib against PI3K α and PI3K δ in pre-clinical research. This Phase I study (NCT03510767) assessed the safety, tolerability, pharmacokinetics and antitumor activity of TQ-B3525 in Chinese patients with advanced malignancies. **Methods:** Patients with relapsed or refractory (R/R) lymphoma who have experienced at least two prior systemic anti-cancer treatments, and advanced solid tumor who have failed standard anti-cancer treatment, were enrolled. TQ-B3525 was administered orally from 2mg, 5mg, 10mg, 20mg once daily (qd) to 10mg, 20mg twice daily (bid). DLT was observed in the first cycle (28 days) of dose-escalation phase. Dose-expansion phase started at the dose level which objective response occurs. **Results:** Between June 2018 and December 2019, a total of 40 patients were enrolled, Including 27 patients with R/R lymphoma and 13 patients with advanced solid tumor. Three DLTs (both grade 3 hyperglycemia) were observed: two in the 20mg bid dose cohort and one in the 10mg bid. The common AEs of all grades were hyperglycemia (65.0%), glycosylated hemoglobin increased (35.0%) and diarrhea (32.5%). Grade 3 or 4 treatment-related AEs occurred in 11 patients (27.5%), with the most common one also being hyperglycemia (10.0%). TQ-B3525 was rapidly absorbed (T_{max}: 1-2 h) and moderately eliminated ($T_{1/2}$: 10-12 h). At steady state, the geometric mean $AUC_{0\text{-}24}$ and C_{trough} of TQ-B3525 at 20mg qd were 1060.7 ± 198.6 h*ng/mL and 23.4 ± 9.5 ng/mL, which was above IC_{50} (4.2 ng/ml). 23 lymphoma patients were evaluable for clinical response per 2014 Lugano Classification. The overall response rate (ORR) was 60.9% (95% CI, 38.5-80.2). The ORR at ≥10mg qd was 70.0% (14/20, [95% CI, 49.9-90.1]). For R/R FL, the ORR was 72.7% (8/11, [95% CI, 46.4-99.1]). At data cut-off (2nd February, 2020), the median PFS for lymphoma was not reached (events rate: 33.3%). The longest duration of response at data cutoff was 11.8 months in a patient with FL. **Conclusions:** TQ-B3525 is well-tolerated in Chinese patients with advanced malignancies, and demonstrated high promising antitumor activity in R/R lymphoma patients. Recommended phase II dose was established at 20mg qd. A single-arm phase 2 trial of TQ-B3525 in patients with R/R FL is currently underway. Clinical trial information: NCT03510767. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

8059 Poster Session (Board #392), Fri, 8:00 AM-11:00 AM

The BCR repertoire comparison, lymphoma typing model and OS predicted model in 5 different pathological lymphomas: T-LBL/ALL, PTCL-NOS, B-MCL, B-FL, and DLBCL. *First Author: Wenhua Jiang, Second Hospital of Tianjin Medical University, Tianjin, China*

Background: Lymphatic system cancer is characterized by high heterogeneity in histology and clinical manifestations, B-cell antigen receptor (BCR) plays a vital role in anti-tumor immune responses. This study aimed to compare the BCR repertoire and identify some specific immune markers for different pathological lymphomas. **Methods:** 5 pathological types of non-Hodgkin's lymphoma (T-LBL/ALL, PTCL-NOS, B-MCL, B-FL, DLBCL) were collected, with reactive lymph node (RLN) hyperplasia as control. All patients were tested by high-throughput immunohistochemical sequencing (HTS-IR) to analyze the correlation between B-cell immunohistochemistry and clinical indicators, and constructed new strategy typing and overall survival (OS) predicted models for lymphomas. **Results:** The BCR repertoire had the highest diversity in RLN, followed by T-LBL/ALL, PTCL-NOS, DLBCL, B-MCL and B-FL. The diversity of BCR repertoire and similarity of B cell antigens were higher in B-MCL and B-FL patients. Similar to RLN, T-LBL/ALL and PTCL-NOS had broad and diverse V-J pairs, and rare in B-MCL, B-FL and DLBCL. RLN patients were with the highest average number of amino acids, followed by T-LBL/ALL, DLBCL, PTCL-NOS, B-MCL and B-FL. The expressed amino acid sequencing of ARDLIALDY, ARRPGSFDY, ARDIAGWGAVAGLLGRAYYGMDV, and ARDGPYGGNSVEYFQH were markedly different among 5 groups. Patients tended to recurrence expressed ASLDSSPSGFC, ARGMTTVTTAPNY, ARVPLYDDQNINDV and AGGVGGYDWGSYYFDY (P = 0.01605, 0.02869, and 0.01569), and prone to metastasis with expressions of ARVKEFYGILTGYDY, AHSIIGSSWYNWFDP and VRDGGWQSNNWLGFDV (P = 0.04259, 0.0450 and 0.0481). For all patients, 18 (7 negative, 11 positive) and 12 (10 negative, 2 positive) IGH V-J pairs were respectively associated with lymphoma recurrence and metastasis. The top 3 most significant pairs were IGHV7-4-1_IGHJ4, IGHV3-53_IGHJ5 and IGHV3-7_IGHJ5 bound up with recurrence (P = 0.0019, 0.0020 and 0.0021), and IGHV3-74_IGHJ1, IGHV1-69_IGHJ3 and IGHV1-2_IGHJ1 related to metastasis (P = 0.0022, 0.010 and 0.019). The accuracy of typing model in training and test sets was 78.125% (25/32) and 60% (6/10), respectively. The OS model can predict long (≥ 24 months) or short (< 24 months) OS. **Conclusions:** Our study identified new biomarkers, constructed novel lymphoma typing model and OS predicted model based on B cell repertoire. It provides a comprehensive understanding of immune response, and contributes to the diagnosis and prognosis of non-Hodgkin's lymphoma. Research Sponsor: National Natural Science Foundation of China.

8060 Poster Session (Board #393), Fri, 8:00 AM-11:00 AM

REFLECT real-world evidence (RWE) prospective study update: Efficacy and safety results of Sandoz biosimilar rituximab (SDZ-RTX) for the treatment of diffuse large B-cell lymphoma (DLBCL). *First Author: Manfred Welslau, Onkologische Schwerpunktpraxis am Klinikum, Onkologie Aschaffenburg, Aschaffenburg, Germany*

Background: SDZ-RTX (Rixathon) is approved in more than 20 countries and regions, including highly regulated markets e.g. Europe, Japan and Switzerland for all labeled indications of reference rituximab. REFLECT is the first prospective post-approval study to evaluate a rituximab biosimilar as a curative therapy in untreated pts with $CD20^+$ DLBCL. This interim analysis adds up efficacy and additional safety results on the previously presented data (Welslau et al, ASCO and EHA 2019). **Methods:** Adult patients (pts) were treated with SDZ-RTX and cyclophosphamide, doxorubicin, vincristine, prednisone (R-CHOP) according to the product label. The primary endpoint is to evaluate the effectiveness of Rixathon measured by complete response (CR) rate at the end of treatment. Secondary endpoints are overall response rate (ORR), progression-free survival at 24 months and adverse events (AEs). Data were collected at baseline and all scheduled treatment and follow-up visits, which is still ongoing. No imputation was made for missing values, and endpoints are summarized descriptively. **Results:** As of Sep 30, 2019, 170 pts were enrolled, and R-CHOP treatment was close to completion. The median age of pts was 70 years, and 52% were women. Overall, 38% of pts completed the first 12-month observation period, 41% were ongoing, while 21% of pts discontinued. Most of the pts (~80%) had an ECOG score of 0 (35%) or 1 (46%). Early staging (I–II2), low to intermediate disease risk (IPI 0-2), and known B symptoms were reported for 55%, 50%, and 30% of pts, respectively. CR rate at the end of treatment was 57% (defined as the revised response criteria for malignant lymphoma by Cheson et al, 2007 that excludes complete remission/unconfirmed [CRu]). Summary of efficacy is reported in the Table. Overall, 83% of pts experienced AEs, the most common being anemia (23%), fatigue (21%), and polyneuropathy (15%). Treatment-related AEs were reported for 28% of pts. Rates of any serious AEs (SAEs) and treatment-related SAEs were 37% and 6.5%, respectively. On-treatment deaths and all deaths were reported in 2.4% and 4.7% of pts, respectively. **Conclusions:** REFLECT is the first prospective post-approval study to evaluate a rituximab biosimilar as a curative therapy in untreated pts with DLBCL. This interim analysis results re-confirms the expected safety and efficacy profile for DLBCL patients treated with R-CHOP. Research Sponsor: Sandoz Group, a Novartis Division.

Summary of response.

Response (%)	All patients (N = 170)
ORR	88%
CR	57%
PR	31%
Not available	3%
Missing	9%

8061 Poster Session (Board #394), Fri, 8:00 AM-11:00 AM

Clinicopathologic features and outcomes of de novo transformed indolent lymphoma. *First Author: Collin K Chin, The University of Texas MD Anderson Cancer Center, Department of Lymphoma/Myeloma, Houston, TX*

Background: Untreated transformed indolent lymphoma (unTIL) can present as a composite lymphoma (COM), 2 or more separate sites of disease with one site transformed (discordant; DIS) or following indolent lymphoma sequentially (SEQ). Current practices are guided by small retrospective studies or extrapolated from trials involving non-transformed lymphomas. **Methods:** 353 patients (pts) with biopsy-proven unTIL treated with curative chemoimmunotherapy between 01/2000 to 01/2019 were included (intention to treat). All indolent B-cell lymphomas (iNHL) were included except CLL/SLL. Patients with MCL and non-DLBCL transformation were excluded. Prior therapy for iNHL was not allowed except one line of non-chemotherapy-based therapy. Kaplan-Meier method was used for time-to-event analysis including progression-free (PFS) and overall survival (OS). **Results:** 252 (71%) pts presented with COM, 50 (14%) DIS and 51 (14%) SEQ lymphoma. The underlying iNHL was: 308 (87%) follicular lymphoma, 37 (10%) nodal MZL, 7 (2%) MALT lymphoma, and 1 (0.3%) WM. Frontline therapy (FLT) included: RCHOP for 271 (77%), DAEPOCHR for 60 (17%), clinical trial for 7 (2%), BR for 4 (1%), RHCVAD for 2 (1%), RCEOP for 2 (1%), radiation therapy for 2 (1%), RFND for (1%) 2, RCVP for 2 (1%), and rituximab only for 1 (0.3%). 9 (3%) pts had ASCT in first remission. 50 (15%) pts received maintenance rituximab (MR) with fewer cases of HGBL-DH compared to the non-MR cohort (0% *v* 10%). With a median follow-up of 3.4 years (range 0.1-19.1), 4-year PFS and OS rates were 59% and 88%. By univariate analysis (UVA) the underlying type of iNHL, cell-of-origin and choice of induction therapy (DAEPOCHR *v* RCHOP) were not associated with inferior outcomes. SEQ transformations were associated with inferior OS on UVA ($P = 0.02$) which was not significant on multivariable analysis (MVA) ($P = 0.3$). MVA identified ECOG PS $>$ 1, B symptoms and HGBL-DH as independent prognostic factors for inferior PFS and OS. In patients who achieved PR or greater following FLT, MR was associated with improved PFS on MVA (HR 0.6, 95% CI 0.3-0.9, $P = 0.04$) without an OS benefit ($P = 0.2$). 39 (31%) pts relapsed with iNHL only (mPFS 2.4 yrs, 4-yr OS 94%) and 88 (69%) relapsed with transformed lymphoma (mPFS 1.1 yrs, 4-yr OS 69%) with no significant difference in pattern of relapse with MR ($P = 0.2$). **Conclusions:** The clinicopathologic features of unTIL are similar to those of *de novo* DLBCL. Escalation of therapy beyond R-CHOP may not be required in the absence of HGBL-DH. unTIL should be included in future clinical trials involving *de novo* DLBCL given the similar clinicopathologic features. Research Sponsor: None.

8062 Poster Session (Board #395), Fri, 8:00 AM-11:00 AM

Alternative anti-CD20 antibody versus desensitization for lymphoma patients with drug hypersensitivity reactions requiring discontinuation of rituximab, obinutuzumab, or ofatumumab. *First Author: Paola Ghione, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Immunotherapy with anti CD20 is often associated with mild easily manageable infusion reactions. In rare cases, patients experience severe drug hypersensitivity reactions (DHR) serum sickness or anaphylaxis. These in turn may lead to discontinuation of the drug. In our experience, switching to a different anti-CD20 agent is a feasible alternative to discontinuation or desensitization protocols. **Methods:** From our pharmacology database we identified all the patients that received rituximab and/or obinutuzumab, and/or ofatumumab, and/or all the patients who received a flat dose of less than 50 mL of the same drugs and were followed at our institution. From the medical record, we identified all the cases where the anti-CD20 antibody was changed due to allergy, serum sickness or other types of DHR, and all those who received minimal doses of anti-CD20 in the context of a desensitization protocol. DHRs were evaluated either by an allergist, or by retrospective review following the World Allergy Organization guidelines. Our primary comparison, was to assess the proportion of pts able to completed planned infusion of abs using either approach (Fisher's exact Test). **Results:** Among 343 patients receiving at least two different anti-CD20 antibodies or a flat dose of $<$ 50 mL, we identified 44 patients experiencing severe DHRs needing intervention. At the time of the reaction, 16 (36%) received the anti-CD20 as single agent, 24 (54%) in combination with chemotherapy, 4 (9%) in combination with ibrutinib or lenalidomide. In 9 (20%) patients the reaction was defined as anaphylactoid (8 rituximab; 1 obinutuzumab) and in 8 (18%) patients, all receiving rituximab, as serum sickness. Episodes of DHR were addressed with either desensitization (n = 29) or change of anti-CD20 agent (n = 25), 9 patients received both of these approaches, one patient switched anti-CD20 antibodies twice. Overall, 21 desensitizations were successful (72.4%), 8 failed; 23 changes of anti-CD20 were successful (92%) and 2 failed ($p = 0.09$). **Conclusions:** In patients with DHR use of an alternative anti-CD20 antibody is safe and is an alternative or complementary approach to anti-CD20 desensitization. Research Sponsor: None.

8063 Poster Session (Board #396), Fri, 8:00 AM-11:00 AM

CNS involvement by North American-ATLL (NA-ATLL) is associated with discrete patterns and molecular profile involving XPO1 E571 and KLF2/PI3KCD in selected cases. *First Author: Nishi Shah, Montefiore Einstein Center for Cancer Care, Bronx, NY*

Background: Information on central nervous system (CNS) involvement with NA-ATLL is limited. In this study, we describe CNS involvement in ATLL patients at a tertiary hospital in New York City. **Methods:** We considered CNS involvement if one of the following criteria was met 1) cerebrospinal fluid (CSF) cytology or flow cytometry was positive 2) CNS imaging was positive for disease involvement or 3) Physical exam findings were compatible with neurologic involvement. **Results:** Of 94 NA-ATLL patients, 21 (22.3%) had CNS involvement by ATLL. CSF was involved in 13/21 and 5/21 patients at diagnosis and relapse respectively. At diagnosis, MRI showed CNS involvement in brain and spine in 5/21 (24%) and 3/21 (14%) cases respectively. At relapse, imaging revealed brain and spine involvement in 2 patients each. Neurological exam was abnormal in 7 (33%) and 3 (14%) cases at diagnosis and relapse respectively. Next generation exon targeted sequencing was performed in 9 cases. Table shows the mutations (mtn) and functional groups with frequencies. XPO1 E571K mutation was present in 2 patients with extensive CNS disease and refractory to conventional treatment with an overall survival (OS) of 2 months. To our knowledge, this is the first time that XPO1 E571K is reported in a T-Cell malignancy. We also describe here a second set of mutations with CNS involvement (KLF2 and PI3KCD) in 2 patients. Median OS was 8.5 months, Median RFS was 6.5 months in our series. In most cases, the lymphomatous phenotype appeared to have direct mass-like extension (5/21) with several cases of accompanying osteolytic spine or skull lesions, whereas cases with hematogenous involvement tends to spread to the CSF by traversing the brain blood barrier. **Conclusions:** In this report we describe patterns of CNS involvement in ATLL and the associated mtns. We also describe two unique cases of XPO1E571K mtn in a TCL. Research Sponsor: None.

List of mtns in CNS-ATLL pts grouped by predominant pathway.

Cell cycle and DNA maintenance	ATM	2
	CDKN2A	2
	CDKN2B	1
	TP53	1
	SETBP1	1
Class I MHC protein complex	B2M	1
Epigenetic and histone modification	ARID1A	1
	HIST1H1E	1
	EP300	1
	SMARCB1	1
G-coupled receptor	P2RY8	1
JAK/STAT	JAK3	1
NFKB	REL	1
NOTCH	NOTCH1	3
	SPEN	1
Nuclear export signal-dependent protein transport	XPO1	2
Other	FAS	2
	CDH1	1
	ZFHX4	1
	NTRK1	1
PI3K/AKT/MTOR	PIK3CD	2
Ras	HRAS	1
	NRAS	1
	NF1	1
Receptor tyrosine kinases	ALK	1
	ERBB3	1
Splicing factor mtn	SF3B1	1
Transcriptional regulation (TR)	TBL1XR1	3
	KLF2	3
	AR	2
	MYC	1
	GATA2	1
	GATA3	1
	TCF3	1
TR of granulopoiesis	CSF3R	1
Wnt-B catenin	APC	2
	FAT1	1
	CTNNB1	1

8064 Poster Session (Board #397), Fri, 8:00 AM-11:00 AM

Safety of acalabrutinib (Acala) monotherapy in hematologic malignancies: Pooled analysis from clinical trials. *First Author: Richard R. Furman, Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY*

Background: Acala is a next-generation, highly selective, covalent Bruton tyrosine kinase inhibitor approved in the US for patients (pts) with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and previously treated mantle cell lymphoma (MCL). We evaluated the safety profile of acala monotherapy (monotx) in multiple B cell malignancies. **Methods:** Data from pts with activated B-cell diffuse large B-cell lymphoma, CLL, follicular lymphoma, MCL, multiple myeloma, prolymphocytic leukemia, Richter syndrome, SLL, or Waldenström macroglobulinemia treated with ≥1 dose of acala monotx in 9 studies were pooled. Acala was administered at 100 mg BID in most pts (100–400 mg total dose daily). Adverse events (AE) were assessed. **Results:** A total of 1040 pts were included (median age: 67 y [range: 32–90]; ECOG status ≤1: 93%; median exposure duration: 24.6 mo [range: 0–58.5]). A total of 360 (34%) pts discontinued acala, most commonly due to progressive disease (PD; 17%). AEs led to acala discontinuation in 97 (9%) pts; those in > 2 pts were pneumonia (n = 5) and thrombocytopenia (n = 4). Incidence of AEs, including the most common (any grade and grade ≥3), are shown in the Table. Events of clinical interest (ECIs) included atrial fibrillation (afib) of any grade in 46 (4%) pts and grade ≥3 in 13 (1%) pts; major hemorrhage (any grade) in 37 (4%) pts; grade ≥3 infection in 183 (18%) pts; hypertension (any grade) in 79 (8%) pts and grade ≥3 in 36 (4%) pts; and second primary malignancies (SPM) excluding non-melanoma skin cancer (NMSC; any grade) in 68 (7%) pts. Median (range) time to first onset in days for each ECI (any grade) was: afib, 522 (8–1280); major hemorrhage, 293 (4–1327); infections, 92 (1–1317); hypertension, 157 (2–1345); SPM excluding NMSC, 339 (7–1499). Death was reported in 139 (13%) pts, most commonly due to PD (6%) and AEs (5%). **Conclusions:** Acala monotx has a favorable tolerability profile with increased exposure across multiple mature B cell malignancies. Additional analyses will further explore the longitudinal characteristics of AEs. Research Sponsor: Acerta Pharma, a member of the AstraZeneca group.

Incidence of any AEs, serious AEs, and most common AEs (any grade occurring in ≥15% of pts and grade ≥3 occurring in ≥5% of pts).

	Any Grade, n (%)	Grade ≥3, n (%)
Any AEs	1001 (96)	563 (54)
Serious AEs	405 (39)	360 (35)
Common AEs		
Headache	393 (38)	11 (1)
Diarrhea	382 (37)	27 (3)
Upper respiratory tract infection	229 (22)	8 (1)
Contusion	226 (22)	0
Nausea	226 (22)	12 (1)
Fatigue	222 (21)	18 (2)
Cough	218 (21)	1 (< 1)
Arthralgia	119 (19)	7 (1)
Anemia	138 (13)	81 (8)
Neutropenia	128 (12)	116 (11)
Pneumonia	90 (9)	53 (5)

8065 Poster Session (Board #398), Fri, 8:00 AM-11:00 AM

A phase I/II study to assess safety and dose of ixazomib in combination with cyclophosphamide and dexamethasone in newly diagnosed patients with light chain (AL) amyloidosis. *First Author: Keren Osman, Rockefeller Univ, New York, NY*

Background: AL amyloidosis is an incurable clonal plasma cell disorder characterized by tissue deposits of immunoglobulin light chain fragments leading to organ dysfunction and death. Standard treatment for newly diagnosed patients (pts) has traditionally included oral melphalan + dexamethasone as well as high-dose melphalan + ASCT. Here we report preliminary results of a Phase 1/2, open-label, multi-institution study of ixazomib (I) in combination with cyclophosphamide (Cy) and dexamethasone (D) in newly diagnosed AL amyloidosis. **Methods:** Eligible pts are ≥18 years with newly diagnosed, untreated biopsy-proven AL amyloidosis. A total of up to 30 pts will be enrolled, with up to 18 in the dose escalation arm (phase 1) and 12 in the maximum tolerated dose (MTD) expansion arm (phase 2) according to a classical 3+3 design. Four dose levels were evaluated in phase 1. I and Cy are given orally (PO) on days 1, 8, 15, and D 20mg PO on days 1, 8, 15, 22 of each 28-day cycle. Treatment continues for a total of 6 cycles or until disease progression, significant toxicity or withdrawal. The primary study objective in phase 1 is to establish the MTD and in phase 2 is to determine hematologic/organ response rate. **Results:** As of February 2020, 120 pts have been enrolled; 16 in phase 1 and 4 in phase 2. The MTD was established at dose level 3 (I 4mg and Cy 500mg). Median age is 65 years (range 46-79), 12 (67%) are male. Light chain isotype is lambda in 14 (78%). Seven pts (39%) have cardiac, 10 (56%) renal, 4 (22%) gastrointestinal, 1 (6%) hepatic, 2 (11%) soft tissue involvement, with 22% having multi-organ involvement. Four pts (22%) completed 6 cycles of therapy and 6 (33%) remain on study with a median of 3 cycles completed. Eight of 16 pts (50%) had at least 1 drug-related adverse event (AE) (any grade), most commonly edema (19%), fatigue (19%), dizziness/lightheadedness (13%) and lymphopenia (13%). Grade 3/4 AEs were rare with grade 3 lymphopenia, anemia, and hyponatremia occurring in 13%, 6%, and 6% of pts, respectively. Of 18 evaluable pts, 7 (39%) achieved ≥VGPR with the median time to best response 2 cycles (1-5). **Conclusions:** The combination of ICyD for pts with newly diagnosed AL amyloidosis is safe and well tolerated. Phase 1 is completed and the recommended phase 2 dose has been established. Deep hematologic responses (≥VGPR) have occurred and time to response appears similar to standard of care induction regimens, ie CyBorD. Phase 2 response data will be updated at the meeting. Research Sponsor: Takeda.

TPS8066 Poster Session (Board #399), Fri, 8:00 AM-11:00 AM

Trial in progress: a phase II, multicenter, single-arm study of zanubrutinib (BGB-3111) in patients with previously treated chronic lymphocytic leukemia/small lymphocytic lymphoma intolerant of prior treatment with ibrutinib. *First Author: Ian Flinn, Sarah Cannon Research Institute/ Tennessee Oncology, Nashville, TN*

Background: Ibrutinib (ibr), a Bruton tyrosine kinase inhibitor (BTKi), was shown to improve patient outcomes in chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL); however, adverse events (AEs) were the most common reason for discontinuing ibr (50% and 63% of discontinuations in relapse/refractory (R/R) and frontline patients, respectively; *Haematologica.* 2018:103:874). Zanubrutinib, an approved BTKi for mantle cell lymphoma, was specifically engineered to optimize selectivity. Pooled clinical data from 6 zanubrutinib monotherapy trials in B-cell malignancies (N=682 patients; R/R CLL/SLL [n=91]) suggested that zanubrutinib monotherapy was well tolerated and demonstrated a low rate of treatment discontinuation from AEs (9%; Tam, EHA 2019). Presented here is a trial-in-progress that will evaluate whether zanubrutinib monotherapy may serve as a therapeutic option for patients with CLL/SLL who have become ibr intolerant. **Methods:** The ongoing phase II, multicenter, US, single-arm, open-label study (NCT04116437, BGB-3111-215) will evaluate zanubrutinib monotherapy (160mg twice daily) as a treatment option for patients with CLL/SLL intolerant to prior ibr treatment. Approximately 60 patients will be enrolled from ~30 community medical centers. Key inclusion criteria include CLL/SLL requiring treatment per International Workshop on CLL criteria (*Blood.* 2018;131:2745) before ibr therapy, intolerance to ibr (defined as an unacceptable AE for which, per investigator's opinion, ibr treatment should be discontinued despite optimal supportive therapy), resolution of ibr-related AEs to grade ≤1 or baseline, and an ECOG PS 0-2. Key exclusion criteria include having an intervening cancer therapy between ibr and zanubrutinib, a documented disease progression during ibr treatment up to the time of enrollment, and a history of central nervous system (CNS) hemorrhage. The primary endpoint is frequency and severity of protocol-specified treatment-emergent AEs (diarrhea, myalgia, muscle spasm, arthralgia, hypertension, fatigue, rash, atrial fibrillation, and hemorrhage excluding CNS hemorrhage). The secondary endpoints include overall response rate, progression-free survival, and patient-reported outcomes. An exploratory endpoint was added to evaluate clinical effects (physical activity, treatment-related symptoms, and quality of life) using a smartphone app. Recruitment is ongoing. Clinical trial information: NCT04116437. Research Sponsor: BeiGene.

TPS8067 Poster Session (Board #400), Fri, 8:00 AM-11:00 AM

An intergroup collaboration for advanced stage classical Hodgkin lymphoma (cHL) in adolescents and young adults (AYA): SWOG S1826. *First Author: Sharon M. Castellino, Emory University, Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta, Atlanta, GA*

Background: Treatment for pediatric cHL varies considerably from that in adult cHL. Hence there are gaps in risk prediction and optimal therapy for de-novo advanced stage disease across the adolescent and young adult (AYA) age spectrum. Early access to novel agents for AYA could be facilitated via collaboration with adult research groups through the U.S. National Cancer Institute's National Clinical Trials Network (NCTN). The PD-1 inhibitor Nivolumab (Nivo) has safety and efficacy in relapsed and refractory disease in children and adults, but has not been evaluated in de-novo disease to date. **Methods:** North American cooperative group lymphoma chairs, Cancer Therapy Evaluation Program (CTEP) representatives and patient advocates met to establish consensus on the comparison arms and study design, based on recent historical approaches across adult and pediatric groups. Study champions were identified across North American cooperative groups and include expertise in imaging, radiation oncology, biology and patient-reported outcomes. A therapeutic study was designed with the primary aim being to compare progression-free survival with novel targeted agents in advanced stage cHL. S1826 (NCT03907488), led by SWOG Cancer Research Network, opened to accrual in July 2019. Eligibility criteria include age > 12 years, and Stage III or IV cHL. Patients are randomized (1:1) to 6 cycles of either Nivo-Adriamycin, Vinblastine, Dacarbazine (AVD) or Brentuximab vedotin (Bv)-AVD. Enrollment is stratified by age, baseline International Prognostic Score, and provider intent to use involved site radiation therapy (ISRT). Protocol-prescribed ISRT is response-adapted, based on end of therapy imaging. The primary endpoint is a comparison of progression-free survival between arms. Secondary clinical endpoints include comparison of: overall survival, metabolic response at the end of therapy, physician-reported adverse events, patient-reported adverse events, and health-related quality of life (overall, and specific to fatigue and neuropathy). This unique intergroup collaboration demonstrates the process and the feasibility of consensus study designs toward early adoption of targeted therapies and harmonization of treatment approaches for AYA populations. Clinical trial information: NCT03907488. Research Sponsor: U.S. National Institutes of Health.

TPS8068 Poster Session (Board #401), Fri, 8:00 AM-11:00 AM

Brentuximab vedotin in combination with nivolumab, doxorubicin, and dacarbazine in newly diagnosed patients with advanced-stage Hodgkin lymphoma (Trial in Progress). *First Author: Judah D. Friedman, University Hospitals Seidman Cancer Center, Cleveland, OH*

Background: Brentuximab vedotin (BV, ADCETRIS) is approved for the treatment of adults with treatment-naïve Stage III or IV cHL in combination with AVD (Connors 2017). Nivolumab is approved for treatment of adults with relapsed/refractory cHL. Both agents have been well tolerated with promising activity when combined with multi-agent chemotherapy. The combination of BV plus nivolumab was evaluated as a frontline treatment option for patients (pts) with cHL who are over 60 years and ineligible for or declined conventional combination chemotherapy (Friedberg, 2018). The ongoing study reported an ORR of 82% in 11 pts and appears well tolerated in this population. In another trial in 93 patients in the first salvage setting, the combination produced a 67% CR rate (Herrera 2018, Moskowitz 2019) and the majority of patients were able to undergo subsequent stem cell transplant. It is reasonable to expect that the combination of BV, nivolumab, A, and D (AN + AD) will result in high response rates and be well tolerated, with potentially less toxicity. **Methods:** SGN35-027 (NCT03646123) is a phase 2 study designed to evaluate the efficacy and safety of A+AVD when administered with growth factor prophylaxis in pts with stage III/IV cHL (Part A). Part B will evaluate the combination of AN + AD in a similar patient population. The primary objective of Part B is to estimate the CR rate at EOT in pts with treatment-naïve advanced cHL. Patients in Part B will have Ann Arbor Stage IIB/III/IV cHL or Stage IIA cHL with bulky mediastinal disease. Enrollment is ongoing in both parts of the study. Approximately 50 pts will be enrolled in Part B. All pts will be treated with BV 1.2 mg/kg, nivolumab 240 mg, doxorubicin 25 mg/m^2, and dacarbazine 375 mg/m^2, administered separately by IV infusion on Days 1 and 15 of each 28-day cycle for up to 6 cycles. Efficacy will be assessed by PET/CT scans at C2 and EOT. Disease assessments will be performed periodically during follow up. Disease response and progression will be assessed using Lugano with the incorporation of LYRIC (Cheson 2016). Clinical trial information: NCT03646123. Research Sponsor: Seattle Genetics, Inc.

TPS8069 Poster Session (Board #402), Fri, 8:00 AM-11:00 AM

Frontline brentuximab vedotin in Hodgkin lymphoma and CD30-expressing peripheral T-cell lymphoma for older patients and those with comorbidities. *First Author: Christopher A. Yasenchak, Willamette Valley Cancer Institute and Research Center/US Oncology Research, Eugene, OR*

Background: Older patients and those with significant comorbidities have not attained outcomes seen in younger patients with classical Hodgkin lymphoma (cHL) and CD30-expressing peripheral T-cell lymphoma (PTCL). Five-year progression-free survival (PFS) was 30%–45% in older HL patients treated with combination chemotherapy versus 75%–80% in younger patients (Evens 2008; Proctor 2009). Similarly, when adjusted for age, a Charleston Comorbidity Index ≥2 was independently associated with worse overall survival (HR=1.63) and PFS (HR=1.54) (Ellin 2018). Brentuximab vedotin (BV, ADCETRIS), a CD30-directed antibody-drug conjugate, has robust activity in cHL patients refractory to several lines of chemotherapy. BV monotherapy in 27 cHL patients aged ≥60 years had a 92% objective response rate (ORR) and 73% achieved complete remission (Forero-Torres, 2015). BV was also active and well-tolerated in CD30-expressing PTCL patients with relapsed or refractory disease (Horwitz 2014). Frontline BV monotherapy may have the potential to be an active and well-tolerated treatment for cHL and PTCL patients who are older or have significant comorbidities, which are populations with high unmet need. **Methods:** This phase II, open-label study, SGN35-015 (NCT01716806), has added 2 cohorts to evaluate the efficacy and tolerability of BV monotherapy in treatment naive patients with cHL, (Part E), or CD30-expressing PTCL (Part F, n~50 each) who are unsuitable for conventional combination therapy due to comorbidity-related factors as determined by a Cumulative Illness Rating Scale (CIRS) score ≥10 or dependence on others for any instrumental activities of daily living. Eligible patients must also have an Eastern Cooperative Oncology Group (ECOG) performance status ≤3 and measurable disease ≥1.5 cm per radiographic techniques. BV (1.8 mg/kg) will be administered as a single intravenous infusion on day 1 of each 2-day cycle. Patients achieving a complete remission, partial remission, or stable disease will receive up to 16 cycles of treatment. Response will be assessed by blinded independent central review of spiral CT and PET scans at Cycles 2, 6, 11, and at end of treatment to be graded per Lugano 2014. The primary objective of these cohorts is to assess ORR of frontline therapy with single-agent BV in patients who have significant comorbidities. Clinical trial information: NCT01716806. Research Sponsor: Seattle Genetics.

TPS8070 Poster Session (Board #403), Fri, 8:00 AM-11:00 AM

POLARGO: Randomized Phase III study of polatuzumab vedotin plus rituximab, gemcitabine, and oxaliplatin (R-GemOx) in relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL). *First Author: Corinne Haioun, Lymphoïd Malignancies Unit, Groupe Hospitalier Henri Mondor, Créteil Cedex, France*

Background: The antibody-drug conjugate polatuzumab vedotin (pola; POLIVY) targets CD79b on B-cell malignancies. Pola plus bendamustine and rituximab (BR) has significantly improved efficacy vs BR alone in patients (pts) with R/R DLBCL. As a result, pola-BR was approved by the FDA for pts with R/R DLBCL after ≥2 prior therapies. This year, the EU granted conditional marketing authorization for pola-BR in pts with stem cell transplant (SCT)-ineligible R/R DLBCL. A range of therapies are used for R/R DLBCL; one recommended option is R-GemOx. Platinum-based chemotherapies such as oxaliplatin are a preferred salvage therapy. In the POLARGO study, the safety and efficacy of pola-R-GemOx vs R-GemOx alone will be assessed in pts with R/R DLBCL. **Methods:** POLARGO (MO40598; NCT04182204) is a multicenter, open-label, Phase III study, comprising a safety run-in stage (pola-R-GemOx; n=10) and a randomized controlled trial (RCT) stage (pola-R-GemOx vs R-GemOx alone; expected n=206). Pts must have histologically confirmed R/R DLBCL and ECOG PS of 0–2. Exclusion criteria include prior allogeneic SCT and/or planned autologous/allogeneic SCT, and baseline grade >1 peripheral neuropathy (PN). Pts in the RCT stage will be recruited from 80–90 sites globally. The primary endpoint of the safety run-in stage is the safety and tolerability of pola-R-GemOx (pola, 1.8mg/kg; R, 375mg/m^2; Gem, 1000mg/m^2; Ox, 100mg/m^2) administered in 21-day cycles, with a focus on PN. In the RCT stage, pts will be stratified by number of prior lines of therapy, outcome of last systemic therapy and age, and randomized (1:1) to receive up to eight 21-day cycles of pola-R-GemOx or R-GemOx. The RCT stage primary endpoint is overall survival. Key secondary endpoints are independent review committee-assessed complete response (CR) and objective response rate (ORR; Lugano 2014 criteria). Other secondary efficacy endpoints include investigator-assessed best overall response, CR rate and ORR. Safety and health-related quality of life during treatment will be assessed. PET-CT and CT scans will be obtained at screening, during, and after the treatment period; follow-up will continue for up to 2 years. POLARGO is currently open and recruiting. Acknowledgment: POLARGO is sponsored by F. Hoffmann-La Roche Ltd. Third-party medical writing assistance, under the direction of Prof. Haioun, Dr McMillan and Dr Hernandez, was provided by Lucinda Sinclair of Gardiner-Caldwell Communications and was funded by F. Hoffmann-La Roche Ltd. Clinical trial information: NCT04182204. Research Sponsor: F. Hoffmann-La Roche Ltd.

TPS8071 Poster Session (Board #404), Fri, 8:00 AM-11:00 AM

Trial in progress: A phase III, randomized, open-label study comparing zanubrutinib plus rituximab versus bendamustine plus rituximab in patients with previously untreated mantle cell lymphoma (MCL). *First Author: Martin H. Dreyling, University Hospital Großhadern, Ludwig Maximilians-University, Munich, Germany*

Background: Bruton tyrosine kinase (BTK) mediates B-cell proliferation, migration, and adhesion. BTK inhibition has emerged as a strategy for targeting B-cell malignancies, including MCL. Zanubrutinib is a next-generation BTK inhibitor that was designed to maximize BTK occupancy and minimize off-target inhibition of TEC- and EGFR-family kinases, with favorable pharmacokinetic and pharmacodynamic properties. Zanubrutinib monotherapy has been evaluated in 118 patients (pts) with relapsed/refractory MCL in 2 single-arm studies: BGB-3111-206 [NCT03206970] and BGB-3111-AU-003 [NCT02343120]. The overall response rate (ORR) by independent review committee (IRC) in both trials was 84% with median durations of response of 19.5 and 18.5 months, respectively. First-line treatment for MCL has failed to cure most pts, particularly elderly or transplant-ineligible groups, and chemotherapy-based approaches result in cumulative, long-term risks. The study described herein is designed to evaluate the safety and efficacy of zanubrutinib plus rituximab versus bendamustine plus rituximab in elderly pts and pts with comorbidities with previously untreated MCL who are ineligible for stem cell transplant. **Methods:** This ongoing phase 3, open-label study will enroll ≈500 pts to be randomized 1:1, stratified by MCL International Prognostic Index score (low vs intermediate/high), age (< 70 vs ≥70 years), and geographic region (North America/Europe vs Asia-Pacific). In arm A, pts will receive up to six 28-day cycles of oral zanubrutinib 160 mg twice daily in combination with intravenous (IV) rituximab 375 mg/m^2 on day 1 of each cycle. After 6 cycles, zanubrutinib will continue as a monotherapy until progressive disease, unacceptable toxicity, or withdrawal of consent. In arm B, pts will receive up to six 28-day cycles of IV bendamustine 90 mg/m^2 on days 1 and 2 of each cycle and rituximab 375 mg/m^2 on day 1 of each cycle, followed by observation. Eligible pts must have histologically confirmed MCL and be aged ≥70 years, or 65-69 years with defined comorbidities. Disease response will be assessed per the 2014 Lugano Classification for non-Hodgkin lymphoma. The primary endpoint is progression-free survival (PFS) determined by IRC. Key secondary end points include PFS by investigator assessment, ORR, time to and duration of response, overall survival, and safety. Recruitment is ongoing. Clinical trial information: NCT04002297. Research Sponsor: BeiGene.

TPS8072 Poster Session (Board #405), Fri, 8:00 AM-11:00 AM

A phase I and randomized phase II etctn study of KW-0761 (Mogamulizumab) and MK-3475 (Pembrolizumab) in relapsed and refractory diffuse large B-cell lymphoma. *First Author: Erel Joffe, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Diffuse large B-cell lymphoma (DLBCL) escapes host immune responses via inhibition of the B2M and CD58 pathways and upregulation of PD-1 ligands. However, treatment results with PD-1 blockade have been disappointing. One potential mechanism is the recruitment of intra-tumoral regulatory T-cells (Tregs) which suppress anti-tumor immunity and inhibit NK cell cytotoxicity. Targeting regulatory T cells with the CCR4 antibody mogamulizumab (KW-0761) represents a molecularly informed strategy to overcome this resistance. Mogamulizumab has been safely administered in combination with pembrolizumab (MK-3475) in patients with solid malignancies and may promote CD8 T-cell dependent effector and NK cell-dependent cytotoxicity in lymphomas. **Methods:** This is a multi-center NIH-ETCTN phase Ib/randomized phase II study. The phase I will evaluate the safety and tolerability of mogamulizumab in combination with pembrolizumab in patients with R/R DLBCL and determine the recommended phase II dose (RP2D). A traditional 3+3 design with a starting dose of pembrolizumab 200mg IV on day 1 of a 21-day cycle and mogamulizumab 1mg/kg IV on days 1, 8, 15 and then 1.5 mg/kg IV every 21 days. The phase II will evaluate the efficacy of the combination by PFS (primary endpoint) ORR and CR (secondary endpoints). This will be a randomized 1:1 study with allowed crossover, comparing the combination to single agent pembrolizumab Correlative studies will evaluate the association of tumor infiltrating CD8 and NK cells with response to treatment, somatic mutations in B2M and CD58 and with MHC-I expression on DLBCL cells. Functional characterization of circulating immune cells in the peripheral blood and measurement of pro and anti-inflammatory cytokines will be used to assess the levels, activation status and effector function of Tregs and circulating T cells. Inclusion criteria include measurable disease, $\geq$2 prior lines of therapy including or ineligible for autologous stem cell transplant, ECOG $\leq$ 2 and normal organ function. Prior or planned allogeneic stem cell transplant, as well as prior treatment with an anti PD-1/PD-L1/CTLA4 antibody, preexisting autoimmune disease or CNS involvement by lymphoma are exclusion criteria. The study aims to enroll up to 12 patients on the phase I and up to 58 patients on the phase II and can be opened at any ETCTN participating site. To date it has been opened at two sites and is accruing the first patients for the phase I portion. Clinical trial information: NCT03309878. Research Sponsor: U.S. National Institutes of Health.

TPS8073 Poster Session (Board #406), Fri, 8:00 AM-11:00 AM

Phase I/II study of R-ICE (rituximab-ifosfamide-carboplatin-etoposide) with lenalidomide (R2-ICE) in patients with first-relapse/primary refractory diffuse large B-cell lymphoma (DLBCL) in academic and community cancer research united (ACCRU) network. *First Author: Francis Guerra-Bauman, Mayo Clinic, Rochester, MN*

Background: Response rates to salvage immunochemotherapy in patients with DLBCL relapsing after or refractory (R/R DLBCL) to front line therapy remain unsatisfactory. Lenalidomide (Len) has significant single agent activity in relapsed/refractory DLBCL. The addition of lenalidomide (Len) days 1-7 to rituximab plus ifosfamide-carboplatin-etoposide (RICE) was shown to be feasible with promising efficacy in phase 1b study (Feldman T, et al. BJH, 2014). We developed phase I/II study to evaluate the safety and efficacy of the addition of Len (extended to 14 day schedule) to RICE (R2-ICE) for R/R-DLBCL patients who are candidates for stem cell transplant. **Methods:** The phase I portion was designed to determine the maximally tolerated dose Len in combination with RICE using the standard cohort 3+3 design. The escalation dose levels were 15 mg and 20 mg daily x 14 days. Prophylactic aspirin and growth factor support is mandatory. After 2 cycles of therapy response is evaluated with a PET/CT scan; the responding patients are eligible for 1-2 additional cycles of R2ICE as a bridging before HDC/SCT. The estimated overall response rate for two cycles of R-ICE in R/R DLBCL to RCHOP was estimated to be approximate 45%. We hypothesize that the addition of lenalidomide in the relapse setting could increase the overall response rate by approximately 20%. The one-stage design with an interim analysis being utilized in phase 2 requires 45 evaluable patients (one sided alpha = 0.09, power 90%). For Phase I, all types of B-cell lymphomas were eligible. For phase II portion only DLBCL patients are eligible per central pathology review. Other eligibility criteria include: received one line of previous anti-lymphoma therapy, $\geq$ 2 weeks from completion of prior anti-lymphoma therapy, candidate for HDC and SCT, adequate organ (creatinine clearance $\geq$ 60ml/min by Cockcroft-, total bilirubin $\leq 2 \times$ ULN) and bone marrow function (ANC) $\geq$1500/mm^3; platelet count $\geq$75,000/mm3). The use of steroids and/or rituximab up to 1 week prior to registration for management of symptoms is allowed. 9 patients cleared phase 1 without DLT and dose of 20 mg days 1 -14 was recommend for phase 2 part (RP2D) of the study. The phase 2 study passed interim futility analysis and accrual continues. Correlatives include cell of origin by Nanostring, Myc/bcl2 expression and by FISH and minimal residual disease. PET scans are centrally reviewed including metabolic tumor volume. Clinical trial information: NCT02628405. Research Sponsor: Celgene/BMS.

TPS8074 Poster Session (Board #407), Fri, 8:00 AM-11:00 AM

A phase II study of MT-3724, a novel CD20-targeting engineered toxin body, to evaluate safety, pharmacodynamics, and efficacy in subjects with relapsed or refractory diffuse large B-cell lymphoma. *First Author: Adolfo Enrique Diaz Duque, University of Texas Health at San Antonio, San Antonio, TX*

Background: Engineered toxin bodies (ETBs) are comprised of a proprietarily engineered form of Shiga-like Toxin A subunit (SLT-A) genetically fused to antibody-like binding domains. ETBs work through novel mechanisms of action and are capable of forcing internalization, self-routing through intracellular compartments to the cytosol, and inducing potent cell-kill via the enzymatic and permanent inactivation of ribosomes. MT-3724 represents a novel ETB modality comprised of an anti-CD20 single-chain variable fragment genetically fused to SLT-A. It is capable of efficient internalization once bound to CD20 and can induce potent direct cell-kill via enzymatic ribosome inactivation. MT-3724 is currently being studied in three ongoing Phase 2 studies for relapsed or refractory diffuse large B-cell lymphoma (r/rDLBCL). **Methods:** The primary objective of this single-arm, Phase 2 study (NCT02361346) is to determine the efficacy of MT-3724 monotherapy in r/rDLBCL based on overall response rate (ORR), defined as the proportion of subjects with a complete/partial response according to the Lugano criteria, as assessed by independent, central review. Key secondary objectives include safety, progression-free survival, investigator-assessed ORR, duration of response, overall survival, and pharmacodynamics. Adverse events will be assessed and documented according to Common Terminology Criteria for Adverse Events version 5.0. Key eligibility criteria include adult subjects with histologically confirmed, r/rDLBCL, with $\geq$2 prior standard of care systemic NHL treatment regimens, and $\geq$1 measurable lesion. As rituximab and other CD20-targeting antibodies compete with MT-3724 for the same CD20 domain, minimum washout periods from these agents must be observed. Subjects remain eligible post stem cell transplant or chimeric antigen receptor T-cell therapy. Subjects will receive 50 μg/kg MT-3724 IV over 1 hour on Days 1, 3, 5, 8, 10 and 12 of a 21-day treatment cycle. The anticipated sample size is N = 100. Interim analyses will be performed to confirm minimum efficacy thresholds based on the encouraging data observed in the completed phase 1 portion of the study [Hamlin et al. Blood 2019;134(Suppl 1):4098]. Multiple global sites are enrolling subjects. Clinical trial information: NCT02361346. Research Sponsor: Molecular Templates, Inc.

TPS8075 Poster Session (Board #408), Fri, 8:00 AM-11:00 AM

Phase I study of radiotherapy (RT) & durvalumab in relapsed/refractory diffuse large B-cell lymphoma (DLBCL) & follicular lymphoma (FL): The RADD study. *First Author: Eliza Anne Hawkes, Austin Health and Olivia Newton-John Cancer Research Institute, Heidelberg, Australia*

Background: Most DLBCL & FL responds well to first line treatment, yet relapsed disease outcomes are poor. PD1/PDL1 inhibitors yield high response rates in some lymphomas, but single agent therapy in heavily pretreated pts are disappointing. RT stimulates anti-tumor immunity through several mechanisms and may enhance response to immune checkpoint inhibition (ICI). Concurrent ICI & RT is synergistic in preclinical studies & solid tumors, improving local & distant (abscopal) response. RT to multiple disease sites may broaden the spectrum of tumor antigen release and overcome clonal variation between disease sites to further augment the immune response. **Methods:** RaDD (NCT03610061) is a phase I, 3+3 dose escalation study to determine the safety profile of escalating dose & number of sites of RT in combination with Durvalumab (anti-PD-L1 antibody) in RR DLBCL & FL. Eligible pts (i.e. $\geq$1 prior therapy, ineligible for auto-SCT, no contraindication to PDL1i) receive 5 fractions of external beam RT to target site(s). 5 RT dose & site levels are included (dose range 2.5Gy-20Gy to 1-3 sites). Durvalumab 1500mg IV commences day 2 of RT and continues 4-weekly until confirmed disease progression. The DLT period is 28 days from start of RT. Primary endpoint is the recommended phase two dose (RP2D) of RT in combination with durvalumab. Secondary endpoints include response rates, PFS & OS. Correlative studies will examine the tumour-immune system interaction; an exploratory PET substudy with novel tracers for durvalumab (^{89}Zr-Durvalumab) & CD8+ T cells (^{89}Zr -Df-IAB22M2C) will also be performed. Projected enrollment for determination of maximum tolerated dose (MTD) & RP2D is 6-30 pts pending toxicity. Recruitment will continue to 36 pts for secondary endpoint analysis. 9 pts are enrolled across cohorts 1-3 to date. Clinical trial information: NCT03610061. Research Sponsor: Victorian Cancer Agency (grant funding - TRP16006), Pharmaceutical/Biotech Company.

8500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

First-in-human phase I study of the novel CELMoD agent CC-92480 combined with dexamethasone (DEX) in patients (pts) with relapsed/refractory multiple myeloma (RRMM). *First Author: Paul G. Richardson, Dana-Farber Cancer Institute, Boston, MA*

Background: CC-92480 is a novel cereblon E3 ligase modulator (CELMoD) agent designed for rapid, maximal degradation of Ikaros and Aiolos. In vitro, it has enhanced antiproliferative and tumoricidal activity in MM cell lines, including those resistant to lenalidomide (LEN) and pomalidomide (POM), with strong immune stimulatory activity. **Methods:** A phase 1, multicenter, dose-escalation study evaluated the maximum tolerated dose (MTD), recommended phase 2 dose, safety, tolerability, and pharmacokinetics of CC-92480 + DEX in heavily pretreated RRMM pts. Eligible pts had progression on or within 60 days of their last MM therapy and were either resistant or intolerant to, or not otherwise candidates for currently available therapies. Several treatment schedules tested escalating doses of CC-92480 + DEX (40 mg; 20 mg if ≥75 yrs). **Results:** As of Dec 24, 2019, 66 pts had received CC-92480 + DEX. Median age was 67 yrs (range 40–78), median number of prior regimens was 6 (range 2–13). Prior therapies included stem cell transplantation (67%), bortezomib (92%), LEN (89%), POM (83%), and anti-CD38 antibodies (78%). CC-92480 doses explored included 0.1–1.0 mg QD (10/14 days × 2), 0.8–1.0 mg QD (21/28 days), 0.2–0.8 mg BID (3/14 days × 2), and 1.6–2.0 mg QD (7/14 days × 2). MTD was 1.0 mg for both 10/14 × 2 and 21/28 schedules. Grade 3–4 treatment-emergent adverse events (TEAEs) were reported in 58 (88%) pts. Most frequent grade 3–4 TEAEs included neutropenia (53%), infections (30%), anemia (29%), and thrombocytopenia (17%), with 9% grade 3 fatigue. Among different cohorts, 10 pts had dose-limiting toxicities (the majority related to neutropenia). Overall response rate (ORR) was 21% (9 very good partial responses [VGPRs]; 5 PRs) for efficacy evaluable population (n = 66). Efficacy was dose and schedule dependent; across two 1.0 mg QD schedules (10/14 × 2 and 21/28), 10 of 21 (48%) pts responded (7 VGPR and 3 PR), with response independent of immunomodulatory drug (IMiD) refractoriness. Plasma exposure increase and peripheral blood Ikaros and Aiolos degradation were dose dependent. Ikaros and Aiolos significantly decreased in bone marrow plasma cells of LEN- and POM-refractory pts. **Conclusions:** TEAEs of CC-92480 were mainly related to myelosuppression in heavily pretreated, including triple-class-refractory, RRMM pts. Promising activity with 48% ORR at therapeutic doses was observed. The study is ongoing to further optimize dose and schedule, with combination studies underway and dose expansion cohorts planned. Clinical trial information: NCT03374085. Research Sponsor: Bristol-Myers Squibb.

8501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Weekly selinexor, bortezomib, and dexamethasone (SVd) versus twice weekly bortezomib and dexamethasone (Vd) in patients with multiple myeloma (MM) after one to three prior therapies: Initial results of the phase III BOSTON study. *First Author: Meletios A. Dimopoulos, National and Kapodistrian University of Athens School of Medicine, Athens, Greece*

Background: Selinexor is an oral, selective inhibitor of XPO1-mediated nuclear export, leading to the reactivation of tumor suppressor proteins. In a phase 1b/2 study, the combination of once weekly (QW) selinexor with bortezomib and dexamethasone (SVd) was well tolerated with anti-MM activity in patients (pts) with PI-sensitive and PI-refractory disease. While twice weekly (BIW) bortezomib in combination therapy is efficacious, prolonged use is limited due to peripheral neuropathy (PN, 50-60%). The BOSTON study was designed to determine if SVd improves progression free survival (PFS), overall response rates (ORR) and reduces the rate of PN vs Vd. **Methods:** BOSTON is a global, phase 3, randomized study of QW SVd vs BIW Vd after 1-3 prior anti-MM regimens. The primary endpoint is PFS. Secondary endpoints include ORR, overall survival (OS) and PN (rates and EORTC QLQ-CIPN20 outcomes). Randomization is stratified by treatment with prior PI therapies, number of prior anti-MM regimens (1 vs > 1), and Revised International Staging System (R-ISS; Stage III vs I or II). Following confirmation of progressive disease, pts on Vd could cross over to either: 1) SVd for pts able to tolerate continued bortezomib or 2) selinexor and dexamethasone for pts with bortezomib intolerance. **Results:**402 pts were enrolled; 195 and 207 to SVd and Vd, respectively. Median age was 67 (range: 38-90). Most (59.6%) pts were > 65 years and 57.1% were male. R-ISS stage at the time of MM diagnosis was III for 18.5% of pts. Baseline characteristics were balanced across the 2 arms. SVd significantly prolonged PFS vs Vd (median 13.93 vs 9.46 months, HR = 0.70, P = 0.0066). SVd was associated with a significantly higher ORR (76.4% vs 62.3%, P = 0.0012). Median OS was not reached on SVd vs 25 months on Vd (P = 0.28). Most frequent treatment-related adverse events (grade ≥3) for SVd vs Vd were thrombocytopenia (35.9% vs 15.2%), fatigue (11.3% vs 0.5%) and nausea (7.7% vs 0%). Clinically important differences were reported on the motor, autonomic and sensory scales on CIPN20. PN rates (grade ≥2) were significantly lower with SVd vs Vd (21.0% vs 34.3%, P = 0.0013). **Conclusions:** BOSTON is the first phase 3 study to evaluate the clinical benefit of SVd for relapsed/refractory MM. The study met the primary endpoint: once weekly SVd significantly improved PFS and ORR compared to twice weekly Vd. Rates of PN were significantly reduced with numerically fewer deaths on SVd vs Vd. Full dataset will be presented at the meeting. Clinical trial information: NCT03110562. Research Sponsor: Karyopharm Therapeutics Inc.

8502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

DREAMM-6: Safety and tolerability of belantamab mafodotin in combination with bortezomib/dexamethasone in relapsed/refractory multiple myeloma (RRMM). *First Author: Ajay K. Nooka, Emory University Hospital, Winship Cancer Institute, Atlanta, GA*

Background: Belantamab mafodotin, a B-cell maturation antigen targeting immunoconjugate, demonstrated clinically meaningful, single-agent activity in patients with heavily pre-treated RRMM refractory to an immunomodulatory agent, a proteasome inhibitor, and refractory and/or intolerant to an anti-CD38 monoclonal antibody (DREAMM-2, NCT03525678, *Lancet Oncol*.2020). The multimodal mechanism of action and manageable safety profile make belantamab mafodotin a promising candidate for use in different RRMM combination regimens. **Methods:** DREAMM-6 (NCT03544281) is an ongoing, two-part, two-arm, study evaluating the safety, tolerability, and clinical activity of belantamab mafodotin in combination with bortezomib/dexamethasone (BorDex) and lenalidomide/dexamethasone in patients previously treated with ≥1 prior therapy line. Here, we present data for belantamab mafodotin in combination with BorDex. Part 1 (dose escalation) and Part 2 (dose expansion) evaluated belantamab mafodotin (2.5 and 3.4 mg/kg) administered as SINGLE (Day 1) or SPLIT dose (divided equally on Days 1 and 8) in combination with BorDex. **Results:** As of February 6, 2020, 52 patients were enrolled: 6 patients were enrolled at 2.5 mg/kg single dose and 7 at 3.4 mg/kg single dosing in Part 1, and 45 patients in Part 2. No dose-limiting toxicities were observed. Corneal events (including keratopathy, blurred vision, and dry eye) and thrombocytopenia were the most frequently reported AEs and were clinically manageable. **Conclusions:** In DREAMM-6, preliminary data demonstrate that the combination of belantamab mafodotin and BorDex has an acceptable safety profile, with no new safety signals identified. Funding: GlaxoSmithKline (207497). Drug linker technology licensed from Seattle Genetics; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa. Clinical trial information: NCT03544281. Research Sponsor: GlaxoSmithKline.

8503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Idecabtagene vicleucel (ide-cel; bb2121), a BCMA-targeted CAR T-cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): Initial KarMMa results. *First Author: Nikhil C. Munshi, Dana-Farber Cancer Institute, VA Boston Healthcare System, and Harvard Medical School, Boston, MA*

Background: Outcomes are poor in triple-class exposed RRMM patients (pts) who progress on immunomodulatory agents (IMiDs), proteasome inhibitors (PIs), and CD38 antibodies (mAbs). Ide-cel, a BCMA targeted CAR T cell therapy, showed promising tolerability and efficacy in RRMM pts in the phase I CRB-401 study (*NEJM*2019;380:1726). We present primary efficacy and safety data from the pivotal phase II KarMMa trial of ide-cel in RRMM (NCT03361748). **Methods:** Enrolled pts had ≥3 prior regimens (including IMiD, PI, and CD38 mAb) and were refractory to their last regimen per IMWG criteria. After lymphodepletion (cyclophosphamide 300 mg/m^2+ fludarabine 30 mg/m^2 x 3), pts received 150–450 × 10^6 CAR+ T cells (target dose range). Endpoints included overall response rate (ORR; primary), complete response (CR) rate, duration of response (DoR), and PFS. **Results:** Of 140 pts enrolled, 128 received ide-cel. Median age was 61 y; median no. of prior regimens was 6; 84% were triple- and 26% were penta-refractory. Most pts (88%) had bridging therapy. At data cutoff (16 Oct 2019), median follow up was 11.3 mo. ORR was 73% and median PFS was 8.6 mo; both increased with higher dose (Table). All subgroups had an ORR ≥50%, including older and high-risk pts. Most common any-grade (Gr) toxicities were cytopenias (97%) and cytokine release syndrome (CRS; 84%). CRS was mainly Gr 1/2; 5 pts (5%) had Gr 3, 1 had Gr 4, and 1 had Gr 5 (at 300 × 10^6). Neurotoxicity developed in 23 pts (18%); 4 (3%) Gr 3 and 0 Gr ≥4. Median peak CAR+ T cell expansion occurred at 11 d. Expansion was higher in responders and parameters (AUC_{0-28d}, C_{max}) increased with higher dose, with exposure overlap across doses. Persistence was durable, with CAR+ T cells detected in 29/49 (59%) and 4/11 pts (36%) at 6 and 12 mo. **Conclusions:** Ide-cel demonstrated deep, durable responses in heavily pretreated RRMM pts. Efficacy and safety reflected prior reports and support a favorable ide-cel clinical benefit-risk profile across the target dose range. Clinical trial information: NCT03361748. Research Sponsor: Bristol-Myers Squibb and bluebird bio.

Dose, × 10^6 CAR+ T cells	150 (n=4)	300 (n=70)	450 (n=54)	Total (N=128)
ORR, n (%)	2 (50)	48 (69)	44 (82)	94 (73)
CR/sCR, n (%)	1 (25)	20 (29)	19 (35)	40 (31)
Median DoR*, mo	†	9.9	11.3	10.6
Median PFS*, mo	†	5.8	11.3	8.6
CRS overall / Gr ≥3, n (%)	2 (50) / 0	53 (76) / 4 (6)	52 (96) / 3 (6)	107 (84) / 7 (5)
Median onset / duration, d	7 / 5	2 / 4	1 / 7	1 / 5
NT overall / Gr ≥3, n (%)	0 / 0	12 (17) / 1 (1)	11 (20) / 3 (6)	23 (18) / 4 (3)
Median onset / duration, d	NA	3 / 3	2 / 5	2 / 3

NT, investigator identified neurotoxicity; sCR, stringent CR.
*Kaplan-Meier estimate.
†Not reported due to small n.

8504 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Orvacabtagene autoleucel (orva-cel), a B-cell maturation antigen (BCMA)-directed CAR T cell therapy for patients (pts) with relapsed/refractory multiple myeloma (RRMM): update of the phase 1/2 EVOLVE study (NCT03430011). *First Author: Sham Mailankody, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Orva-cel is an investigational, BCMA-directed CAR T cell product with a fully human binder. Over 100 pts have been treated in the EVOLVE phase 1 study. Pts treated at 50 and 150 $\times$ 10^6 CAR+ T cells were previously reported (Mailankody ASH 2018 #957). We now report results of the higher dose levels (DLs) in 51 pts who received orva-cel manufactured using the process intended to support commercial use. **Methods:** Pts with RRMM who had $\geq$3 prior regimens, a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 monoclonal antibody (mAb), received orva-cel at 300, 450, and 600 $\times$ 10^6 CAR+ T cells after lymphodepletion with fludarabine/cyclophosphamide. **Results:** Median pt age was 61 (range, 33–77) y; median time from diagnosis was 7.0 (range, 1.7–23.6) y, with a median of 6 (range, 3–18) prior regimens. Overall, 92% of pts were penta-exposed (2 IMiDs, 2 PIs, and an mAb); 61% of pts received bridging therapy (77% were refractory to bridging therapy). Two pts had dose-limiting toxicities: grade 3 neurological event (NE) for $>$7 d at 300 $\times$ 10^6 CAR+ T cells and grade 4 neutropenia for $>$28 d at 450 $\times$ 10^6 CAR+ T cells. Key efficacy and safety outcomes are shown in the Table. Cytokine release syndrome (CRS)/NEs were managed with tocilizumab and/or steroids (78%), anakinra (14%), and/or vasopressors (6%). Grade $\geq$3 anemia, neutropenia, and thrombocytopenia at 29 d occurred in 21%, 55%, and 44% of pts (median time to resolution to grade $\leq$2 of any cytopenia, $\leq$2.1 mo). Grade $\geq$3 infections occurred in 14%. After a median follow-up (F/U) of 5.9 mo, median progression-free survival was not reached. **Conclusions:** Orva-cel at 300, 450, and 600 $\times$ 10^6 CAR+ T cells demonstrated manageable safety (CRS grade $\geq$3: 2%; NE grade $\geq$3: 4%) and compelling efficacy in heavily pretreated pts with RRMM, with a 91% objective response rate (ORR) and 39% complete response (CR)/stringent CR (sCR) rate. Updated results will be presented, including minimal residual disease, durability of response, and recommended phase 2 dose. Clinical trial information: NCT03430011. Research Sponsor: Juno Therapeutics, a Bristol-Myers Squibb company.

n (%)	300 $\times$ 10^6CAR+ T cells	450 $\times$ 10^6CAR+ T cells	600 $\times$ 10^6CAR+ T cells	All DLs
Efficacy	**N = 19**	**N = 18**	**N = 7**	**N = 44**
ORR (sCR + CR + VGPR + PR)	18 (95)	17 (94)	5 (71)	40 (91)
sCR + CR	5 (26)	9 (50)	3 (43)	17 (39)
VGPR	8 (42)	3 (17)	0	11 (25)
PR	5 (26)	5 (28)	2 (29)	12 (27)
Median F/U, mo (Min–max)	6.1 (1.7–9.2)	5.8 (0.9–9.2)	1.7 (0.9–3.0)	5.9 (0.9–9.2)
Safety	**N = 19**	**N = 19**	**N = 13**	**N = 51**
CRS grade ≥3	0	1 (5)	0	1 (2)
NE grade ≥3	1 (5)	1 (5)	0	2 (4)

PR, partial response, VGPR, very good PR.

8505 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Update of CARTITUDE-1: A phase Ib/II study of JNJ-4528, a B-cell maturation antigen (BCMA)-directed CAR-T-cell therapy, in relapsed/refractory multiple myeloma. *First Author: Jesus G. Berdeja, Sarah Cannon Research Institute, Nashville, TN*

Background: JNJ-68284528 (JNJ-4528) is a chimeric antigen receptor T (CAR-T) cell therapy containing 2 BCMA-targeting single-domain antibodies. Here we present updated CARTITUDE-1 (NCT03548207) phase 1b results with longer follow-up. **Methods:** Pts had MM per IMWG criteria, measurable disease, received $\geq$3 prior regimens or were double refractory to a PI and IMiD, and received anti-CD38 antibody. Cyclophosphamide 300 mg/m^2+ fludarabine 30 mg/m^2 over 3 days were used for lymphodepletion. JNJ-4528 (median, 0.73x10^6 CAR+ viable T cells/kg) was given as a single infusion. Cytokine release syndrome (CRS) was graded by Lee *et al*2014 and neurotoxicity by CTCAE, v5.0 and ASTCT grading. Response was assessed per IMWG criteria. **Results:** As of 17 Jan 2020, median follow-up is 9 mo (3–17). Phase 1b enrollment is complete (N = 29 treated; median 5 (3–18) prior lines, 76% penta-exposed, 86% triple-refractory, 31% penta-refractory, 97% refractory to last line of therapy). Most frequent adverse events (AEs) were neutropenia (100%), CRS (93%), and thrombocytopenia (93%). Grade (Gr) $\geq$3 hematologic AEs were neutropenia (100%), thrombocytopenia (69%), and leukopenia (59%). 27 (93%) pts had CRS; 25 Gr 1–2, 1 Gr 3, and 1 Gr 5 (day 99 subsequent to dose-limiting toxicity of prolonged Gr 4 CRS). Median time to onset of CRS was 7 days (2–12). 4 pts had treatment-related neurotoxicity: 3 Gr 1–2 and 1 Gr 3. ORR was 100%, with 22 (76%) stringent complete responses (sCRs), 6 (21%) very good partial responses (VGPRs), and 1 (3%) PR. Median time to $\geq$CR was 2 mo (1–9). 26/29 pts are progression-free, with 6-mo progression-free survival rate of 93% and longest response ongoing at 15 mo. 1 death due to CRS and 1 to acute myeloid leukemia (not treatment-related) occurred during the study. All 16 pts (14 sCR, 2 VGPR) evaluable at 6 mo were minimal residual disease negative at 10^{-5} or 10^{-6}. JNJ-4528 CAR+ T cell expansion peaked between day 10–14. At 6-mo individual follow-up, 22/28 pts had JNJ-4528 CAR+ T cells below the level of quantification (2 cells/μL) in peripheral blood, suggesting CAR-T persistence in peripheral blood did not seem to correlate with deepening of response. At peak expansion, preferential expansion of CD8+ CAR-T cells with a central memory phenotype was observed in peripheral blood. **Conclusions:** JNJ-4528 treatment led to responses in all pts. These responses were early, deep, and durable at a low dose of CAR-T cells with 26/29 (90%) pts progression free at median 9-mo follow-up. CRS was manageable in most pts, supporting outpatient dosing. Clinical trial information: NCT03548207. Research Sponsor: Janssen Research & Development, LLC.

8506 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Long-term follow-up of BMT CTN 0702 (STaMINA) of postautologous hematopoietic cell transplantation (autoHCT) strategies in the upfront treatment of multiple myeloma (MM). *First Author: Parameswaran Hari, CIBMTR (Center for International Blood and Marrow Transplant Research), Department of Medicine, Medical College of Wisconsin, Milwaukee, WI*

Background: STaMINA was a phase III trial comparing progression-free survival (PFS) among 758 pts randomized to: 1. second autoHCT then lenalidomide (Len) maintenance (Auto/Auto, n = 247); 2. consolidation with Len/bortezomib/dexamethasone (RVD) followed by Len maintenance (Auto/RVD, 254); 3. Len maintenance (Auto/Len, 257). All three arms were similar (Stadtmauer JCO 2018). Len maintenance was designed to continue for 3 years and amended to allow continuation until disease progression through a follow up protocol (07LT, NCT#02322320). We report 6 yr follow up for STaMINA and the results of Len discontinuation beyond 3 years. **Methods:** 07LT was offered to pts who were progression-free at 38 mo; completed planned Len maintenance and were within 4 years of BMT CTN 0702 follow up. Among 431 07LT eligible patients, 273 enrolled and 179 opted to continue maintenance until disease progression. All patients enrolled in STaMINA were reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) and long-term outcomes for patients not enrolled on 07LT (N = 166) were available through this mechanism. Before combining 07LT data and CIBMTR data for LTFU analysis, outcomes in both databases were analyzed separately and confirmed to be comparable. **Results:** Using intent-to-treat (ITT), 6yr PFS and overall survival (OS) was the same among Auto/Auto (43.9%; 73.1%), Auto/RVD (39.7%, 74.9%) and Auto/Len (40.9%, 76.4%)(p = 0.6; p = 0.8). Protocol defined high risk disease, (HR = 1.53, p $<$ 0.0001) and age (p = 0.03) were adverse risks for PFS. In as treated analysis, 6yr PFS were 49.4%, 39.7% and 38.6% for Auto/auto (170), Auto/RVD (222) and Auto/Len (361), respectively (p = 0.01). 6yr PFS in high risk pts as treated analysis were 43.6% and 26% for Auto/auto and Auto/Len, respectively (p = 0.03). Landmark analysis at 38 mo included 215 pts who continued Len maintenance (either on 07LT study or commercial Len) vs. 207 who stopped. Baseline demographics; study arm on 0702, induction pre-autoHCT were similar. Len discontinuation after 38 mo was associated with inferior PFS (79.5% vs. 61% at 5yr; HR = 1.91, p = 0.0004) but similar OS. Incidence of all second primary malignancies (SPM)(81 cases with 43 heme-malignancies) was associated with age. **Conclusions:** Long term outcomes are similar using ITT, but as treated analysis suggested a PFS benefit for tandem autoHCT, driven mainly by pts with high risk MM. Len discontinuation even at 38 mo was associated with inferior PFS. Clinical trial information: NCT02322320. Research Sponsor: U.S. National Institutes of Health.

8507 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Primary analysis of the randomized phase II trial of bortezomib, lenalidomide, dexamthasone with/without elotuzumab for newly diagnosed, high-risk multiple myeloma (SWOG-1211). *First Author: Saad Zafar Usmani, Levine Cancer Institute, Atrium Health, Charlotte, NC*

Background: The introduction of immunomodulatory agents, proteasome inhibitors, and autologous stem cell transplantation (ASCT) has improved outcomes for patients with multiple myeloma (MM), but those with high risk MM (HRMM) have a poor long-term prognosis. To date, no trials have addressed optimal treatment for these patients. **Methods:** S1211 is a randomized phase II trial (NCT01668719) comparing 8 cycles of lenalidomide, bortezomib and dexamethasone (RVd) induction followed by dose-attenuated RVd maintenance until disease progression with or without elotuzumab. Stem cell collection was allowed, but ASCT was deferred until progression. HRMM was defined by one of the following: gene expression profiling high-risk (GEP^{hi}), t(14; 16), t(14; 20), del(17p) or amplification 1q21, primary plasma cell leukemia (pPCL) and elevated serum LDH ($>$ 2X ULN). Median progression-free survival (PFS) was the primary end-point, using a one-sided stratified log-rank test at a one-sided significance level of 0.1. Secondary endpoints included overall response rate (ORR), adverse events (AE), serious adverse events (SAE) and OS. Response was assessed using the IMWG 2009 criteria. **Results:** S1211 enrolled 103 evaluable patients, RVd n = 54, RVd-Elo n = 49. 75% had ISS II/III, 47% amp1q21, 38% del17p, 12% t(14; 16), 9% GEP^{hi}, 7% pPCL, 5% t(14; 20) and 4% elevated serum LDH (18.5% $>$ 1 feature). With median follow-up of 53 months (mos.), no difference in median PFS was observed [RVd-Elo = 31 mos., RVd = 34 mos.,HR = 0.968 (80% CI = 0.697-1.344), p = 0.449]. No difference in OS was observed [RVd-Elo = 68 mos, RVd = not reached, HR = 1.279 (80% CI: 0.819, 2.000), p-value = 0.478]. 72% pts had $>$ Grade 3 AEs, no differences in the safety profile were observed except $>$Grade 3 infections (RVd 8%, RVd-Elo 16%), $>$Grade 3 sensory neuropathy (RVd 8%, RVd-Elo 13%). **Conclusions:** In the first randomized HRMM study reported to date, the addition of elotuzumab to RVd induction and maintenance did not improve patient outcomes. However, the PFS and OS seen in both arms of the study exceeded the original statistical assumptions and support the role for PI/IMiD combination maintenance therapy for this patient population. The S1211 data will serve as an important benchmark for future HRMM clinical trials. Clinical trial information: NCT01668719. Research Sponsor: U.S. National Institutes of Health.

8508 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Depth of response to isatuximab, carfilzomib, lenalidomide, and dexamethasone (Isa-KRd) in front-line treatment of high-risk multiple myeloma: Interim analysis of the GMMG-CONCEPT trial. *First Author: Katja Weisel, University Medical Center of Hamburg-Eppendorf, Hamburg, Germany*

Background: High-risk (HR) multiple myeloma (MM) still has a significant impaired prognostic outcome. Addition of CD38 monoclonal antibodies to standard-of-care regimens significantly improved response rates and depth of response in newly diagnosed (ND) and relapsed/refractory MM patients (pts). Here, we report the prespecified end of induction interim analysis (IA) of the investigator-initiated GMMG-CONCEPT trial (NCT03104842), evaluating the quadruplet regimen isatuximab plus carfilzomib, lenalidomide and dexamethasone (Isa-KRd) in HR NDMM pts. **Methods:** 153 pts with HR NDMM are planned to be included into the trial. HR MM is defined by the presence of del17p or t(4;14) or t(14;16) or >3 copies 1q21 and ISS 2 or 3 stage disease. Pts receive 6 cycles of Isa-KRd induction, 4 cycles of Isa-KRd consolidation and Isa-KR maintenance. Transplant eligible pts (arm A) undergo high-dose therapy. Transplant ineligible pts (arm B) receive 2 additional cycles of Isa-KRd induction. The primary endpoint is MRD negativity measured by next-generation flow after consolidation. This IA reports on overall response rates (ORR) after induction. Additional MRD analysis will be presented. **Results:** 50 pts (46 arm A, 4 arm B) were included in the IA population for ORR. HR MM was defined by del17p in 52%, t(4;14) in 38%, t(14;16) in 12% and >3 copies 1q21 in 42%. 39/46 pts in arm A and 4/4 pts in arm B completed induction treatment. ORR was 100%, with 5 pts (10.0%) showing partial response (PR), 22 (44.0%; including 4 in arm B) very good partial response (VGPR) and 23 (46.0 %) complete response (CR). Median stem cell yield was 6.6×10^6CD34+ cells/kg. Grade 3/4 treatment-emergent adverse events ($\geq$ 10%) with Isa-KRd included neutropenia (34.0%), leukopenia (26.0%) and thrombocytopenia (14.0%). Main non-hematologic toxicities grade 3/4 were hypertension (12.0%) and infection (8.0%). **Conclusions:** To the best of our knowledge, we report for the first time on a trial investigating solely HR NDMM and Isa-KRd quadruplet treatment. Isa-KRd induction induces deep responses in HR MM pts. The overall safety profile of Isa-KRd is expected and consistent with previous reports. The study is ongoing, with pts continuing to be included. Clinical trial information: 03104842. Research Sponsor: Sanofi, Celgene, Amgen.

8509 Poster Discussion Session; Displayed in Poster Session (Board #409), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Updated results from BELLINI, a phase III study of venetoclax or placebo in combination with bortezomib and dexamethasone in relapsed/refractory multiple myeloma. *First Author: Shaji Kumar, Mayo Clinic, Rochester, MN*

Background: Venetoclax (Ven) is a selective, potent, oral BCL-2 inhibitor. In the Phase 3 BELLINI trial, addition of Ven to bortezomib (B) + dexamethasone (d) significantly improved response rates and progression-free survival (PFS) vs placebo (Pbo) and showed significant efficacy in patients (pts) with either t(11;14) or BCL2high gene expression. Here we present updated safety and efficacy data from the prespecified second interim overall survival (OS) analysis. **Methods:** In this multicenter, randomized, double-blind study (NCT02755597), pts with relapsed/refractory multiple myeloma (RRMM) with 1-3 prior lines of therapy were randomized 2:1 to Ven (800 mg) or Pbo in combination with B (1.3 mg/m2) and d (20 mg). The primary endpoint was PFS; key secondary endpoints included overall response and overall survival (OS). **Results:** 291 pts were randomized; 194 to Ven, 97 to Pbo. Pt characteristics were well balanced among arms. In the Ven arm, median age was 66, 17% had high-risk cytogenetics, 11% had t(11;14), and 34% had BCL2high gene expression. As of 13 Sept 2019, 59 pts were still on study, 45 (23%) Ven vs 14 (14%) Pbo. At a median follow-up of 28.6 months, there were 64 (33%) deaths in the Ven arm vs 24 (25%) in Pbo. At the initial data cutoff (26 Nov 2018), PFS HR was 0.63 (0.44,0.90) and OS HR was 2.03 (1.04,3.95). Table shows updated PFS and OS. Most common treatment-emergent adverse events (TEAEs) with Ven were diarrhea (59%), nausea (37%), and constipation (35%). Most common grade 3/4 AEs (Ven/Pbo) were neutropenia (21%/8%), thrombocytopenia (15%/30%), anemia (16%/15%), diarrhea (15%/12%), and pneumonia (18%/13%). Serious AEs occurred in 54% Ven and 52% Pbo pts. 24% discontinued Ven due to AEs vs 12% Pbo. There were 14 treatment-emergent deaths in the Ven arm and 1 in Pbo. **Conclusions:** The addition of Ven to Bd significantly improves PFS but resulted in increased mortality vs Pbo in the total population. Greatest PFS improvement with Ven was observed in pts with t(11;14) or BCL2high gene expression, where Ven shows a favorable benefit-risk profile. The study continues for final OS analysis. Clinical trial information: NCT02755597. Research Sponsor: Abbvie, Inc, Pharmaceutical/Biotech Company.

PFS and OS by subgroup.

	N	VEN	PBO	HR (95% CI)
Median PFS, mo, all pts	291	23.2	11.4	0.60 (0.43,0.82)
t(11;14)	35	NR	9.3	0.09 (0.02,0.41)
t(11;14) or *BCL2^{high}*	114	NR	9.9	0.31 (0.18,0.53)
non-t(11;14), *BCL2^{low}*	164	15.3	11.5	0.84 (0.55,1.28)
Median OS, mo, all pts	291	33.5	NR	1.46 (0.91,2.34)
t(11;14)	35	NR	NR	0.72 (0.14,3.6)
t(11;14) or *BCL2^{high}*	114	NR	NR	0.97 (0.43,2.17)
non-t(11;14), *BCL2^{low}*	164	32.8	NR	1.74 (0.93,3.25)

8510 Poster Discussion Session; Displayed in Poster Session (Board #410), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Selinexor, daratumumab, and dexamethasone in patients with relapsed/refractory multiple myeloma (MM). *First Author: Cristina Gasparetto, Duke University Cancer Center, Durham, NC*

Background: Selinexor is a first-in-class oral Selective Inhibitor of Nuclear Export (SINE) compound that binds and inactivates exportin 1 (XPO1). Selinexor in combination with low dose dexamethasone (Sel-dex) was approved by the FDA, based on data from the STORM study, wherein Sel-dex induced an overall response rate (ORR) of 26.2% in patients (pts) with relapsed/refractory MM (RRMM). Single agent daratumumab has demonstrated an ORR of 29% in MM reftactory to proteasome inhibitors (PIs)/immunomodulatory drug (IMiDs). We evaluated the safety, tolerability and preliminary efficacy of the combination of Sel-dex and daratumumab (SDd) in pts with MM refractory to PIs/IMiDs. **Methods:** This is a multicenter, open-label, phase 1b/2 dose escalation and expansion study. Pts were eligible if they had received $\geq$ 3 prior lines of therapy, including a PI and an IMiD, or whose MM was refractory to a PI and an IMiD. In the expansion phase, pts were required to be anti-CD38 monoclonal antibody-naïve. One dose level was tested at each schedule: selinexor once-weekly (QW at 100 mg) or twice-weekly (BIW at 60 mg) with dexamethasone 40 mg. Daratumumab 16 mg/kg IV was administered per label. Primary objective was to determine the maximum tolerated dose and recommended phase 2 dose (RP2D), and assess safety, tolerability and efficacy of SDd in pts with RRMM. **Results:** A total of 34 pts were enrolled; 3 in the 60 mg BIW and 31 in the 100 mg QW cohorts. Median age was 69 and median number of prior treatment regimens was 3 (range, 1–10). Out of 34 pts, 62% and 65% were refractory to bortezomib and lenalidomide respectively. Common treatment related adverse events (all grades, grades 3/4) included: thrombocytopenia (71%, 47%), fatigue (62%, 18%), nausea (71%, 9%), anemia (62%, 32%) and neutropenia (50%, 26%). Two dose limiting toxicities (DLTs) were reported in the 60 mg BIW cohort: Grade 3 thrombocytopenia and Grade 2 fatigue requiring dose reduction in selinexor to 100 mg QW. In the 100 mg QW escalation cohort (n = 6), no DLTs occured. 32 patients were evaluable for efficacy. The ORR was 73% (11 VGPR, 11 PR) for 30 daratumumab-naïve pts. Median progression-free survival was 12.5 months in both groups. **Conclusions:** Based on tolerability and efficacy, the RP2D of SDd is selinexor 100 mg, daratumumab 16 mg/kg and dexamethasone 40 mg, administered QW. In pts with PI and IMiD refractory MM, weekly SDd demonstrated promising activity with an ORR of 73% in daratumumab-naïve pts and a median PFS of 12.5 months. This supports further development of a novel non-PI, non-IMiD backbone in earlier lines of therapy. Clinical trial information: NCT02343042. Research Sponsor: Karyopharm Therapeutics Inc.

8511 Poster Discussion Session; Displayed in Poster Session (Board #411), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Updated analysis of a phase I/II study of venetoclax in combination with daratumumab and dexamethasone, +/- bortezomib, in patients with relapsed/refractory multiple myeloma. *First Author: Jonathan L. Kaufman, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: Venetoclax (Ven) is a selective, potent, oral BCL-2 inhibitor that induces apoptosis in multiple myeloma (MM) cells *in vitro.* It has shown synergistic activity with bortezomib (V) and dexamethasone (d). Combination of the CD38 monoclonal antibody daratumumab (D) with Ven is hypothesized to further increase anti-myeloma activity based on dual mechanisms of pro-apoptotic effects on tumor cells and enhanced immune stimulation. **Methods:** This ongoing Phase 1/2, nonrandomized, multicenter study (NCT03314181) is evaluating safety, efficacy and pharmacokinetics (PK) of VenDd +/- V in patients (pts) with relapsed/refractory MM. In Part 1, pts with t(11;14) who received $\geq$1 prior line of therapy (PI and an immunomodulatory drug) were treated with VenDd [Ven QD + D 16 mg/kg IV + d 40 mg weekly]. In Part 2, pts irrespective of t(11;14) status, non-refractory to PIs and who received 1–3 prior lines of therapy were treated with VenDVd [Ven QD + D 16 mg/kg IV + V (1.3 mg/m^2) + d (20 mg)]. A randomized, open-label expansion (Part 3) will further evaluate and compare safety and efficacy of VenDd (400 or 800 mg Ven dose levels) with control DVd in pts with t(11;14). **Results:** As of Dec 05, 2019, 48 pts were enrolled. Part 1 included 24 pts with t(11;14), median age 63 (range 51–76). Part 2 included 24 pts, median age 65 (range 41–80) of which 6 (25%) had t(11;14). Frequent adverse events (AEs; VenDd/VenDVd) were fatigue (71%/25%), diarrhea (58%/46%), nausea (46%/50%), insomnia (33%/50%), upper respiratory tract infection (33%/21%), cough (42%/9%), and dyspnea (25%/25%). Frequent Grade $\geq$ 3 AEs in pts on VenDd were neutropenia (17%), hypertension (12%), fatigue and hyperglycemia (8% each), and in pts on VenDVd were insomnia (21%), diarrhea and thrombocytopenia (8% each). Nine pts had infection-related Grade $\geq$ 3 AEs (5 VenDd, 4 VenDVd). Eighteen pts had a serious AE (11 VenDd, 7 VenDVd) with pyrexia (n = 3) being most common. One pt on VenDVd died of progressive disease. PK analyses showed that addition of D and V did not impact Ven exposure. Median follow-up time (VenDd/VenDVd) was 10 and 9 months. Overall response rate in VenDd/VenDVd was 96%/92% and 96%/79% had $\geq$ very good partial response rate. Median progression free survival and duration of response were not reached. **Conclusions:** Pts treated with VenDd +/- V continue to demonstrate a tolerable safety profile with encouraging efficacy, notably among pts with t(11;14) treated with VenDd. Safety, efficacy, PK, and cytogenetics analyses will be updated for presentation. Clinical trial information: NCT03314181. Research Sponsor: AbbVie.

8512 Poster Discussion Session; Displayed in Poster Session (Board #412), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Analysis of treatment efficacy in the GEM-CESAR trial for high-risk smoldering multiple myeloma patients: Comparison between the standard and IMWG MRD criteria and QIP-MS including FLC (QIP-FLC-MS). *First Author: Noemí Puíg, Hospital Universitario de Salamanca, Salamanca, Spain*

Background: The GEM-CESAR trial is a potentially curative strategy for high-risk smoldering multiple myeloma (HRsMM) patients (pts) in which the primary endpoint is the achievement of sustained minimal residual disease (MRD) negativity in the bone marrow (BM) by next generation flow (NGF). The value of BM MRD assessment in MM is proven, but alternative, non-invasive methods, accurately reflecting disease burden are needed. **Methods:** Pts received six 4-week cycles of KRd as induction (K:36mg/m2 twice weekly, R: lenalidomide 25mg po od days 1-21 and d:dexamethasone 40mg po weekly) followed by melphalan 200mg/m2, two further cycles of KRd as consolidation and up to 2 years of Rd (R: 10mg/d, d:20mg/week). Efficacy was analyzed in parallel in BM samples by NGF and in serum by SPEP/IFE and QIP-MS/QIP-FLC-MS in 52 out of the 90 pts enrolled in the trial. Standard and MRD responses were carried out as per the IMWG guidelines. For QIP-MS serum immunoglobulins were purified using polyclonal antibodies (anti-IgG, -IgA, -IgM, -total κ and -total λ light chain, -free κ and -free λ light chain). Mass spectra were generated on a MALDI-TOF-MS system. **Results:** Overall response rate (ORR) was 98% post-induction, 98% post-ASCT, and 100% post-consolidation; 38.4%, 61.5% and 68.6% of pts reached ≥ complete response at each time-point and, among them, 23%, 44% and 55% achieved flow MRD-negativity. Using the combination of QIP-MS/QIP-FLC-MS, the percentage of pts without detectable disease at each timepoint lowered to 12%, 27% and 38% reflecting the higher sensitivity of the method. Against NGF, QIP-MS/QIP-FLC-MS provided negative predictive values of 67%, 92% and 89% (p = 0,0206; p < 0,001; p = 0,003) and identified disease in 95%, 97% and 92% of pts that were positive by NGF-MRD at each respective timepoint. Three pts from this cohort have progressed so far: two were NGF+/MS+ at the three timepoints whilst 1 remained NGF- but QIP-MS/FLC-MS+ throughout. **Conclusions:** The GEM-CESAR treatment strategy induces a high ORR in HRsMM pts, and the % of cases achieving flow-MRD negativity post-ASCT meets the primary endpoint of the trial. The combined use of QIP-MS and FLC-MS offers higher sensitivity relative to standard methods and may provide relevant information about the right timing for performing a BM aspirate/biopsy. Clinical trial information: NCT02415413. Research Sponsor: None.

8513 Poster Discussion Session; Displayed in Poster Session (Board #413), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Measurable residual disease (MRD) assessed by mass spectrometry (MS) in peripheral blood versus next generation sequencing (NGS) in bone marrow in multiple myeloma treated on phase II trial of KRd+ASCT. *First Author: Benjamin Avi Derman, University of Chicago Medical Center, Chicago, IL*

Background: MRD-negativity in multiple myeloma (MM) assessed by NGS in bone marrow (BM) aspirate is associated with longer progression free survival (PFS) and overall survival. MS can detect monoclonal protein at a heightened sensitivity in peripheral blood (PB). We sought to assess the concordance of MS in PB and NGS in BM, comparing outcomes by MRD status. **Methods:** MRD was tested on paired PB and BM samples from transplant (ASCT)-eligible pts with newly diagnosed secretory MM who received treatment on a phase II clinical trial (NCT01816971) with KRd for 4 cycles, ASCT, KRd for 14 cycles, and lenalidomide maintenance (LM). Both NGS and MS were evaluable in 36 pts after a total of 18 cycles of KRd (C18) and in 24 pts after 1 year of LM. MS signatures were identified in pretreatment PB samples. C18 and after 1 year of LM PB samples were evaluated using both MALDI-TOF and liquid-chromatography-MS (LCMS) by the Binding Site Group. Paired MRD by NGS was performed by ClonoSEQ. 20/60 samples reached the limit of detection for 10^{-6} and 40/60 for 10^{-5}. **Results:** There was substantial concordance between NGS and MALDI-TOF among the 60 samples (κ= 0.667, 83% agreement) and fair concordance between NGS and LCMS (κ= 0.348, 63% agreement). However, all 22 discordant samples (8 with NGS depth 10^{-6}, 14 with NGS depth 10^{-5}) were $NGS^{-}/LCMS^{+}$. 4/16 (25%) of these pts converted to NGS^{+}, and 3/16 (19%) clinically progressed. There was stronger concordance between LCMS and NGS 10^{-6}(κ= 0.615) than with NGS 10^{-5}(κ= 0.375). At a median follow-up of 56 months, C18 $LCMS^{-}$(n = 9) was associated with superior PFS vs all $LCMS^{+}$(n = 27; p = 0.03) and independently vs $NGS^{-}/LCMS^{+}$ (n = 14; p = 0.04). There were 10 events (including 4 deaths) in the C18 $LCMS^{+}$ group vs 0 in the $LCMS^{-}$ group. **Conclusions:** MRD assessment by LCMS in PB appears to reach and possibly exceed the sensitivity of MRD by NGS in BM at a depth of 10^{-5}-10^{-6}. LCMS positivity predicted conversion from NGS^{-} to NGS^{+} in 25% of discordant cases, and LCMS negativity was a better predictor of superior PFS than MRD negativity by NGS. These observations need confirmation in larger prospective studies. Research Sponsor: None.

8514 Poster Discussion Session; Displayed in Poster Session (Board #414), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Clinical implications of loss of minimal residual disease (MRD) negativity in multiple myeloma. *First Author: Meera Mohan, UAMS Myeloma Center, Little Rock, AR*

Background: Attainment of MRD negativity in multiple myeloma (MM) patients is increasingly considered an optimal therapeutic endpoint, but little is known about the MRD evolution in those who achieve this milestone. We investigated the clinical implication of loss of MRD negativity or MRD conversion in patients with ≥VGPR. **Methods:** We identified and followed 606 patients achieving a sustained ≥VGPR with bone marrow MRD negativity(≥ 2 consecutive reading) following treatment on a total therapy protocol and with a median follow-up of 10 y. All patient had negative PET and MRI DWIBS at enrollment. Serial BM aspirate MRD was determined by 8-color next generation flow (NGF, EuroFlow) with a minimal sensitivity of 10^{-5} cells. **Results:** Most MM patients were considered low risk with a UAMS GEP70 score of ≤ 0.66 (92%; 495/538) . While 60% (364/606) of patients had sustained MRD negativity, the remaining 40% (242/606) experienced MRD conversion with a 5.7 y median time from ASCT and 6.3 y from diagnosis. The risk of clinical relapse was significantly elevated in patients with MRD conversion compared to sustained MRD negativity (73%, 177/242 *vs.* 5%, 18/364; R.R. = 3.5; P< 0.0001). The median level of MRD positivity (> 0.2 ratio of MM cells to normal plasma cells) also highly correlated with relapse (P< 0.0001). Loss of MRD negativity preceded clinical relapse by a median time of 1.1 years. Loss of MRD negativity without clinical relapse was seen in 27% (65/242). MRD conversion was associated with an inferior PFS and OS (PFS: 10.2 y *vs.* NR; P < 0.0001, H.R. 18.7; 95% CI 13.3 - 26.3 and OS: 26.1 y *vs.* NR; P= 0.01, H.R. 1.7; 95% CI 1.1 - 2.6). Furthermore, when MRD conversion was within 5 y of diagnosis compared > 5 y, patients had a worse OS (P < 0.0001, H.R. 17.2; 95% CI 7.8 – 37.8). We also observed that MRD conversion later than 5 years from diagnosis did not affect the OS. In a subset of patients (n = 144) the timing of first MRD negativity following treatment was available. Attainment of MRD negativity within 6 months of diagnosis compared to any time after 6 months was predictive of future MRD conversion (65%, 17/26 *vs.*42%, 49/118; P = 0.03) and clinical relapse (54%, 14/26 *vs.*28%, 33/118; P = 0.02). **Conclusions:** MRD conversion occurs in a significant proportion of MM patients (40%) on long-term follow-up and predicts future clinical relapse. Significance of MRD conversion has a temporal relationship from diagnosis and portray inferior clinical outcome particularly within 5 years of diagnosis. Research Sponsor: None.

8515 Poster Discussion Session; Displayed in Poster Session (Board #415), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Bortezomib induction prior to autologous hematopoietic cell transplantation (AHCT) for newly diagnosed light chain amyloidosis (AL): A study of 426 patients. *First Author: Robert F. Cornell, Vanderbilt University Medical Center, Nashville, TN*

Background: AL is a clonal plasma cell (PC) disorder causing multiorgan dysfunction from amyloid fibril deposition. While bortezomib (B) induction has been used prior to AHCT recently, AHCT without prior induction has been a common practice. The primary objective of this study was to compare outcomes of AL patients who proceeded to AHCT without induction to those receiving pre-AHCT induction with B. **Methods:** Outcomes of 426 systemic AL AHCT recipients between 2014-2018 reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) were reviewed. Patients receiving induction with therapy other than B, AHCT occurring > 9 months after diagnosis, no documented AL end-organ involvement, myeloma-defining events and conditioning other than melphalan (MEL) monotherapy were excluded. Multivariate analysis (MVA) was conducted to identify prognostic factors associated with relapse, PFS and overall survival (OS). **Results:** 286 patients received B induction therapy vs 140 patients receiving no induction. Age, gender, number and type of organs involved, and AL AHCT center volume were similar between the groups. Patients receiving induction had greater PC burden compared with no induction (PC ≥ 10%, 41% vs 11%, p < 0.01). Induction was B, cyclophosphamide and dexamethasone (D) in 83% followed by B, lenalidomide and D (10%) or B+D (7%). Median follow-up was 24.9 months. At 2 years, B induction vs. no induction was associated with 13% (95% CI 10-17%) vs 22% (95% CI 15-30%) relapse risk (p = 0.03); 83% (95% CI 79-87%) vs 74% (95% CI 66-81%) PFS (p = 0.04); 93% (95% CI 90-95%) vs 94% (95% CI 89-97%) OS (p = 0.7). On MVA, the B induction group had improved PFS (HR 0.46, 95% CI 0.3-0.7, p < 0.001) with similar OS (HR 0.6, 95% CI 0.3-1.2, p = 0.1) compared with no induction. Creatinine < 2 mg/dl (HR 0.55, 95% CI 0.3-0.9, p = 0.02) and Karnofsky score ≥90 (HR 0.51, 95% CI 0.33-0.78, p < 0.01) were also associated with improved PFS. MEL dose < 180 mg/m^2 was associated with inferior PFS (HR 2.17, 95% CI 1.31-3.61, p < 0.01) and OS (HR 3.6, 95% CI 1.5-8.6, p < 0.01). No deaths were seen in the first 100 days post-AHCT. At last follow-up, 32 deaths occurred, 26 (81%) due to AL. **Conclusions:** Compared with prior CIBMTR analyses, B induction use has increased in AL AHCT recipients and a higher PC burden was the only clinical determinant. Furthermore, B induction was associated with lower relapse and improved PFS at 2 years with no OS difference despite higher proportion of patients with > 10% PC, which has been associated with poor outcomes. Research Sponsor: U.S. National Institutes of Health.

8516 Poster Discussion Session; Displayed in Poster Session (Board #416), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Depth of response prior to autologous stem cell transplantation to predict survival in light chain amyloidosis. *First Author: Iuliana Vaxman, Israel Sackler Faculty of Medicine Tel-Aviv University, Tel-Aviv, Israel*

Background: The role of induction therapy prior to autologous stem cell transplant (ASCT) in immunoglobulin light chain (AL) amyloidosis remains controversial. Data on the prognostic impact of response to induction in a transplanted cohort are lacking. The aim of this study was to assess the impact of response to induction therapy on survival in patients undergoing ASCT for AL amyloidosis. **Methods:** We conducted a retrospective study of all newly diagnosed AL amyloidosis patients who received induction prior to ASCT between January 2007 and August 2017 at Mayo Clinic, Rochester, Minnesota. Patients receiving only corticosteroids prior to transplant were excluded as were those with an involved light chain of less than 5 mg/dL (not measurable for response). **Results:** 134 patients met inclusion criteria. The median age at diagnosis was 60 (range 36-74) and 85 (63%) were men. The most commonly used induction regimen was proteasome inhibitor-based (73.1%, n=98). The overall response rate to induction was 83% (complete response 17%, very good partial response 30% and partial response 36%). With a median follow up of 56.5 months, the median PFS and OS was 48.5 months and not reached, respectively. Response depth to induction therapy was associated with improved PFS and OS and was independent of the bone marrow plasma cell percentage. The median PFS was not reached for patients achieving ≥VGPR prior to ASCT and 33.8 months for patient achieving PR or less (P=0.001). The median OS was longer in patients with deeper responses (not reached for patients achieving ≥VGPR vs. 128 months for patients achieving PR or less (P=0.02). On multivariable analysis, independent predictors of OS were melphalan conditioning dose (RR= 0.38; P=0.018) and depth of response prior to transplant (RR 2.52; P=0.039). **Conclusions:** Hematologic response prior to transplant predicts post-transplant outcomes in patients with AL amyloidosis. Research Sponsor: None.

Univariable and multivariable analysis for overall survival.

	Univariable		Multivariable	
Variable	**RR (95% CI)**	**P**	**RR (95% CI)**	**P**
Age ≥ 65 years	3.5 (0.99 to 4.99)	0.05	1.76 (0.76 to 4.05)	0.185
More than 2 organs involved	1.63 (0.27 to 3.9)	0.268		
BMPC≥10%	0.45 (0.8 to 2.36)	0.83		
Mayo stage 2012 III/IV versus I/II	1.65 (0.23 to 3.72)	0.24		
Conditioning melphalan dose 200 mg/m^2 versus 140 mg/m^2	0.38 (0.19 to 0.83)	0.0164	0.38 (0.17 to 0.85)	0.018
Hematologic responseCR/VGPR versus PR or less	2.7 (1.2 to 6.37)	0.027	2.52 (1.04 to 6.09)	0.039
Post-transplant treatment	0.92 (0.5-1.65)	0.7		

8517 Poster Discussion Session; Displayed in Poster Session (Board #417), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Will adding alkylating agent to bortezomib improve survival of newly diagnosed AL amyloidosis patients? *First Author: Yumeng Zhang, University of South Florida, Tampa, FL*

Background: The combination of bortezomib (Bort) and alkylating agent (AA) is a frequently used first-line therapy for AL amyloidosis. Kastritis et al. compared melphalan and dexamethasone with or without bortezomib as primary therapy and demonstrated increased hematologic response rate with the bortezomib and melphalan combination. However, the role of AA is unclear. This study aimed to evaluate if adding AA to Bort improved patient outcomes in AL amyloidosis. **Methods:** We retrospectively reviewed clinical data on 209 patients with systemic AL Amyloidosis at Moffitt Cancer Center between 2008 and 2020. We excluded patients with localized amyloidosis or amyloid other than AL. Patients were divided into two groups based on upfront therapy: A) Bort and B) Bort + AA. All patients also received dexamethasone. The staging was per Mayo 2012. Organ involvement, response, and progression were defined based on the 2005 criteria. Overall survival (OS) was defined as the time from initial diagnosis until death or last contact. Time to next therapy (TTNT) was calculated in patients with the documented hematologic response from the time of initiation of therapy to time of the next therapy/last follow up/death. **Results:** Of 209 patients, 36% (n=76) received Bort+AA; 30% (n=62) received Bort. No significant difference in clinical characteristics was seen in both groups except for age (which was higher for arm A: median 65 and 62 years, respectively, p=0.043) (table). In addition, Bort+AA became more commonly used as a frontline therapy after 1/1/2014 (p=0.001). Group A and B had similar median OS (69.9 months [95% CI. 44.7-95.2] and 64.4 mo [95% CI 40.5-88.3] respectively, p=0.60). 86% of patients in group B achieved a hematologic response as compared to 74% of patients in group A (p=0.15). Similarly, 47% of patients in group B achieved an organ response as compared to 34% of patients in group A (p=0.22). TTNT was higher in group A than group B (16.9 mo [95% CI, 0-41.5] and 7.8 mo [95% CI, 3.5-12.0], respectively, p=0.08). **Conclusions:** While Bort+AA is a commonly used regimen for amyloidosis, the addition of AA to Bort did not result in superior OS, TTNT compared to Bort alone in this retrospective study. This finding should be confirmed in prospective studies. Baseline Characteristics. Research Sponsor: None.

Baseline characteristics.

Characteristic	**Group A n=62**	**Group B n=76**	**P value**
Male, %	60	63	0.73
Age at diagnosis, median	65	62	0.04
Date of diagnosis before 1/2014, %	50	22	0.001
Stage I, %	30	18	0.50
Stage II, %	22	27	
Stage III, %	28	32	
Stage IV, %	20	23	
Hematologic response	36/49 (73%)	55/64 (85%)	0.15
Organ Response	15/44 (34%)	24/51 (47%)	0.22

8518 Poster Discussion Session; Displayed in Poster Session (Board #418), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Impact of lenalidomide-bortezomib-dexamethasone (RVd) induction on patients with newly diagnosed multiple myeloma and renal impairment: Results from the Connect MM Registry. *First Author: Sikander Ailawadhi, Mayo Clinic, Jacksonville, FL*

Background: Patients (pts) with newly diagnosed multiple myeloma (NDMM) and renal impairment (RI) are often excluded from clinical trials. Data are limited on the effects of induction treatment in these pts, who may also be ineligible for autologous stem cell transplant (SCT) due to severity of RI. This analysis investigated the impact of RVd induction on renal function in transplant eligible (TE) and noneligible (TNE) pts from the Connect MM Registry, a US, multicenter, prospective, observational study. **Methods:** Eligible pts were ≥ 18 y and had symptomatic MM diagnosed ≤ 2 mos prior to enrollment, as defined by the International Myeloma Working Group criteria. For this analysis, pts that received frontline RVd for ≥ 3 cycles were grouped per transplant eligibility and renal function at baseline (BL; creatinine clearance [CrCl] < 30, 30-50, > 50-80, and > 80). Pts with progressive disease at BL were excluded. Renal function at 3 mos was measured. Median unadjusted progression-free survival (PFS) was calculated from start of regimen in TE and TNE populations, with pts grouped by CrCl (≤ 60 or > 60) at BL. **Results:** As of 7/23/19, 421 TE and 212 TNE pts received RVd for ≥ 3 cycles. TE and TNE pts were grouped by BL CrCl of < 30 (20 and 16 pts), 30-50 (36 and 50 pts), > 50-80 (117 and 63 pts), and > 80 (248 and 83 pts). Renal function improvement was observed in all pts receiving RVd, including those with moderate (30-50 CrCl) and severe (< 30 CrCl) RI at BL (Table). In pts with > 60 CrCl and ≤ 60 CrCl at BL, median PFS in TE pts was 48.6 mos and 43.2 mos, respectively. In TNE pts, median PFS was 36.4 mos and 30.6 mos, respectively. **Conclusions:** The results from the Connect MM Registry indicate that pts with NDMM and RI (including moderate and severe) who receive front-line RVd for ≥ 3 cycles may see improvement in renal function at 3 mos, regardless of transplant eligibility. RVd therefore can potentially be used in pts with RI. This analysis provides real-world data that support further investigation of RVd treatment in pts with moderate or severe RI. Clinical trial information: NCT01081028. Research Sponsor: Celgene Corporation.

Change in renal function from BL to 3 mos in pts receiving ≥ 3 cycles of RVd.

Population	**TE**	**TE**	**TE**	**TE**	**TNE**	**TNE**	**TNE**	**TNE**
Renal Function 3 Mos Post-BL, %	**BL Normal (n = 248)**	**BL Mild (n = 117)**	**BL Moderate (n = 36)**	**BL Severe (n = 20)**	**BL Normal (n = 83)**	**BL Mild (n = 63)**	**BL Moderate (n = 50)**	**BL Severe (n = 16)**
Normal	85	**42**	**14**	**10**	76	**33**	**20**	**13**
Mild	*3*	44	**47**	**15**	*10*	51	**30**	**6**
Moderate	0	*3*	28	**30**	*1*	*6*	40	**25**
Severe	0	*2*	*3*	35	0	0	0	44
Missing/not reported	13	10	8	10	13	10	10	13

Bold, improvement from BL; *italics*, worsening from BL; underline, unchanged from BL.

8519 Poster Discussion Session; Displayed in Poster Session (Board #419), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

DREAMM-2: Single-agent belantamab mafodotin (GSK2857916) in patients with relapsed/refractory multiple myeloma (RRMM) and renal impairment. *First Author: Hans Chulhee Lee, MD Anderson Cancer Center, Houston, TX*

Background: Renal impairment, a frequent complication and poor prognostic factor in RRMM, often leads to poor tolerability of standard regimens. We report outcomes in patients with renal impairment receiving single-agent belantamab mafodotin (2.5 or 3.4 mg/kg; B-cell maturation antigen targeting immunoconjugate not renally metabolized) from the DREAMM-2 post-hoc analysis (NCT03525678). **Methods:** Eligible patients with RRMM had no active renal conditions and adequate renal function (based on albumin/creatinine ratio [<500 mg/g] and eGFR [mL/min/1.73 m^2]: normal [≥90], mild impairment [mild, ≥60≤90], moderate impairment [mod, ≥30≤60]). **Results:** Overall response rates (95% CI) in patients with mild/mod impairment (2.5 mg/kg: 32% [21.4–44.0]; 3.4 mg/kg: 36% [25.6–48.5]) were similar to those in the overall population (*Lancet Oncol.*2020). The median duration of response (DoR) was not reached (NR) in 2.5 mg/kg mild/mod subgroup (95% CI estimate: 4.2 months–NR); median DoR was 7.5 months (4.9–NR) in 3.4 mg/kg mild/mod subgroup. Rates of keratopathy and albuminuria were similar regardless of renal function; rates of anemia, pyrexia, and thrombocytopenia were more frequent in patients with impaired renal function (Table). eGFR did not change or changed to normal in most patients. **Conclusions:** Following treatment with single-agent belantamab mafodotin, patients with mild/mod renal impairment achieved a similar efficacy and safety profile as patients with normal renal function. Funding: GlaxoSmithKline (205678). Drug linker technology licensed from Seattle Genetics; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa. Clinical trial information: NCT03525678. Research Sponsor: GlaxoSmithKline.

AEs and lab changes based on renal function.

n (%)	**2.5: Normal (n=19)**	**2.5: Mild (n=48)**	**2.5: Mod (n=24)**	**3.4: Normal (n=18)**	**3.4: Mild (n=52)**	**3.4: Mod (n=22)**
Keratopathy	18 (95)	33 (69)	15 (63)	14 (78)	40 (77)	14 (64)
Anemia	1 (5)	13 (27)	7 (29)	5 (28)	21 (40)	12 (55)
Pyrexia	2 (11)	9 (19)	9 (38)	3 (17)	17 (33)	5 (23)
Thrombocytopenia	3 (16)	11 (23)	6 (25)	6 (33)	26 (50)	12 (55)
Nausea	5 (26)	10 (21)	7 (29)	4 (22)	16 (31)	9 (41)
AST increased	5 (26)	12 (25)	2 (8)	1 (6)	16 (31)	6 (27)
Serious AEs	7 (37)	16 (33)	12 (50)	8 (44)	25 (48)	11 (50)
Worst post-baseline albumin creatinine ratio <500 mg/g*	11/14 (79)	38/45 (84)	15/20 (75)	9/14 (64)	28/37 (76)	13/20 (65)
eGFR change to normal or no change	5/6 (83)	20/27 (74)	15/16 (94)	14/16 (88)	25/35 (71)	14/14 (100)

AEs in >30% with mild/mod are listed; *Patients with albumin creatinine ratio <500 mg/g at baseline

8520 Poster Discussion Session; Displayed in Poster Session (Board #420), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase II, single-arm study of denosumab in multiple myeloma patients with renal insufficiency. *First Author: Elizabeth O'Donnell, Massachusetts General Hospital Cancer Center, Boston, MA*

Background: Bone destruction is a devastating consequence of multiple myeloma (MM). An unmet medical need exists for the management of skeletal complications in MM patients with renal insufficiency. Despite the effectiveness of intravenous bisphosphonates, their use is limited in situations where renal dysfunction is present. Denosumab is a fully human monoclonal IgG2 antibody to RANKL that has been shown to be non-inferior to zoledronic acid for SRE rates in MM (Raje, et al. Lancet Oncol). More importantly, it does not have the same renal toxicity as the bisphosphonates. We hypothesize that denosumab can be safely and effectively administered in MM patients with renal insufficiency to improve bone health. This may fill a gap in clinical care for bone-directed therapy in this patient population. **Methods:** This multi-center study will include forty adult patients with newly diagnosed or relapsed MM with a creatinine clearance of less than 30 mL/min (NCT02833610). All patients will receive a subcutaneous injection of denosumab 120 mg Q4W for a total of 12 cycles. In addition, it is required that all subjects receive daily vitamin D and calcium supplementation at standard doses (at least 2000 mg calcium citrate and1000 IU of vitamin D), unless documented hypercalcemia develops on study. The primary objective is to assess the effect of denosumab 120 mg Q4W on serum c-terminal telopeptide (sCTX). Secondary objectives include evaluation of safety and tolerability of denosumab in patients with renal insufficiency, incidence of hypocalcemia, effect on bone mineral density, effect on urinary n-terminal telopeptide, and proportion of patients who have a documented skeletal-related event. **Results:** At the time of this analysis, a total of 20 out of a planned 40 patients have been enrolled, including 9 women, 11 men. Of those treated, 8 patients have completed the planned 12 cycles of therapy. Hypocalcemia was observed in 7 (35%) patients. Four patients (20%) experienced grade 3 hypocalcemia, 3 (15%) grade 2 or less. Two patients developed osteonecrosis of the jaw, one (5%) grade 1 and one (5%) grade 4 event. Data for the analysis of the primary endpoint of sCTX levels will be presented. **Conclusions:** Investigation of denosumab in MM patients with renal insufficiency defined as a creatinine clearance less than 30 mL/min is ongoing. Early data support that denosumab can be safely administered in this population. However, incidence of hypocalcemia despite aggressive prophylactic calcium dosing underscores the importance of the trial to inform safe practice in this more fragile population. Clinical trial information: NCT02833610. Research Sponsor: Amgen.

8521 Poster Session (Board #421), Fri, 8:00 AM-11:00 AM

Bortezomib, lenalidomide, and dexamethasone (VRD) is superior to lenalidomide, adriamycin, and dexamethasone (RAD) prior to risk-adapted transplant in newly diagnosed myeloma. *First Author: Stefan Knop, Medizinische Klinik und Poliklinik II, Julius Maximilians Universität Würzburg, Würzburg, Germany*

Background: High-dose chemotherapy (HDT) followed by autologous stem cell transplant (SCT) remains a standard of care in patients (pts) with newly diagnosed (ND) multiple myeloma (MM). While lenalidomide (R) maintenance is acknowledged to improve outcomes, intensified consolidation (such as tandem-SCT) has yielded conflicting results. Allogeneic (allo) SCT holds the promise of curative potential at the cost of higher treatment-related mortality (TRM). In a previous phase 2 study, we showed a very low TRM rate (6.1%) and feasibility of 12 months (mos) of R maintenance (maint), with auto/allo SCT after R/adriamycin/dexamethasone (RAD). This prompted us to compare, on a randomized rather than a "biological assignment" basis, a second auto- versus (vs) an allo-SCT in pts with an unfavorable prognosis. **Methods:** The current protocol (DSMM XIV, NCT01685814) was set up according to a double 2x2-factorial design. Post-induction (PInd) CR rate was the efficacy endpoint for the comparison of RAD vs bortezomib (V)/RD (VRD; 3 cycles each). If pts had achieved >VGPR to HDT, a second randomization (2ndR) compared immediate R maint (arm A2) with a second auto-SCT (B2). In case of < VGPR, pts were randomized between a second auto- (C2) and allo-SCT (D2). Planned R maint. duration was 36 mos, except after allo (12 mos). **Results:** Between 05/2012-06/2016, 476 pts were randomized and 469 received at least one dose of study drug. Pts' median age was 55 (range, 32–65) years. 11.3% of pts had FISH del17p; 11.6% had t(4;14); and 4.4% had t(14;16). PInd CR rate was 11.8% (90% CI, 7.9%-16.3%) with RAD and 13.0% (90% CI, 8.9-18.0) with VRD (P = .697). 382 pts underwent R2 with 279 pts. (73%) in >VGPR and 103 (27%) in < VGPR, respectively. Median duration of R maint (N = 298) was 21.2 mos for A2, 23.1 mos for B2, 27.4 mos for C2, and 11.0 mos. for D2. At a median follow-up of 40.2 (0.5-87.0) months, median PFS from first randomization with RAD was 41.7 (95% CI, 35.4-48.5) mos vs. 53.7 (95% CI, 46.2-63.1) mos with VRD (P = .0439). Median PFS from 2ndR was 38.7 (95% CI, 30.3-47.3) mos for the 181 RAD vs. 50.7 (95% CI, 44.4-64.9) mos for the 201 VRD pts (P = .0126). Median overall survival (OS) cannot be estimated. With 47 deceased RAD vs 36 VRD pts, HR was .671 (95% CI, .435-1.037; P = .0703). **Conclusions:** In this study, median PFS benefit was 12 mos in favor of VRD vs. RAD despite comparable PInd CR. We show for the first time a len-PI to be superior to a len-chemo triplet, confirmed with positive OS trends. 3-year PFS for all consolidation arms will be presented. Clinical trial information: NCT01685814. Research Sponsor: Celgene, AMGEN.

8522 Poster Session (Board #422), Fri, 8:00 AM-11:00 AM

Genetic polymorphisms associated with clostridium difficile infection in multiple myeloma patients undergoing autologous stem cell transplantation. *First Author: Issam Hamadeh, Levine Cancer Institute, Charlotte, NC*

Background: CDI is the primary cause of infectious diarrhea in immunocompromised patients including those undergoing autologous stem cell transplant (SCT). Given the key role of gut microbiome and its interaction with host immune system, we investigated whether polymorphisms in innate immunity genes (identified through Ingenuity Pathway Analysis) were associated with CDI. **Methods:** We queried our database to identify MM patients who underwent an autologous SCT between April 2015-June 2019. Patients who had their buccal swabs collected through an IRB approved specimen collection protocol were included herein. Data were collected on age, conditioning regimen, CDI diagnosis, time from admission until CDI diagnosis, absolute neutrophil count (ANC) at time of CDI diagnosis, and antibiotic prophylaxis. Genomic DNA was extracted from buccal swabs and genotyped for 62 single nucleotide polymorphisms (SNPs) in *ASPH, RLBP1L1, ATP7B, IL-8, FAK, TNFRSF14, CTH, TLR* and *IL-4*. Univariate and multivariate logistic regression analyses were performed to assess association between CDI and presence of SNPs in these genes. **Results:** A total of 83 patients were identified (25 cases and 58 controls). Baseline characteristics were comparable between two groups. Median age was 67 years (range: 50-79). All patients received high dose melphalan as conditioning, and the same antibiotic prophylaxis during peri-transplant period. Median time from hospitalization until CDI diagnosis was 10 days (IQR:9 days), and median ANC was 0.7/mL (IQR:1.6/mL). Two SNPs (rs2227307 T > G in *IL-8* and rs2234167 G > A in *TNFRSF14*) were significantly associated with CDI risk in both univariate and multivariate logistic regression analyses (Table). **Conclusions:** Our findings suggest that rs227307G (in *IL-8*) and rs2234167A (in *TNFRSF14*) alleles are potential risk factors for CDI after autologous SCT. Our findings, if validated in a larger cohort, would support genetic testing as a screening tool to identify patients who might benefit from prophylaxis against CDI. Research Sponsor: Carolinas Myeloma Research Foundation.

Results of univariate/multivariate logistic regression.

	Univariate analysis			Multivariate analysis		
SNP	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
rs2227307	1.8	0.4-9.1	0.40	2.3	0.4-12	0.30
G/G vs T/T	4.2	1.0-16.7	0.03	4.3	1.1-17.5	0.04
T/G vs T/T	-	-	0.03	-	-	0.05
rs2234167	3.3	1.1-10.2		3.1	1.0-10.2	
A/A vs G/G						
G/A vs G/G						

8523 Poster Session (Board #423), Fri, 8:00 AM-11:00 AM

A first-in-class ex vivo combination between cytokine-induced memory like (CIML) NK cells and a CD38 targeting antibody recruiting molecule (ARM) as a novel approach to target NK cells without cellular engineering for the treatment of multiple myeloma. *First Author: Luca Rastelli, Kleo Pharmaceuticals, New Haven, CT*

Background: Cytokine-induced memory-like (CIML) NK cells differentiate after a brief preactivation with interleukin-12 (IL-12), IL-15, and IL-18 and exhibit enhanced responses to cytokine or activating receptor restimulation for several weeks to months. Antibody Recruiting Molecules (ARM) are bifunctional molecules that simultaneously bind a given tumor marker and engage endogenous IgG antibodies, therefore binding and activating NK cells via their FcR and targeting them to kill tumors cells. A first in class therapy that has the potential to improve the activity of CIML NK cells by combining them with KP1237, a CD38-ARM is presented for the treatment of newly diagnosed multiple myeloma (MM) patients who are minimal residual disease positive (MRD+) and eligible for autologous stem cell transplant (ASCT). **Methods:** Specific killing of CD38 expressing MOLP-8 cells by CIML NK cells alone or in combination with KP1237 was measured. Additionally, NK and CIML NK cells from healthy volunteers and MM patients at various stages of the disease were tested for activity against autologous and allogeneic tumor cell targets. In these experiments, surface phenotype and activation status of NK cells were determined. **Results:** A statistically significant increase in specific killing was observed when KP1237 was used in combination with CIML NK cells in an ADCC assay against CD38 expressing MOLP-8 ($p = 0.0105$, mean 61.8 ± SD 9.1 and mean 83.7 ± SD 13.58 for CIML NK alone and CIML NK+KP1237, respectively). This effect was accompanied by an increase in plasma membrane retention of CD107a. Surface phenotype of NK and CIML NK cells from healthy volunteers and MM patients was compared since the functional activity of NK cells from such patients is debated. We report surface expression of CD56, CD16, CD57, NKG2D, Nkp44, Nkp46, CD107a, KIR2DL2/3/DS2, and CD69 as well as frequencies of CD57hi CD56+ mature versus CD57lo CD56+ immature NK cell subsets. Further, autologous CIML NK cells + KP1237 exhibit cytotoxicity towards patient plasma cells. **Conclusions:** The activity of CIML NK cells towards CD38 expressing MM target cells is improved by the addition of KP1237 avoiding the need for cellular engineering with chimeric antigen receptors. This led to the development of the combination drug product consisting of patient autologous CIML NK cells, KP1237 and IVIG. Clinical development is under way for (MRD+) MM patients eligible for ASCT. Research Sponsor: Kleo Pharmaceuticals.

8524 Poster Session (Board #424), Fri, 8:00 AM-11:00 AM

Prospective evaluation of spatial heterogeneity at single cell resolution in multiple myeloma. *First Author: Maximilian Merz, Roswell Park Cancer Institute, Buffalo, NY*

Background: Osteolytic lesions (OL) characterize symptomatic multiple myeloma (MM). It is still unclear why plasma cells (PC) cause OL in certain regions of the body while other areas show no signs of bone destruction despite significant bone marrow infiltration. We conducted the first study of single cell RNA sequencing (scRNA-seq) and whole-exome sequencing (WES) of PC obtained from random bone marrow samples (RS) and paired OL. **Methods:** As part of a prospective clinical trial, patients consented to an imaging-guided biopsy of new OL identified by PET/CT in addition to the RS from the iliac crest. Both samples were acquired in the same session. On the same day PC were isolated using a CD138 positive selection kit and single cell gene expression libraries were generated for scRNA-seq. Frozen PC were subjected to DNA extraction and WES. **Results:** We sequenced 93569 purified, viable PC from paired samples from 15 different locations in the first 7 consecutive patients (median PC from location: 7203; range 1121-10279). Quality assessment of scRNA-seq data revealed no differences between PC in OL and RS. Based on scRNA-seq, 9-24 different subpopulations of PC in individual patients were identified. Over 90% of clusters found in the RS were also present in corresponding OL suggesting a common ancestor. This was true for patients with overlapping as well as divergent mutational profiles in RS and OL as shown by WES. In each patient we found PC clusters that were predominantly present in OL. Respective clusters were characterized by expression of Wnt-signaling inhibitors like DKK-1, Frzb and sFRP-2 and other genes linked to MM bone disease (HGF, CXCL-12, CCL3). Lysosome-associated membrane protein-like molecule 5 (LAMP5) and J-chain were overexpressed in OL clusters. Analysis of genes (IKZF1 and IKZF3) associated with response to treatment and outcome revealed vast heterogeneity and differences in risk scores (UAMS70 and IFM15) on a single cell level from different locations in individual patients. **Conclusions:** Our study provides the first evidence that PC from OL have distinct transcriptomic profiles that link site-specific gene expression to development of bone disease and adverse outcome. Research Sponsor: German Cancer Aid.

8525 Poster Session (Board #425), Fri, 8:00 AM-11:00 AM

KarMMa-RW: A study of real-world treatment patterns in heavily pretreated patients with relapsed and refractory multiple myeloma (RRMM) and comparison of outcomes to KarMMa. *First Author: Sundar Jagannath, Mount Sinai Medical Center, New York, NY*

Background: RRMM patients (pts) triple-class exposed (to immunomodulatory drugs [IMiDs], proteasome inhibitors [PIs] and anti-CD38 monoclonal antibodies [mAbs]) have limited treatment (tx) options. The ongoing phase II KarMMa study (NCT03361748) is examining idecabtagene vicleucel (ide-cel; bb2121), a BCMA targeted CAR T cell therapy, in RRMM pts with ≥3 prior regimens (IMiD, PI and CD38 mAb inclusive) who are refractory to their last tx per IMWG criteria. This study aimed to 1) assess tx patterns and outcomes in real world (RW) RRMM pts similar to the KarMMa population and; 2) compare outcomes with SoC in a synthetic cohort vs ide-cel in KarMMa. **Methods:** In this global, noninterventional, retrospective study (KarMMa-RW), pt-level data from clinical sites, registries and databases were collated into a single data model. RW pts meeting KarMMa eligibility criteria (eligible cohort; EC) were compared with KarMMa (N = 128) using trimmed stabilized inverse probability of tx weighted propensity scores (IPTW PS) for pts in both studies with Poisson regression for ORR and ≥VGPR, and Cox models with study as a term for PFS. All models were adjusted for unbalanced covariates. **Results:** Of 1949 RW pts, 1171 were refractory to last regimen (median age, 68 y; median no. of prior regimens, 5; triple-class refractory, 41%). Further selection for subsequent tx, organ function and no comorbidities yielded 190 EC pts who had > 90 distinct tx regimens. With a median follow-up of 11.3 mo (KarMMa) and 10.2 mo (EC) at data cutoff (Oct 30, 2019), ORR, ≥VGPR and PFS were significantly improved in KarMMa vs EC (Table). **Conclusions:** Results from the KarMMa-RW study confirm that there is no clear SoC for heavily pretreated RW RRMM pts and responses are suboptimal with currently available therapies. Ide-cel showed deep, durable responses and significantly improved PFS in RRMM pts, representing a potential new tx option in RRMM. Clinical trial information: tbd. Research Sponsor: Bristol-Myers Squibb and bluebird bio.

Baseline Characteristic	EC (N = 190)	KarMMa* (N = 128)
Median age, y	64	61
R-ISS disease stage III, %	4	16
High-risk cytogenetics, %	30	35
Median no. prior regimens	5	6
Triple-class refractory/plasmacytoma, %	43/11	84/39
Effectiveness†		
ORR, % (95% CI)	32 (24-42)	76 (69-86)
	RR, 2.4 (1.7-3.3);	*P*< 0.0001
≥VGPR‡, % (95% CI)	14 (9-22)	57 (47-70)
	RR, 4.2 (2.4-7.2);	*P*< 0.0001
Median PFS, mo	3.5 (3.2-3.7)	11.3 (9.5-13.1)
	HR, 0.48 (0.33-0.69);	*P*< 0.0001

HR, hazard ratio; RR, risk ratio
*Across all target doses
†Derived for both studies using trimmed stabilized IPTW PS
‡CR not reported due to missing biopsy data in EC to confirm CR

8526 Poster Session (Board #426), Fri, 8:00 AM-11:00 AM

Efficacy and safety of carfilzomib, dexamethasone, daratumumab (KdD) twice-weekly at 56 mg/m^2 and once-weekly at 70 mg/m^2 in relapsed or refractory multiple myeloma (RRMM): Cross-study comparison of candor and MMY1001. *First Author: Xavier Leleu, Hopital Claude Huriez, Lille, France*

Background: CANDOR, a randomized phase 3 study, showed significantly improved progression-free survival (PFS) and overall response rate (ORR) for twice-weekly KdD 56 mg/m^2(TW KdD56) vs Kd in RRMM, with a 37% risk reduction in disease progression or death (Usmani, 2019). The benefit of once-weekly carfilzomib (K) at 70mg/m^2 for the same triplet, KdD (OW KdD70), in RRMM was shown in the nonrandomized MMY1001 study. We performed robust cross-study comparisons to investigate how TW KdD56 compares to OW KdD70. **Methods:** For alignment of inclusion criteria, the primary analysis set for this cross-study comparison included individual data from CANDOR pts with prior exposure to bortezomib and immunomodulatory drug, and all pts in MMY1001. Propensity score method (Rambaldi, 2019; Kumar, 2019) allowed reliable cross-study comparison, controlling for baseline prespecified covariates such as age, creatinine clearance, performance status, prior treatment exposure/refractoriness, and time from initial diagnosis and relapse. Propensity score adjustment based on inverse probability of treatment weighting (IPTW) was implemented on efficacy endpoints, while safety was evaluated side-by-side. **Results:** The unadjusted and adjusted propensity score comparison of CANDOR and MMY1001 showed similar efficacy in terms of ORR and PFS in the TW KdD56 and OW KdD70 groups (Table). As propensity score comparisons were for efficacy only, safety comparisons between CANDOR and MMY1001 included differing sample sizes and treatment duration (Table). The safety of KdD56 and KdD70 was consistent with the known safety profiles of individual study treatments. **Conclusions:** OW KdD70 is an efficacious dosing option with favorable benefit-risk, comparable to TW KdD56. The OW KdD70 dosing option represents a more convenient regimen that might encourage adherence and potentially lead to better outcomes for RRMM pts. Clinical trial information: NCT03158688. Research Sponsor: Amgen, Inc.

	Unadjusted		Adjusted*	
	TW KdD56 (n = 185)	OW KdD70 (n = 85)	TW KdD56 (n = 89.3)	OW KdD70 (n = 85)
ORR, % (95% CI)	83.2 (77.1–88.3)	81.2 (71.2–88.8)	79.6 (71.2–87.9)	81.2 (72.9–89.5)
Median PFS (OW/TW), mo (95% CI)	NE (18.4–NE)	25.8 (19.4–NE)	NE (12.0–NE)	25.8 (19.4–NE)
HR, (OW/TW) (95% CI)	–		0.80 (0.49–1.32)	
Median follow-up, mo	16.8	23.5	–	–
Grade ≥3 AEs‡, n (%)	156 (84.3)	70 (82.4)	–	–
AEs leading to K discontinuation‡, n (%)	39 (21.1)	16 (18.8)	–	–
Fatal AEs‡, n (%)	20 (10.8)	3 (3.5)	–	–

*propensity score adjustment using IPTW; ‡treatment-emergent; NE, not estimable

8527 Poster Session (Board #427), Fri, 8:00 AM-11:00 AM

Ixazomib vs placebo maintenance for newly diagnosed multiple myeloma (NDMM) patients not undergoing autologous stem cell transplant (ASCT): The phase III TOURMALINE-MM4 trial. *First Author: Meletios A. Dimopoulos, National and Kapodistrian University of Athens School of Medicine, Athens, Greece*

Background: Maintenance therapy delays disease progression in non-ASCT NDMM patients. However, in practice, currently used maintenance therapies may be limited to fixed duration due to toxicity and route of administration; additional options are needed. **Methods:** 706 non-ASCT NDMM patients who received 6–12 months of standard-of-care induction therapy and achieved at least a partial response (≥PR) were randomized 3:2, double-blind, to the oral proteasome inhibitor (PI) ixazomib (n = 425; 3 mg, cycles 1–4, then, if tolerated, 4 mg, cycle 5 onwards) vs placebo (n = 281) on days 1, 8, and 15 of 28-day cycles for ≤2 yrs. Patients were stratified by prior PI exposure (yes vs no), pre-induction International Staging System (ISS) disease stage (I/II vs III), age (< 75 vs ≥75 yrs), and post-induction best response (complete or very good partial response [CR/VGPR] vs PR). Primary endpoint was progression-free survival (PFS). **Results:** Baseline characteristics were well balanced. Overall median age was 73 yrs, 38% of patients were aged ≥75 yrs, 35% were ISS stage III, and 22%/40%/38% had CR/VGPR/PR post induction. Overall, 82% of patients received a PI and 33% an immunomodulatory drug as part of their induction regimen. At a median follow-up of 21.1 months, median PFS was 17.4 months with ixazomib vs 9.4 months with placebo (hazard ratio [HR] 0.659, 95% confidence interval [CI] 0.542–0.801, p < 0.001). Significant (p < 0.001) PFS benefit was seen in patients who achieved CR/VGPR post induction (Table). Overall survival data are not yet mature (19% of events); follow-up is ongoing. Treatment-emergent adverse events (TEAEs) were mostly grade 1–2 (37% vs 23% of patients had grade ≥3 TEAEs with ixazomib vs placebo). Common TEAEs for ixazomib vs placebo included nausea (27% vs 8%), vomiting (24% vs 4%), and diarrhea (23% vs 12%); 5% vs 6% of patients had new primary malignancies. No cumulative toxicities were observed. **Conclusions:** Ixazomib maintenance therapy in non-ASCT NDMM patients showed a clinically meaningful 34% reduction in the risk of progression or death, with a well-tolerated safety profile. Ixazomib is the first oral PI maintenance option for non-ASCT NDMM patients. Clinical trial information: NCT02312258. Research Sponsor: Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

		Ixazomib	Placebo	HR (95% CI)
Median PFS, months	All	17.4	9.4	0.659 (0.542–0.801)
	CR/VGPR post induction	25.6	12.9	0.586 (0.449–0.765)
	Pre-induction ISS stage III	16.6	7.8	0.695 (0.499–0.967)
	Age ≥75 yrs	16.7	10.6	0.738 (0.537–1.014)
Safety, %	Any TEAE	91	82	
	Grade ≥3 TEAE	37	23	
	Serious TEAE	22	17	
	Discontinuation due to TEAE	13	8	
	On-study death	3	2	

8528 Poster Session (Board #428), Fri, 8:00 AM-11:00 AM

Multiple myeloma (MM) vaccination (influenza, FV and pneumococcal, PV) rates worldwide and impact on infection, hospitalization, and death. *First Author: Michael A. Thompson, Aurora Cancer Care, Aurora Research Institute, Advocate Aurora Health, Milwaukee, WI*

Background: MM is a cancer of the immune system. Infections are common reasons for hospitalization and death in MM. As MM patients (pts) are living longer, with prolonged exposure to systemic therapy, there is a need to vaccinate pts and to determine the effectiveness of these vaccines. Vaccination in MM pts is underutilized, based on a study of vaccination patterns in a large health system (Alemu JPCRR 2017) and data collected via a pt self-report online portal (Thompson ASCO 2020). We analyzed FV and PV patterns and associated outcomes in INSIGHT MM, the largest global, prospective, observational study in MM to date. **Methods:** INSIGHT MM aims to understand MM pt and disease characteristics at diagnosis and relapse, treatment patterns, clinical outcomes, and treatment-associated tolerability, effectiveness, quality of life, and healthcare resource utilization. INSIGHT MM has enrolled 4318 MM pts from 15 countries worldwide; pts are being followed up prospectively for ≥5 yrs. Vaccine status is collected at study entry and yearly. We analyzed FV and PV patterns and associated outcomes of pts enrolled in July 2016–2019. **Results:** At data cutoff (Sep 1, 2019), 2562/2523 pts had study entry data on FV/PV status. Overall vaccination rates were low (FV 40%, PV 30%) and varied by region: FV 56%/38%/27%/4% and PV 43%/28%/21%/5% in US/Europe/Latin America/Asia. In evaluable pts, lack of vaccination was associated with higher infection and hospitalization rates for FV, and with increased risk of death (univariate analysis) for both FV and PV (Table; multivariate analysis underway). Infections, including influenza and pneumonia, were the cause of death in 19% (43/226) / 8% (9/108) (P = 0.018) of pts who did not receive FV / received it in the past 2 yrs and 19% (46/236) / 9% (9/100) (P = 0.027) of pts who did not receive PV / received it in the past 5 yrs, and in 7%/15%/20%/40% of pts who died in US/ Europe/Latin America/Asia (P < 0.0001). **Conclusions:** Global vaccination rates in MM pts were low and varied by region. Lack of vaccination correlated with rates of infection (FV), hospitalization (FV), and death (FV and PV). Further MM datasets should be analyzed to confirm the findings. Vaccination data should be collected in prospective clinical trials as it may affect survival. Vaccination is important in MM and should be encouraged. Clinical trial information: NCT02761187. Research Sponsor: Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

	Total	Deceased	Alive	P value
FV status available from past 2 yrs, n	2275	355	1920	P < 0.0001
Yes (2 FV)	4%	1%	4%	
Yes (1 FV)	39%	31%	40%	
No (0 FV)	57%	68%	56%	
PV status available from past 5 yrs, n	2254	356	1898	P = 0.0001
Yes	38%	29%	40%	
No	62%	71%	60%	

8529 Poster Session (Board #429), Fri, 8:00 AM-11:00 AM

Updates from a phase Ib study of isatuximab (Isa), bortezomib (V) and dexamethasone (D) plus cyclophosphamide (C) or lenalidomide (R) in transplant-ineligible, newly diagnosed multiple myeloma (NDMM). *First Author: Enrique M. Ocio, Marqués de Valdecilla University Hospital (IDIVAL), University of Cantabria, Santander, Spain*

Background: We report updated data from a Phase Ib study of Isa, a CD38 monoclonal antibody, plus VCd or VRd in transplant ineligible patients (pts) with NDMM (NCT02513186). **Methods:** Isa-VCd: Isa (10 or 20 mg/kg; weekly [QW] cycle 1 [C1], then Q2W), V (1.3 mg/m^2; twice weekly C1, then QW), C (300 mg/m^2; QW C1, then Days [D] 1, 8, 15 to C12), d (20 mg; twice weekly C1, then D1, 2, 8, 9, 15, 16, 22, 23 to C12). Isa-VRd: Isa (10 mg/kg), V and d as described above; R (25 mg/day; D1–14 and D22–35). Efficacy and safety were evaluated. Conventional (M-protein levels) and minimal residual disease (MRD) IMWG response assessments were compared. MRD negativity was assessed at 10^{-5} by next-generation sequencing and flow. Mass Spectrometry (MS) negativity (no detectable serum M-protein) was assessed for 13 pts by Immuno-Capture and Liquid Chromatography coupled to High Resolution MS. **Results:** As of Nov 18, 2019, 17 pts were treated with Isa-VCd (10 mg/kg, n = 13; 20 mg/kg, n = 4), 27 with Isa-VRd; 53% and 63% remained on treatment, respectively. Infusion reactions were seen in 53% of Isa-VCd and 63% of Isa-VRd pts; Grade ≥3 infections in 23% and 37%; serious adverse events in 47% and 52%. See table for efficacy. 3 MRD positive pts were MS positive with persistent detectable M-protein (> 10 μg/mL). 8/10 MRD negative pts were MS positive (4 at 5-10 μg/mL; 4 at > 10 μg/mL) and 2/10 were MS negative (< 5 μg/mL). Stable residual M-protein was observed by MS up to 23 months post-MRD negativity. All pts tested by MS are still progression-free. **Conclusions:** Isa-VCd/VRd shows encouraging efficacy and tolerability in NDMM. MS seems to be more sensitive than MRD; low levels of M-protein were detectable even in MRD negative pts. Clinical trial information: NCT02513186. Research Sponsor: Sanofi.

Efficacy	Isa-VCd (n = 15)	Isa-VRd (n = 26)
ORR, n (%)	14 (93)	26 (100)
≥CR	10 (67)	11 (42)
VGPR	2 (13)	14 (54)
PR	2 (13)	1 (4)
≥VGPR MRD negative	8 (53)	10 (38)
2 yr PFS, probability (95% CI)	0.93 (0.61-0.99)	0.96 (0.75-0.99)
Events/pts censored	5/10	2/24
Median follow-up duration, mo	37.1	21.5

CI, confidence interval; CR, complete response; PFS, progression free survival; ORR, overall response rate; PR, partial response; VGPR, very good partial response.

8530 Poster Session (Board #430), Fri, 8:00 AM-11:00 AM

Once weekly selinexor, carfilzomib, and dexamethasone (SKd) in patients with relapsed/refractory multiple myeloma (MM). *First Author: Cristina Gasparetto, Duke University Cancer Center, Durham, NC*

Background: Selinexor is a novel, first-in-class selective inhibitor of nuclear export (SINE), which blocks exportin 1 (XPO1), forcing the nuclear retention and activation of tumor suppressor proteins. Selinexor in combination with low dose dexamethasone (Sel-dex) was approved by the FDA, based on data from the STORM study wherein Sel-dex induced an overall response rate (ORR) of 26.2% in patients (pts) with refractory MM. We hypothesize that once weekly (QW) SKd may be an active well tolerated regimen and evaluated this combination in a dose escalation/expansion study. **Methods:** STOMP is a phase 1b/2 study evaluating various doses and enrolled pts with carfilzomib naive relapsed MM. Oral selinexor was dosed QW at 80 or 100 mg. Carfilzomib was dosed QW (on days 1, 8 and 15 of 28-day cycle) at 56 mg/m^2 or 70 mg/m^2. Dexamethasone was dosed at 40 mg QW. The primary objectives of the study are to assess the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), as well as explore the efficacy and safety of SKd. **Results:** As of January 2020, 18 pts were enrolled. Median age was 71 years (range: 50-76). Median number of prior regimens was 4 (range: 1-8). All pts (n = 18) were previously treated with bortezomib and lenalidomide, and 50% and 56% pts were refractory to bortezomib and lenalidomide respectively. Nine (50%) pts received prior pomalidomide treatment and 8 (44%) pts were refractory. Eleven (61%) pts received prior daratumumab treatment and 9 (50%) were refractory. The MTD was selinexor 80 mg QW, carfilzomib 56 mg/m^2 QW and dexamethasone 40 mg QW. The ORR and CBR were 72% and 79% respectively with 4 complete responses, 7 very good partial responses, 2 partial responses, and 1 minimal response. Stable disease was observed in 3 pts. With a median follow-up period of 4.7 (1.8-16.3) months, median progression-free survival has not been reached. Common treatment-related adverse events (total, Grade ≥3) were thrombocytopenia (83.3%, 66.7%), nausea (66.7%, 0%), anemia (55.6%, 11.1%), fatigue (50%, 11.1%), anorexia (44%, 5.6%), weight loss (44%, 0%), and neutropenia (33.3%, 11.1%). **Conclusions:** Once weekly SKd demonstrated an encouraging ORR of 72% in pts with a median of 4 lines of prior therapy. The majority of responses are deep and predominantly CR and VGPR. The combination is well tolerated with no new safety signal, no Grade ≥3 nausea, vomiting, diarrhea, weight loss or anorexia. The side effects are a function of the dose and schedule and can be managed with dose modification and supportive care. Enrolment is ongoing and supports a phase 3 study of SKd. Clinical trial information: NCT02343042. Research Sponsor: Karyopharm Therapeutics Inc.

8531 Poster Session (Board #431), Fri, 8:00 AM-11:00 AM

Pharmacodynamic (PD) responses drive dose/schedule selection of CC-92480, a novel CELMoD agent, in a phase 1 dose-escalation study in relapsed/refractory multiple myeloma (RRMM). *First Author: Lilly Wong, Bristol-Myers Squibb, San Diego, CA*

Background: CC-92480 is a novel cereblon (CRBN) E3 ligase modulator (CELMoD) agent under investigation in a first-in-human phase 1 study (NCT03374085) in RRMM patients (pts). In preclinical studies, CC-92480 demonstrated efficient and sustained degradation of Ikaros/Aiolos leading to broad antiproliferative effects and induction of apoptosis in MM cell lines, and enhanced immune stimulatory effects. **Methods:** Eligible RRMM pts received escalating doses of CC-92480 + dexamethasone. Several dosing schedules were evaluated in parallel; more continuous with 4-day or 7-day breaks and intensive with longer breaks in a 28-day cycle. Peripheral blood and bone marrow aspirates (BMA) were taken before and during treatment at multiple time points. Levels of Ikaros/Aiolos in T cells, and effects on immunomodulation were assessed by flow cytometry. Weekly levels of free light chain (sFLC) and B-cell maturation antigen (sBCMA) were determined in serum during the first 2 cycles of treatment. BMA clots were analyzed by immunohistochemistry for CRBN, Ikaros, Aiolos, ZFP91, c-Myc, and IRF-4. **Results:** The rate and depth of Ikaros/Aiolos degradation in T cells increased with dose and reached maximal at ≥0.6 mg QD with sustained degradation over 24 hrs. Substrate recovery occurred during drug holidays with faster recovery at lower doses, and reached full recovery with ≥7-day break for all dose levels tested. B cells decreased with increasing dose, and T-cell proliferation was demonstrated at all doses/schedules. Substrate degradation was also evident in bone marrow plasma cells including in the setting of low CRBN levels. In these heavily pretreated, including triple-class-refractory, RRMM pts, CC-92480 dosing periods led to rapid and sustained decreases in sFLC and sBCMA. This was dose and schedule dependent and correlated with plasma exposure; the longer breaks in the intensive schedules led to rapid rebound of these markers, while the more continuous schedules maintained the depth of suppression. **Conclusions:** PD responses correlated with dose and schedule. PD samplings at multiple time points during treatment allowed dynamic changes and kinetics of each biomarker in all schedules to be followed and to inform next steps. Ikaros/Aiolos degradation and recovery, coupled with changes in sFLC and sBCMA, guided the adjustment of the dosing schedule during dose escalation in order to optimize efficacy and tolerability. The study is ongoing and selection of the recommended phase 2 dose is pending. Research Sponsor: Bristol-Myers Squibb.

8532 Poster Session (Board #432), Fri, 8:00 AM-11:00 AM

Diagnostic performance of skeletal survey versus 18F-FDG-PET/CT for detecting lytic lesions in smoldering multiple myeloma. *First Author: Elizabeth M. Hill, NCI/NHLBI, Bethesda, MD*

Background: Per NCCN Guidelines for smoldering multiple myeloma (SMM), whole body radiography, i.e. skeletal survey (SS), should be used to rule out osteolytic bone lesions. If negative, more sensitive imaging techniques such as whole body ^{18}F-FDG-PET/CT(PET/CT), MRI, or low dose CT should be used to differentiate between SMM and multiple myeloma (MM). The false-negative rate of SS is high (30-70%). The frequency of false-positive SS in SMM is less well known but important because of its common use in community practice. We examine the specificity of SS in patients with a presumed diagnosis of SMM and question if SS is still warranted prior to modern imaging techniques to confirm a diagnosis of SMM. **Methods:** Records of patients sequentially referred from the community and evaluated for a presumed diagnosis of SMM at the National Institutes of Health Myeloma Program between April 2010 to January 2020 were reviewed. Patients with a SS and PET/CT performed within 30 days were included. Positive findings on PET/CT were defined per the 2014 IMWG criteria as one or more sites of osteolytic bone destruction seen on CT. The sensitivity and specificity of SS were calculated using PET/CT as the reference test. **Results:** Charts from 144 patients with presumed SMM were reviewed. A total of 76 SMM patients had both a SS and PET/CT performed within 30 days of each other. Sixty-four patients (84.2%) showed concordant results. Twelve (15.8%) patients had discordant imaging results. SS was falsely negative in 3 (4.7% (95% CI: 1.2%-14.2%)) patients and falsely positive in 9 (69.2% (95% CI: 38.9%-89.6%)) patients. SS had a sensitivity of 57.1% (95% CI: 20.2%-88.2%) and a specificity of 86.9% (95% CI: 76.2-93.5). **Conclusions:** In patients presumed to have SMM, disease burden is low thus highly sensitive imaging modalities are needed to rule out bone disease. This study confirms the low sensitivity of SS in the SMM population. It more importantly points out the low specificity of SS in SMM. The IMWG no longer recommends conventional SS prior to whole body CT (or PET/CT) as first imaging choice in SMM. While the argument may be made that SS should still be used upfront due to low cost and widespread availability, this study shows the risk of overestimating disease. Over 10% of patients in this series had false positive disease on SS and thus at risk of receiving unnecessary treatment. Not only concerning for patient toxicity but more so financial toxicity. If SS is used, it is important to review positive findings directly with a radiologist and consider follow-up confirmatory imaging. Research Sponsor: None.

8533 Poster Session (Board #433), Fri, 8:00 AM-11:00 AM

Multiparameter flow cytometry (MFC) and next generation sequencing (NGS) for minimal residual disease (MRD) evaluation: Results of the FORTE trial in newly diagnosed multiple myeloma (MM). *First Author: Stefania Oliva, GIMEMA, European Myeloma Network, Italy*

Background: The role of MRD by MFC and NGS is well known in MM, with few data on the concordance of the two techniques. We analyzed and compared MRD data from the FORTE trial both by MFC and NGS. **Methods:** Newly diagnosed MM patients (pts) ≤65 years were randomized to: carfilzomib, lenalidomide, dexamethasone (KRd) induction-autologous stem cell transplant (ASCT) - KRd consolidation (KRd_ASCT); 12 KRd cycles (KRd12); carfilzomib, cyclophosphamide, dexamethasone (KCd) induction-ASCT-KCd consolidation (KCd_ASCT). Pts were then randomized to maintenance: lenalidomide alone or plus carfilzomib. MRD was assessed by 8-color second generation flow cytometry (sensitivity 10^{-5}) in pts with ≥very good partial response (VGPR) before maintenance. In a subgroup of these pts, next generation flow (NGF; sensitivity 10^{-5}-10^{-6}) was performed. In ≥CR pts, MRD pre-maintenance was also assessed by NGS (Adaptive Biotechnologies; sensitivity 10^{-5}-10^{-6}). Thus, both MFC and NGS evaluations were available only in ≥CR pts. 1-year sustained MRD negativity by MFC and NGS was also analyzed in pts with at least one sample available at least 1 year apart. **Results:** MFC and NGS data were available in 184/233 (79%) CR pts (66 KRd_ASCT, 67 KRd12 and 51 KCd_ASCT). Median age of this ≥CR population was 57 years (IQR 52-62), 13% had International Staging System (ISS) III and 27% high risk cytogenetics by FISH [either del(17p) or t(4;14) or t(14;16)]. Table reports MRD negativity rate by MFC and NGS at a cut-off of 10^{-5} and 10^{-6} among ≥CR negative pts in the 3 arms. NGS negativity at a cut-off 10^{-6} was found in 36/133 (27%) ≥CR pts (for 51/184 CR pts 10^{-6} sensitivity was not reached). In evaluable pts, 1-year sustained 10^{-5} MRD negativity by MFC and NGS was superimposable (83%). We evaluated concordance of MRD results by the two techniques and observed agreement was 86% for MFC and NGS at 10^{-5} evaluable samples (n: 335; r: 0.61) and 78% for MFC and NGS at 10^{-6} evaluable samples (n: 56; r: 0.77). **Conclusions:** In pts who achieved ≥CR, similar rate of pre-maintenance 10^{-5} negativity by MFC and NGS has been reached in each arm, with 83% pts maintaining 1-year MFC or NGS 10^{-5} sustained MRD negativity. Concordance between MFC and NGS was good, particularly when the same sensitivity was reached. Longer follow up is needed to draw definitive conclusions. Clinical trial information: NCT02203643. Research Sponsor: Amgen.

	≥ 10^{-5} MFC MRD NEG	10^{-5} NGS MRD NEG	10^{-6} NGS MRD NEG *
KRD-ASCT	83%	76%	34%
KRD12	79%	69%	23%
KCD-ASCT	69%	70%	27%

*calculated on NGS 10^{-6} evaluable pts

8534 Poster Session (Board #434), Fri, 8:00 AM-11:00 AM

Association of elevated red cell distribution width and overall survival in multiple myeloma. *First Author: Sam Rubinstein, Vanderbilt University Medical Center, Nashville, TN*

Background: The most widely used multiple myeloma (MM) staging system, the Revised International Staging System (R-ISS), is based on lactate dehydrogenase, albumin, cytogenetics, and beta-2 microglobulin (B2M). B2M has limited clinical utility, is often only obtained to compute R-ISS, and is often a send-out test. Prior studies have shown that elevated red cell distribution width (RDW), a common test that is part of the routine complete blood count, is associated with reduced overall survival (OS) in MM. We hypothesized that a MM staging system could be constructed replacing B2M with RDW. **Methods:** Patients treated at Vanderbilt University Medical Center from 2000 to 2018 with cancer registry-confirmed MM diagnoses were included. OS was computed by registry-curated death and diagnosis dates; living patients were censored at date last known alive or of last follow up. A Cox proportional hazards model determining the independent effects of R-ISS, age, and RDW on OS was built. An alternate staging system (RDW-SS) was developed, replacing the B2M cutoffs in R-ISS with RDW (stage 1: RDW $<$ 14.0% stage 2: RDW 14.0-15.5%; stage 3: RDW $>$ 15.5%). Cox models comparing RDW-SS and R-ISS after adjustment for age and category of induction therapy (proteasome inhibitor [PI] and immunomodulatory drug [IMiD]), PI only, IMiD only, other) were built. **Results:** In 604 MM patients with available data, RDW was independently associated with OS after adjustment (HR = 1.069 per 1% RDW increase, $p < 0.001$). RDW-SS stages were associated with reduced OS (RDW-SS 2 HR 1.52, 95% CI 1.09 – 2.11, $p = 0.01$; RDW-SS 3 HR 2.13, 95% CI 1.37 – 3.28, $p < 0.001$) after adjustment; R-ISS stages were not (Table). **Conclusions:** RDW at MM diagnosis was independently associated with reduced OS, after adjustment for the clinical factors of age and treatment exposure; notably, R-ISS was not. The RDW-SS is simpler to obtain than R-ISS and may have improved prognostic value pending independent validation. If confirmed, mechanistic study of the etiology of this relationship is warranted. Research Sponsor: U.S. National Institutes of Health.

Cox models for R-ISS and RDW-SS.

Variable	R-ISS HR (95% CI)	P	RDW-SS HR (95% CI)	P
Age (per year)	1.04 (1.03-1.05)	*	1.04 (1.03-1.05)	*
Stage II (vs. I)	1.15 (0.92-1.52)	.20	1.52 (1.09-2.11)	.01
Stage III (vs. I)	1.30 (0.90-1.97)	.15	2.13 (1.37-3.28)	*
PI only induction (vs. PI + IMiD)	1.86 (1.27-2.67)	.001	1.87 (1.29-2.71)	*
IMiD only induction (vs. PI + IMiD)	1.55 (1.11-2.22)	.01	1.48 (1.04-2.12)	.003
Other induction (vs. PI + IMiD)	2.24 (1.52-3.28)	*	2.22 (1.51-3.27)	*

* = < 0.001

8535 Poster Session (Board #435), Fri, 8:00 AM-11:00 AM

Oncolytic virus pelareorep plus carfilzomib phase I trial in carfilzomib-refractory patients (NCI 9603): Responses with cytokine storm. *First Author: Douglas Weston Sborov, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT*

Background: Viral oncolytic therapy with intravenous Pelareorep, the infusible form of reovirus, is supported by preclinical data indicating that its antitumor activity results from direct cytolysis and an immune response against infected MM cells. Our preclinical data has shown that monocytes serve as carriers of reovirus from the peripheral blood to the bone marrow (Dona et al, ASH, 2019). In this abstract we present patients treated to date that were Carfilzomib refractory at enrollment. **Methods:** Pelareorep (P), Carfilzomib (K), and dexamethasone (d) were all infused on days 1, 2, 8, 9, 15 and 16 of a 28-day cycle. Patients were pretreated with dexamethasone 20 mg intravenously, then Carfilzomib 20 mg/m^2 on days 1 and 2 of cycle 1, and 56 mg/m^2 thereafter. Pelareorep dose levels were at $3x10^{10}$, $4.5*10^{10}$, and planned $9*10^{10}$ median tissue culture infectious dose ($TCID_{50}$). **Results:** All 6 evaluable patients showed reovirus infection in the post-treatment marrow aspirates cycle 1 day 9. Despite all patients having Carfilzomib-refractory disease, 2 patients achieved partial responses, two patients with short duration stable disease but few side effects, and 2 patients with PD. Of the two responders, one patient developed fever and grade 4 thrombocytopenia during cycle 1 and withdrew mid cycle. The other patient with a PR developed a cytokine storm - this patient presented cycle 1 day 3 hypoxemic with pneumonia, systolic failure (LVEF 69%-- $>$ 26%), with biochemical evidence of hemophagocytic syndrome with elevated IL-2R, IL-6, and ferritin $>$ 25K. This patient responded to tocilizumab, but ultimately died two weeks later with sepsis. Autopsy revealed pneumonia, no areas of reovirus infection other than in myeloma cells, and reovirus productive infection in 5-35% of myeloma cells (i.e. capsid protein). **Conclusions:** While infection of myeloma cells was seen in all evaluable patients on cycle 1 day 9, those with a clinical response demonstrated concomitant CD8 & NK cell recruitment, PD L1 upregulation, activated caspase-3 expression, increased viral protein production within the myeloma cells, and these patients demonstrated mild to severe signs and symptoms consistent with secondary HLH. This is the first report of cytokine storm after oncolytic virus in a patient with a blood cancer, a syndrome thought to be related to T-cell activation from the combination treatment. This trial was supported by the NCI Division of Cancer Treatment & Diagnosis Cancer Therapy Evaluation Program (CTEP). Clinical trial information: NCT02101944. Research Sponsor: U.S. National Institutes of Health, Other Government Agency.

8536 Poster Session (Board #436), Fri, 8:00 AM-11:00 AM

Pivotal DREAMM-2 study: Single-agent belantamab mafodotin (GSK2857916) in patients with relapsed/refractory multiple myeloma (RRMM) refractory to proteasome inhibitors (PIs), immunomodulatory agents, and refractory and/or intolerant to anti-CD38 monoclonal antibodies (mAbs). *First Author: Sagar Lonial, Emory University Hospital, Winship Cancer Institute, Atlanta, GA*

Background: Single-agent belantamab mafodotin (B-cell maturation antigen targeting immunoconjugate) showed clinically meaningful activity and manageable safety in patients with heavily pre-treated RRMM (DREAMM-2, NCT03525678, *Lancet Oncol.*2020). We report updated results (median follow-up 9 months). **Methods:** DREAMM-2 is an ongoing single-agent belantamab mafodotin (2.5 or 3.4 mg/kg) study in patients with RRMM after ≥3 prior therapy lines and refractory to an immunomodulatory agent, a PI, and refractory and/or intolerant to an anti-CD38 mAb. Primary endpoint: overall response rate (ORR; ≥partial response per independent review committee). **Results:** ORR was 31% in the 2.5 mg/kg (19% with ≥very good partial responses [VGPR]) and 35% (24% with ≥VGPR) in the 3.4 mg/kg groups (Table). Duration of response (DoR) was not reached (NR) in the 2.5 mg/kg and 6.2 months in the 3.4 mg/kg groups; 1-year overall survival (OS) estimate was 53%. Common Grade 3/4 AEs (> 10% in either group) were keratopathy (2.5: 29%; 3.5: 24%), thrombocytopenia (2.5: 21%; 3.4: 32%), anemia (2.5: 20%; 3.4: 27%), pneumonia (2.5: 6%; 3.4: 13%), and neutropenia (2.5: 11%; 3.4: 16%). AEs were managed with dose delays (2.5: 54%; 3.4: 62%) and reductions (2.5: 34%; 3.4: 43%); discontinuations due to AEs were uncommon (2.5: 9%; 3.4: 12%). **Conclusions:** Single-agent belantamab mafodotin was well-tolerated, and clinically meaningful responses were sustained despite dose modifications with longer follow-up. Funding: GlaxoSmithKline (205678). Drug linker technology licensed from Seattle Genetics; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa. Clinical trial information: NCT03525678. Research Sponsor: GlaxoSmithKline.

Outcomes.

	2.5 mg/kg (n = 97)[a]	3.4 mg/kg (n = 99)[b]
Median number of cycles (range)	3 (1–15)	3 (1–14)
ORR (97.5% CI), %	31 (20.8–42.6)	35 (24.8–47.0)
DoR[c], m	NR (4.2–NR)	6.2 (4.8–NR)
Probability of DoR ≥6 m, % (95% CI)	70 (48–84)	58 (39–72)
Progression-free survival (PFS)[c], m	2.8 (1.6–3.6)	3.9 (2.0–5.8)
PFS: patients with ≥minimal response[c], %	NR (7.5–NR)	8.4 (6.9–13.8)
Probability of OS at 12 m, % (95% CI)	53 (38–66)	53 (41–63)

[a]41 on study; 17/41 on treatment; [b]47 on study; 18/47 on treatment; [c]median (95% CI estimates). m, months

8537 Poster Session (Board #437), Fri, 8:00 AM-11:00 AM

Corticosteriod tapering in patients (Pts) with relapsed or refractory multiple myeloma (RRMM) receiving subcutaneous daratumumab (DARA SC): Part 3 of the open-label, multicenter, phase Ib PAVO Study. *First Author: Hareth Nahi, Karolinska Institute, Department of Medicine, Division of Hematology, Karolinska University Hospital at Huddinge, Stockholm, Sweden*

Background: Intravenous DARA (DARA IV) is approved for the treatment of MM. In Part 2 of PAVO, DARA SC, a concentrated, pre-mixed SC co-formulation of DARA and recombinant human hyaluronidase PH20 (rHuPH20), was well tolerated, with a low infusion-related reaction (IRR) rate, and showed consistent serum concentrations and similar efficacy to DARA IV in RRMM pts. In PAVO Part 3, we evaluated the safety of pre- and post-dose corticosteroid tapering during DARA SC administration. **Methods:** RRMM pts with ≥2 prior lines of treatment, including a proteasome inhibitor (PI) and immunomodulatory drug (IMiD), received DARA SC (DARA 1,800 mg + rHuPH20 30,000 U in 15 mL) by manual SC injection per approved IV monotherapy dosing schedule. Pts received a 3-week (wk) tapering schedule (corticosteroid-free by Cycle [C] 1 Day [D] 22), with methylprednisolone (MP) given PO/IV pre-dose (C1D1, 100 mg; C1D8, 60 mg; C1D15, 30 mg) and PO post-dose (C1D1, 20 mg for 2 days; C1D8, 20 mg for 1 day; C1D15, 20 mg for 1 day), or a 2-wk tapering schedule (corticosteroid-free by C1D15), with MP given PO/IV pre-dose (C1D1, 100 mg; C1D8, 60 mg) and PO post-dose (C1D1, 20 mg for 2 days; C1D8, 20 mg for 1 day). **Results:** Pts (3-wk group, n = 15; 2-wk group, n = 15) received a median of 2 (range: 2-7) prior lines of therapy, with 37% refractory to a PI and an IMiD. The 3-wk and 2-wk groups received a median (range) of 14 (2-19+) and 8 (2-16+) DARA SC doses without corticosteroids, respectively. No IRRs were reported in the 3-wk group. 3 pts (20%) in the 2-wk group experienced IRRs on C1D1 (grade 3 hypertension, grade 2 chills, grade 1 pyrexia, grade 1 oropharyngeal pain, and grade 1 tachycardia). IRRs occurred within 2 h of the first DARA SC administration; no IRRs were reported at later administrations. Most common (≥25%) treatment emergent adverse events (TEAEs) were upper respiratory tract infection (40%) and fatigue and nausea (27% each). Most common (≥5%) grade 3/4 TEAEs were anaemia, lymphopenia, neutropenia, and hypertension (7% each). At median follow-up of 6.8 mo (3-wk group) and 2.4 mo (2-wk group), the overall response rates were 40% (95% CI, 16-68%) and 27% (95% CI, 8-55%) and ≥very good partial response rates were 13% (95% CI, 2-40%) and 7% (95% CI, 0-32%), respectively. **Conclusions:** Rapid corticosteroid tapering over 2 wks is safe in RRMM pts receiving DARA SC. These data help guide future DARA SC combinations (ie, T-cell redirectors, CAR-T, or checkpoint inhibitors), where limiting concurrent corticosteroids may be preferred. Clinical trial information: NCT02519452. Research Sponsor: Janssen Research & Development, LLC.

8538 Poster Session (Board #438), Fri, 8:00 AM-11:00 AM

Daratumumab + bortezomib, thalidomide, and dexamethasone (D-VTd) in transplant-eligible newly diagnosed multiple myeloma (TE NDMM): Baseline SLiM-CRAB based subgroup analysis of CASSIOPEIA. *First Author: Cyrille Touzeau, Centre Hospitalier Universitaire, Nantes, France*

Background: In the phase 3 CASSIOPEIA study, D-VTd significantly improved outcomes vs VTd in TE NDMM pts at an 18.8-mo median follow-up. To allow earlier diagnosis and treatment of MM, the IMWG added 3 validated biomarkers (≥60% clonal bone marrow plasma cells, serum free light chain ratio ≥100, and > 1 focal bone lesion by MRI; "slim") to the conventional "CRAB" diagnostic criteria. We present a subgroup analysis of CASSIOPEIA based on baseline slimCRAB criteria. **Methods:** TE NDMM pts were randomized 1:1 to 4 pre-ASCT induction and 2 post-ASCT consolidation cycles of D-VTd or VTd. The "slim-only" subgroup excludes pts with ≥1 conventional CRAB criterion based on data collected at baseline; the remaining pts were included in the "CRAB" subgroup. **Results:** Of 1085 randomized pts (543 D-VTd; 542 VTd), 81 were included in the slim-only subgroup (36 D-VTd; 45 VTd) and 1004 were included in the CRAB subgroup. In slim-only vs CRAB pts, 22% vs 54% had an ECOG score of ≥1, 4% vs 16% had ISS Stage III disease, and 11% vs 16% had high-risk cytogenetics. For D-VTd vs VTd pts in the slim-only group, these rates were 22% vs 22%, 8% vs 0%, and 6% vs 16%, respectively. Overall response rates (ORR) and rates of sCR, ≥CR, and MRD negativity were similar between slim-only and CRAB pts; for slim-only pts, rates were significantly higher for D-VTd vs VTd (Table). After an 18.8-mo median follow-up, progression-free survival (PFS) was not significantly different in slim-only vs CRAB pts, or in D-VTd vs VTd slim-only pts (Table). For D-VTd vs VTd CRAB pts, 18-mo PFS rates were 92% vs 84%, and 24-mo PFS rates were 89% vs 76%. **Conclusions:** Baseline characteristics indicate that slim-only pts were slightly fitter and of lower risk status vs CRAB pts; however, response rates, MRD-negativity rates, and PFS did not differ significantly between these groups. Among slim-only pts, significantly higher response and MRD-negativity rates were achieved with D-VTd vs VTd. Among CRAB pts, PFS rates were higher with D-VTd vs VTd. Clinical trial information: NCT02541383. Research Sponsor: Janssen Research & Development, LLC.

	Slim-only	CRAB	*P*value	Slim-only		
				D-Vth	Vth	
	(n = 81)	(n = 1004)		(n = 36)	(n = 45)	*P*value
ORR, %	90	91	0.4053	97	84	0.0377
sCR	25	25	0.9776	36	16	0.0083
≥CR	32	33	0.9690	50	18	0.0003
MRD neg(MFC, 10^{-5}), %	46	54	0.1261	67	29	< 0.0001
Median PFS, mo	NR	NR	-	NR	NR	-
PFS HR (95% CI)	0.73 (0.36-1.50)		0.3888	1.19 (0.30-4.78)		0.8023

MFC, multiparametric flow cytometry; NR, not reached.

8539 Poster Session (Board #439), Fri, 8:00 AM-11:00 AM

A phase Ib study of TAK-079, an investigational anti-CD38 monoclonal antibody (mAb) in patients with relapsed/ refractory multiple myeloma (RRMM): Preliminary results. *First Author: Amrita Y. Krishnan, City of Hope, Duarte, CA*

Background: TAK-079 is a subcutaneously (SC) administered mAb with multiple modes of action for killing target cells. Here we report data from an ongoing dose finding study of TAK-079 monotherapy in patients with RRMM (NCT03439280). **Methods:** Pt were eligible after ≥ 3 lines of therapy and previous exposure to immunomodulatory drug (IMiD), proteasome inhibitor (PI), alkylating agent, and corticosteroid; prior anti-CD38 therapy allowed. Patients were refractory or intolerant to at least 1 PI and 1 IMiD. TAK-079 given as a SC injection weekly for 8 doses, every other week for 8 doses, then monthly until disease progression (PD) or unacceptable toxicity. SC injection was 2 mL administered in ≤ 1 minute. **Results:** 34 patients were enrolled across 5 fixed dose cohorts (TAK-079 45-135-300-600-1200 mg SC) as of 09 December 2019. Median age was 65 (50–81) years. At study entry, 65% were refractory to both an IMiD and PI; 82% refractory to last line of therapy, 21% of patients were previously exposed to at least 1 anti-CD38 monoclonal antibody. Median number of prior therapies was 4 (2,12). No ≥ Grade 1 early or late systemic infusion reactions (IRR) reported. Three (< 1%) injection site reactions described in > 1200 injections administered; 2 mild pruritis and 1 moderate swelling. Drug related adverse events (AEs), any grade, occurring in at least 10% of patients were: fatigue (21%), anemia (18%), neutropenia (18%), leukopenia (15%). Neutropenia was the only drug related grade 3 AEs in 2 or more patients (n = 2); only drug related SAE was 1 Grade 3 diverticulitis. No drug-related grade 4 AEs, AEs leading to study discontinuation, or on-study deaths reported. Recommended phase 2 dose (RP2) is to be 600 mg based on no reported DLTs, no MTD identified, and preliminary efficacy (PFS and response [ORR]). At the RP2 dose, 9 patients received at least 6 cycles of therapy by the data cutoff; their ORR was 33%, median duration of response was not estimable. The clinical benefit rate (minimal response or better) in all 12 patients enrolled at the RP2 dose was 67%. At a median follow-up of 7.5 months, PFS not estimable at the RP2 dose. **Conclusions:** TAK-079 monotherapy is safe, generally well tolerated, and active in patients with RRMM through tested doses. Clinical activity occurred early and was durable. With no MTD identified, no IRRs, no significant hematologic toxicity, the RP2 dose is 600 mg. PFS, with a median FU of 7.5 months at the data-cut off, is not estimable at the RP2 dose. Updated safety and efficacy data will be presented. Clinical trial information: NCT03439280. Research Sponsor: Takeda Pharmaceuticals, Inc.

8540 Poster Session (Board #440), Fri, 8:00 AM-11:00 AM

Efficacy of daratumumab in the treatment of multiple myeloma with high-risk cytogenetics: Meta-analysis of randomized phase III trials. *First Author: Smith Giri, University of Alabama at Birmingham, Birmingham, AL*

Background: The addition of Daratumumab (D) to backbone multiple myeloma (MM) regimens leads to improved response rates and progression free survival (PFS). Whether improved outcomes are also seen among patients with high-risk cytogenetics (HRC) remains unclear, particularly in first-line (FL) setting. **Methods:** We conducted a systematic search of bibliographic databases, clinical trials registries and meeting libraries from inception to December 2019, for phase III randomized trials that compared backbone MM regimens vs. same regimen plus D either in FL or relapsed/refractory (R/R) setting and reported outcomes by cytogenetic risk (HRC vs standard risk cytogenetics, SRC). We defined HRC as presence of t(4;14), t(14;16) or del(17p). The primary endpoint was PFS. We pooled relative log-hazard ratios using DerSimonian-Laird random-effects model. We assessed heterogeneity using Cochran's Q and the I^2 statistic. **Results:** Of 3,070 studies screened, 6 phase III trials were included. This included 3 trials in FL setting (Alcyone, Maia and Cassiopeia, 2,528 patients, 358 HRC) and 3 trials in R/R setting (Castor, Pollux and Candor, 1,533 patients, 222 HRC). The addition of D to FL backbone regimens among patients with HRC led to improved PFS (pooled HR 0.67; 95% CI 0.47-0.95, p = 0.02) with little heterogeneity (Cochran's Q p = 0.77, I^2= 0), similar to R/R setting (pooled HR 0.45; 95% CI 0.30-0.67, p < 0.01, Cochran's Q = 0.63, p < 0.01, I^2= 0). Similar results were seen in SRC MM patients in FL setting (pooled HR 0.45; 95% CI 0.37-0.54, p < 0.01, Cochran's Q p = 0.49, I^2= 0) and R/R setting (pooled HR 0.38; 95% CI 0.25-0.56; p < 0.01, Cochran's Q p = 0.04, I^2= 70%). **Conclusions:** Incorporating D to backbone regimens led to improved PFS among patients with HRC MM in both FL and R/R setting. Lack of substantial heterogeneity suggests benefit of D regardless of backbone regimen. D based regimens are appropriate choices in FL and R/R setting for both SRC and HRC patients. Longer follow up with mature overall survival data is needed to validate these findings. Research Sponsor: None.

Impact of Daratumumab on PFS among MM patients with high-risk cytogenetics.

Study Name	Intervention	Control	Hazard Ratio	95% CI	p-Value
Alcyone	DaraVMP	VMP	0.78	0.43-1.42	0.42
Maia	DaraRD	RD	0.57	0.32-1.03	0.06
Cassiopeia	DaraVTD	VTD	0.67	0.35-1.29	0.23
Pooled Effect Size ($I^2$0%, Cochran's Q p = 0.77)			**0.67**	**0.47-0.95**	**0.025**
Castor	DaraVD	VD	0.41	0.21-0.83	0.01
Pollux	DaraRD	RD	0.37	0.18-0.76	0.01
Candor	DaraKD	KD	0.58	0.30-1.12	0.11
Pooled Effect Size (($I^2$0%, Cochrans Q p = 0.63)			**0.45**	**0.30-0.67**	**< 0.001**

8541 Poster Session (Board #441), Fri, 8:00 AM-11:00 AM

DREAMM-2: Single-agent belantamab mafodotin (GSK2857916) in patients with relapsed/refractory multiple myeloma (RRMM) and high-risk (HR) cytogenetics. *First Author: Adam D. Cohen, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA*

Background: Patients with RRMM and HR cytogenetics have a poor prognosis and need effective therapies. In DREAMM-2 (NCT03525678), single-agent belantamab mafodotin (an immunoconjugate targeting B-cell maturation antigen) demonstrated clinically meaningful activity and a manageable safety profile in patients with heavily pretreated RRMM (*Lancet Oncol*.2020). We present outcomes in patients with HR-cytogenetics (9-month follow-up). **Methods:** Patients with RRMM received single-agent belantamab mafodotin (2.5 or 3.4 mg/kg). For this post hoc analysis, HR-cytogenetics included t(4;14), t(14;16), 17p13del, or 1q21+ (tested locally). **Results:** The median number of cycles was 3 (2.5: range: 1–15) and 4 (3.4: range: 1–14). Overall response rate (ORR; ≥partial response [PR] per independent review committee) was 27% in the 2.5 mg/kg group (22% with ≥very good partial response [VGPR]) and 40% in the 3.4 mg/kg group (27% with ≥VGPR). The median duration of response (DoR) was not reached in the 2.5 mg/kg group and was 6.2 months in the 3.4 mg/kg group. The most common adverse events (> 30% in either group) were consistent with the overall population (*Lancet Oncol*.2020): keratopathy (2.5: 59%; 3.4: 79%), thrombocytopenia (2.5: 44%; 3.4: 65%), nausea (2.5: 27%; 3.4: 33%), anemia (2.5: 24%; 3.4: 42%), and blurred vision (2.5: 20%; 3.4: 42%). **Conclusions:** Patients with HR-cytogenetics maintain deep and durable clinical responses with single-agent belantamab mafodotin, comparable to that reported in the overall population. The safety profile remained consistent with previous reports. Funding: GlaxoSmithKline (205678). Drug linker technology licensed from Seattle Genetics; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa. Clinical trial information: NCT03525678. Research Sponsor: GlaxoSmithKline.

Efficacy outcomes in patients with HR-cytogenetics

	2.5 mg/kg (n = 97)[a]	3.4 mg/kg (n = 99)[b]
ORR (≥PR), % (95% CI)	27 (14.2–42.9)	40 (25.8–54.7)
Median DoR (95% CI), months	NR (1.4–NR)	6.2 (4.8–NR)
Probability of DoR at 9 months, (95% CI[c]), %	52 (20–77)	47 (23–68)
Median PFS (95% CI), months	2.1 (0.8–3.7)	5.8 (1.5–6.9)
Probability of PFS ≥6 months, (95% CI[c]), %	30 (16–45)	46 (31–60)
Median OS (95% CI), months	9.4 (4.3–13.1)	13.8 (NE–NE)
Probability of OS at 12 months, (95% CI[c]), %	45 (27–61)	68 (25–80)

[a]n = 41 on study, n = 8 on study treatment; [b]n = 48 on study, n = 11 on study treatment; [c]95% CI estimate. NE, not evaluable; NR, not reached.

8542 Poster Session (Board #442), Fri, 8:00 AM-11:00 AM

Prevalence and significance of clonal hematopoiesis of indeterminate prognosis (CHIP) in multiple myeloma. *First Author: Leslie Jane Padrnos, Mayo Clinic, Scottsdale, AZ*

Background: Clonal hematopoiesis of indeterminate potential (CHIP) is defined by the presence of leukemia-associated somatic mutations in clonally expanded hematopoietic stem cells with a VAF of ≥2%. CHIP has been associated with myeloid malignancies and increased all cause mortality largely from atherovascular disease. The prevalence and impact of CHIP in patients with myeloma (MM) is yet to be defined. Aims: Evaluate the prevalence and significance of CHIP in 101 lenalidomide exposed patients with multiple myeloma. **Methods:** 101 MM patients, the majority exposed to > 2 years of lenalidomide (Len), with stored mononuclear blood samples were identified for Next Generation Sequencing (NGS) using a panel encompassing 42 gene mutations associated with CHIP. Electronic medical records were reviewed and outcomes of secondary malignancy, macrocytosis, thrombosis and mortality were extracted. **Results:** Thirty of 101patients were found to have CHIP with the most frequent mutations: DNMT3A (12%), TET2 (5%), and TP53 (4%). One third of patients with CHIP had > 1 mutation (37%). At 68 months median follow up over a quarter of patients experienced thrombosis (31%) and 13% developed subsequent malignancy/premalignant condition including myelodysplastic syndrome (3%). There was no significant difference in age, gender, duration of Len prior to NGS testing, thrombosis complication, or survival in those with versus without a CHIP mutation. At last F/U 30% had died, 25% remained on therapy, 27% were on maintenance therapy and 11% were on observation alone. **Conclusions:** CHIP mutations are common in plasma cell neoplasms, with 30% of patients in this study retrospectively found to have CHIP mutations by NGS testing. CHIP mutations have been associated with cardiovascular events and malignancy development, however no associations were identified in this small study. Limitations to this study include small sample size, retrospective nature and duration of follow up. Further study of this very common finding in MM patients regarding timing of development and subsequent impact of these mutations could help risk stratify and inform therapy selection. Research Sponsor: U.S. National Institutes of Health, Mayo Clinic Center for Individualized Medicine.

	No CHIP mutation N=71	CHIP Mutation N=30	Total N=101
Age at diagnosis, mean, years	58.2	60.3	58.8
Duration of Len prior to NGS collection, mean, months	8.4	8.7	8.5
Duration of Len, mean, months	31	28	30
Secondary malignancy or premalignant condition, (%)	9 (13)	4 (13)	13 (13)
Any Thrombosis, (%)	21 (30)	10 (33)	31 (31)
Venous thromboembolism(%)	17 (24)	9 (30)	26 (26)
Arterial Event, (%)	5 (8)	1 (4)	6 (7)
Follow up, median, months	70	62	68

8543 Poster Session (Board #443), Fri, 8:00 AM-11:00 AM

FDA analysis: Impact of BMI on efficacy outcomes in multiple myeloma trials. *First Author: Rachel Ershler, U.S. Food and Drug Administration, Silver Spring, MD*

Background: Obesity has been implicated as a risk factor for the development of certain types of cancers, including multiple myeloma. Previous studies in other tumor types suggest that overweight subjects may have better outcomes, however, in relapsed/refractory multiple myeloma (RRMM), it is unknown whether body weight affects outcomes to therapy. **Methods:** We conducted a retrospective analysis of 13 RRMM clinical trials submitted to the FDA between 2012-2018. Patients were divided into four groups, underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5- < 25 kg/m^2), overweight (BMI 25.0- < 30 kg/m^2) and obese (BMI > 30.0 kg/m^2). A multivariate analysis for progression free survival (PFS) and overall survival (OS), stratified by study and adjusted for age, cytogenetic risk group (Standard, High, Unknown), immunoglobin subtype (IgG Y/N), ECOG status (0-1, > 1, UNK), sex (M/F) was used to estimate the HR. **Results:** A total of 5898 patients were included in this analysis. The median age was 65 years (range 30-91 years). A total of 87(1.5%) patients were underweight, 1853 (31%) were normal weight, 2212 (38%) were overweight, 1332 (23%) were obese, and 414 (7%) had missing BMI. The results of the multivariate analysis of PFS and OS are shown in the Table. **Conclusions:** Exploratory analysis of patients with RRMM found that patients who were overweight and obese had a trend towards slightly improved PFS and OS when compared to normal weight patients. Similar trends were observed in the analyses of overall response rate and BMI (not presented in the abstract). These results are consistent with previous studies in other malignancies. Limitations include the lack of adjustment for multiple testing, the small sample of patients in the underweight category, and heterogeneity in the treatment regimens and PFS assessments in the clinical trials included in the analysis. Future studies are needed to evaluate safety and impact of treatment regimens on efficacy outcome measures based on body weight. Research Sponsor: None.

Multivariate analysis of PFS and OS.

BMI Category	PFS HR (95% CI)	OS HR (95%CI)
Under vs Normal	1.15 (0.86,1.54)	1.10 (0.77,1.56)
Over vs Normal	0.90 (0.82, 0.99)	0.91 (0.81, 0.99)
Obese vs Normal	0.88 (0.79, 0.97)	0.84 (0.75, 0.95)
Missing vs Normal	1.48 (1.21, 1.81)	1.20 (0.93, 1.56)

8544 Poster Session (Board #444), Fri, 8:00 AM-11:00 AM

The significance of beta-II microglobulin (β2M) and International Staging System (ISS) in multiple myeloma (MM) patients (pts.) with renal impairment (RI). *First Author: Gloria Lin, Medical College of Wisconsin, Milwaukee, WI*

Background: ISS stage which underlies prognostic models used in MM, is derived from albumin and β_2M at diagnosis. β_2M, a low molecular polypeptide, is present on all nucleated cells and is elevated in pts. with RI. In MM, although the association between β_2M and prognosis has been interpreted to reflect a higher tumor burden, RI by itself may explain at least in part the higher levels of β_2M seen with this disease. Historically, those presenting with MM and severe RI had a poor prognosis and quite likely the β_2M elevation irrespective of kinetics predicted poor prognosis. In this study, we investigated the significance of β_2M and ISS staging in MM patients in the setting of RI in the modern era when renal recovery is more common after induction. **Methods:** MM pts. treated at our institution from 2012-2014 were included and divided into two groups by creatinine (Cr) level at diagnosis: <2 and ≥ 2 mg/dl. Demographic and disease characteristics were compared between the two groups using ANOVA and chi-square tests as appropriate. COX regression was used for the multi-variate analysis for survival and the effect of β_2M levels, adjusting for albumin levels, on survival was allowed to vary by Cr level to evaluate potential interaction. **Results:** Of 201 total pts., 163 (81.6%) had Cr <2 mg/dL and 38 (18.4%) $\geq$ 2mg/dL at diagnosis with higher β_2M and ISS stage in Cr$\geq$2 group. On adjusted analysis, albumin was significantly associated with overall survival (OS) (hazard ratio, HR 0.60; 95% CI 0.36-1; p = 0.04); however, β_2M was associated with OS only when Cr <2 mg/dl (HR 1.13, 95% CI 1.06-1.19; p $<$ 0.0001) but not when Cr$\geq$2 mg/dl (HR 0.98, 95% CI 0.91-1.06; p = 0.65) with significant interaction (p = 0.004). Likewise, the effect of β_2M on progression-free survival was significant when Cr <2 (HR 1.1, 95% CI 1.05-1.19; p = 0.0002), but not Cr$\geq$2 (HR 1.02; 95% CI 0.97-1.08; p = 0.42) with significant interaction (p = 0.03). **Conclusions:** Our results show that in the era of modern induction therapy and rapid improvement in kidney function, a high β_2M may not impact prognosis as adversely, at least in those with RI, since an elevated β_2M may be disproportionate to true tumor burden. Thus, ISS staging in these patients should be reevaluated after induction and potential renal recovery. Novel biomarkers may refine MM staging independent of the level of kidney function. Research Sponsor: None.

8545 Poster Session (Board #445), Fri, 8:00 AM-11:00 AM

Sporadic late-onset nemaline myopathy with monoclonal paraprotein as a malignancy rather than disimmunity and treatment with chemotherapy-based approach. *First Author: Rouslan Kotchetkov, Simcoe Muskoka Regional Cancer Program, Barrie, ON, Canada*

Background: A subset of sporadic late-onset nemaline myopathy (SLONM) associated with monoclonal gammopathy of undetermined significance (MGUS) has more aggressive course, often fatal. Whether SLONM+MGUS is a malignancy or dysimmunity is unclear. Two approaches are used to treat SLONM+MGUS: 1) immunosuppression (IS) ± plasmapheresis/exchange; 2) chemotherapy (ChT) ± autologous stem cell transplantation (ASCT). Due to the rare occurrence of the disease the best treatment modality is not known. **Methods:** We conducted a literature search to identify previous treatment for patients with SLONM+MGUS using PubMed, Elsevier, Medline, and CINAHL databases from 1975 to 2019. All publications were carefully reviewed to remove "duplicate" patients. Overall, 28 reports were included for the final analysis. **Results:** 38 unique patients with SLONM+MGUS received either IS (n = 19) or ChT ± ASCT (n = 19). The median age was 48 years [24-75]. In the IT group 74% (n = 14) were males vs 53% (n = 10) in the ChT group. All patients had IgG monoclonal protein (MP): kappa in 57% (n = 11) in the IT, 42% (n = 8) in the ChT group. In the IT group MP values were 0.42 & 0.2 g/L (n = 2); in the ChT group median MP was 2.7 g/L [0.1-14, n = 14]. In the IT group 84% (n = 16) received steroids, 26% (n = 5) plasmapheresis, 53% (n = 10) non-steroid immunosuppressants, 11% (n = 2) rituximab, and 53% (n = 10) IVIG. Six patients (32%) had one IT modality; 13 (68%) had 2 or 3. In the ChT group 10 patients (53%) had ASCT; 6 patients (31%) had CyBorD or Lenalidomide+Dexamethasone + ASCT; 3 patients (16%) had chemotherapy without ASCT. 10 patients in IT group had neurological improvement (NI): 53% overall response (OR) with 16% (n = 3) complete remission (CR), and 37% (n = 7) partial response (PR). No improvement/progression had 9 patients (47%). In 2 patients (10%), neurological CR was associated with resolution of MP. Mean time to best response was 19 months. In ChT group 18 patients achieved NI: 94.7% OR with CR in 73.7% (n = 14) and PR in 21.0% (n = 4). Only one patient had no response to therapy. The best NI correlated with resolution of MP. Mean time to best response was 10 months. **Conclusions:** Our study with the most extensive cohort of patients with SLOMN+MGUS supports ChT ± consolidative ASCT aimed at complete elimination of the malignant plasma cell clone as the preferred treatment. Superior clinical benefits of ChT suggest that the presence of MP has clinical rather than undetermined significance, and SLOAN + MP should be considered as a malignancy rather than dysimmunity. Research Sponsor: None.

8546 Poster Session (Board #446), Fri, 8:00 AM-11:00 AM

Ixazomib-dexamethasone (Ixa-Dex) vs physician's choice (PC) in relapsed/refractory (RR) primary systemic AL amyloidosis (AL) patients (pts) by prior proteasome inhibitor (PI) exposure in the phase III TOURMALINE-AL1 trial. *First Author: Efstathios Kastritis, Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece*

Background: The PI bortezomib is commonly used in first-line therapy of AL, but new therapies are needed that are tolerable in the context of multi-organ dysfunction and that, in RRAL, offer improved outcomes following prior bortezomib. Ixazomib is an oral PI, and in TOURMALINE-AL1, the first phase 3 trial conducted in RRAL, while the first primary endpoint of hematologic overall response rate (ORR) was not met, all clinically relevant time-to-event endpoint data favored Ixa-Dex vs PC (Dispenzieri et al, ASH 2019). **Methods:** RRAL pts with 1–2 prior therapies were randomized (1:1) to Ixa-Dex (n = 85) or PC (n = 83; Dex plus lenalidomide [n = 47], melphalan [n = 24], cyclophosphamide [n = 10], or thalidomide [n = 2]), stratified by cardiac stage, relapsed vs refractory disease, and prior PI exposure. The primary endpoints were hematologic ORR and 2-yr rate of vital organ deterioration or death. We report subgroup analyses of ORR and outcomes by prior PI exposure. **Results:** Of the 168 pts enrolled, 90 were PI-naïve and 78 PI-exposed (46 and 39 in the Ixa-Dex arm; 44 and 39 in the PC arm) per stratification; 28 and 27 pts in the Ixa-Dex and PC arms had received bortezomib in their last prior line. Hematologic ORR was 63% vs 50% for Ixa-Dex vs PC (odds ratio [OR] 1.71; 95% confidence interval [CI] 0.74–3.96) in PI-naïve pts, and 41% vs 51% (OR 0.66; 95% CI 0.27–1.62) in PI-exposed pts. For time-to-event outcomes (Table), hazard ratios (HRs) were 0.46–0.85 in favor of Ixa-Dex vs PC in both PI-naïve and PI-exposed pts. **Conclusions:** Hematologic ORR was higher with Ixa-Dex vs PC in PI-naïve pts but lower in PI-exposed pts (although not statistically significant), and long-term clinically relevant outcomes favored Ixa-Dex in both groups. Based on HRs, the magnitude of benefit appeared similar or greater in PI-naïve vs PI-exposed pts. Clinical trial information: NCT01659658. Research Sponsor: Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

	PI-naïve			PI-exposed		
Median, mos	Ixa-Dex	PC	HR (95% CI)	Ixa-Dex	PC	HR (95% CI)
Time to vital organ deterioration or death	44.9	28.0	0.53 (0.24–1.18); p = 0.112	27.0	26.1	0.52 (0.27–1.01); p = 0.050
Composite progression-free survival	30.4	9.8	0.56 (0.31–1.02); p = 0.054	7.0	5.5	0.77 (0.46–1.28); p = 0.309
Time to treatment failure	16.2	5.3	0.46 (0.27–0.79); p = 0.004	7.0	5.2	0.76 (0.47–1.23); p = 0.262
Time to subsequent therapy	61.4	16.3	0.57 (0.29–1.09); p = 0.084	15.7	12.1	0.66 (0.37–1.18); p = 0.156
Overall survival	Not reached	71.1	0.81 (0.37–1.80); p = 0.610	40.9	32.4	0.85 (0.46–1.60); p = 0.616

8547 Poster Session (Board #447), Fri, 8:00 AM-11:00 AM

Evaluation of minimal residual disease in relapsed/refractory multiple myeloma patients treated with venetoclax or placebo in combination with bortezomib and dexamethasone: BELLINI study analyses. *First Author: Philippe Moreau, Hematology Department, CHU Nantes, Nantes, France*

Background: Venetoclax (Ven) is a selective, potent BCL-2 inhibitor that has synergistic activity with bortezomib (B) and dexamethasone (d). In the Phase 3 BELLINI trial, addition of Ven to Bd significantly improved median progression-free survival (PFS) and response rates, including minimal residual disease (MRD) negativity, but resulted in increased mortality vs placebo (Pbo). Here, we determine whether MRD negativity was associated with longer PFS and OS in relapsed/refractory multiple myeloma (RRMM) patients treated with Ven+Bd in the BELLINI dataset. **Methods:** In BELLINI (NCT02755597), RRMM patients (pts) sensitive or naïve to proteasome inhibitors with 1-3 prior lines of therapy were randomized 2:1 to Ven (800 mg) or Pbo plus B (1.3 mg/m^2) and d (20 mg). Next-gen sequencing MRD assessments were done on bone marrow aspirates at the time of suspected CR/sCR, and 6- and 12-months post confirmation of CR/sCR. Patients with a missing or indeterminate assessment were considered MRD positive. Evaluation of MRD in biomarker-defined subgroups (cytogenetics and *BCL2* expression) was also performed and will be presented. **Results:** In total, 291 pts were randomized; 194 to Ven, 97 to Pbo. As of 13 Sep 2019, the median follow-up was 29 months. Ven + Bd demonstrated significantly higher MRD negativity rates ($< 10^{-5}$), including a higher proportion of pts achieving sustained MRD negativity (Table). In the Ven arm, the median (m)PFS was not reached for MRD negative pts vs 16.2 months for MRD positive pts (HR = 0.23, 95% CI: 0.10-0.54, p $<$ 0.001). While the mOS was not reached in the Ven arm, OS was significantly longer for MRD negative vs MRD positive pts (HR = 0.25, 95% CI: 0.08-0.80, p = 0.0194). **Conclusions:** The addition of Ven to Bd resulted in deep and durable responses, including higher rates of MRD negativity. MRD negativity in the context of Ven was associated with prolonged survival in patients with RRMM, consistent with the broader MRD body of evidence with other therapies in MM. Clinical trial information: NCT02755597. Research Sponsor: AbbVie and Genentech.

MRD negativity rates in the ITT population.

MRD negativity status ($< 10^{-5}$), % (n/N)	**Ven + Bd**	**Pbo + Bd**	**p-value**
MRD negativity rate	**15%** (29/194)	**2%** (2/97)	p = 0.0016
MRD negative ≥CR rate	**13%** (26/194)	**1%** (1/97)	p = 0.0013
MRD negativity rate in pts achieving ≥CR	**46%** (26/57)	**14%** (1/7)	p = 0.2386
≥6-month sustained MRD negativity rate in pts achieving ≥CR	**16%** (9/57)	**0%** (0/7)	p = 0.5768
≥12-month sustained MRD negativity rate in pts achieving ≥CR	**7%** (4/57)	**0%** (0/7)	p = 1.0000

8548 Poster Session (Board #448), Fri, 8:00 AM-11:00 AM

Castleman disease spectrum. *First Author: Johnson Khor, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA*

Background: Castleman disease (CD) describes a group of lymphoproliferative disorders that share characteristic histopathology. Unicentric CD (UCD) and idiopathic multicentric CD (iMCD) are differentiated by the number of enlarged lymph node (LN) regions: UCD involves 1 region and iMCD involves > 1 region. UCD typically has mild or no symptoms whereas iMCD requires abnormal labs and symptoms for diagnosis and can progress to life-threatening multi-organ failure. Review of an international natural history registry of CD revealed patients across a broad spectrum with regards to number of enlarged LN regions and disease severity. We hypothesize that there is a positive correlation between disease activity and the number of enlarged LNs and that the spectrum of CD is more complex than a binary UCD-iMCD dichotomy. **Methods:** Herein, enrolled UCD and iMCD patients whose diagnosis was confirmed by an expert-panel were selected for analysis (N = 81). A standardized disease activity score (scale 0-1) was computed for each patient using available diagnostic values of C-reactive protein, hemoglobin, and albumin (CHA score). **Results:** We looked at the association between number of enlarged LNs and CHA and found a significant positive correlation (R = 0.65, $p < 0.0001$). Given this, we divided the cohort into groups of mild, moderate, and extensive lymphadenopathy according to the number of regions of enlarged LNs at the time of diagnosis: group 1 (1 enlarged LN region); group 2 (2-4 enlarged LN regions); and group 3 (≥5 enlarged LN regions). We identified 20 patients in group 1, 19 in group 2, and 42 in group 3 with no statistical differences in sex, race, or age at diagnosis. Histopathological subtype differed significantly among groups. Group 1 was 89% hyaline vascular (HV)/ hypervascular (HpV) and 11% mixed (Mx); group 2 was 74% HV/HpV, 21% Mx, and 5% plasmacytic (Pl); and group 3 was 64% HV/HpV, 32% Mx, and 5% Pl. We then looked at CHA score in these groups and found that group 3 patients have a significantly greater CHA score (median [IQR]: 0.46 [0.49]) than both group 2 (0.08 [0.14]) and group 1 (0.0 [0.10]) (adjusted $p < 0.001$ for both) while there was no difference between groups 1 and 2. **Conclusions:** These results suggest that disease severity is positively associated with the number of enlarged LNs. The different proportions of histopathological subtypes between the three groups could indicate different pathologic mechanisms are involved. Further work is needed to determine if patients with a few enlarged LNs exhibit disease more closely to UCD or iMCD and to understand long-term outcomes for these patients. Research Sponsor: EUSA Pharma.

8549 Poster Session (Board #449), Fri, 8:00 AM-11:00 AM

Correlation between 24-hour proteinuria and spot urine albumin to creatinine ratio in systemic light chain amyloidosis. *First Author: Alissa Visram, Mayo Clinic, Rochester, MN*

Background: Proteinuria evaluation is essential for diagnosing and monitoring of renal involvement in light chain (AL) amyloidosis. A 24 hour protein collection (24h UP) is the gold standard for proteinuria assessment however it is cumbersome and can be inaccurate. A spot urine albumin to creatinine ratio (uACR) has been proposed as a convenient method to estimate 24hUP. We aimed to validate the correlation between uACR and 24hUP in a large cohort of patients. **Methods:** We retrospectively studied systemic AL amyloidosis patients evaluated between 2010 and 2019 at Mayo Clinic, with a uACR and 24hUP collected less than 7 days apart. Linear regression analysis was used to construct a prediction model for 24hUP with uACR as the primary predictor. Possible confounders (age, gender, body mass index, morning versus afternoon spot urine collection, estimated glomerular filtration rate) for the primary relationship between uACR and 24h UP were evaluated in the model. We used receiver operating characteristic (ROC) analysis to identify the best uACR cutoff to predict significant proteinuria (defined as a 24hUP > 500mg). **Results:** We included 665 patients, with a median age of 66 years (IQR 59-72). The spot urine was collected in the morning (before 1200 hours) in 382 (57%) patients, and in the afternoon in 283 (43%) patients. The median 24hUP was 321 (IQR 129-2512.5) mg, median uACR was 107 (IQR 13.5-1845) mg/g, and median serum creatinine was 1.2 (IQR 1-1.8) mg/dL. The uACR correlated well with 24h UP (Pearson's r= 0.83, 95% CI 0.80-0.85). Linear regression showed that $E(24h\ UP_i) = 362 + 1.05(uACR_i)$, and this model was statistically and clinically significant ($p < 0.001$ and R^2 of 0.68, respectively). Age, gender, body mass index, eGFR, and time of day of spot urine collection did not confound the primary relationship between uACR and 24hUP, and no collinearity was observed. A uACR cutoff of > 280 mg/g was the best predictor of a 24hUP > 500 mg (area under the ROC curve 0.98, sensitivity 92%, specificity 97%). For simplicity, we assessed the predictive value of uACR > 300 mg/g for 24h UP > 500 mg. Among patients with 24huACR > 300 mg/g 264 (96%) had a 24hUP > 500 mg, and 31 (7%) of patients with uACR < 300 mg/g had a 24h UP > 500 mg ($p < 0.001$). **Conclusions:** In systemic AL amyloid patients, we showed that uACR on a random urine sample correlated well with 24h UP, and can be used to estimate proteinuria with a linear regression model. Based on these findings, and the convenience of uACR testing for patients, we propose that uACR should be used to monitor renal response to AL amyloidosis therapy. Research Sponsor: None.

8550 Poster Session (Board #450), Fri, 8:00 AM-11:00 AM

Characteristics and outcome of patients with MYD88 wild-type Waldenström Macroglobulinemia. *First Author: Saurabh Zanwar, Mayo Clinic, Rochester, MN*

Background: Waldenström Macroglobulinemia (WM) is a rare lymphoplasmacytic malignancy characterized by the presence of a recurrent point mutation in the *MYD88* gene ($MYD88^{L265P}$) in 80-95% of cases. Patients with $MYD88^{WT}$ genotype comprise a small subset that responds poorly to ibrutinib and other Bruton tyrosine kinase inhibitors. We examined the characteristics and outcome of WM patients with $MYD88^{WT}$ genotype predominantly treated with non-BTK inhibitor based therapies. **Methods:** Patients with a diagnosis of WM seen at Mayo Clinic, Rochester, between 1996 and 2018 were included. Their characteristics and outcomes were assessed from the time of active disease. Marrow MYD88 genotyping was assessed with an allele specific PCR assay (analytic sensitivity 1%). Categorical and continuous variables were compared using Chi square and Wilcoxon tests, respectively. Time-to-event analyses were performed using Kaplan Meier test. **Results:** Of 986 patients with active WM, MYD88 genotype data were available in 331 (34 %) patients; 72 (22%) and 260 (78%) patients harbored $MYD88^{WT}$ and $MYD88^{L265P}$ genotypes, respectively. The median follow-up was 5.8 years (95% CI: 5.0-6.5 years) from active WM; 6 years $MYD88^{WT}$ vs 5.4 years for $MYD88^{L265P}$ cohort. Median age was 63 years and 66 years in the $MYD88^{WT}$ and $MYD88^{L265P}$ cohorts, respectively ($p = 0.07$) with 46% and 53% patients being ≥65 years of age, respectively ($p = 0.36$). Pre-treatment marrow lymphoplasmacytic (LPL) infiltrate (median 40% for $MYD88^{WT}$ vs 60% for $MYD88^{L265P}$; $p = 0.001$) and beta-2 microglobulin (median 3 μg/mL for $MYD88^{WT}$ vs 3.9 μg/mL for $MYD88^{L265P}$; $p = 0.02$) were lower in the $MYD88^{WT}$ compared to the $MYD88^{L265P}$ cohort; other laboratory parameters at active disease were comparable. Per IPSSWM prognostic criteria, $MYD88^{WT}$ had fewer patients in the high risk group (18% for $MYD88^{WT}$ vs 42% $MYD88^{L265P}$; $p = 0.03$). Patients with $MYD88^{WT}$ had higher likelihood of histological transformation [18% for $MYD88^{WT}$ vs 4% for $MYD88^{L265P}$; odds ratio 5.8 (95% CI: 2.5-13.5; $p < 0.0001$)]. Among patients with treatment data available, only 35 (11%) patients received ibrutinib. The 5-year overall survival (OS) from active disease was comparable (85% in $MYD88^{WT}$ vs 82% in $MYD88^{L265P}$ cohort; $p = 0.7$). **Conclusions:** $MYD88^{WT}$ genotype in WM is associated with lower marrow LPL infiltration, lower likelihood of high-risk IPSSWM categorization and a higher likelihood of histological transformation in comparison to $MYD88^{L265P}$ mutant subpopulation. MYD88 genotype does not affect the OS from active disease in predominantly non-BTK inhibitor treated patients. Research Sponsor: None.

TPS8551 Poster Session (Board #451), Fri, 8:00 AM-11:00 AM

GO39775: A multicenter phase I trial evaluating the safety, pharmacokinetics, and activity of BFCR4350A, a FcRH5/CD3 T-cell dependent bispecific antibody, in patients with relapsed or refractory multiple myeloma. *First Author: Adam D. Cohen, Abramson Cancer Center and University of Pennsylvania, Philadelphia, PA*

Background: Multiple myeloma (MM) remains an incurable disease, with estimated median survival of 8–9 months in patients with relapsed or refractory (R/R) disease (Kumar et al. 2014; Usmani et al. 2016). There is no uniform standard of care for R/R MM, and combinations used in later lines have diminishing responses, especially after re-exposure to previously received classes of therapy (Gandhi et al. 2019). New targets and treatment modalities are needed. Fragment crystallizable receptor-like 5 (FcRH5) is expressed on myeloma cells across lines of therapy, and is overexpressed by myeloma cells with 1q21 gain; expression in healthy tissue is restricted to the B-cell lineage, and is retained in plasma cells (Li et al. 2017). BFCR4350A is an IgG-based T-cell-dependent bispecific antibody that was specifically engineered to target the most membrane-proximal domain of FcRH5 on myeloma cells and cluster of differentiation 3 (CD3) on T cells, with dual binding resulting in efficient immune synapse formation and T-cell killing of myeloma cells. BFCR4350A demonstrates potent killing of plasma cells and patient-derived myeloma cells (including those with low levels of FcRH5 expression) *in vitro*, and complete depletion of bone marrow plasma cells in primates, without severe or prolonged cytokine release (Li et al. 2017). GO39775 (NCT03275103) is an open-label, multicenter Phase I dose-escalation and dose-expansion trial evaluating the safety, pharmacokinetics (PK), and activity of BFCR4350A monotherapy in patients with R/R MM. **Methods:** Patients must be aged ≥18 years and must have R/R MM for which no established therapies are available or appropriate, or be intolerant to those therapies. Patients with prior CAR-T therapy and/or prior BCMA-directed therapy are not excluded. BFCR4350A is administered by intravenous infusion, and q3w dosing with Cycle 1 single-step or multi-step dosing is being investigated in dose-escalation (Arms A and B, respectively). Enrolment into both arms is ongoing, with patients receiving up to 17 cycles of treatment until disease progression or unacceptable toxicity. Primary objectives are to evaluate safety (including the maximum tolerated dose and dose-limiting toxicities) and to identify a recommended Phase II dose. Secondary objectives include assessment of PK, activity, immunogenicity, and pharmacodynamic biomarkers. Clinical trial information: NCT03275103. Research Sponsor: Genentech, Inc. Third-party medical writing assistance, under the direction of Adam Cohen and James Cooper, was provided by Stephanie Lacey of Gardiner-Caldwell Communications, and was funded by F. Hoffmann-La Roche Ltd.

TPS8552 Poster Session (Board #452), Fri, 8:00 AM-11:00 AM

DREAMM-5 platform trial: Belantamab mafodotin in combination with novel agents in patients with relapsed/refractory multiple myeloma (RRMM). *First Author: Paul G. Richardson, Dana-Farber Cancer Institute, Boston, MA*

Background: Single-agent belantamab mafodotin (GSK2857916), a B-cell maturation antigen targeting immunoconjugate, induced deep and durable responses in patients with RRMM, with a manageable safety profile (DREAMM-2, NCT03525678, *Lancet Oncol.*2020). A platform trial design allows efficient evaluation of belantamab mafodotin in combination with other anti-myeloma agents, such as a humanized wild-type IgG1 anti-OX40 agonist, an IgG4 inducible T-cell costimulatory (ICOS) agonist, and a gamma-secretase inhibitor. The unique, multimodal mechanisms of action (MoAs) of belantamab mafodotin, in combination with MoAs of these agents, has the potential to achieve synergistic effects in MM, to further enhance anti-myeloma activity without compromising safety. **Methods:** DREAMM-5 (NCT04162210) utilizes a master protocol with separate sub-studies comprised of sequential dose exploration (DE) and cohort expansion (CE) phases, to identify promising, effective belantamab mafodotin combinations when compared with a shared belantamab mafodotin monotherapy control arm (CE phase only). DE phases consist of multiple dosing cohorts with belantamab mafodotin combinations where patients are assigned to treatment slots by predetermined algorithmic approach (modified toxicity probability interval; N≤10 per cohort). Recommended phase 2 doses (RP2D) will be based on dose-limiting toxicities, safety, and pharmacokinetics. Interim analyses, based on overall response rate (ORR), determine if a RP2D is moved forward to a CE phase (N≥35 per cohort). Patients in the CE (stratified by number of prior therapies) will be randomized equally to open sub-studies. Eligible patients will have received ≥3 prior therapy lines which must include ≥1 immunomodulatory agent, proteasome inhibitor, and anti-CD38 antibody. The primary objectives are to identify RP2D for each combination (DE phase) and ORR (≥partial response, CE phase). Sub-studies 1 (combination with GSK3174998, OX40 agonist antibody) and 2 (combination with GSK3359609, ICOS agonist antibody) are currently enrolling. Sub-study 3 (combination with nirogacestat [PF-03084014; SpringWorks Therapeutics]) is projected to begin enrollment in the first half of 2020. Additional sub-studies will be explored based on scientific rationale and/or preclinical combination study results. Funding: GlaxoSmithKline (207495). Drug linker technology licensed from Seattle Genetics; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa. Clinical trial information: NCT04162210. Research Sponsor: GlaxoSmithKline.

TPS8553 Poster Session (Board #453), Fri, 8:00 AM-11:00 AM

Subcutaneous daratumumab in patients with multiple myeloma who have been previously treated with intravenous daratumumab: A multicenter, randomized, phase II study (LYNX). *First Author: Nizar J. Bahlis, University of Calgary, Arnie Charbonneau Cancer Institute, Calgary, AB, Canada*

Background: The intravenous (IV) formulation of daratumumab (DARA), a human CD38-targeted monoclonal antibody, is approved in many countries for use as monotherapy in relapsed/refractory multiple myeloma (RRMM) and in combination with standard-of-care regimens in RRMM or newly diagnosed MM. A subcutaneous (SC) formulation of DARA is under investigation in several ongoing studies. In the phase 3 COLUMBA study, DARA SC was shown to be non-inferior to DARA IV, demonstrating similar efficacy and pharmacokinetics, with a significantly decreased rate of infusion-related reactions and reduced administration time. The phase 2 LYNX (MMY2065) study will evaluate the efficacy and safety of retreatment with DARA. **Methods:** In this ongoing, multicenter, open-label, randomized phase 2 study, ~230 patients (pts) with prior exposure to DARA will be randomized 1:1 to receive carfilzomib and dexamethasone (Kd) ± DARA. Pts must have received 1 to 2 prior lines of therapy (at least one of which included DARA IV), with DARA-based therapy completed ≥3 months prior to randomization. Eligible pts have achieved a partial response or better (IMWG criteria) to DARA-based therapy, with a duration of response of ≥4 months. Pts must not have discontinued DARA due to a related adverse event or received prior treatment with carfilzomib. Pts will receive 20 mg/m^2 carfilzomib IV on Day 1 of Cycle 1, escalated to 70 mg/m^2 on Days 8 and 15; carfilzomib 70 mg/m^2 will be administered on Days 1, 8, and 15 of each 28-day cycle thereafter. Dexamethasone 40 mg will be administered (IV or PO) QW for Cycles 1-9 and then on Days 1, 8 and 15 from Cycle 10 onwards. Pts in the D-Kd group will also receive DARA SC (1,800 mg co-formulated with recombinant human hyaluronidase PH20 [rHuPH20; Halozyme]) QW in Cycles 1-2, Q2W in Cycles 3-6, and Q4W thereafter. The primary endpoint is the rate of pts achieving a very good partial response or better. Secondary endpoints include overall response rate, rate of pts achieving complete response or better, progression-free survival, overall survival, overall minimal residual disease-negativity rate, time to next treatment, pharmacokinetics, and safety. Clinical trial information: NCT03871829. Research Sponsor: Janssen Research & Development, LLC.

TPS8554 Poster Session (Board #454), Fri, 8:00 AM-11:00 AM

A phase III, randomized, multicenter, open-label study of venetoclax or pomalidomide in combination with dexamethasone in patients with t(11;14)-positive relapsed/refractory multiple myeloma. *First Author: Maria--Victoria Mateos, Hospital Clinico Univ de Salamanca, Salamanca, Spain*

Background: BCL-2 is an anti-apoptotic protein important for myeloma cell survival. Venetoclax (Ven) is a highly selective, potent, oral BCL-2 inhibitor, that has shown promise in clinical studies as monotherapy or in combination with other agents in patients with t(11;14)-positive relapsed/refractory multiple myeloma (RRMM; Kumar et al. *Blood.* 2017; Costa et al. ASH 2018. Abstr. #303; Harrison et al. ASH 2019. Abstr. #142; Bahlis et al. ASH 2019. Abstr. #925; Kaufman et al. ASH 2019. Abstr. #926). Notably, t(11;14)-positive MM is more dependent on BCL-2 for cell survival, which, together with these clinical data, suggests that Ven combined with dexamethasone (Dex) may provide greater clinical benefit versus standard therapies, like pomalidomide (Pom), in this biomarker-defined patient population. This ongoing Phase 3 study (CANOVA; NCT03539744) aims to evaluate the safety and efficacy of VenDex vs PomDex in t(11;14)-positive RRMM. **Methods:** Eligible patients (≥18 years) must have t(11;14)-positive RRMM per central lab, an ECOG performance status ≤2, received ≥2 prior lines of therapy, previously received a proteasome inhibitor, and must be refractory to lenalidomide and last line of therapy. Patients cannot have history of treatment with Ven, Pom, or other BCL-2 inhibitors. Patients will be randomized 1:1 to Ven (800 mg orally, once-daily) or Pom (4 mg orally, once-daily on days 1-21 of 28-day cycles). Patients in both groups will receive 40 mg Dex (20 mg for patients ≥75 years) once weekly. Treatment will continue until disease progression, unacceptable toxicity, or withdrawal from study. Patients will be stratified based on age at randomization (< 65 vs ≥65 years), prior lines of therapy (2 to 3 vs ≥4), and International Staging System stage at screening (I vs II vs III). The primary endpoint is progression-free survival (PFS) per independent review committee (IRC) assessment based on International Myeloma Working Group criteria. The final PFS analysis will be performed when approximately 147 PFS events per IRC are observed. Secondary endpoints are response rate, patient-reported outcomes, overall survival, duration of response, times to response and progression, minimal residual disease negativity rate, safety, and Ven pharmacokinetics. Approximately 244 patients will be enrolled; as of January 21, 2020, 28 patients have been randomized (from 19 sites in 12 countries) and enrollment is ongoing. Clinical trial information: NCT03539744. Research Sponsor: Abbvie, Inc, Pharmaceutical/Biotech Company.

TPS8555 Poster Session (Board #455), Fri, 8:00 AM-11:00 AM

Open-label pilot study of genetically engineered NY-ESO-1–specific t cells (GSK3377794) alone or in combination with pembrolizumab in relapsed/refractory multiple myeloma. *First Author: Aaron Rapoport, University of Maryland Greenebaum Comprehensive Cancer Center and School of Medicine, Baltimore, MD*

Background: Adoptive cellular therapy may be practice-changing in relapsed/refractory multiple myeloma (MM). NY-ESO-1 TCR T (GSK3377794) are autologous polyclonal T cells transduced by a self-inactivating lentiviral vector to express an affinity-enhanced TCR capable of recognizing NY-ESO-1 or LAGE-1a antigenic peptides in complex with HLA-A*02. GSK3377794 has shown clinical activity in synovial sarcoma, melanoma, myxoid/round cell liposarcoma, and MM after autologous stem cell transplant. NY-ESO-1 and LAGE-1a are cancer/testis antigens frequently overexpressed in MM and linked to poor clinical outcome. PD-1 expression on CD8 T cells, which has been observed in MM patients previously treated with GSK3377794 as well as with CD19 CAR T-cell therapy, can limit adaptive immune response. We hypothesize that GSK3377794 alone, or in combination with the anti-PD-1 inhibitor pembrolizumab, may result in an antitumor effect in MM. **Methods:** This is an open-label, pilot study (NCT03168438) of GSK3377794 in patients with relapsed/refractory MM positive for HLA-A*02:01, HLA-A*02:05, ± HLA-A*02:06 and NY-ESO-1/LAGE-1a. Patients (n = 20) who have received ≥3 prior therapies containing ≥1 immunomodulatory imide, proteasome inhibitor, alkylator, CD38 monoclonal antibody, or glucocorticoid will be assigned to either single-infusion GSK3377794 (Arm 1, n = 10) or single-infusion GSK3377794 + pembrolizumab 200 mg IV every 3 weeks (Arm 2, n = 10). Arm 1 enrollment will be completed first. In Arm 2, pembrolizumab will begin in Week 3 (Week 6 if precluded by toxicity). Patients in both arms will provide cells via leukapheresis to manufacture autologous NY-ESO-1–specific T cells, undergo lymphodepletion (fludarabine + cyclophosphamide), and then receive GSK3377794 infusion ($1-8 \times 10^9$ transduced T cells). Primary and secondary objectives are to assess safety/tolerability and antitumor activity, respectively, of GSK3377794 (± pembrolizumab). Arm 2 enrollment will pause for a 3-week safety review after 3 patients have received a first dose of pembrolizumab. Efficacy, safety, and biomarkers will be assessed every visit. The treatment phase will last 108 weeks, or until disease progression; follow-up will last ≤15 years. As of January 2020, 3 patients have been treated. Funding: GlaxoSmithKline (208470) Clinical trial information: NCT03168438. Research Sponsor: GlaxoSmithKline.

TPS8556 Poster Session (Board #456), Fri, 8:00 AM-11:00 AM

DREAMM-9: Phase III study of belantamab mafodotin plus VRd versus VRd alone in transplant-ineligible newly diagnosed multiple myeloma (TI NDMM). *First Author: Saad Zafar Usmani, Levine Cancer Institute, Charlotte, NC*

Background: Bortezomib, lenalidomide, and dexamethasone (VRd) is the standard of care for transplant-eligible and TI NDMM, but relapse is usually inevitable. The median progression-free survival (PFS) is ~3 years for patients with TI NDMM, and with each relapse, the duration of response (DoR) diminishes, highlighting the need for novel, effective, targeted agents. Single-agent belantamab mafodotin is a first-in-class B-cell maturation antigen–binding, humanized, afucosylated, monoclonal immunoconjugate, showing deep and durable responses in heavily pretreated patients with relapsed/refractory multiple myeloma (*Lancet Oncol*2020). Preclinical work suggests belantamab mafodotin plus bortezomib or lenalidomide enhances anti-myeloma activity. Therefore, studying clinical activity of belantamab mafodotin in combination with these agents is warranted. **Methods:** DREAMM-9 (NCT04091126) is a two-part, open-label study to determine efficacy and safety of single-agent belantamab mafodotin with VRd vs. VRd alone in patients with TI NDMM. Patients aged ≥18 years with ECOG status 0–2 and adequate organ system functions will be eligible. Part 1 (dose selection) will evaluate safety/tolerability of belantamab mafodotin with VRd administered by single (Day 1) or split dosing (Days 1 and 8) in ≤5 cohorts (n = 12/cohort): 1.9 mg/kg, 2.5 mg/kg split and single, and 3.4 mg/kg split and single. Six more patients may be added to cohort(s) most likely to be selected as recommended Phase III dose (RP3D). Dose-limiting toxicities and adverse events (AEs) will be assessed, and belantamab mafodotin RP3D determined through modified toxicity probability interval criteria. Part 2 (randomized Phase III) will determine efficacy and safety of belantamab mafodotin at RP3D with VRd vs. VRd alone (n = 750) in two arms randomized 1:1. Dual primary endpoints will be rate of minimal residual disease (MRD) negativity and PFS. Secondary endpoints will be response rates (overall response, complete response, very good partial response or better, sustained MRD negativity), DoR, time to progression, and overall survival. Safety assessment will include AEs, serious AEs and ocular findings. In both parts, belantamab mafodotin will be given with VRd for eight induction cycles and then with Rd for maintenance until disease progression or unacceptable toxicity. Funding: GlaxoSmithKline (209664). Drug linker technology licensed from Seattle Genetics; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa. Clinical trial information: NCT04091126. Research Sponsor: GlaxoSmithKline.

9000 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Randomized phase II clinical trial of cisplatin/carboplatin and etoposide (CE) alone or in combination with nivolumab as frontline therapy for extensive-stage small cell lung cancer (ES-SCLC): ECOG-ACRIN EA5161. *First Author: Ticiana Leal, University of Wisconsin Carbone Cancer Center, Madison, WI*

Background: Immune checkpoint inhibition is now given in combination with chemotherapy for first line (1L) therapy of extensive stage small cell lung cancer (ES-SCLC). We conducted a randomized phase II study of nivolumab (anti-PD1) in combination with platinum-etoposide (CE) as 1L treatment for patients with ES-SCLC (EA5161, NCT03382561). **Methods:** Patients with measurable (RECIST v1.1) ES-SCLC, ECOG performance status 0 or 1, who had not received prior systemic treatment for ES-SCLC were enrolled. Patients were randomized 1:1 to nivolumab 360 mg + CE every 21 days for 4 cycles followed by maintenance nivolumab 240 mg every 2 weeks until progression or up to 2 years (arm A) or CE every 21 days for 4 cycles followed by observation (arm B). Prophylactic cranial irradiation (PCI) was permitted at the investigator's discretion. Investigator's choice of cisplatin or carboplatin was allowed across both arms. The primary endpoint was PFS in eligible and treated patients. Secondary endpoints included OS, ORR, and safety. Adverse events (AEs) were graded per NCI-CTCAE v4.0. **Results:** This study was activated in May 2018 and completed accrual in December 2018. 160 patients were enrolled. Baseline characteristics were well balanced between arms. In the ITT population (n = 160), nivolumab + CE significantly improved the PFS compared to CE with HR 0.65 (95% CI, 0.46, 0.91; p = 0.012); mPFS 5.5 versus 4.6 months, respectively. Secondary endpoint of OS was also improved with nivolumab + CE versus CE with HR 0.67 (95% CI, 0.46, 0.98; p = 0.038); mOS 11.3 versus 8.5 months. Among patients who initiated study therapy, nivolumab + CE significantly improved the PFS compared to CE with HR 0.68 (95% CI, 0.48, 1.00; p = 0.047); mPFS 5.5 versus 4.7 months, respectively; in this population, OS was also improved with nivolumab + CE versus CE with HR 0.73 (95% CI, 0.49, 1.11; p = 0.14); mOS 11.3 versus 9.3 months. The ORR was 52.29% versus 47.71%. The incidence of treatment-related grade 3/4 AEs was 77% versus 62% and AEs leading to discontinuation 6.21% versus 2.07%. Ten patients remain on maintenance nivolumab. Lethal adverse events independent of treatment were similar between the two arms (9 in arm A; 7 in arm B). **Conclusions:** The addition of nivolumab to CE as 1L treatment for ES-SCLC significantly improved PFS and OS. No new safety signals were observed. Clinical trial information: NCT03382561. Research Sponsor: ECOG-ACRIN.

9001 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

KEYNOTE-604: Pembrolizumab (pembro) or placebo plus etoposide and platinum (EP) as first-line therapy for extensive-stage (ES) small-cell lung cancer (SCLC). *First Author: Charles M. Rudin, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Pembro monotherapy showed durable antitumor activity as third-line or later therapy for metastatic SCLC, leading to FDA approval in that setting. KEYNOTE-604 was a double-blind, phase 3 study of pembro + EP vs placebo + EP as first-line therapy for ES-SCLC (NCT03066778). **Methods:** Eligible patients (pts) with previously untreated ES-SCLC and no untreated CNS metastases were randomized 1:1 to pembro 200 mg Q3W or saline placebo for up to 35 cycles plus 4 cycles of standard-dose EP. Pts with CR or PR after cycle 4 could receive PCI at investigator discretion. Randomization was stratified by platinum choice (carboplatin vs cisplatin), ECOG PS (0 vs 1), and LDH (≤ULN vs > ULN). Primary endpoints were OS and PFS (RECIST v1.1, blinded central review) in the ITT population. ORR, DOR, and safety were secondary endpoints. OS and PFS treatment differences were assessed by the stratified log-rank test. The protocol specified 2 interim analyses (IAs) and a final analysis (FA). Prespecified efficacy boundaries were one-sided $P = 0.0048$ for PFS at IA2 (prespecified final PFS analysis) and 0.0128 for OS at FA. **Results:** 453 pts were randomized. 223/228 pts assigned to pembro + EP and 222/225 assigned to placebo + EP received ≥1 dose of assigned treatment; 1 pt assigned to pembro + EP received placebo + EP in error. Median age was 65 y, 74% had ECOG PS 1, and 57% had LDH > ULN; more pts in the pembro + EP arm had baseline brain metastases (14% vs 10%). At FA (median follow-up, 21.6 mo), 9% of pts in the pembro + EP arm and 1% in the placebo + EP arm remained on study treatment; 12% and 14% received PCI. At IA2 (median follow-up, 13.5 mo), pembro + EP significantly improved PFS in the ITT population (HR 0.75 [95% CI 0.61-0.91], $P = 0.0023$; median 4.5 vs 4.3 mo). At FA, pembro + EP prolonged OS in the ITT population, but the significance threshold was not met (HR 0.80 [95% CI 0.64-0.98], $P = 0.0164$; median 10.8 vs 9.7 mo). In a post hoc analysis of OS in the as-treated population, the nominal P value was smaller than the significance threshold (HR 0.78 [95% CI 0.63-0.97], $P = 0.0124$). ORR at FA was 71% for pembro + EP vs 62% for placebo + EP; median DOR was 4.2 vs 3.7 mo. Observed AEs were as expected; any-cause AEs were grade 3-4 in 77% vs 75%, grade 5 in 6% vs 5%, and led to discontinuation in 15% vs 6%. **Conclusions:** Pembro + EP significantly improved PFS and prolonged OS compared with placebo + EP as first-line therapy for pts with ES-SCLC. No unexpected toxicities were seen with pembro + EP. These data support the benefit of pembro-containing regimens for ES-SCLC. Clinical trial information: NCT03066778. Research Sponsor: Merck & Co., Inc., Kenilworth, NJ, USA.

9002 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Durvalumab ± tremelimumab + platinum-etoposide in first-line extensive-stage SCLC (ES-SCLC): Updated results from the phase III CASPIAN study. *First Author: Luis G. Paz-Ares, Hospital Universitario 12 de Octubre, Madrid, Spain*

Background: CASPIAN is an open-label, Phase 3 study of durvalumab (D) ± tremelimumab (T) + etoposide and either cisplatin or carboplatin (EP) for pts with 1L ES-SCLC. At the planned interim analysis (data cutoff Mar 11, 2019; 63% maturity), D + EP demonstrated a statistically significant improvement in OS compared with EP alone (HR 0.73 [95% CI 0.59–0.91]; p=0.0047). Here we present a planned updated analysis of OS for D + EP vs EP and the first results for D + T + EP vs EP. **Methods:** Treatment-naïve pts with ES-SCLC (WHO PS 0/1) were randomized 1:1:1 to D 1500 mg + EP q3w, D 1500 mg + T 75 mg + EP q3w, or EP q3w. In the IO arms, pts received 4 cycles of EP + D ± T, followed by maintenance D 1500 mg q4w until disease progression. Pts received one additional dose of T 75 mg post EP in the D + T + EP arm. In the EP arm, pts received up to 6 cycles of EP and optional PCI (investigator's discretion). The two primary endpoints were OS for D + EP vs EP and for D + T + EP vs EP. **Results:** 268, 268 and 269 pts were randomized to D + EP, D + T + EP and EP, respectively; baseline characteristics were generally well balanced across arms. As of Jan 27, 2020, the median follow-up was 25.1 mo, 82% maturity. D + EP continued to demonstrate improvement in OS vs EP, with a HR of 0.75 (95% CI 0.62–0.91; nominal p=0.0032); median OS 12.9 vs 10.5 mo, respectively. 22.2% of pts were alive at 2 y with D + EP vs 14.4% of pts with EP. D + T + EP numerically improved OS vs EP, however this did not reach statistical significance per the prespecified statistical plan: HR 0.82 (95% CI 0.68–1.00; p=0.0451 [p≤0.0418 required for stat sig]); the median OS was 10.4 mo and 23.4% of pts were alive at 2 y. Secondary endpoints of PFS and ORR remained improved with D + EP vs EP and will be presented. Confirmed investigator-assessed ORR was similar for D + T + EP vs EP (58.4% vs 58.0%). Median PFS was similar for D + T + EP vs EP (4.9 mo vs 5.4 mo), but the 12-mo PFS rate was numerically higher (16.9% vs 5.3%); PFS HR 0.84 (95% CI 0.70–1.01). In the D + EP, D + T + EP and EP arms, respectively, incidences of all-cause AEs of Grade 3/4 were 62.3%, 70.3% and 62.8%; AEs leading to discontinuation 10.2%, 21.4% and 9.4%; and AEs leading to death 4.9%, 10.2% and 5.6%. **Conclusions:** The addition of durvalumab to EP continued to demonstrate improvement in OS compared with a robust control arm, further supporting this regimen as a new standard of care for 1L ES-SCLC offering the flexibility of platinum choice. No additional benefit was observed when T was combined with D + EP in this pt population. Safety findings in all arms remained consistent with the known safety profiles of all agents. Clinical trial information: NCT03043872. Research Sponsor: AstraZeneca.

9003 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

PrE0505: Phase II multicenter study of anti-PD-L1, durvalumab, in combination with cisplatin and pemetrexed for the first-line treatment of unresectable malignant pleural mesothelioma (MPM)—A PrECOG LLC study. *First Author: Patrick M. Forde, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

Background: First-line CP was FDA-approved in 2004 for unresectable MPM. Given the role of inflammation in MPM and promising responses to PD-1 pathway blockade in pretreated MPM, we conducted a phase 2 single arm study of the anti-PD-L1 antibody, durvalumab (durva), combined with CP for patients (pts) with untreated MPM of any subtype. **Methods:** Eligible pts were treatment-naïve with surgically unresectable MPM. Primary endpoint was overall survival (OS); pts received up to 6 cycles of durva-CP, followed by maintenance durva up to 1 year. Carboplatin was permitted for pts with baseline hearing or renal impairment. The first 15 pts were monitored for dose-limiting toxicities (DLTs). Secondary endpoints included toxicity, objective response by modified RECIST, progression-free survival (PFS), and correlative analyses. With a sample size of 55 patients and 32 events, the study had 90% power to detect a 58% improvement in median OS from 12 months (m) (historical control) to 19 m with durva-CP. **Results:** PrE0505 enrolled 55 patients at 15 US-based sites between 06/2017 and 06/2018. Histologic subtypes were epithelioid (75%), biphasic (11%), sarcomatoid (13%), and desmoplastic (2%). There were no DLTs during the run-in period. As of January 2020 the median follow up is 20.6 m and 29 deaths have occurred. The median OS at the time of report is 21.1 m. The 12 m OS rate was 70% with a 2 sided 95% confidence interval (56%, 81%) and two-sided 80% CI (62%, 78%). Analyses for the secondary endpoints were ongoing at abstract submission. Exome sequencing, TCR sequencing and dual PD-L1/CD8 staining have been completed on baseline tumors from at least 45 of the 55 patients enrolled as well as RNA sequencing for those with adequate tissue. Initial results show that tumors harbored an average tumor mutation burden of 22 somatic sequence alterations and varying levels of aneuploidy were detected. **Conclusions:** The combination of chemotherapy with durvalumab delivered a promising median OS for previously untreated pts with unresectable MPM. Full results from the study along with the extensive correlative analyses performed will be reported. The phase 3 PrE0506/DREAM3R trial evaluating CP-durvalumab versus CP alone will commence enrollment in the United States and Australia in 2020. Clinical trial information: NCT02899195. Research Sponsor: AstraZeneca, U.S. National Institutes of Health.

9004 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Randomized phase II study on gemcitabine with or without ramucirumab as second-line treatment for advanced malignant pleural mesothelioma (MPM): Results of Italian Rames Study. *First Author: Maria Pagano, Oncology Unit, Clinical Cancer Center, AUSL-IRCCS Reggio Emilia, Reggio Emilia, Italy*

Background. The RAMES Study (EudraCT Number 2016-001132-36) is a multicenter, double-blind, randomized phase II trial exploring the efficacy and the safety of the addition of ramucirumab to gemcitabine as the second-line treatment in MPM patients (pts) after platinum/pemetrexed regimens. **Methods.** The pts were assigned (1:1) to receive Gemcitabine 1000 mg/m^2 i*v* on days 1 and 8 every 21 days with Placebo (Arm A) or Ramucirumab 10 mg/kg i*v* on day 1, of a 21-day cycle (Arm B), until tolerability or progressive disease. Pts was stratified by ECOG/PS (0-1 vs 2), age ($\leq$ 70 vs $>$ 70 yrs), histology (epithelioid vs non-epithelioid) and time to progression (TTP) after first-line therapy. The primary endpoint was overall survival (OS). Assuming a proportion of OS equal to 40% at 1 year in arm A, a 12% absolute improvement in OS at 1 yrs was expected in Arm B (hazard ratio = 0.70).114 events (156 subjects) are required for a one-sided log-rank test with α = 0.15 to have 80% power. **Results.** From December 2016 to July 2018, 164 pts were randomized, 81 pts in Arm A and 80 Arm B; 3 pts were randomized but not treated. Characteristics of pts were: median age 69 yrs (44-81), males 119 (73.9%), females 42 (26.1%); ECOG/PS0 96 (59.6%) ECOG/PS1-2 65 (40.4%); histotype epithelioid 132 (81.9%), non-epithelioid 29 (18.1%); stage III 98 (60.7%), stage IV 60 (37.3%), 3 (2.0%) missing; asbestos exposure assessed 80 (49.7%). Median of courses was 3.50 in Arm A and 7.50 in Arm B. OS was significantly longer in Arm B with median 13.8 mths (70% CI 12.7-14.4) vs Arm A with 7.5 mths (70% CI 6.9-8.9), HR 0.71 (70% CI 0.59-0.85, p = 0.057). OS at 6 and 12 mths was in Arm A 63.9% and 33.9%, and in Arm B 74.7% and 56.5%, respectively. In Arm B OS was not correlated to TTP at first-line therapy (13.6 mths in TTP $\leq$6 mths and 13.9 mths in TTP $>$ 6 mths) and histotypes (13.8 months in the epithelioid and 13.0 months in non-epithelioid). No significant differences in thromboembolism G3-4 events were observed in Arm A vs Arm B (p= 0.64). None hypertension G3-4 was reported in Arm A vs 5 pts (6.3%) in Arm B (p= 0.022). No significant differences in G3-4 haematological toxicities between the two arms were reported. **Conclusion:** In the RAMES Study the addition of Ramucirumab to Gemcitabine significantly improved OS regardless of age of pts, tumor histotype and TTP at the first-line treatment. Gemcitabine plus Ramucirumab can be considered a manageable regimen in second-line treatment of advanced MPM pts.Clinical trial information: NTC03560973. Research Sponsor: None.

9005 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

CTONG1104: Adjuvant gefitinib versus chemotherapy for resected N1-N2 NSCLC with EGFR mutation—Final overall survival analysis of the randomized phase III trial 1 analysis of the randomized phase III trial. *First Author: Yi-Long Wu, Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, School of Medicine, South China University of Technology, Guangzhou, China*

Background: ADJUVANT-CTONG1104, a randomized phase 3 trial showed adjuvant gefitinib treatment significantly improved disease-free survival (DFS) vs standard doublet chemotherapy in patients (pts) with epidermal growth factor receptor (*EGFR*) mutation-positive resected stage II-IIIA (N1-N2) non-small-cell lung cancer (NSCLC). 5-year survival rate of N1N2 were 38%-50% in IASLC staging system. Here, we present the final overall survival (OS) results from the study. **Methods:** From Sep 2011 to April 2014, 222 patients, aged 18-75 years, with *EGFR* activating mutation through completely resection and diagnosed as stage II-IIIA (N1-N2) NSCLC pathologically from 27 sites were enrolled. The enrolled patients were 1:1 randomized to receive adjuvant gefitinib (250 mg once per day) for 24 months (G, n=111) or vinorelbine (25 mg/m^2, d1 and d8) plus cisplatin (75 mg/m2, d1) every 3 weeks for 4 cycles (C, n=111). The primary endpoint was DFS in the ITT population. Secondary endpoints included OS, 3 and 5-year DFS rate, 5-year OS rate. The subsequent therapy data were collected, including crossover from C to G, re-challenge TKI and other treatment. Data cut-off date was Jan. 13, 2020. **Results:** A median follow-up was 76.9 months. The median OS (mOS) was 75.5 months based on 95 (42.8%) events in ITT whole population. The mOS was 75.5m in G arm and 79.2m in C arm (HR 0.96, 95%CI 0.64-1.43, p=0.823). The 3, 5-year OS rate were 68.6%, 53.8% in G and 67.5%, 52.4% in C respectively. DFS in 3, 5-y were 40.3%, 23.4% in G and 33.2%, 23.7% in C, respectively ($P_{3\text{-}y}$=0.395, $P_{5\text{-}y}$=891). All predefined subgroups including age, gender, lymph node, EGFR mutation type had no significant difference in statistics but in favor of G arm in trend. Subsequent treatment especially targeted therapy contributed most to OS (HR = 0.46, 95% CI 0.26 – 0.83). Median OS of patients receiving subsequent target therapy was75.5m (n=35), 36.4m in other treatment (n=33; (P$<$0.001). For G mOS were 75.5 (n=15; target therapy) and 35.0 (n=18; other, p$<$0.001), for C 62.8m (n=20) and 46.8m (n=15; p=0.251). The RR was 26.7%, DCR 66.7%, mPFS 14.1m and mOS 19.6m for patients with rechallenged EGFR TKI in G arm (n=15). No novel unexpected SAE was observed during follow up. **Conclusion** The DFS survival advantage did not translate to OS difference in ADJUVANT trial. The OS with 75.5m was the best one of survival in completely resected N1N2 NSCLC comparing with historical data and sequent TKI treatment contribute to overall survival. Clinical trial information: NCT01405079. Research Sponsor: Chinese Thoracic Oncology Group (CTONG), Chinese Thoracic Oncology Group (CTONG).

9006 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Randomized phase III study of irinotecan/cisplatin (IP) versus etoposide/cisplatin (EP) for completely resected high-grade neuroendocrine carcinoma (HGNEC) of the lung: JCOG1205/1206. *First Author: Hirotsugu Kenmotsu, Division of Thoracic Oncology, Shizuoka Cancer Center, Shizuoka, Japan*

Background: In the WHO classification, small cell lung cancer (SCLC) and large cell neuroendocrine carcinoma (LCNEC) are considered as high-grade neuroendocrine carcinoma (HGNEC) of the lung. Although there were no randomized trials evaluating adjuvant chemotherapy for patients (pts) with resected HGNEC, EP was considered to be a standard regimen for this population. A phase III study showed the superiority of IP to EP in pts with extensive stage SCLC (JCOG9511). **Methods:** Pts with completely resected HGNEC were randomized in a 1:1 ratio to receive either etoposide (100 mg/m^2, days 1-3)/cisplatin (80 mg/m^2, day 1) or irinotecan (60 mg/m^2, days 1, 8, 15)/cisplatin (60 mg/m^2, day 1), using the minimization method according to sex, pathologic stage, histology and institution. The primary endpoint was changed from overall survival (OS) to relapse-free survival (RFS) during the study period. We assumed a 3-year RFS of 59% of EP arm and 72% of IP arm (hazard ratio (HR) of 0.623). Planned sample size was 220 in total to give a power of 80% with a one-sided alpha of 5%, an accrual period of 6 years and a follow-up period of 3 years. **Results:** Between April 2013 and October 2018, 221 pts with a median age of 66 years, pathological stage I (54%), SCLC (53%), were randomly assigned to the EP arm (n = 111) or the IP arm (n = 110). In the second interim analysis, the predictive probability that IP would be superior to EP at the time of the primary analysis was 15.9%, which led to early termination of the trial. With a median follow-up of 24.1 months, 3-year RFS was 65.4% versus 69.0% with HR of 1.076 (95% CI, 0.666-1.738; log-rank test, one-sided *P*= 0.619). In the subgroup analyses of histology, 3-year RFS in SCLC was 65.2% versus 66.5% with HR of 1.029 (95% CI, 0.544-1.944), and 3-year RFS in LCNEC was 66.5% versus 72.0% with HR of 1.072 (95% CI, 0.517-2.222). Overall survival at 3 years was 84.1% versus 79.0% with HR of 1.539 (95% CI, 0.760-3.117). Proportions of treatment completion were 87.4% (EP) and 72.7% (IP). Incidences (EP/IP) of grade 3 or 4 febrile neutropenia (20.2/3.7%) or neutropenia (97.2/35.8%) were more common in EP. Grade 3 or 4 diarrhea (0.9/8.3%) or anorexia (6.4/11.1%) were more common in IP. One treatment-related death due to tracheal bleeding was observed in IP. **Conclusions:** This study failed to show the superiority of IP to EP in RFS for pts with completely resected HGNEC. EP is still a standard treatment for this population. Clinical trial information: UMIN000010298. Research Sponsor: the Japan Agency for Medical Research and Development.

9007 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Randomized phase II trial comparing the efficacy of standard-dose with high-dose twice-daily thoracic radiotherapy (TRT) in limited disease small-cell lung cancer (LD SCLC). *First Author: Bjorn Henning Gronberg, Department of Clinical and Molecular Medicine, NTNU, Norwegian University of Science and Technology and Department of Oncology, St. Olav's Hospital, Trondheim University Hospital, Trondheim, Norway*

Background: Concurrent chemoradiotherapy is the standard treatment of LD SCLC. Some patients are cured, but most relapse and better treatment is needed. 45 Gy in 30 fractions BID is the most recommended TRT-schedule. Studies suggest that a higher TRT-dose might prolong survival, but hitherto, this has not been confirmed in randomized trials. We aimed to investigate whether high-dose BID TRT of 60 Gy in 40 fractions was feasible, tolerated, and improved survival. **Methods:** Patients $>$ 18 years, performance status (PS) 0-2 and confirmed LD SCLC were to receive 4 courses of platinum/etoposide and were randomized to BID TRT of 60 or 45 Gy. Responders were offered prophylactic cranial irradiation of 25-30 Gy. Primary endpoint was 2-year survival; secondary endpoints were toxicity, progression free survival (PFS), and overall survival (OS). To demonstrate a 25% improvement of 2-year survival from 53% to 66% with a one-sided α = .10 and β = .80, 75 patients were required on each arm. **Results:** Between 2014-2018, 176 patients were enrolled at 22 Scandinavian hospitals. 160 completed TRT per protocol and were eligible for the present analyses (60 Gy: n = 84, 45 Gy: n = 76). Median age was 65, 58% women, 90% PS 0-1. There were no significant differences in grade 3–4 esophagitis (60 Gy: 19%, 45 Gy: 18%, p = .92) or grade 3–4 pneumonitis (60 Gy: 4%, 45 Gy: 0%, p = .10). There was a trend towards more neutropenic infections on the 45 Gy arm (60 Gy: 21%, 45 Gy: 36%, p = .05). There were no significant differences in other grade 3-4 toxicity. Three patients died during the study treatment period (60 Gy: one neutropenic infection and one aortic dissection; 45 Gy: one thrombocytopenic bleeding). There were no statistically significant differences in response rates (60 Gy: 88% [95% CI 81-95], 45 Gy: 85% [95% CI 76-93], p = .52) or median PFS (60 Gy: 20 months [95% CI 11-29], 45 Gy: 14 months [95% CI 10-19], p = .31). Significantly more patients on the 60 Gy arm were alive after 2 years (60 Gy: 73% [95% CI 63-83], 45 Gy: 46% [95% CI 36-60], p = .001), and they had a significantly longer median overall survival (60 Gy: 42 months [95% CI 32-51], 45 Gy: 23 months [95% CI 17-28], HR .63 [95% CI .41-.96], p = .031). **Conclusions:** LD SCLC patients who received BID TRT of 60 Gy had a statistically significant and numerically substantial benefit in terms of 2-year survival (primary endpoint) and median overall survival compared with those who received BID TRT of 45 Gy. The higher TRT dose did not cause more toxicity than the standard dose. Clinical trial information: NCT02041845. Research Sponsor: The Norwegian Cancer Society and The Liaison Committee for Education, Research and Innovation in Central Norway.

9008 Poster Discussion Session; Displayed in Poster Session (Board #201), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II study of pembrolizumab (pembro) plus platinum doublet chemotherapy and radiotherapy as first-line therapy for unresectable, locally advanced stage III NSCLC: KEYNOTE-799. *First Author: Salma K. Jabbour, Department of Radiation Oncology, Rutgers Cancer Institute of New Jersey, Robert Wood Johnson Medical School, Rutgers University, New Brunswick, NJ*

Background: KEYNOTE-799 (NCT03631784) evaluates pembro plus concurrent chemoradiation therapy (CCRT) in pts with unresectable, locally advanced stage III NSCLC. **Methods:** In this phase 2, nonrandomized, open-label trial, pts with previously untreated, unresectable, pathologically confirmed stage IIIA–C NSCLC with measurable disease (RECIST 1.1) received up to 17 cycles of pembro 200 mg Q3W starting with cycle 1 plus standard thoracic radiotherapy (60 Gy in 30 daily 2-Gy fractions) in cycles 2–3 and investigator's choice of paclitaxel 200 mg/m^2 + carboplatin AUC 6 Q3W for cycle 1, then paclitaxel 45 mg/m^2 + carboplatin AUC 2 QW for cycles 2–3 (cohort A), or cisplatin 75 mg/m^2 + pemetrexed 500 mg/m^2 Q3W (nonsquamous only) in cycles 1–3 (cohort B). Primary endpoints were ORR (CR/PR per RECIST 1.1 by blinded independent central review) and rate of grade ≥3 pneumonitis (per NCI CTCAE v4.0). CIs were estimated using the Clopper-Pearson method. Safety was assessed in all treated patients; efficacy was assessed in pts with ≥15 wks follow-up. **Results:** As of Jan 3, 2020, 112 and 73 pts have been enrolled in cohorts A and B, respectively; 63 in cohort A and 52 in cohort B continue on treatment. Median (range) follow up was 8.3 (0.7–14.0) mo in cohort A and 5.8 (0.2–13.7) mo in cohort B. ORR (90% CI) was 67.0% (58.9%–74.3%) in cohort A and 56.6% (44.4%–68.2%) in cohort B (Table). Grade ≥3 pneumonitis occurred in 9 pts (8.0%; 90% CI, 4.3%–13.6%) in cohort A and 4 pts (5.5%; 90% CI, 1.9%–12.1%) in cohort B. Treatment-related grade ≥3 AEs occurred in 72 pts (64.3%) in cohort A and 30 pts (41.1%) in cohort B. 4 pts had treatment-related grade 5 pneumonitis (all in cohort A). Enrollment is complete for cohort A and ongoing in cohort B. **Conclusions:** Pembro plus CCRT shows promising antitumor activity in pts with unresectable, locally advanced stage III NSCLC. Toxicity was as anticipated with pembro plus CCRT. Clinical trial information: NCT03631784. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	Cohort A* N=112	Cohort B* N=53
ORR, % (90% CI)	67.0 (58.9–74.3)	56.6 (44.4–68.2)
Median (range) duration of response, mo	NR (1.6+ to 10.5+)	NR (1.7+ to 10.5+)
DOR ≥ 6 mo,† %	91.1	100
6-mo PFS rate,† %	81.4	85.2
6-mo OS rate,† %	87.2	94.8

*Pts with ≥15 wks follow-up.
†Kaplan-Meier estimate.

9009 Poster Discussion Session; Displayed in Poster Session (Board #202), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase I safety and feasibility study of neoadjuvant chemoradiation plus pembrolizumab followed by consolidation pembrolizumab in resectable stage IIIA non-small cell lung cancer. *First Author: Christopher Lemmon, Cleveland Clinic Foundation, Cleveland, OH*

Background: Patients (pts) with resectable stage IIIA non-small cell lung cancer (NSCLC) have high rates of recurrence despite concurrent chemoradiation (CRT) followed by surgery. Immune checkpoint inhibitor consolidation has improved outcomes in unresectable stage III pts. Here we report the addition of concurrent neoadjuvant pembrolizumab (P) to CRT in stage IIIA patients to determine the safety and feasibility of this approach. **Methods:** Pts with stage IIIA NSCLC deemed resectable by a thoracic surgeon received neoadjuvant CRT consisting of cisplatin, etoposide, and concurrent P (200mg every 3 weeks x 3) with 45 Gy in 25 fractions. Pts without progression underwent resection followed by 6 months of consolidation P. The primary objective was feasibility and safety (defined as ≤30% grade 3 or higher pulmonary toxicity or any grade 4/5 nonhematologic toxicity). Ten pts were to be enrolled in Part 1, and if 2 or fewer pts had events then an additional 10 pts were to be enrolled. Secondary objectives were progression free survival (PFS), overall response rate (ORR), and pathologic complete response rate (pCR). **Results:** The median age of 9 enrolled pts was 66 years (range 49-76). 67% were female. 8 pts were assessable for radiographic response with an ORR of 75%. One pt came off study for progression prior to surgery and one had pleural metastases found during surgery so resection was aborted. Six pts underwent complete resection with a pCR rate of 67% (4/6). Consolidation P was started on 4 pts, with 3 completing treatment and 1 declined further treatment after 3 cycles. Median follow-up is 19.6 months and median PFS has not been reached. None of the patients who underwent resection have recurred. Serious adverse events were reported in all 9 pts with most significant being 2 grade 5 events: 1 due to pneumocystis pneumonia after resection but prior to consolidation, and 1 due to cardiac arrest during the neoadjuvant phase. Grade 3 events included 1 episode each of pneumonitis, bronchopleural fistula, acute kidney injury, colon perforation, and febrile neutropenia. **Conclusions:** The addition of P to neoadjuvant CRT in resectable stage IIIA pts resulted in a high pCR rate at resection. Although the relationship between grade 5 events and the addition of P was not clear, the stopping rule for infeasibility was met. As other larger studies are underway, the trial was halted rather than amended. This investigator initiated trial was funded by Merck. Clinical trial information: NCT02987998. Research Sponsor: Merck.

9010 Poster Discussion Session; Displayed in Poster Session (Board #203), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Consolidation nivolumab/ipilimumab versus nivolumab following concurrent chemoradiation in patients with unresectable stage III NSCLC: A planned interim safety analysis from the BTCRC LUN 16-081 trial. *First Author: Melissa Yan, Indiana University Melvin and Bren Simon Cancer Center, Indianapolis, IN*

Background: Consolidation PD-1/PD-L1 inhibition after chemoradiation (CRT) for unresectable stage III NSCLC improves overall survival. In stage IV NSCLC, the combination of nivolumab/ipilimumab improved overall survival compared to chemotherapy in patients with PD-L1 > 1% and performed favorably in patients with PD-L1 < 1%. The safety of consolidation nivolumab/ipilimumab after CRT has not been previously assessed. **Methods:** In this randomized, multi-center, phase II study, a total of 105 planned pts with unresectable stage IIIA/IIIB NSCLC will receive chemoradiation, then randomize 1:1 to either nivolumab 480mg IV q4 wks (Arm A) or nivolumab 3mg/kg IV q2 wks + ipilimumab 1mg/kg IV q6 wks (Arm B), for up to 24 wks. In this planned interim analysis, the safety of the first 50 patients, with 25 patients treated on each arm, is assessed. **Results:** From 9/2017 to 6/2019, the first 50 patients were accrued and analyzed for this planned safety analysis. Baseline characteristics for Arm A/B: median age 64/62, stage IIIA 17/16, stage IIIB 8/9, nonsquamous 14/13, squamous 11/12. The median number of cycles completed in Arm A was 6 (range 1-6, cycle length q4 wks) and in Arm B was 4 (range 1-4, cycle length q6 wks). The rate of treatment-related adverse events leading to discontinuation of therapy was 16% in Arm A and 40% in Arm B. The percentage of patients with any > grade 3 adverse event (AE) was 32% in Arm A and 44% in Arm B. With respect to immune-related AE (irAEs), the percentage of patients with any ≥grade 2 was 44% in Arm A and 60% in Arm B; any ≥ grade 3 irAEs was 16% in Arm A and 32% in Arm B. The incidence of > grade 2 pneumonitis was 16% in Arm A and 36% in Arm B. The percentage of patients with > grade 3 pneumonitis was 4% in Arm A and 20% in Arm B. No treatment-related deaths were reported on either arm. **Conclusions:** In the post chemoradiation setting, the incidence of > grade 3 toxicity was greater in the consolidative nivolumab/ipilimumab arm, which resulted in a higher rate of treatment discontinuation than nivolumab alone. The Data and Safety Monitoring Board recommended continued enrollment without modification to the trial and the study currently remains open to accrual (66 of 105 patients have been enrolled as of 1/17/2020). Clinical trial information: NCT03285321. Research Sponsor: Bristol-Myers Squibb.

9011 Poster Discussion Session; Displayed in Poster Session (Board #204), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Atezolizumab plus stereotactic ablative therapy for medically inoperable patients with early-stage non-small cell lung cancer. *First Author: Karen Kelly, University of California Davis Comprehensive Cancer Center, Sacramento, CA*

Background: Stereotactic ablative radiation therapy (SABR) is the standard-of-care for medically inoperable, early stage non-small cell lung cancer (NSCLC), but regional and distant failures remain problematic. Based on our *in vivo* data showing synergy between radiation and immune checkpoint inhibitors (ICI) and the known efficacy and mild toxicity profile of ICI in NSCLC, we conducted a phase I study to determine the maximum tolerated dose of neoadjuvant, concurrent, and adjuvant atezolizumab with SABR for early stage NSCLC patients (pts). **Methods:** Eligible pts had histologically confirmed T1-3 NSCLC with at least one feature predictive of increased recurrence risk: diameter ≥1 cm, SUV ≥6.2 on PET, or moderately/poorly differentiated histology, were medically inoperable or refused surgery and had a Zubrod PS ≤2. Patients received 6 cycles of atezolizumab. A 3+3 dose finding design was employed with 3 dose levels: 3 mg/kg, 10 mg/kg, and 1200 mg flat dosing. SABR was delivered starting cycle 3 to 50 Gy over 4-5 fractions. Dose limiting toxicity (DLT) was assessed during the first 9 weeks. **Results:** 20 pts were enrolled, 15 pts in the dose finding and 5 pts at the recommended phase II dose (RP2D). Patient factors: Medlan age 77; 45% male, 85% smoking history, 85% PS 0-1 and 35% squamous. One pt on dose level 2 had a DLT – a grade 3 rash. Atezolizumab 1200 mg flat dosing was the RP2D. Grade 3 pneumonitis was not observed. Partial responses after 2 cycles were seen in 3/17 evaluable pts (18%) and 1 pt had a minor response. No patient progressed on treatment. PD-L1 expression was 0% 8/13 (62%), >1% - 50% 4/13 (31%), >50% 1/13 (8%) in pts with sufficient tissue. Of 5 pts with PD-L1 expression 3 (60%) were responders and 1 (12.5%) of 8 pts with 0% PD-L1 expression responded. Multi-plex Quantitative Immunofluorescence (QIF) using a T cell activation panel demonstrated to correlate with ICI response was performed on 9 samples (including 2 responders, 1 minor responder). The CD3 QIF score was > two-fold higher in the responders compared to non-responders, and the levels of proliferating and activated T cells were likewise > two-fold higher. Comprehensive stool and serial blood analyses have been completed. Correlative endpoints will be reported along with additional efficacy outcomes. **Conclusions:** Atezolizumab plus SABR is feasible, safe and shows an efficacy signal in medically inoperable early stage NSCLC. This combination will be tested in a randomized phase III trial SWOG/NRG S1914. Funding: This work was supported by the DOD CDMRP W81XWH-15-2-0063 and Genentech. Clinical trial information: NCT02599454. Research Sponsor: DEPARTMENT OF DEFENSE - CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAM, Pharmaceutical/Biotech Company.

9012 Poster Discussion Session; Displayed in Poster Session (Board #205), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

***KEAP1/NFE2L2* mutations to predict local recurrence after radiotherapy but not surgery in localized non-small cell lung cancer.** *First Author: Michael S Binkley, Stanford University School of Medicine, Stanford, CA*

Background: Tumor genotyping in localized non-small cell lung cancer (NSCLC) is not broadly performed due to lack of actionable associations of mutations with treatment or outcome. We sought to identify recurrent mutations in localized NSCLC that are associated with local recurrence (LR) after radiotherapy (RT) or surgery. **Methods:** We identified consecutive patients with NSCLC treated with chemoradiotherapy (CRT), stereotactic ablative radiotherapy (SABR) or surgery from 2009-2018 at our institution with stage IA1-IIIC NSCLC who had genotyping performed on tumor tissue using a targeted gene panel. Our primary objective was to identify somatic tumor mutations that predicted LR after RT but not surgery. We also performed functional screening assays by expressing open reading frame constructs harboring patient-derived mutations in knock-out cell lines generated by CRISPR-Cas9 and evaluating effects on in vitro radioresistance. **Results:** We identified 232 consecutive patients with localized NSCLC (87.1% adenocarcinoma, 10.3% squamous, 2.3% other) who received tumor biopsy or resection specimen and underwent tumor genotyping. 47 patients with locally advanced NSCLC received CRT, 50 patients with early stage NSCLC received SABR, and 135 patients with early stage NSCLC underwent surgical resection. Of all recurrent mutations ($>$ 5% mutation frequency), only mutations in Kelch-like ECH-associated protein 1 (*KEAP1)* or Nuclear Factor Erythroid 2-Related Factor 2 (*NFE2L2)* genes *(K/N^{MUT})* were significantly associated with LR after CRT or SABR, with 2-year LR in the combined RT cohort of 42.4% for K/N^{MUT} versus 12.5% for wildtype (P = 0.005). Furthermore, K/N^{MUT} were present in nearly half of all LR events. Strikingly, there was no significant difference in LR for K/N^{MUT} tumors following CRT versus SABR (P = 0.47). Local recurrence was rare for patients who received surgery (n = 2) and was not associated with *K/N* mutation status (P = 0.60). Functional evaluation by expression of *K/N* mutations in knock-out cell lines revealed that LR only occurred in patients with mutations that induced radioresistance (i.e. pathogenic) but not passenger mutations (P = 0.04). In contrast to genotyping, NFE2L2 target gene expression analysis via RNA-seq did not predict LR (P = 0.93). **Conclusions:** Our findings suggest that *KEAP1/NFE2L2* mutations are a predictive biomarker of clinical radioresistance and a dominant cause of LR after RT. Genotyping for *KEAP1/NFE2L2* mutations could therefore facilitate treatment personalization in localized NSCLC. Research Sponsor: U.S. National Institutes of Health.

9013 Poster Discussion Session; Displayed in Poster Session (Board #206), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase II trial of atezolizumab and bevacizumab in patients with relapsed/refractory and unresectable malignant peritoneal mesothelioma. *First Author: Kanwal Pratap Singh Raghav, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Malignant peritoneal mesothelioma (MPeM) is an orphan malignancy. No recommended/FDA approved therapies exist for salvage treatment beyond first-line platinum and pemetrexed based chemotherapy. While immune checkpoint inhibition has shown preliminary efficacy in mesotheliomas, data and efficacy is limited in MPeM patients (pts) [objective response rate (ORR) ~ 11%; median progression-free survival (mPFS) ~ 4 months (m); median overall survival (mOS) ~ 11 m]. We aimed to prospectively assess the safety and efficacy of combined anti-PD1 (atezolizumab) and VEGF (bevacizumab) blockade (AtezoBev) in pts with MPeM. **Methods:** In this phase 2 study, eligible pts with histologically confirmed MPeM, ECOG PS 0-1, and prior platinum and pemetrexed treatment were treated with 1200 mg of atezolizumab and 15 mg/kg of bevacizumab IV every 21 days until disease progression, unacceptable toxicity, or withdrawal. Primary endpoint was confirmed ORR by RECIST 1.1 by independent radiology review. Duration of response (DOR), PFS and OS were prespecified secondary endpoints. **Results:** Among 20 enrolled pts (3/2017 - 2/2019), median age was 63 (range, 33-87) years, 12 (60%) were female, 12 (60%) had PS 0, and 2 (10%) had biphasic MPeM. Among 20 evaluable pts (median cycles 14), confirmed ORR was 35% (7 pts; 95% CI: 15.4-59.2) (median DOR 8.8 m). Responses were ongoing in 5/7 (71.4%) pts at data cutoff. The median follow-up was 20.5 months. Six deaths were observed during follow-up, and the 1-year OS was 79% (95% CI: 52 – 91) (median OS ~ NR). Median PFS was estimated as 17.6 m (95% CI: 9.1 – NR). The 1-year PFS was 54% (95% CI: 28 – 74). Grade 3 (no grade 4/5) treatment-emergent adverse events occurred in 10 (50%) pts; most common being hypertension (40%) and anemia (10%). Two (10%) pts had grade 3 immune-related adverse events. Translational studies are ongoing. **Conclusions:** AtezoBev showed promising and durable efficacy in relapsed/refractory MPeM with acceptable safety profile. Ongoing multiomic analyses of pre and on-treatment tissue/liquid biopsies obtained on all these pts will provide additional insight into mechanisms and biomarkers of response and resistance. Clinical trial information: NCT03074513. Research Sponsor: Genentech Inc., MD Anderson Cancer Center

9014 Poster Discussion Session; Displayed in Poster Session (Board #207), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

PIT-1: Randomized phase II trail of pemetrexed-cisplatin plus bevacizumab or concurrent thoracic radiation therapy followed by surgery in stage IIIA (N2) nonsquamous non-small cell lung cancer. *First Author: Kazuya Takamochi, Department of General Thoracic Surgery, Juntendo University School of Medicine, Tokyo, Japan*

Background: PIT-1 (Personized Induction Therapy-1) is a multicenter, open-label, randomized phase II study using selection design of platinum doublet chemotherapy plus angiogenesis inhibitor or concurrent thoracic radiation therapy (TRT) as induction therapy followed by surgery in patients with stage IIIA (N2) nonsquamous non-small cell lung cancer (NSCLC) to investigate the efficacy and safety of these treatment strategies. **Methods:** Patients with stage IIIA (pathologically proven N2) nonsquamous NSCLC randomly received (1:1) induction therapy consisting of pemetrexed (500 mg/m^2) and cisplatin (75 mg/m^2) plus bevacizumab (15 mg/kg) intravenously every 3 weeks for three cycles (arm A) or concurrent TRT (45 Gy in 25 fractions) (arm B) followed by surgery. The primary endpoint was 2-year progression-free survival (PFS) rate and key secondary endpoints included overall survival (OS), the objective response rate (ORR) as defined by the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, the pathological complete remission (pCR) rate, feasibility and toxicity. **Results:** Eighty-eight patients were randomly assigned (each arm, n = 44) between October 2013 and June 2017 and 82 (arm A, n = 42; arm B, n = 40) were treated. Patient demographics were balanced between the two arms. The percentage of patients who received induction therapy followed by surgery was 88.1% (37/42) in arm A and 92.5% (37/40) in arm B. The complete resection rate was 81.1% (30/37) in arm A, and 91.9% (34/37) in arm B. The 2-year PFS rate was 36.8% (95% CI: 22.4-51.2) in arm A, and 50.0% (95% CI: 33.8-64.2) in arm B. The 2-year OS rate was 80.5% (95% CI: 64.7-89.7) in arm A, and 80.0% (95% CI: 64.0-89.5) in arm B. The ORR was 50.0% (21/42) in arm A and 60.0% (24/40) in arm B. The pCR rate was 8.1% (3/37) in arm A and 10.8% (4/37) in arm B. Grade 3 or 4 toxicities occurred during induction therapy in 35.7% of the patients in arm A and 22.5% of the patients in arm B. Grade 3 or 4 surgical complications occurred in 21.4% of the patients in arm A and 20.0% of the patients in arm B. Although no fatal toxicity was observed during induction therapy in either arm, two patients in arm A died after surgery due to bronchopleural fistula. **Conclusions:** The 2-year PFS rate in arm B was higher than that in arm A. Fatal surgical complications were only observed in arm A. Therefore, we chose pemetrexed-cisplatin plus concurrent thoracic radiation therapy as the investigational induction treatment strategy for a future phase III study. Clinical trial information: 000011941. Research Sponsor: None.

9016 Poster Discussion Session; Displayed in Poster Session (Board #209), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

SAKK 16/14: Anti-PD-L1 antibody durvalumab in addition to neoadjuvant chemotherapy in patients with stage IIIA(N2) non-small cell lung cancer (NSCLC)—A multicenter single-arm phase II trial. *First Author: Sacha Rothschild, Department of Medical Oncology, University Hospital Basel, Basel, Switzerland*

Background: For patients (pts) with resectable stage IIIA(N2) non-small cell lung cancer (NSCLC) neoadjuvant chemotherapy (chemo) with 3 cycles cisplatin (cis)/docetaxel (doc) followed by surgery is an accepted standard of care leading to a 1-year (yr) event-free survival (EFS) of 48% and a 5-yr overall survival (OS) of 37%. PD-1/PD-L1 inhibitors have recently shown to lead to high response rates in resectable NSCLC. **Methods:** SAKK 16/14 is an open-label single-arm phase II study including 68 pts with resectable NSCLC stage IIIA(N2) (T1-3 N2 M0), irrespective of histological subtype, genomic aberrations or PD-L1 expression status. Neoadjuvant treatment consisted of 3 cycles of cis 100 mg/m^2 and doc 85 mg/m^2 q3w followed by 2 cycles of durvalumab 750 mg q2w. Durvalumab was continued after surgery q2w for 1 yr. The primary endpoint is EFS at 1 yr. The statistical hypothesis is to improve EFS at 1 yr from 48% based on the SAKK 16/00 study to 65%. Here, we report the primary endpoint and response data from 67 evaluable pts included in the study. **Results:** 68 pts were included from 06/16 to 01/19 and 67 pts (35 males, 32 females) were evaluable. Median age was 61 yrs (range, 41-74). 52 pts (77.6%) had a WHO PS of 0. 95.5% were current or former smokers. The majority of tumors were adenocarcinoma (55.2%) followed by squamous cell histology (32.8%). Clinical stage T1, T2 and T3 were present at diagnosis in 22.4%, 49.3% and 28.4%, respectively. 81.1% of pts underwent resection. The main reason for not undergoing surgery was disease progression (33.3%). Pneumonectomy was performed in 5 pts (9.1%), 43 pts underwent lobectomy and 7 pts bilobectomy. 30-day postoperative mortality was observed in one patient (1.8%). One patient died due to a bleeding complication after surgery most likely not related to neoadjuvant therapy. Radiographic response was 44.8% (95%CI: 32.6-57.4) after neoadjuvant chemo and 59.7% (95%CI: 46.4-71.9) after additional neoadjuvant immunotherapy. 1-yr EFS was 73.3% (90%CI: 62.5-81.4). Results for pathologic remission rate as well as correlation with PD-L1 status will be presented during the meeting. **Conclusions:** We report on treatment outcomes of the largest cohort of pts with resectable stage IIIA(N2) NSCLC receiving perioperative immune checkpoint inhibitor therapy. The addition of perioperative durvalumab to standard of care cis/doc is safe and leads to a high response rate and a very encouraging 1-yr EFS rate that appears substantially higher than with chemo alone. Clinical trial information: NCT 02572843. Research Sponsor: AstraZeneca, Other Foundation.

9017 Poster Discussion Session; Displayed in Poster Session (Board #210), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The anti-disialoganglioside (GD2) antibody dinutuximab (D) for second-line treatment (2LT) of patients (pts) with relapsed/refractory small cell lung cancer (RR SCLC): Results from part II of the open-label, randomized, phase II/III distinct study. *First Author: Martin Edelman, Fox Chase Cancer Center, Philadelphia, PA*

Background: Although SCLC is highly responsive to initial therapy, most pts relapse < 1 y. Topotecan (T) and irinotecan (I) are used in 2LT of SCLC; however, treatment response is low: ≤10-25% and median survival is ~4-5 months. Preclinical studies support GD2 as an SCLC target. This study evaluated the combination of D+I vs. I alone or T alone in 2LT of SCLC pts. **Methods:** Pts with RR SCLC, Eastern Cooperative Oncology Group 0-1, were randomized 2:2:1 to receive D 16-17.5 mg/m^2 intravenously (IV) plus I 350 mg/m^2 IV (Day 1 q21d), I 350 mg/m^2 IV (Day 1 q21d), or T 1.5 mg/m^2 IV (Days 1-5 q21d). Randomization was stratified by duration of response to prior platinum therapy. Primary endpoint was overall survival (OS) in pts treated with D+I vs. I alone and was analyzed using stratified log-rank test and COX regression. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and clinical benefit rate, ORR + stable disease (CBR). Safety was assessed. **Results:** 471 pts were randomized to D+I (n = 187), I (n = 190), or T (n = 94). Baseline characteristics were balanced (24.2% women; mean ± SD age 61.6 ± 8.7 y). Median OS was similar in pts receiving D+I (6.9 [3.5,10.9] months) vs. I alone (7 [3.6,13.1] months) (HR [95% CI]: 1.12 [0.9,1.4]; P = 0.3132) or T alone (7.4 [3.8,12.8] months) (HR [95% CI]: 1.05 [0.8,1.37]; P = 0.7233). Median PFS was similar in pts receiving D+I (3.5 [1.5,6.2] months) vs. I (3 [1.4,5.7] months) or T (3.4 [1.6, 6.1] months) alone. ORR was similar in pts receiving D+I (17.1%) vs. I (18.9%) or T (20.1%) alone. CBR was similar in pts receiving D+I (67.4%) vs. I (58.9%) or T (68.1%) alone. Grade 3 or higher adverse events were experienced by 77% D+I, 69.5% I, and 86.4% T pts. **Conclusions:** Treatment with D+I was not superior to established 2LT for RR SCLC. Exploratory analyses are ongoing to evaluate GD2 expression in circulating tumor cells, select protein biomarkers, and any correlative impact on observed response. Clinical trial information: NCT03098030. Research Sponsor: United Therapeutics.

9018 Poster Discussion Session; Displayed in Poster Session (Board #211), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Molecular subtypes and clinical outcomes to initial systemic treatment in patients with small cell lung cancer. *First Author: Wei-Chu Victoria Lai, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Investigators have proposed that differential expression of the transcription regulators ASCL1 and NeuroD1 can be used to define molecular subtypes of small cell lung cancers (SCLCs). Here we evaluate SCLC subtypes based on ASCL1 and NeuroD1 expression in patients (pts) treated with first-line (1L) chemotherapy profiled with targeted next-generation sequencing (NGS). **Methods:** We used NGS (MSK-IMPACT) to profile tumors from pts with SCLCs. We performed IHC to assess ASCL1 (A) or NeuroD1 (N). Objective response rate (ORR) to therapy was determined using RECIST. PFS and OS were analyzed using Kaplan-Meier. **Results:** 281 pts with SCLCs were profiled with NGS (102 LS-SCLC; 179 ES-SCLC). Most frequently mutated genes were *TP53* (90%), *RB1* (68%), *KMT2D* (22%), *NOTCH1* (15%), *FAT1* (14%), *PTPRD* (12%). Mutations in *BIRC3*, *FOXL2*, *TENT5C*, *TET1*, *NRAS*, *KIT*, *TSHR*, *ESR1* were enriched in ASCL1-/NeuroD1+ (A-/N+), and mutations in *KMT2D* and *EP300* were enriched in A-/N- ($p<0.05$). Copy number alterations in *WWTR1*, *ATR*, *IKZF1*, *PALB2*, *PIK3CB* were enriched in A-/N+ ($p<0.05$). IHC for ASCL1 and NeuroD1 was performed on 78 samples: 11 A-/N-, 32 A+/N-, 4 A-/N+, 31 A+/N+. Overall survival at 1 year based on subtype was 25% in A-/N- (2/9), 60% in A-/N+ or A+/N- (13/32), and 55% in A+/N+ (10/25). For the 10 pts who survived 2 years, 5 were A+/N- and 5 were A+/N+. 146 pts treated with 1L platinum had RECIST-evaluable disease. ORR was 75% (110/146; 95% CI 68-82%). Median PFS was 7 months with CR/PR and 3.5 months with SD/PD (HR 0.32; 95% CI 0.18-0.56). Median OS was 17 months with CR/PR and 11 months with SD/PD (HR 0.55; 95% CI 0.34-0.9). Mutations in *RUNX1*, *EPHA7*, *CDKN2A*, *FLT1* and copy number alterations in *FGFR1*, *CCND1* were enriched in patients with SD/PD ($p<0.05$). PFS rate at 6 months was 25% in A-N- (1/4), 60% in A-/N+ or A+/N- (9/15), and 55% in A+/N+ (6/11). For the 7 pts who survived 2 years, 3 were A+/N- and 4 were A+/N+. **Conclusions:** Molecular subtypes defined by ASCL1 and NeuroD1 encompass molecular characteristics that may predict patient outcomes. Further investigation is needed to delineate the underlying biological differences among the various subtypes to help define therapeutic vulnerabilities of each subtype of SCLC. Completion of IHC for ASCL1, NeuroD1 and additional key transcription factors POU2F3 and YAP1 are in progress for the entire cohort. WES and RNA sequencing are occurring in parallel and will be correlated with IHC results and clinical outcomes. Research Sponsor: None.

9019 Poster Discussion Session; Displayed in Poster Session (Board #212), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

YAP1 positive small-cell lung cancer subtype is associated with the T-cell inflamed gene expression profile and confers good prognosis and long term survival. *First Author: Taofeek Kunle Owonikoko, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: The dominant expression of transcription factors ASCL1, NeuroD1, YAP1 or POU2F3 characteristically defines four small cell lung cancer (SCLC) subtypes (SCLC-A, SCLC-N, SCLC-Y and SCLC-P). The clinical validation and biological relevance of these emerging SCLC subtypes is currently lacking. **Methods:** Using the Illumina TruSeq RNA Exome Kit, we generated RNA-Seq data from 61 cases of SCLC and pulmonary carcinoid to interrogate gene expression differences in SCLC subtypes as well as in survival outliers (top and bottom decile) matched for clinically relevant prognostic factors and treatment. We also assessed YAP1 protein expression in a blinded fashion by immunohistochemistry in 130 SCLC cases. **Results:** We successfully classified 68% of SCLC into one of the four SCLC subtypes whereas 81.5% of carcinoids did not fit into any of these categories. GSEA for differentially expressed genes between outlier subgroups showed significant upregulation of interferon gamma and interferon alpha response genes in late survivors. Moreover, a previously validated 18-gene T-cell inflamed gene expression profile was upregulated in late survivors and in the SCLC-Y subtype. Furthermore, the SCLC-Y subtype and late survivors showed higher expression of HLA gene family and reduced expression of cancer testis antigens. The median (95% CI) OS was 14 (4.3, 28.8), 16.7 (0.9, NA), 8.1 (2, 9.7) and 20.1 (0.6, 39.5) months respectively, for SCLC-A, N, P and Y subtypes. YAP-1 protein expression was positive in 17 of 130 (13%) SCLC cases. The majority of cases with positive YAP1 expression by immunohistochemistry, 12 of 17 cases (70.6%), were limited stage SCLC at the time of original diagnosis. **Conclusions:** SCLC subtypes have clinical implication as predictive and prognostic biomarker. SCLC-Y subtype is enriched for T-cell inflamed phenotype and long term survival, and may predict for clinical benefit of immunotherapy. Research Sponsor: Novartis Oncology.

9020 Poster Session (Board #213), Fri, 8:00 AM-11:00 AM

Validation of tumor DNA in bronchial lavage as a diagnostic tool in lung cancer. *First Author: Sara Witting Christensen Witting Christensen Wen, Department of Oncology, Vejle Hospital, University Hospital of Southern Denmark, and Institute of Regional Health Research, University of Southern Denmark, Vejle, Denmark*

Background: Diagnosing lung cancer requires invasive procedures with risk of complications for the patient. The HOXA9 gene is highly methylated in lung cancer, and methylated tumor DNA (meth-tDNA) in bronchial lavage has previously shown potential as a diagnostic biomarker. The aim of the present study was to validate these preliminary results. **Methods:** Patients were referred by the general practitioner on suspicion of lung cancer. The Danish diagnostic package includes chest and abdominal CT scan, bronchoscopy, blood tests, and histopathological or cytological verification. Twelve ml lavage fluid was collected at bronchoscopy for analysis of meth-tDNA based on droplet digital PCR according to our published method. A positive test was defined as ≥ 4 droplets containing meth-tDNA and a ratio between HOXA9 and Albumin of > 0.15%. The analysis was performed blinded to clinical data and meth-tDNA status was compared with the final diagnosis. **Results:** The study population was 204 consecutively enrolled patients. The material consisted of a discovery cohort (n = 105, presented at ASCO 2019) used for establishing the cut-points, and a validation cohort (n = 99). Six were excluded from analysis due to malignancy other than lung cancer and one due to failed analysis. In the discovery cohort, the sensitivity was 68.7% (95% CI 56.2-79.4%), specificity 88.2% (95% CI 72.6-96.7%), and positive predictive value (PPV) 92.0% (95% CI 80.8-97.8%). In the validation cohort, the same values were 76.9% (95% CI 63.2-87.5%), 77.3% (95% CI 62.2-88.5%), and 80.0% (95% CI 66.3-90.0%), respectively. Analyzing the entire patient material (n = 197) the sensitivity, specificity, and PPV were 72.3% (95% CI 63.3-80.1%), 82.1% (95% CI 71.7-89.8%), and 86.0% (95% CI 77.6-92.1%), respectively. The false positive samples were equally distributed among patients with cryptogenic organizing pneumonia, granulomatous inflammation, and acute inflammatory disease. The false negative samples were mainly from patients with peripheral tumor, no radiologically detectable tumor, and mesothelioma. **Conclusions:** Meth-tDNA in bronchial lavage holds potential as a supplementary tool in the diagnosis of lung cancer with a clinically relevant sensitivity and specificity. Routine clinical application awaits further validation in a clinical trial. Research Sponsor: The grant for early detection of cancer, Region of Southern Denmark, Denmark.

meth-tDNA status	Lung cancer	No lung cancer
Discovery: Positive	46	4
Discovery: Negative	21	30
Validation: Positive	40	10
Validation: Negative	12	34
Total: Positive	86	14
Total: Negative	33	64

9022 Poster Session (Board #215), Fri, 8:00 AM-11:00 AM

Role of adjuvant chemotherapy in patients with pathological stage I NSCLC with high-risk features. *First Author: Lubina Arjyal, Gundersen Health System, La Crosse, WI*

Background: Lobectomy is the current standard of care for patients with stage I non-small cell lung cancer (NSCLC). There is a lack of prospective data on the benefit of adjuvant chemotherapy (CT) in patients with negative margins but with high-risk features: lympho-vascular invasion (LVI) or visceral pleural invasion (VPI). We aimed to investigate the benefit of adjuvant CT in patients with pathological stage I NSCLC with high-risk features. **Methods:** The 2016 National Cancer Database was queried to identify patients with pathological stage I NSCLC (8^{th} edition AJCC staging) diagnosed from 2010-2015 who received lobectomy/pneumonectomy with clear surgical margins. Patients were stratified into high risk (tumor size ≥2 cm with LVI and/or VPI) or low risk group. Multivariate Cox proportional hazards regression and propensity score matched Kaplan-Meier survival analysis were used to compare overall survival between those who received adjuvant CT and those who did not. **Results:** 34,556 patients were identified with 1114 (3.2%) receiving adjuvant CT. On multivariate Cox regression analysis, high risk tumors (hazard ratio [95% confidence interval] = 1.31 [1.25-1.38]) and lack of adjuvant chemotherapy (1.25 [1.09-1.44]) were associated with worse overall survival (OS). Additionally, male sex, age ≥ 60 years, higher comorbidity burden, lack of insurance, low facility volume, low median income, non-squamous histology were associated with worse OS. After propensity score matching, Kaplan-Meier survival analysis of the high risk subgroup (n = 2923) showed a significant difference in overall survival (OS) between those who received adjuvant CT (n = 1032, 5 year OS, 74.7%; 95% CI, 70.9%-78.0%) and those who did not (n = 1891, 5 year OS, 66.9%; CI, 63.9%-69.6%; p = 0.0002). In patients with no high risk factors for recurrence (n = 384), OS was not significantly different between the patients who received adjuvant CT (n = 78, 5 year OS, 75.8%; CI, 61.3%-85.5%) and those who did not receive adjuvant CT (n = 306, 5 year OS, 77.1%; CI, 70.0%-82.7%; p = 0.3). **Conclusions:** Our study showed better survival with adjuvant CT in patients with pathological stage I NSCLC who have tumor size greater than 2 cm, LVI and/or VPI. Research Sponsor: None.

9023 Poster Session (Board #216), Fri, 8:00 AM-11:00 AM

Circulating tumor DNA (ctDNA) analysis predicts recurrence following surgery in patients with stage I-IIIA non-small-cell lung cancer (NSCLC): Results of GASTO1035 and GASTO1018. *First Author: Si-Yu Wang, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: Circulating tumor DNA can be detected in the plasma and serum of patients with solid tumors and has emerged as a noninvasive biomarker for dynamically monitoring tumor. Postsurgical ctDNA analysis of early-stage NSCLC may identify patients at high risk of recurrence and facilitate early intervention and personalized cancer therapy. **Methods:** These studies recruited 123 patients with newly diagnosed resectable stage I-IIIA NSCLC. Preoperative and postoperative plasma and postoperative tissue samples were subjected to next-generation sequencing (Nanjing Shihe Jiyin Biotechnology Inc.) using a 425 cancer-related genes panel. Peripheral blood samples were collected before surgery, postoperatively within 1 month, and every 3-6 months for up to 3 years. Plasma samples with at least 1 variants detected in tissue samples were defined as ctDNA positive. **Results:** After 4 exclusions, 119 eligible patients were enrolled from June 2016 to February 2019. Presurgical ctDNA was detectable in 31 of 117 (26.5%) patients and was associated with inferior recurrence-free survival (HR, 3.90, 95% CI, 1.44-10.58, P = 0.004). Similarly, ctDNA was detected in 13 of 116 (11.2%) of the first postsurgical samples and was associated with shorter RFS (HR, 3.54, 95% CI, 1.22-10.23, P = 0.002). During surveillance after surgery, ctDNA-positive patients (38/119, 31.9%) were more than 9 times more likely to experience disease recurrence than ctDNA-negative patients (HR, 9.17, 95% CI, 2.60-32.42, P < 0.001). Serial ctDNA detection preceded radiologic disease recurrence by a median lead time of 4.23 months (95% CI, 0.91-7.54 months). We also observed a positive correlation between the ctDNA detection rate and the disease stage. **Conclusions:** These results suggest that detection of ctDNA before and after surgery is associated with the identification of a high risk of disease recurrence of resectable NSCLC. Perioperative ctDNA analyses identify disease recurrence earlier than standard-of-care radiologic imaging, and thus could facilitate personalized cancer treatment at early time points. Clinical trial information: NCT03465241 and NCT03172156. Research Sponsor: None.

9024 Poster Session (Board #217), Fri, 8:00 AM-11:00 AM

Validation of 4-marker protein panel for the early detection of lung cancer using PLCO samples. *First Author: Johannes Fahrmann, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: We have previously demonstrated that a protein panel consisting of ProSFTPB, CEA, CA125 and CYFRA21.1 may improve lung cancer risk assessment and has potential to define eligibility for computed tomography screening. Herein, we aimed to validate the classifier performance of the 4-marker protein panel using pre-diagnostic serum samples from the PLCO cohort. We additionally explored the additive value of diacetylspermine (DAS) with the 4-marker protein panel for identifying lung cancer cases. **Methods:** ProSFTPB, CEA, CA125 and CYFRA21.1 levels were measured in baseline sera of 537 lung cancer cases (76 SCLC/461 NSCLC) diagnosed within 6 years of baseline blood draw and 3772 cancer-free controls using bead-based immunoassays. DAS was measured using ultrahigh performance liquid chromatography mass spectrometry. Samples were analyzed in a double-blinded randomized fashion. **Results:** Overall classification performance (receiver operating characteristic area under the curve (ROAUC)) of the 4-marker panel for delineating lung cases diagnosed within 1 year and 1 to 2 years of baseline blood draw from cancer-free controls was 0.78 (95% CI: 0.74-0.82) and 0.73 (95% CI: 0.68-0.78), respectively. Classification performances of the 4-marker panel amongst lung cancer cases diagnosed within 1 year of baseline blood draw stratified into adenocarcinoma, squamous cell carcinoma and small cell lung cancer subtypes yielded ROAUCS of 0.78 (95% CI: 0.72-0.85), 0.76 (95% CI: 0.69-0.83) and 0.79 (95% CI: 0.68-0.90), respectively. Sub-analyses adjusting for smoking status yielded comparable ROAUC point estimates. Comparison of the 4-marker performance amongst non-NLST and NLST eligible lung cancer patients diagnosed within 1 year of baseline blood draw in comparison to matched cancer-free controls resulted in ROAUCs of 0.71 (95% CI: 0.63-0.79) and 0.74 (95% CI: 0.69-0.80), respectively. Analyses evaluating the additive classifier performance of serum DAS with that of the 4-marker protein panel revealed statistically significant improvement (McNemar Exact Test 2-sided $p < 0.05$) in sensitivity at high specificity derived from youden index for SCLC and squamous cell carcinoma cases diagnosed within 2 years from baseline blood draw, respectively, in comparison to the 4-marker protein panel alone. **Conclusions:** We have validated the performance of the 4-marker panel for early detection of lung cancer in the PLCO pre-diagnostic cohort. We further demonstrate that DAS can complement the 4-marker protein panel and identify more SCLC and squamous cell carcinoma cases. Research Sponsor: U.S. National Institutes of Health.

9025 Poster Session (Board #218), Fri, 8:00 AM-11:00 AM

Reliable detection of the presence of pulmonary carcinoma on whole-slide images by a deep learning model. *First Author: Gouji Toyokawa, Department of Thoracic Surgery, Clinical Research Institute, National Hospital Organization, Kyushu Medical Center, Fukuoka, Japan*

Background: Lung cancer is one of the leading causes of cancer-related death worldwide, and its histopathological diagnosis is crucial for deciding on optimum treatment strategies. Recently, artificial intelligence (AI) models have been widely shown to be useful in various medical fields, particularly image and pathological diagnoses; however, AI models for the pathological diagnosis of pulmonary lesions that have been validated in large-scale test sets are yet to be seen. **Methods:** We trained a convolution neural network based on the Efficient Net B3 architecture to classify carcinoma from whole slide images (WSIs) using a training dataset of 3640 images. WSI diagnoses were available. We used a transfer learning approach, in which the starting weights were obtained from a pre-trained model on ImageNet. The model was then trained on our dataset using multiple instance learning, a semi-supervised learning approach. To classify a WSI, the model was applied in a sliding window fashion with an input tile size of 512x512 and a stride of 256. The maximum probability was then used as a WSI diagnosis. **Results:** We evaluated our model on a total of 2680 WSIs originating from five independent sources (two hospitals in Japan and three public datasets from around the world). The model achieved a Receiver Operator Curve Area Under the Curves (ROC AUCs) of 0.974, 0.974, 0.996, 0.988, and 0.981, respectively. **Conclusions:** We successfully established a reliable AI model for differentiating between lung carcinoma and non-neoplasm with a high ROC AUC on five independent test sets. If used in clinical practice, our model could help reduce the burden on pathologists and be useful for diagnosing pulmonary lesions in areas in which there are shortages of pathologists. Further prospective multicenter studies are warranted in order to validate the results obtained in the current study. Research Sponsor: None.

9026 Poster Session (Board #219), Fri, 8:00 AM-11:00 AM

Role of T0 status in overall survival for unresectable stage III non-small cell lung cancer. *First Author: Takefumi Komiya, Parkview Cancer Institute, Fort Wayne, IN*

Background: Occult (T0) primary non-small cell lung cancer (NSCLC) with mediastinal involvement is a known but rare clinical condition. Its prognosis has not been evaluated well in the literature. **Methods:** Using National Cancer Database (NCDB), cases diagnosed between 2004 and 2016 with unresectable clinical stage III NSCLC with N2 or N3 involvement were selected and assigned to T0 or T1-4 group according to AJCC staging version 6th or 7th. Clinical demographics including use of chemotherapy/immunotherapy in first course of treatment were collected. As validation, independent data using Surveillance, Epidemiology, and End Results Program (SEER) was analyzed accordingly. Survival analyses were conducted using Kaplan-Meier and log-rank tests. **Results:** A total of 458 and 84,263 cases met criteria for unresectable, N2/N3 stage III NSCLC with T0 and T1-4 status, respectively. T0 status was associated with younger age, recent diagnosis, adenocarcinoma histology, N3, and use of chemotherapy. Overall survival (OS) was improved in T0 over T1-4 group ($p < 0.0001$) with a five-year survival rate of 30.5% and 12.7%, respectively, with a validation with multivariate proportional hazard models. Propensity score matching analyses using all 458 patients in each group demonstrated a significant difference in OS ($p < 0.0001$). The difference was also significant in a subset of those who have undergone chemoradiation ($p < 0.0001$). Independent analysis using SEER data confirmed its superior survival of T0 over T1-4 with a five-year survival rate of 35.3% and 13.5%, respectively. **Conclusions:** Both NCDB and SEER analyses demonstrated better survival of T0 than T1-4 counterpart in the setting of unresectable stage III NSCLC, irrespective of chemotherapy status. This group may require a distinct assignment to new staging group after further investigation. Research Sponsor: None.

9027 Poster Session (Board #220), Fri, 8:00 AM-11:00 AM

Base excision repair (BER) inhibitor TRC 102 (Methoxyamine) combined with pemetrexed (PEM)-based chemo-radiation (CRT) for locally advanced non-squamous non-small cell lung cancer (NS-NSCLC): Results of a phase I trial. *First Author: Tithi Biswas, University Hospitals Seidman Cancer Center, Case Western Reserve University, Cleveland, OH*

Background: About 35% of all NSCLC presents with locally advanced disease and chemo-radiation results in 5-year OS of only ~31%. PEM-platinum combination is approved in stage IV NSCLC and has similar efficacy to platinum-etoposide in stage 3 NSCLC and a favorable toxicity profile (Proclaim trial). TRC102 is an oral small molecule inhibitor of BER. TRC102 potentiates the cytotoxicity of antimetabolites and alkylators and reverses chemotherapy resistance by rapidly and covalently binding to chemotherapy-induced abasic sites in DNA. TRC102 increased radio-sensitization by PEM of NSCLC cell lines and H1299 and A549 xenografts. **Methods:** Between 11/2015 and 5/2019, 15 patients were enrolled in a 3+ 3 design: 12 with stage III and 3 with oligometastatic stage IV NS-NSCLC. The primary objective was to determine dose-limiting toxicities (DLT's) and recommended Phase 2 dose (RP2D) of TRC102 in combination with PEM, cisplatin and radiotherapy. Secondary objectives were to assess toxicity, tumor response and PFS at 6 months. Based on pre-clinical data, PEM-TRC102 was given on day 1, and cisplatin/radiotherapy was initiated on day 3. This schedule was duplicated on day 21 and day 23 of the second cycle. After completion of radiotherapy, two additional cycles of PEM-cisplatin were given. Toxicities were assessed by NCI CTACAE version 4 and 5. **Results:** Median patient age was 69 years (45-79) and median follow up was 16.6 months (3.1-38.6). There were no DLTs or grade 5 toxicity. Hematologic and GI toxicities were the most common adverse events (Table) and radiation pneumonitis was not seen. The RP2D of TRC102 was 200 mg when given with cisplatin/radiotherapy and PEM. Of 15 evaluable patients, 3 had CR (20%) and 12 had PR (80%). The 2-year PFS rate was 49%. **Conclusions:** PEM-TRC102 combined with cisplatin/radiotherapy in non-squamous NSCLC was safe and well tolerated, and did not cause safety signals beyond those expected from CRT. Preliminary response data and PFS in this cohort was encouraging. A phase 2 trial, integrating post-CRT immunotherapy with this aggressive DNA-damaging regimen is warranted. Clinical trial information: NCT02535325. Research Sponsor: Lucille and Robert Gries Endowed Fund, the Vincent K. Smith Fund, and Early Phase Clinical Research Support (EPCRS) P30 Funding at the Case Comprehensive Cancer Center.

	Grade 1	Grade 2	Grade 3	Grade 4	Total (n = 15)
Hematological toxicity					
Anemia	6	4	3		13
Lymphopenia		3	7	3	13
Decreased neutrophil count			6	1	7
Decreased Platelet count	10	2			12
GI toxicity					
Nausea	5	6			11
Vomiting	1	3			4
Dehydration		3	2		5
Esophagitis	1	7			8
Fatigue	1	3	1		5
Anorexia	2	2	3		7
Weight Loss			3		3
Pulmonary Toxicity					
Pneumonitis					0
Cough	1	2			3
Skin toxicity					
Dermatitis	2	2			4

9030 Poster Session (Board #223), Fri, 8:00 AM-11:00 AM

Detection of early-stage lung cancer by exhaled volatile organic compounds using a high-pressure photon ionization time-of-flight mass spectrometry. *First Author: Mantang Qiu, Peking University People's Hospital, Beijing, China*

Background: Exhaled breath-based test is an attractive option for cancer detection due to its non-invasive nature. Exhaled volatile organic compounds (VOCs) are produced in various biochemical processes and might be sensitive tumor biomarkers. Here, we reported an exploratory study to investigate the performance of exhaled VOCs for detection of early-stage lung cancer using a high-resolution high-pressure photon ionization time-of-flight mass spectrometry (HPPI-TOFMS). **Methods:** Treatment-naïve patients with pulmonary nodules who received surgery at our department and without history of cancer were enrolled. Exhaled breath samples were collected before surgery and stored in Tedla bags. A CO_2 sensor was applicated during sample collection to ensure only "alveolar air" was collected. Exhaled samples were directly detected by HPPI-TOFMS, which has a resolution > 3000. Deep learning algorithm was used to build detection model based on HPPI-TOFMS data. **Results:** A total of 171 patients were included in this study, including 139 patients with lung cancer (114 of TNM stage I, 14 of stage II, 9 of stage III, and 2 of stage IV) and 32 patients with benign nodules. Mass spectrum peaks with $m/z <$ 500 detected by HPPI-TOFMS were retained and 32500 features were extracted from each exhaled breath samples. Based these extracted features, participants who were pathologically diagnosed as lung cancer could be discriminated from those with benign diseases with an accuracy of 96.19%, sensitivity of 96.43%, and specificity of 84.38%. Discrimination of lung cancer patients with lymph node metastasis (n = 12) from those without lymph node metastasis (n = 127) had an accuracy of 83.23%. **Conclusions:** Exhaled VOCs as detected by a high-resolution HPPI-TOFMS might be sensitive biomarkers for detection of early-stage lung cancer. Research Sponsor: None.

9031 Poster Session (Board #224), Fri, 8:00 AM-11:00 AM

CT and PET radiomic features associated with major pathologic response to neoadjuvant immunotherapy in early-stage non-small cell lung cancer (NSCLC). *First Author: Erica C. Nakajima, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

Background: An early biomarker of response to immunotherapy (IO) is needed urgently to identify the patients (pts) who will derive benefit. We reported the first clinical trial of neoadjuvant IO (nIO) in resectable non-small cell lung cancer (NSCLC) (NCT02259621). In this study, we investigated whether there was an association between MPR and radiomic features (RF) in [^{18}F]-fluorodeoxyglucose ([^{18}F]-FDG) PET and standard CT images obtained at baseline and after nIO in early stage NSCLC tumors. **Methods:** Prior to receiving neoadjuvant nivolumab or nivolumab/ipilimumab, patients with Stage I-IIIA NSCLC underwent two [^{18}F]-FDG PET-CTs and/or plain CTs: a baseline scan at enrollment (PRE), and after nIO (POST). After neoadjuvant treatment, tumors were resected and evaluated for MPR. Volumes of interest (VOIs) were drawn around primary tumors on the scans. Using our novel radiomic software, Imager-4D, VOIs were evaluated for 20 RFs assessing [^{18}F]-FDG standard uptake value (SUV) or Hounsfield unit (HU) heterogeneity and spatial distribution in PET and CT images respectively. The baseline, post-treatment, and percent change in RFs before and after nIO were compared between tumors with and without MPR. Wilcoxon test was used for the comparisons. **Results:** The PRE and POST scans of 24 pts were analyzed. All pts had PRE and POST CTs performed, and 17 pts had PRE and POST [^{18}F]-FDG PET-CT scans. 7 of 24 (29%) had MPR. In the CT scan analysis, HU-based RFs of voxel count, total volume, energy, entropy, homogeneity, contrast, and dissimilarity in POST CT scans each significantly association with MPR. In the PET scan analysis, SUV mean and voxel count RFs in the POST scans, and the percent change in the cluster shade RF between PRE and POST scans were significantly associated with MPR. **Conclusions:** Collectively, we identified a significant increase in heterogeneity in the POST CT images of NSCLC tumors that had MPR. This association may reflect increased T cell infiltration or tumor necrosis. In contrast, most [^{18}F]-FDG-based RFs did not distinguish MPR vs non-MPR tumors, although the sample size was limited. We will further investigate these HU-based RFs as non-invasive markers of response to IO in conjunction with pathologic markers of IO response and in a larger patient cohort. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

9032 Poster Session (Board #225), Fri, 8:00 AM-11:00 AM

The association between immune-related adverse events and efficacy outcomes with consolidation pembrolizumab after chemoradiation in patients with stage III NSCLC: an analysis from HCRN LUN 14-179. *First Author: Nikhil Shukla, Indiana University, Indianapolis, IN*

Background: Consolidation checkpoint inhibitor therapy (CPI) for up to 1 year following chemoradiation (CRT) is a current standard of care for pts with inoperable stage III NSCLC. However, some pts are not able to complete 1 year of CPI due to immune-related adverse events (irAES). In multiple retrospective studies, pts with stage IV NSCLC treated with CPI who experience irAEs generally receive fewer cycles of CPI without a significant detrimental effect on efficacy. The association between irAEs and outcomes with consolidation CPI after CRT has never been reported. Here we report the association between irAEs and efficacy outcomes from the HCRN LUN 14-179, a single-arm phase II trial of consolidation pembrolizumab following concurrent CRT in pts with unresectable stage III NSCLC. **Methods:** After completion of CRT eligible pts with stage III NSCLC without PD received pembrolizumab 200 mg IV q 3 wks for up to 1 yr. Demographics, disease characteristics, and number of cycles of pembrolizumab received were reported in pts who had any grade irAEs (except pneumonitis which included grade >2 only) [Group A] and those without irAEs (except grade 1 pneumonitis) [Group B]. Chi-square test (or Fisher's Exact test) were used for comparisons for categorical variables and Wilcoxon test for continuous variables. The Kaplan-Meier method was used to analyze time to metastatic disease (TMDD), PFS, and OS. A log-rank test was used to compare groups. **Results:** 92 eligible pts for efficacy analysis were enrolled from March 2015 to November 2016. 4 yr OS estimate for all pts is 46.2%. Any grade irAEs (except grade I pneumonitis) (n = 37 pts) included pneumonitis (18.5%), colitis (3.3%), increased creatinine (5.4%), elevated transaminases (3.3%), hyperthyroidism (7.6%), hypothyroidism (13.0%). Grade ≥ 2 irAEs (n = 32 pts) included pneumonitis (18.5%), hypothyroidism (10.8%), and colitis (3.3%). Group A/B: male (21/38), female (16/17), current or former smoker (35/52), stage IIIA (20/35), stage IIIB (17/20), non-squamous (21/30), squamous (16/25). Median number of pembrolizumab cycles received in Group A/B pts were 9 vs 15 (p = 0.0942) respectively. 4 yr efficacy endpoints in Groups A/B were TMDD 35.3% vs 41.3% (p = 0.83), PFS 27.8% vs 28.7% (p = 0.97), OS 43.5% vs 47.9% (p = 0.99), respectively. **Conclusions:** Despite receiving fewer cycles of consolidation pembrolizumab, pts who experienced any grade irAEs (excluding grade 1 pneumonitis) did not have significantly reduced efficacy outcomes. Clinical trial information: NCT02343952. Research Sponsor: Merck Sharp & Dohme Corp.

9033 Poster Session (Board #226), Fri, 8:00 AM-11:00 AM

Outcomes of patients with stage III non-small cell lung cancer (NSCLC) that harbor a *STK11* mutation. *First Author: Josiah An, University of Iowa Hospitals and Clinics, Iowa City, IA*

Background: *STK11* mutation ($STK11^m$) in patients with stage IV NSCLC is associated with inferior survival and poor response to immune check point inhibitors (ICI). The significance of $STK11^m$ in patients (pts) with stage III NSCLC treated with concurrent chemoradiation (CCRT) with and without consolidation ICI is unknown. **Methods:** Patient demographics, disease characteristics, treatment received and outcomes in pts with stage III NSCLC that harbor $STK11^m$ were retrospectively reviewed from 4 cancer centers. A cohort of pts with stage III NSCLC and wild type *STK11 (*$STK11^w$*)* from the University of Iowa served as a comparison group. SPSS version 25 was used for data analysis. **Results:** 75 pts with stage III NSCLC who had gene sequencing were included. 16/75 (21%) had $STK11^m$. The clinical characteristics for the 16 $STK11^m$ and 59 $STK11^w$ pts showed ($STK11^m$ vs. $STK11^w$): mean age: 58 vs. 64 yrs, non-squamous histology: 11/16 (69%) vs. 37/59 (63%), *KRAS* co-mutation: 6/16 (38%) vs. 11/59 (19%), *TP53* co-mutation: 9/16 (56%) vs. 15/59 (25%), PD-L1 ≥ 50%: 2/16 (13%) vs. 10/59 (17%), received CCRT 11/16 (69%) vs. 59/59 (100%) and consolidation ICI 6/16 (38%) vs. 17/59 (29%). Regarding the 6 $STK11^m$ pts who received ICI (4 pembrolizumab, 2 durvalumab), the median number of ICI infusions was 8 (range, 3-17) vs. 7 (range, 1-25) in the 17 pts with $STK11^w$ who received ICI (durvalumab). Progression free survival (PFS) for the $STK11^m$ vs. $STK11^w$ pts who received CCRT but not ICI was (4.2 vs. 34.3 months, respectively. P = 0.168), for the $STK11^m$ vs. $STK11^w$ pts who received CCRT and ICI was (11.3 vs. 17.5 months, respectively. P = 0.174), and for the $STK11^m$ vs. $STK11^w$ pts who received CCRT regardless of receiving ICI (11.3 vs. 32.9 months, respectively. P = 0.021). The median overall survival for $STK11^m$ pts (16 pts) was 25.5 months (95% CI, 13.7 to 37.2) while not yet reached for the $STK11^w$ group. **Conclusions:** In stage III NSCLC, $STK11^m$ was associated with inferior clinical outcomes. Larger studies are needed to identify the prognostic implications of $STK11^m$ in stage III NSCLC and whether ICI impacts survival for this subgroup. Research Sponsor: None.

9034 Poster Session (Board #227), Fri, 8:00 AM-11:00 AM

Evaluation of the incidence of pneumonitis in United States veterans with non-small cell lung cancer receiving durvalumab following chemoradiation. *First Author: Theodore Seth Thomas, Washington University, St Louis, MO*

Background: Locally advanced, unresectable non-small cell lung cancer is commonly treated with concurrent chemoradiation therapy (CRT). Durvalumab is a PD-L1 immune checkpoint inhibitor (ICI) administered following completion of CRT. Pneumonitis is a known toxicity of ICI therapy. In the landmark PACIFIC study the incidence of pneumonitis in patients receiving durvalumab was 33.9% (any grade) and 3.4% (grade 3/4) compared to placebo 24.8% and 2.6% (*Antonia et al, NEJM 2017)*. The incidence of pneumonitis is thought to be higher in real-world populations. This study evaluated the incidence of pneumonitis in a cohort of U.S. Veterans. **Methods:** Durvalumab recipients were identified using VA Informatics and Computing Infrastructure databases. Using pharmacy records we confirmed durvalumab and corticosteroid prescriptions. Clinical information was obtained via the electronic medical record. The primary outcome was the development of pneumonitis. We defined asymptomatic pneumonitis as the presence of new radiographic findings consistent with pneumonitis without documented clinical symptoms. We recorded pneumonitis grade as reflected in clinical documentation. If not specifically graded, we used Common Terminology Criteria for Adverse Events (CTCAE v4.0) to assess severity. Logistic regression analysis evaluated associations between pneumonitis and age, comorbidities, radiation dose and stage. Cox proportional hazards analysis evaluated associations between pneumonitis and risk of death. **Results:** A total of 123 veterans received durvalumab through 3/31/2019 (with follow up through 11/15/2019). Asymptomatic radiographic infiltrates occurred in 49 (39.8%) patients. There were 26 cases of clinically important pneumonitis Grade 2: 9(7.3%), Grade 3: 14 (11.4%), Grade 4: 2(1.6%), and grade 5: 1 (.08%). Acute hypersensitivity reactions occurred in five (4.1%) patients. Reported reasons for discontinuation of durvalumab included: disease progression [38 (31%)], toxicity [30 (24.3%)], and patient death [1 (1.6%)]. There was no association between age, time from radiation end to durvalumab initiation, radiation dose, smoking history, chemotherapy used or disease stage on development of pneumonitis. Cox analysis did not demonstrate an association between pneumonitis and risk of death. **Conclusions:** Clinically significant pneumonitis was more frequent in this cohort than reported in prior clinic trial populations. Further studies to identify pneumonitis risk factors are needed. Research Sponsor: None.

9035 Poster Session (Board #228), Fri, 8:00 AM-11:00 AM

I-SABR phase II randomized study of nivolumab immunotherapy and stereotactic ablative radiotherapy in early stage NSCLC: Interim analysis adverse effects. *First Author: Joe Y. Chang, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Stereotactic Ablative Radiotherapy (SABR) provides > 95% local control and has become standard care of medically inoperable stage I NSCLC. However, cumulatively about 40% of patients develop recurrence in the regional lymph nodes, distant organs, or secondary lung cancer. Combined immunotherapy and SABR (I-SABR) may reduce these recurrences by stimulating stronger cancer specific immune response. **Methods:** This is an ongoing phase II randomized study (SABR vs. I-SABR) to evaluate the efficacy and toxicity of I-SABR in medically inoperable, early stage (T1-T3: < 7 cm, including multi-primary tumors), isolated recurrence NSCLC without lymph node or distant metastasis. The primary objective is event-free survival (any recurrence and/or death). Secondary objectives include rates of ≥Grade 2 toxicity. 4-D CT image guided SABR (50 Gy in 4 fractions or 70 Gy in 10 fractions) was delivered to all patients. Patients randomized to I-SABR received additional concurrent Nivolumab (240 mg, every two weeks for total of 7 doses or 480 mg every four weeks for total of 4 doses). 140 patients are anticipated to enroll. We report here interim analysis of toxicity. **Results:** 92 patients (median age: 72, range: 57 to 90) were enrolled and randomized (47 to SABR; 45 to I-SABR). With median follow up of 14.5 months (range 2 to 28 months), there were no treatment-related grade 4/5 adverse events. For the I-SABR arm, there was one case of possible related grade 3 dyspnea, skin rash and 2 cases of probable grade 3 fatigue. There were possible/probable treatment related 2 cases of grade 2 pneumonitis, fatigue, pruritus and 1 case of grade 2 hyperthyroidism and arthralgia. No patients discontinued treatment due to adverse effects. For the SABR arm, there were possible treatment related 1 case of grade 2 fatigue and pneumonitis. All symptoms resolved with or without treatment. **Conclusions:** Combined Nivolumab immunotherapy and SABR (I-SABR) appear to be well-tolerated in this fragile patient population with no grade 4/5 toxicity. All toxicities were tolerable and resolved. The major barrier for patient enrollment and/or randomization is patient's perception of potential toxicities and additional clinic visits. Continued enrollment and additional follow up are needed to validate these findings. Clinical trial information: NCT03110978. Research Sponsor: BMS.

9036 Poster Session (Board #229), Fri, 8:00 AM-11:00 AM

Efficacy of DNA versus RNA NGS-based Methods in MET Exon 14 skipping mutation detection. *First Author: Magdalena Jurkiewicz, Columbia University Medical Center, New York, NY*

Background: Exon 14 skipping mutations in the mesenchymal-epithelial transition (*MET*) gene are reported in 2-5% of lung adenocarcinomas and are mutually exclusive of other driver mutations. Small-molecule *MET* tyrosine kinase inhibitors, capmatinib and tepotinib, showed durable responses in previously treated and treatment-naïve patients harboring *MET*-exon-14 skipping mutations. Studies suggest that for detection of *MET*-ex14 mutations, DNA-based assays alone may be sub-optimal when compared to RNA-based NGS assays. We compared the performance of DNA and RNA-based assays for detection of MET-ex14 variants. **Methods:** We examined NGS-based profiling data of lung adenocarcinomas (or when this diagnosis could not be excluded) to identify MET-ex14 mutations missed by DNA but identified by RNA analysis. The carcinomas were profiled by a DNA-based NGS panel that targets MET exons 2, 14, 16, 18 and 19. Cases without driver mutations were reflexed to an NGS-based RNA fusion panel (Archer's Anchored Multiplex PCR). **Results:** Over a 21-month period, MET-ex14 skipping events were detected in 16/644 (2.5%) lung carcinomas by DNA profiling. RNA analysis on driver-negative cases identified 9 additional MET-ex14 mutations. All 16 MET-ex14 DNA variants occurred at or around the intron 14 splice donor site, as the assay did not include the intron 13 splice acceptor site. Clinical characteristics of the *MET* positive cohort include a male to female ratio of 0.8:1.0, an average age of 76.5 years and 52% non-smoker status. All tumors were adenocarcinomas (including one with a $<$ 10% spindle/pleomorphic component) with the exception of 3 adenosquamous carcinomas and 1 squamous cell carcinoma. **Conclusions:** DNA based NGS-panels can potentially miss MET-ex14 skipping events in lung carcinomas, when the primers do not target both 3′ splice site of intron 13, and the 5′ splice site of intron 14. A reflex work flow interrogating RNA fusions can potentially capture such events. The clinical and molecular characterization of the variants detected only by RNA NGS assays warrants further exploration. Research Sponsor: None.

9037 Poster Session (Board #230), Fri, 8:00 AM-11:00 AM

Artificial intelligence based on deep learning for differential diagnosis between benign and malignant pulmonary nodules: A real-world, multicenter, diagnostic study. *First Author: Tao Xu, Department of Respiratory and Critical Care Medicine, the Affiliated Hospital of Qingdao University, Qingdao, China*

Background: Lung cancer is the most common cancer worldwide. Artificial intelligence (AI) platform using deep learning algorithms have made a remarkable progress in improving diagnostic accuracy of lung cancer. But AI diagnostic performance in identifying benign and malignant pulmonary nodules still needs improvement. We aimed to validate a Pulmonary Nodules Artificial Intelligence Diagnostic System (PNAIDS) by analyzing computed tomography (CT) imaging data. **Methods:** This real-world, multicentre, diagnostic study was done in five different tier hospitals in China. The CT images of patients, who were aged over 18 years and never had previous anti-cancer treatments, were retrieved from participating hospitals. 534 eligible patients with 5-30mm diameter pulmonary nodules identified by CT were planning to confirm with histopathological diagnosis. The performance of PNAIDS was also compared with respiratory specialists and radiologists with expert or competent degrees of expertise as well as Mayo Clinic's model by area under the curve (AUC) and evaluated differences by calculating the 95% CIs using the Z-test method. 11 selected participants were tested circulating genetically abnormal cells (CACs) before surgery with doctors suggested. **Results:** 611 lung CT images from 534 individuals were used to test PNAIDS. The diagnostic accuracy, valued by AUC, in identifying benign and malignant pulmonary nodules was 0.765 (95%CI [0.729 - 0.798]). The diagnostic sensitivity of PNAIDS is 0.630(0.579 – 0.679), specificity is 0.753 (0.693 – 0.807). PNAIDS achieved diagnostic accuracy similar to that of the expert respiratory specialists (AUC difference: 0.0036 [-0.0426 - 0.0497]; p = 0.8801) and superior when compared with Mayo Clinic's model (0.120 [0.0649 - 0.176], p $<$ 0·0001), expert radiologists (0.0620 [0.0124 - 0.112], p = 0.0142) and competent radiologists (0.0751 [0.0248 - 0.125], p = 0.0034). 11 selected participants were suggested negative in AI results but positive in respiratory specialists' result. 8 of them were malignant in histopathological diagnosis with tested more than 3 CACs in their blood. **Conclusions:** PNAIDS achieved high diagnostic accuracy in differential diagnoses between benign and malignant pulmonary nodules, with diagnostic accuracy similar to that of expert respiratory specialists and was superior to that of Mayo Clinic's model and radiologists. CACs may be able to assist CT-based AI in improving their effectiveness but it still need more data to be proved. Clinical trial information: ChiCTR1900026233. Research Sponsor: None.

9038 Poster Session (Board #231), Fri, 8:00 AM-11:00 AM

Clinical impact of targetable gene alterations on therapeutic outcomes in stage II/III locally advanced non-small cell lung cancer patients. *First Author: Yoshitaka Zenke, National Cancer Center Hospital East, Kashiwa, Japan*

Background: The clinical significance of genetic alterations in stage II/III non-small cell lung cancer (NSCLC) patients has not yet been clarified. We have prospectively analyzed NSCLC patients for cancer-related gene alterations and have followed up clinical course of the patients, establishing a large-scale clinico-genomic database in our nationwide genome screening project (LC-SCRUM-Japan). **Methods:** Submitted tumor samples were subjected to a targeted next-generation sequencing (NGS) system, Oncomine™ Comprehensive Assay. Therapeutic and prognostic data were collected and updated every year. **Results:** Since March 2015 to May 2019, 5166 non-squamous NSCLC patients from 263 institutions had been enrolled in the LC-SCRUM-Japan, and 754 of them were diagnosed as stage II/III. The median age of the 754 patients was 67 years (range, 21-92), and 503 (67%) were male, 595 (79%) smokers and 631 (84%) stage III. Of 640 available samples, 258 (40%) had targetable gene alterations, comprising 106 KRAS mut, 42 EGFR mut, 29 BRAF mut, 20 MET ex14skip/amp, 16 ALK fus, 12 ROS1 fus, 11 ERBB2 ex20ins, 8 RET fus, 7 EGFR ex20ins, 5 AKT1 mut, 1 NRG1 fus, 1 FGFR2/3 fus. In patients who received surgery (n = 159), 3-year disease-free survival rate was worse in patients with targetable gene alterations than in those without (40% vs 58% months; p = 0.03). In patients who received cytotoxic chemo-radiotherapy (n = 148), the response rate was similar in patients with targetable gene alterations and those without (70% vs. 77%); however, 3-year progression-free survival rate tended to be shorter in patients with targetable gene alterations than in those without (19% vs 35%; p = 0.08). **Conclusions:** In stage II/III NSCLC, the total frequency of targetable gene alterations was similar to that previously evaluated in our stage IV cohort (45%), and the current standard therapies showed early progression in the targetable gene-altered patients. A novel effective multimodality treatment in combination with targeted therapies is needed for this population. Research Sponsor: Japan Agency for Medical Research and Development.

9039 Poster Session (Board #232), Fri, 8:00 AM-11:00 AM

Real-world survey of pneumonitis/radiation pneumonitis among patients with locally advanced non-small cell lung cancer treated with chemoradiotherapy after durvalumab approval: A multicenter retrospective cohort study (HOPE-005/CRIMSON). *First Author: Go Saito, Department of Respirology, Graduate School of Medicine, Chiba University, Chiba, Japan*

Background: Durvalumab was approved as a consolidation therapy after chemoradiotherapy (CRT) for locally advanced non-small cell lung cancer (NSCLC) and established as the standard of care. However, since the approval of durvalumab, little has been reported on the frequency, severity, or clinical course of pneumonitis/radiation pneumonitis throughout the course of CRT. **Methods:** We conducted a 17-center, retrospective cohort study of consecutive patients with locally advanced NSCLC who received concurrent chemoradiotherapy (CCRT) with platinum-based chemotherapy between May 2018 and May 2019. **Results:** A total of 275 patients were included; their median age was 69.9 (range, 40.3-87.5), mean V_{20} was 19.4% (range, 1.4-37.9), and mean "mean lung dose" was 10.9 Gy (range, 1.5-31.3). Of these, 204 patients received durvalumab consolidation therapy (74.2%). Median follow-up time from the initiation of CCRT was 8.4 months (range, 1.5-15.7). During follow-up, 225 patients (81.8%) developed any-grade pneumonitis/radiation pneumonitis. Of these, more than half (134 of 225) were asymptomatic (grade 1), 18 (6.5%) were ≥grade 3, and 4 patients (1.5%) had fatal pneumonitis/radiation pneumonitis. By the time of initial assessment of response to CCRT, 64 (23.3%) patients had developed radiation pneumonitis. Logistic regression revealed that only V_{20} ≥25 % was an independent risk factor of symptomatic (≥grade 2) pneumonitis/radiation pneumonitis (OR: 2.74, 95% CI: 1.35-5.53, p = 0.0045). Of the 275 patients, 67 were treated with corticosteroids for pneumonitis/radiation pneumonitis (24.7%), and 14 (5.1%) needed home oxygen therapy after the treatment of pneumonitis/radiation pneumonitis. Among patients treated with corticosteroids, 21 patients received durvalumab rechallenge. Of the 21 patients, 6 (29%) showed pneumonitis/radiation pneumonitis relapse, of which 3 (14%) resulted in suspension of durvalumab rechallenge, but none were fatal. **Conclusions:** Although over four-fifths of the patients treated with CCRT after the approval of durvalumab developed pneumonitis/radiation pneumonitis, more than half of them were asymptomatic, and ≥grade 3 events accounted for 6.5%. Sometimes patients needed corticosteroid therapy, which was in many occasions effective, and some also underwent durvalumab rechallenge. V_{20} was an independent risk factor of symptomatic pneumonitis/radiation pneumonitis. Research Sponsor: None.

9040 Poster Session (Board #233), Fri, 8:00 AM-11:00 AM

Prognostic role of mid-treatment PET/CT and plasma cytokines in patients undergoing chemoradiation for locally advanced non-small cell lung cancer (LA-NSCLC). *First Author: Jing Zeng, University of Washington, Seattle, WA*

Background: Patients with unresectable LA-NSCLC are treated with concurrent chemoradiation (CRT) and consolidation immunotherapy with survival that range from months to years or even decades. Early predictive biomarkers have potential to identify patients who are unlikely to benefit from continuing standard of care therapy and require a change in management. We investigated biomarkers that are widely available (PET/CT scan and plasma cytokine levels) to develop early predictors (mid-CRT) of survival in a phase II clinical trial of chemoradiation for LA-NSCLC. **Methods:** 37 Patients with AJCC v7 stage IIB-IIIB NSCLC were prospectively enrolled on the FLARE-RT trial (NCT02773238) from 2016-9. All patients underwent chemoradiation; 18 also received adjuvant durvalumab. PET/CT exams were performed at week 3 of CRT and response status was pre-defined by published metrics. 21 patients consented to peripheral blood collection at baseline and week 3, and plasma levels of 43 common inflammatory cytokines were measured. Bootstrapping over 100 iterations of the least absolute shrinkage and selection operator (LASSO) was performed to reduce feature dimensionality and guard against false discoveries. Cox regression of selected cytokine levels and PET response status, as well as time-dependent receiver-operating characteristic (ROC) analysis, were evaluated for associations to overall survival (OS). **Results:** Median follow-up was 18 months with 1-year OS 81% and PFS 52%. Mid-CRT PET response (as determined by pre-defined metrics) was strongly associated with OS (HR 5.6 [1.4-22.0], p = 0.015) after adjusting for radiation target volume, with 1-yr OS 94% for responders vs. 68% for non-responders (p = 0.017). Plasma TNFα level was also prognostic for OS (HR 1.9 [1.1-3.5], p = 0.030). TNFα retained significance for OS (HR 2.3 [1.2-4.6], p = 0.016) after adjusting for PET response. Bivariate mid-CRT PET response and TNFα generated a parsimonious model to predict OS (AUC = 0.85, 18-month horizon). **Conclusions:** Risk stratification for long-term survival after chemoradiation in patients with LA-NSCLC may be achievable based on mid-chemoradiation assessment of widely available biomarkers (PET imaging and plasma TNFα level). Combined functional imaging and peripheral blood biomarkers will be validated in a larger sample of our trial cohort, along with other independent patient populations. Clinical trial information: NCT02773238. Research Sponsor: U.S. National Institutes of Health.

9041 Poster Session (Board #234), Fri, 8:00 AM-11:00 AM

Peripheral blood T-cell receptor immune repertoire characterization of resectable stage IIIA non-small cell lung cancer patients receiving neoadjuvant chemo-immunotherapy treatment from NADIM study. *First Author: Alberto Cruz Bermudez, Instituto Investigacion Sanitaria Puerta de Hierro-Segovia de Arana, Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain*

Background: Characterization of the peripheral blood T-cell receptor (TCR) repertoire has become a novel approach to predict the clinical benefit to anti-PD1/PDL1 therapy. However, there is lack of knowledge about the clinical relevance of TCR repertoire in terms of pathological response and clinical outcomes (PFS and OS) in chemo-immunotherapy. To answer this question we have analysed samples from the NADIM study (NCT03081689), in which resectable stage IIIA NSCLC patients were treated with neoadjuvant chemo-immunotherapy with Nivolumab. **Methods:** Using ION Torrent-based next-generation sequencing we have analysed TCR repertoire of peripheral blood from 30 patients receiving chemo-immunotherapy. Using 25ng of total RNA from PBMCs, clonal convergence, evenness and diversity were calculated at diagnosis (pre-treatment) and after 3 cycles of Nivolumab plus carboplatin (post-treatment). Regarding pathological responses, patients were classified in 3 groups: complete response (pCR) (0% viable tumour at the resection specimen), mayor response (pMR) ($<$ 10% viable tumour) and incomplete response (pIR) ($>$ 10% of viable tumour). At data analysis, PFS and OS median follow-up times were longer than 20 months. **Results:** No statistically significant differences in TCR repertoire in terms of evenness (p = 0,373), diversity (p = 0,691) or convergence (p = 0,054) between pre- and post-neoadjuvant treatment were observed. Similarly, no significant differences were observed in these metrics between pathological response groups. However, a detailed analysis of the clones showed that the percentage of frequent clones (greater than 0.1%) that increase after neoadjuvant therapy does show differences between the different pathological response groups (pIR vs pMR), being elevated in patients who presented responses greater than 90% (p = 0.0385). Regarding the clinical benefit, having this parameter higher than the median (43,90% in this cohort) is associated with a higher PFS (p = 0.0490) and OS (p = 0.078) using KM Log-rank test. **Conclusions:** Evenness, Diversity and Convergence derived from immune repertoire analysis do not appear to be clinically useful in the context of neoadjuvant chemo-immunotherapy in lung cancer. However, the detailed analysis of the clones seems promising. The increase of the most frequent clones after treatment seems to be associated to different clinical variables such as pathological response and PFS in these patients. Clinical trial information: NCT03081689. Research Sponsor: BRISTOL MYERS SQUIBB.

9042 Poster Session (Board #235), Fri, 8:00 AM-11:00 AM

Clinical characteristics, genomic features, and recurrence risk of early-stage MET exon 14 mutant non-small cell lung cancer (NSCLC). *First Author: Gonzalo Recondo, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute, Boston, MA*

Background: *MET* exon 14 alterations occur in ~3% of patients (pts) with NSCLC. Although clinical and genomic features of *MET* exon 14 mutant (mut) NSCLC are better characterized in the metastatic setting, less is known about early-stage disease for this molecular subtype. **Methods:** Clinicopathologic and genomic data were collected from patients (pts) with resected stage I-III *MET* exon 14 mutant NSCLC at the Dana-Farber Cancer Institute (DFCI) and the Memorial Sloan Kettering Cancer Center (MSKCC). We estimated the disease-free survival (DFS) and overall survival (OS) of patients from the date of surgical resection. The prevalence of *MET* exon 14 mutations in stage I-III NSCLC was assessed using OncoPanel NGS v3.0 at DFCI. **Results:** The prevalence of *MET* exon 14 alterations in resected tumors of pts with stage I-III NSCLC at DFCI using Oncopanel v3 was 2.8% (17/613) overall: 2.9% (16/542) in non-squamous and 1.4% (1/71) in squamous histology. We identified 131 pts with resected stage I-III (I = 73, II = 28, III = 30) *MET* exon 14 mut NSCLC at DFCI (Oncopanel v1-v3) and MSKCC (MSK-IMPACT), with a median age of 71 years (yrs) (range: 43-88). There were no significant differences in sex, smoking status, or type of *MET* alteration across stages. In stage I resected tumors there was a higher proportion of adenocarcinoma histology compared to stages II and III (p = 0.009). The median harmonized TMB (mTMB) was similar across stages (p = 0.43). Common genomic co-alterations included *MET* amplification (amp) (5.3%), *CDK4/6* amp (19.1%), *MDM2* amp (35.1%), *TP53* mut (17.6%) and *CDKN2A/B* loss (9.2%). The median DFS in stage I, II, and III NSCLC was 8.3 yrs (95% CI: 3.1-8.3), 2.6 yrs (95% CI: 1.0-2.6), and 2.1 yrs (95% CI: 0.7-2.7), respectively (p = 0.017). The median OS in stage I, II, and III NSCLC was 9.2 yrs (95% CI: 8.5 -10.5), not reached (NR) (95% CI: NR-NR), and 4.1 yrs (95% CI: 3.6-4.1), respectively (p = 0.052). Concurrent *MET* amp was independently associated with worse DFS (HR: 4.9, 95% CI: 1.8-13.1; p = 0.002) in multivariate analysis. **Conclusions:** *MET* exon 14 mutations are present in 2.8% of resected stage I-III NSCLCs. Given the prevalence of this molecular alteration in early-stage NSCLC, clinical trials exploring the role of adjuvant and neoadjuvant MET targeted therapies in this population may be warranted. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

9043 Poster Session (Board #236), Fri, 8:00 AM-11:00 AM

Contemporary management and associated outcomes of 3,151 patients with stage III non-small cell lung cancer (NSCLC) in a real-world setting: Results of KINDLE, a multicountry observational study. *First Author: Abdul Rahman Jazieh, Oncology Department, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia*

Background: Stage III NSCLC is a heterogeneous disease requiring a multimodality approach. We conducted a global study to characterise the patients (pts), treatment patterns and their associated outcomes for this disease in a real-world setting in the pre-IO era. **Methods:** KINDLE is a retrospective, multicountry, multi-centre study capturing data on patient and disease characteristics, treatments and outcomes. The study included pts with stage III NSCLC diagnosed between January 1st, 2013 and December 31st, 2017 and with at least 9 months of documented follow-up. Descriptive statistics were used to describe patient demographics, disease characteristics and treatment modalities. Inferential statistics was used to correlate various clinical and treatment variables with progression free survival (PFS) and overall survival (OS). **Results:** 3151 patients were enrolled at 125 centres in three geographical regions; 1046 pts in Middle East and North Africa, 1874 pts in Asia and 231 pts in Latin America. Median age was 63 years (range 21-92); 76.5% were male; 69.2% with a smoking history; 55.9% were staged as IIIA (AJCC 7th ed.); 53.7% had adenocarcinoma and 36.6% squamous cell, and 31.7% were known to have an EGFR mutation. 21.4% of patients underwent curative surgical resection. First line therapy included more than 25 different regimens, the most common being concurrent chemo-radiotherapy (cCRT) in 29.4%, chemotherapy (CT) alone in 17%, sequential chemo-radiotherapy (sCRT) in 10.4%, and radiotherapy (RT) alone in 8.5%. Median PFS for the whole cohort was 12.5 mos (95% CI; 12.06 – 13.14) and median OS 34.9 mos (95% CI; 32.00 – 38.01). Stage IIIA patients who were eligible for and underwent surgery + CT, had longer OS than patients who did not undergo surgery, receiving other treatments. Non-surgical approaches included CT, RT, and CRT. In stage IIIB, OS was significantly improved for cCRT vs. CT alone (p = 0.0015) or RT alone (p = $<$ 0.0001) or sCRT (p = 0.0216). Improved survival was observed with sCRT compared with RT alone and chemotherapy vs RT alone. **Conclusions:** KINDLE, a large multicountry observational study, reveals the diversity of treatment practices that exist in stage III NSCLC and provides insights on the outcomes in a real-world setting. The unmet medical need remains high and approaches are required to optimize patient outcomes including implementation of guidelines, physician education and improved access to innovative medicines and quality care. Research Sponsor: AstraZeneca.

9044 Poster Session (Board #237), Fri, 8:00 AM-11:00 AM

A retrospective evaluation of PD-L1 expression on primary non-small cell lung cancer (NSCLC) samples and associated involved hilar or mediastinal lymph nodes (N1 or N2) (REPLICA). *First Author: Eleni Karapanagiotou, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom*

Background: Little is known about the PD-L1 expression in early stage NSCLC as well as the possible heterogeneity of PD-L1 expression in different sites. This study provides information on both PD-L1 expression in stage II and III NSCLC and the relationship between PD-L1 expression in the primary site (lung) and metastatic lymph nodes (LNs) N1 and/or N2. **Methods:** Samples (primary tumor and N1/N2) from 500 patients who underwent lung resection and lymphadenectomy for NSCLC without prior treatments were collected and analyzed for PD-L1 expression using the 22C3 pharmdx Agilent assay. The tumor proportion score (TPS) is documented for each sample according to the following categories: PD-L1: < 1%, 1-49%, ≥ 50%. PD-L1 stained slides were reviewed by two pathologists independently; for discrepant cases the two pathologists reviewed the stains jointly and the consensus score used for the data analysis. Agreement between the two pathologists was assessed by overall agreement and kappa statistic. The association between PD-L1 expression in the primary tumor and lymph node was assessed by cross-tabulation. **Results:** A total of 456 tumors and involved LNs were included in the analysis. Pathologist one assessed 435 primary tumor and LN pairs and pathologist 2 assessed 453 tumor and LNs pairs. The overall agreement between pathologists on PD-L1 expression in primary tumor samples was 77%; K = 0.59 (95% CI 0.57 – 0.63) and in LNs 83%; k = 0.62 (95% CI 0.56 – 0.70). Primary tumors showed PD-L1 < 1% in 235/422 (55,6%), PD-L1 1-49% in 146/422 (34,6%) and PD-L1 > = 50% in 41/422 (9.8%). 77% (327/422) showed no heterogeneity in PD-L1 expression between the primary tumor and involved LNs. In tumors with PD-L1 < 1% expression, 94% of the LNs showed PD-L1 < 1% expression and less than 1% showed PD-L1 > = 50%, 6% of the LNs showed PD-L1 1-49%. When the primary tumor was PD-L1 > = 50% nearly half (46%) of the involved LNs showed the same degree of PD-L1 positivity and 10% of them showed PD-L1 < 1%; 44% of the LNs showed PD-L1 1-49%. When the primary tumor showed 1-49% PD-L1 staining, 60% of the LNs showed the same staining pattern, 36% showed PD-L1 < 1% and only 4% showed PD-L1 > = 50% expression. **Conclusions:** In stage II and III NSCLC, half of the primary tumors show negative PD-L1 expression. Discrepant PD-L1 expression between primary tumors and LN metastases was seen in 23% of the cases, and when present, PD-L1 expression in LN tumors tended to be lower than that in primary tumors. Research Sponsor: MERCK.

9045 Poster Session (Board #238), Fri, 8:00 AM-11:00 AM

AFT-16: Phase II trial of atezolizumab before and after definitive chemoradiation (CRT) for unresectable stage III non-small cell lung cancer (NSCLC). *First Author: Helen J. Ross, Mayo Clinic, Phoenix, AZ*

Background: A minority of the > 40,000 patients (pts) diagnosed with stage III NSCLC annually in the US are cured by CRT, more recently followed by adjuvant immune checkpoint inhibitors (ICI). PD-L1 blockade with CRT may attenuate tumor-related immunosuppression via depletion of regulatory T cells and clonal expansion of effector T cells. Further, CRT may expose otherwise hidden antigens that present additional targets to the reconstituting immune system. Adjuvant ICI has improved survival. Whether ICI before CRT will further improve outcomes is unknown. **Methods:** This Alliance Foundation Trials (AFT) study evaluated safety and efficacy of atezolizumab before and after CRT. 4 cycles of atezolizumab 1200 mg IV q 21 days with restaging after cycles 2 and 4 were followed by carboplatin and paclitaxel (C/P) weekly with 60 Gy radiation and C/P consolidation followed by atezolizumab for 1 year of therapy. Primary endpoint is disease control rate (DCR) (complete response + partial response (PR) + stable disease (SD)) at 12 weeks (wks). Secondary endpoints include overall response rate, progression-free survival, overall survival, safety and quality of life assessed by EORTC QLQ-30. Correlatives include PD-L1 and tumor mutation burden as predictive biomarkers. Tumor tissue was obtained at study entry; plasma and immune cells were isolated at multiple timepoints. **Results:** 64 pts with stage III NSCLC, performance status (PS) 0-1, no active autoimmune disease or significant organ dysfunction enrolled at 13 Alliance sites from 11/2017 to 7/2019. 62 pts received ≥ 1 dose of atezolizumab and are included in the primary analysis; median age 63.9 years (38.1-86.5), 51.6% female, 77.4% white, 61.3% former smokers, 56.5% PS 0. DCR at 12 wks was 77.4% (80% confidence interval 69.2-84.3%) (30.7% PR, 46.8% SD). 54 pts reported adverse events (AEs) during induction, mostly grade (gr) 1. There were 13 serious AEs, most unrelated to study treatment; 1 gr 3 anaphylactic reaction, 1 gr 3 colitis, and 1 gr 4 Guillain-Barre syndrome were attributable to atezolizumab. Baseline PD-L1 status was available for 49 pts. DCR was 82.4% for pts with PD-L1 negative and 90.9% for pts with PD-L1 positive tumors. **Conclusions:** Atezolizumab prior to and following CRT for stage III unresectable NSCLC was well tolerated with an encouraging 12-wk DCR. Analysis of secondary endpoints is ongoing. Further study of induction ICI therapy is warranted in patients with unresectable stage III NSCLC. Support: AFT, Genentech; Clinical trial information: NCT03102242. Research Sponsor: Alliance Foundation Trials, Pharmaceutical/Biotech Company.

9046 Poster Session (Board #239), Fri, 8:00 AM-11:00 AM

A mid-chemoradiation dynamic risk model integrating tumor features and ctDNA analysis for lung cancer outcome prediction. *First Author: Everett J Moding, Stanford University, Stanford, CA*

Background: Circulating tumor DNA (ctDNA) molecular residual disease after curative intent therapy predicts disease progression in localized lung cancer. We hypothesized that integrating pre-CRT features and ctDNA levels during chemoradiation therapy (CRT) can predict patient outcomes earlier to enable response-adapted therapy. **Methods:** We identified pre-CRT features prognostic of disease progression after CRT for Stage II-III non-small cell lung cancer (NSCLC) in a historical "pre-CRT" training cohort of 109 patients. In addition, we applied CAPP-Seq ctDNA analysis pre-CRT and a median of 21 days into CRT (mid-CRT) to a "ctDNA" training cohort of 42 patients treated at MD Anderson and an independent validation cohort of 21 patients treated at Stanford. Prognostic pre-CRT features and mid-CRT ctDNA concentration were integrated using a Bayesian proportional hazards approach to generate a Continuous Individualized Risk Index (Kurtz et al. Cell 2019) for NSCLC (CIRI-NSCLC) to predict freedom from progression (FFP). **Results:** Adenocarcinoma histology (HR 2.6, P = 0.0005) and *KEAP1* mutation (HR 2.7, P = 0.002) but not stage (P = 0.16), age (P = 0.60), or gender (P = 0.98) were significantly associated with FFP in the pre-CRT training cohort. Mid-CRT ctDNA concentration as a continuous variable was significantly associated with FFP in the ctDNA training cohort (HR 1.6, P = 0.04), and applying an optimal threshold identified in the training cohort (3.2 hGE/ml) significantly stratified FFP in the independent ctDNA validation cohort (HR 4.8, P = 0.02). CIRI-NSCLC enabled individualized real-time updating of the probability of FFP as model features became available over the course of CRT. CIRI-NSCLC outperformed individual model features in the independent validation cohort when compared by C-statistic (CIRI-NSCLC: 0.85; mid-CRT ctDNA: 0.76; histology: 0.66; *KEAP1*: 0.60). Across the whole cohort, patients with a greater than 66% risk of progression predicted by CIRI-NSCLC (n = 10) had an FFP of 10.0% at 12 months while patients with a less than 33% risk of progression predicted by CIRI-NSCLC (n = 22) had an FFP of 79.7% at 12 months (HR 15.0, P < 0.001). **Conclusions:** Our results suggest that CIRI-NSCLC can identify patients at very high and low risk of progression. Prospective evaluation will be necessary to test the potential utility of adapting treatment based on CIRI-NSCLC. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

9047 Poster Session (Board #240), Fri, 8:00 AM-11:00 AM

Real-world treatment patterns and clinical outcomes in *EGFR*-mutant unresectable locally advanced NSCLC (LA-NSCLC): A retrospective multicenter study of 367 patients. *First Author: Nan Bi, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital & Shenzhen Hospital, Beijing, China*

Background: The chemoradiation therapy (CRT) is the standard care for unresectable LA-NSCLC. The addition of EGFR-TKIs in first-line treatment of *EGFR*-mutant subpopulation is debatable. **Methods:** We retrospectively collected data for patients with unresectable stage III NSCLC harboring *EGFR* mutations from nine major academic cancer institutions in China from Jan 2012 to December 2018. Patients with *ALK* rearrangements were excluded. Patients were categorized into three subgroups according to the primary treatment: 1) RT+TKI: Combined RT and EGFR-TKI with/out chemotherapy ; 2) no TKI: CRT alone; 3) upfront TKI: EGFR-TKI followed by RT at local-regional progression. PFS and OS were calculated from the date of diagnosis. Log-rank test was used to assess for differences and Cox proportional hazards model was used to adjust for covariates. **Results:** A total of 367 patients met selection criteria were included in the study. Patients receiving TKI were older (≥60 years: 54.7% TKI *v* 36.4% and RT+TKI 33.3% CRT; P = 0.001), and more patients receiving CRT had uncommon *EGFR* mutations (10.3% CRT *v* 2.3% RT+TKI and 4.0% TKI; P = 0.020). Other baseline characteristics were well balanced among groups. With a median follow-up of 40.8 months, the median PFS and OS were 16.6 and 55.4 months for the entire cohort. The median PFS and OS for the three subgroups were shown in the table. On multivariable analysis, after adjusting for age, KPS status, smoking status, stage, and type of *EGFR* mutations, TKI+RT was independently associated with improved PFS (HR, 0.57; 95% CI, 0.41 to 0.78) and OS (HR, 0.61; 95% CI, 0.39 to 0.97) relative to upfront TKI ; TKI+RT was also associated with improved PFS (HR, 0.38; 95% CI, 0.27 to 0.54) relative to CRT, but not OS (HR, 0.66; 95% CI, 0.40 to 1.11). **Conclusions:** The use of upfront EGFR-TKI with deferred RT at progression was associated with inferior OS in patients with *EGFR*-mutant unresectable LA-NSCLC. First-line use of radiotherapy and EGFR-TKI was associated with the longest PFS and OS, which requires further prospective, randomized evaluation. Research Sponsor: National Natural Science Foundation of China (grants 81572971) .

Endpoints	RT+TKI (N = 88) Median (95% CI)	CRT alone (N = 78) Median (95% CI)	Upfront TKI (N = 201) Median (95% CI)	P-value
PFS	21.6 (13.8 to 29.4)	12.6 (10.8 to 14.2)	16.5 (14.1 to 18.9)	< 0.001
OS	67.4 (57.5 to 77.3)	54.2 (40.0 to 68.3)	46.5 (34.5 to 58.6)	0.055

9048 Poster Session (Board #241), Fri, 8:00 AM-11:00 AM

Non-pneumonitis immune-mediated adverse events (imAEs) with durvalumab in patients with unresectable stage III NSCLC (PACIFIC). *First Author: Jarushka Naidoo, Department of Oncology, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD*

Background: The phase 3 PACIFIC trial established durvalumab (durva) after chemoradiotherapy (CRT) as SoC for pts with unresectable stage III NSCLC. We report exploratory analyses to characterize non-pneumonitis (np) imAEs that occurred with durva in PACIFIC. **Methods:** PACIFIC was a double blind trial of pts without disease progression after platinum-based concurrent CRT (≥2 cycles). Pts were randomized 2:1 to receive durva 10 mg/kg or placebo (pbo) IV q2w for ≤12 months, stratified by age, sex and smoking history. We characterized the time to onset, duration, and management/outcomes of np imAEs and their association with (1) baseline pt/disease factors and (2) AEs (excluding all-cause pneumonitis). **Results:** Of 709 treated pts, 19% and 11% experienced imAEs and np imAEs of any grade, respectively; proportionally more had np imAEs with durva (71/475; 15%) vs pbo (5/234; 2%). Thyroid disorders (54/475; 11%), rash/dermatitis (9/475; 2%), and diarrhea/colitis (5/475; 1%) were the most common np imAEs with durva; rash/dermatitis had the shortest time to onset (Table). Among durva treated pts with np imAEs, 11% had grade 3/4 np imAEs, 41% had np imAEs that resolved, and none had fatal np imAEs; interventions included endocrine replacement therapy (73%), systemic corticosteroids (34%), high dose corticosteroids (16%), and discontinuation (10%). There were no apparent differences in baseline factors between pts with or without np imAEs. Durva had a broadly manageable safety profile irrespective of the occurrence of np imAEs. However, a higher proportion of durva treated pts with vs without np imAEs experienced all-cause, grade 3/4 events (41% vs 29%); none were fatal (excl. pneumonitis). **Conclusions:** Np imAEs occurred infrequently in PACIFIC, but were more common with durva vs pbo; thyroid disorders and rash/dermatitis were the most common np imAEs. Of durva treated pts with np imAEs, 11% experienced np imAEs of grade 3/4. Overall, np imAEs were broadly manageable and did not lead to high rates of discontinuation, and no association with baseline factors was seen, suggesting this should not deter use of durva in eligible pts. Clinical trial information: NCT02125461. Research Sponsor: AstraZeneca.

Timing of np imAEs in durva treated pts (≥5 pts with events)

Np imAE category (any grade)	Time to onset from 1st dose, median (range), days [n]*	Duration, median (range), days [n]†
Thyroid disorders	85.0 (14–378) [54]	63.5 (15–224) [20]
Rash/Dermatitis	37.0 (6–111) [9]	117.0 (18–738) [6]
Diarrhea/Colitis	61.0 (2–254) [5]	74.0 (12–151) [5]

*Based on the 1st event reported for each pt. †Excludes ongoing events.

9049 Poster Session (Board #242), Fri, 8:00 AM-11:00 AM

The impact of residual metabolic primary tumor volume after completion of thoracic irradiation in patients with inoperable stage III NSCLC. *First Author: Olarn Roengvoraphoj, Department of Radiotherapy and Radiation Oncology, University Hospital, LMU Munich, Munich, Germany*

Background: The metabolic tumor volume (MTV) is a functional and volumetric PET/CT parameter that has been investigated in recent years with respect to its predictive and prognostic value in different tumor entities. In this study, we investigated the role of residual MTV after completion of thoracic irradiation in inoperable stage III non-small cell lung cancer (NSCLC). **Methods:** We analyzed retrospective and prospective data of 56 patients with inoperable stage III NSCLC treated with chemoradiotherapy (CRT) and chemoradioimmunotherapy (CRT-IO). All patients received an 18F-FDG-PET/CT 3 to max. 6 months after completion of thoracic irradiation. The measurement of the residual MTV of the primary tumor was performed by calculating the SUVmean of the liver + 2SD as threshold. The patients were divided into the following groups: residual-MTV < 1ml; residual-MTV 1-25ml and residual-MTV > 26ml. Survival, local recurrence, and distant metastasis rates were calculated using the Kaplan-Meier method from the last day of thoracic irradiation. **Results:** The median follow-up was 45 months (range 16-74) in the CRT group and 16 months in the CRT-IO group (range13-19). Twenty-two (39%) patients had a residual MTV < 1ml (1st group), 19 (34%) a residual MTV between 1-25ml (2nd group) and 15 (27%) a residual MTV > 25ml (3rd group) after completion of thoracic irradiation. Median overall survival was 61, 20 and 12 months (p = 0.006) in the 1st, 2nd and 3rd groups, respectively. 12-month survival was 86%, 50% and 33% after CRT vs. 88%, 71% and 50% after CRT-IO in the 1st, 2nd and 3rd groups, respectively. The median time to in-field recurrence in the 1st, 2nd and 3rd groups was 51, 20 and 15 months (p = 0.011). The prognostic value of the residual MTV on OS was confirmed exclusively in the CRT patient cohort (p = 0.04), but not in the CRT-IO patient cohort (p = 0.174). Residual MTV demonstrated no influence on the local recurrence rate in the CRT-IO patient cohort, but only in patients treated with CRT (p = 0.007). **Conclusions:** Patients with inoperable stage III NSCLC in whom the residual MTV was < 1ml after completion of thoracic irradiation showed significantly better survival than patients with a residual MTV of 1-25ml and MTV > 25ml. The subgroup analysis confirmed the prognostic value of residual MTV only in patients who received chemoradiotherapy without consolidation immunotherapy. Research Sponsor: None.

9050 Poster Session (Board #243), Fri, 8:00 AM-11:00 AM

Neoadjuvant endobronchial delivery of gene mediated cytotoxic immunotherapy (GMCI) for non-small cell lung cancer (NSCLC): Safety and immunologic activity. *First Author: Laura K. Aguilar, Candel Therapeutics, Needham, MA*

Background: GMCI is a tumor-specific immuno-oncology approach implemented through local delivery of *aglatimagene besadenovec*(AdV-tk) followed by anti-herpetic prodrug. This leads to immunogenic tumor cell death, antigen presenting cell activation, and T cell stimulation resulting in $CD8^+$ T cell dependent protection, as demonstrated in preclinical models and clinical trials in other tumor types. This is the first study to assess endobronchial delivery of AdV-tk for NSCLC. **Methods:** This Phase I dose escalation trial enrolled patients with suspected NSCLC who were candidates for surgery. A single AdV-tk injection was performed by endobronchial ultrasound (n = 11) or mediastinoscopy (n = 1) during the diagnostic staging procedure 3 weeks prior to surgery. Three dose levels were evaluated: $2.5x\ 10^{11}$, $5x10^{11}$, and $1x10^{12}$ vector particles (vp) in a 3+3 design. Valacyclovir was administered for 14 days, starting the day after AdV-tk injection. To assess the local and systemic effects of GMCI, immune biomarkers were evaluated in blood and tumor samples before and after GMCI. **Results:** From 2017-2019, 12 patients (9 men, 3 women, median age 65 [range 55-80]) received GMCI followed by surgery. Average tumor size was 5.1 cm (largest diameter) and final pathologic stage was I (n = 4), II (n = 3), and III (n = 5). Treatment-related adverse events were CTC grade 1 fever (n = 1), flu-like symptoms (n = 1) and nausea/vomiting/diarrhea (n = 1). The only > grade 2 lab abnormality was transient grade 3 lymphopenia (n = 2). A measurable reduction in tumor size was observed in one patient. The average amount of tumor necrosis was 29.4%. Significant infiltration of $CD8^+$T cells (5.2-fold compared to baseline, p = 0.001) was found in tumor 19-22 days after AdV-tk injection. Within the $CD8^+$tumor infiltrating lymphocytes, there was increased expression of CD38 (2.5-fold, p = 0.002), Ki67 (4.8-fold, p = 0.02), PD1 (1.9-fold, p = 0.002), CD39 (2.9-fold, p = 0.04) and CTLA-4 (4.8-fold, p < 0.001), without significant detected differences in Tim3 or TIGIT. Simultaneously, peripheral blood $CD8^+$ cells displayed significant increases in CD38 (3.4-fold, p = 0.006), HLA-DR (4.2-fold, p = 0.002), and Ki67 (5.8-fold, p = 0.017). **Conclusions:** Intratumoral injection of AdV-tk into lung tumors was safe and feasible. Further, AdV-tk effectively induced peripheral blood and intra-tumoral CD8 T cell activation. Consequent upregulation of inhibitory receptors suggests a potential benefit for combination therapies. Clinical trial information: NCT03131037. Research Sponsor: Advantagene.

9051 Poster Session (Board #244), Fri, 8:00 AM-11:00 AM

Neoadjuvant nivolumab (N) plus cisplatin (C)/pemetrexed (P) or cisplatin /gemcitabine (G) in resectable NSCLC. *First Author: Ralph Zinner, University of Kentucky, Department of Medical Oncology, Lexington, KY*

Background: Patients (pts) with resectable stage IB (≥4cm)-IIIA non-small-cell lung cancer (NSCLC) derive modest overall survival benefit with neoadjuvant or postoperative adjuvant chemotherapy. Neoadjuvant therapy can speed the discovery of promising regimens by using pathologic response as a surrogate for OS. Major pathologic response (MPR), defined as < 10% viable tumor, was strongly associated with improved OS. PD-(L)1 checkpoint inhibitors in combination with chemotherapy are standard of care in advanced NSCLC. We hypothesize that the addition of N to neoadjuvant CP or CG will increase the MPR rate compared to historical controls. **Methods:** This is an investigator-initiated trial for pts with newly diagnosed AJCC 8th stage IB (≥4cm)-IIIA squamous or non-squamous EGFR/ALK WT NSCLC with a plan to have surgery. Pts receive 3 courses of N 360mg IV q 3w added to C 75mg/m2 IV q 3w plus P 500 mg/m^2 IV q 3wks or G 1250mg/m^2 IV d1, d8 with surgery 3 wks after the last dose. The primary objective is MPR. To estimate pathologic response, the resected pathology specimens are cut >1 section/cm. Using the Aperio Digital scanning system©, slides were imaged, and then annotated by at least 2 pathologists for viable tumor vs. treatment effect with respective areas then automatically calculated and percentage of viable tumor calculated. Our primary endpoint will be reached if 10/34 (29%) planned pts have at least an MPR. **Results:** From 6/2018-8/2019, 13 pts were enrolled all of whom had surgery. Median age was 69 (49-80), 38% women, 31% nonsquamous, 54% stage IIIA, and 77% PD-L1 positive (≥1%, SP263). Pre-surgical grade 3 toxicity occurred in 2/13 pts, one of whom was changed to carboplatin for courses 2 and 3. Grade 3 toxicities were neutropenia (2/13), anemia (1/13), and renal (1/13). One pt. developed hypothyroidism 4 mos after surgery. One pt died 6 weeks after surgery from complications unrelated to study drugs. Our primary endpoint was met; 11/13 (85%), had at least an MPR with 6/13 (46%) and 5/13 (38%) having an MPR and pCR respectively. Radiologic response rate was 46% (PR 5, CR 1). Pts with either PD-L1+ or PD-L1- had MPRs. With a median follow-up of 10 months there are no recurrences. **Conclusions:** The combination of nivolumab added to platinum doublets was well tolerated. The primary endpoint of MPR in at least 10/34 pts was surpassed with MPR or pCR in 11/13 pts post-surgery. MPR was seen independent of PD-L1 score. Exploratory outcomes assessing markers of immune bias in tumor tissue and plasma are in process. Clinical trial information: NCT03366766. Research Sponsor: Bristol-Myers Squibb.

9052 Poster Session (Board #245), Fri, 8:00 AM-11:00 AM

Efficacy and safety of nivolumab for malignant mesothelioma in the real world. *First Author: Koji Mikami, Division of Respiratory Medicine, Department of Internal Medicine Department of Thoracic Oncology Hyogo College of Medicine, Nishinomiya, Hyogo, Japan*

Background: Until recently, the standard treatment for advanced malignant pleural mesothelioma (MPM) was only cisplatin plus pemetrexed. Nivolumab, an anti-programmed death-1 monoclonal antibody, shows efficacy against pretreated MPM and has been approved in Japan, but the data regarding the efficacy and safety of nivolumab in MPM are limited to those from a small number of patients of the MERIT study. Therefore, it is important to accumulate real-world data on the efficacy and safety of nivolumab for MPM. **Methods:** We retrospectively analyzed all patients with MPM who received nivolumab at Hyogo College of Medicine Hospital from August 2018 to December 2018. **Results:** A total of 77 patients (61 males and 16 females) were included. There were 62, 10, and 5 patients with performance statuses of 0–1, 2, and 3, respectively. There were 63, 8, and 6 patients with epithelioid, sarcomatoid, and bi-phasic histologies, respectively. Nivolumab was administered as second-, third-, and ≥fourth-line treatment to 48, 15, and 11 patients, respectively. In 66 patients who were examined for efficacy, the response rate (RR) was 24.2% and the disease control rate (DCR) was 63.6%. By the histology type, the RR and DCR were 15.1% and 62.3% for the epithelioid type, 62.5% and 87.5% for the sarcomatoid type, and 20.0% and 40.0% for the bi-phasic type, respectively. The median progression-free survival (mPFS) was 4.1 months and the median overall survival (mOS) was 13.3 months. Analyzing the efficacy based on the neutrophil-to-lymphocyte ratio (NLR) in the peripheral blood, the RRswere 14.7% in the NLR≥3.5 group and 25.8% in the NLR $<$ 3.5 group. The mPFS and mOS in the NLR≥3.5 group were 3.1 months and 11.4 months, respectively,whereas those in the NLR $<$ 3.5 group were 5.6 months and not reached, respectively. There were no significant differences in the RR, PFS, and OS between the groups, but a trend of better RRs and longer survivals wasobserved in the NLR $<$ 3.5 group than in the NLR≥3.5 group. Regarding adverse events, fatigue (grades 1 − 2) was observed in 8, hypothyroidism (grade 1–2) in 11, renal dysfunction (grade 1–3) in 6, loss of appetite (grade 1–2) in 2, pneumonitis (grade 3) in 1, rash (grade 1) in 2, and hypopituitarism (grade 3) in 1 patient(s). **Conclusions:** This retrospective study revealed the effectiveness and safety of nivolumab for MPM in the real-world setting.Nivolumab can be used as a standard second-line treatment for MPM. Furthermore, it has been suggested that the NLR may be a predictive marker of the effect of nivolumab for MPM, as pointed out in other carcinomas. Research Sponsor: None.

9053 Poster Session (Board #246), Fri, 8:00 AM-11:00 AM

A gentle therapy: Weekly epirubicin, as second-line treatment in elderly patients with malignant pleural mesothelioma (MPM). *First Author: Roberto Bollina, ASST Rhodense, Rho - Milan, Italy*

Background: MPM is a rapidly progressive tumor with a poor prognosis. Treatment options are limited for patients (pts) with PMP who experience disease progression after first-line pemetrexed-based chemotherapy (CT). This retrospective study wants to evaluate, in the age of immunotherapy, whether a gentle CT can be used as second line of treatment in elderly pts, above all maintaining quality of life (safety and tolerability) and improving progession free survival (PFS). Currently second-line CT is increasingly use, because many elderly pts are fit at the progression of the disease. No standard second/further line CT exist for MPM after failure of first-line pemetrexed based CT. The purpose of the study is to evaluate the clinical activity of weekly epirubicin as second-line CT in elderly with MPM. **Methods:** From July 2015 to March 2019, in Medical Oncology Dept. of ASST Rhodense 98 pts were elegible for analysis. Pts had histologically confermed unresectable MPM. Histology was epithelioid in 86 pts, sarcomatoid in 7 and biphasic in 5 pts. A Carboplatin(AUC4)-pemetrexed doublet was administered in 70 pts and 28 received gemcitabine as single agent how first line. A quality of life questionnaire was administered to each pt and geriatric comprehensive assessment (GCA) was performed. Epirubicin (E) was always administered with a schedule at 20 mg/msq day 1,8,15 every 28 until disease progression or intolerance. The primary endpoint was PFS, and secondary endpoints were the overall response rate (ORR) and QofL an overall survival (OS). **Results:** Of the 98 elegible pts, 71 was males, and 27 was female . Median age: 78 (range 72-86) PS: 0/1/2 was respectively in 32%, 60% and 8% of pts. A median of 5 cycles of E (range 2 -16) was delivered; 3% of pts required dose modification. PFS was of 7 months (range 3-16) . ORR was as follow: 0 CR, 18 PR (17%), 44 SD (44%) and PD occurred in 36 pts (39%). OS was 11 months (range 5-22). No life threatening event occurred. No grade 3-4 toxicities were observed . Liver toxicity grade 1-2in 10 pts (10%), thrombocytopenia grade 1 in 9 pts (9%), neutropenia grade 1-2 in 40 pts (40%), fatigue grade 2 in 33pts (32%), nausea grade 1 in 20 pts (20%). The analitical and stratified data will be exposed. **Conclusions:** Also in the era of immunotherapy, a simple treatment, E in weekly schedule has demonstrated to be a gentle therapy with a possibility to treat in second line, pre-treated elderly pts with MPM in progression after first line therapy, with an acceptable profile . Now this schedule could be considered as a safe and standard secon-line CT in elderly pts. Research Sponsor: None.

9054 Poster Session (Board #247), Fri, 8:00 AM-11:00 AM

Phase II study of olaparib in malignant mesothelioma (MM) to correlate efficacy with germline and somatic mutations in DNA repair genes. *First Author: Raffit Hassan, Thoracic and GI Malignancies Branch, National Cancer Institute, NIH, Bethesda, MD*

Background: BRCA1 associated protein 1 (*BAP1*), a nuclear deubiquitinase involved in DNA double-strand break repair is frequently mutated in MM. Because poly(ADP-ribose) polymerase inhibitors (PARPIs) induce synthetic lethality in *BRCA1/2* mutant cancers, we sought to evaluate efficacy of olaparib in patients with MM and correlate it with pathogenic germline and somatic mutations in DNA repair genes. **Methods:** Phase II single-center study (NCT03531840) enrolled patients with advanced pleural or peritoneal mesothelioma who had progressed on prior therapies, age $>$18 years, ECOG performance status $<$1, adequate organ and bone marrow function. Olaparib 300mg was given twice daily orally in 3 week cycles until disease progression or toxicity. Efficacy was assessed by CT scan every 6 weeks using RECIST criteria. Whole exome sequencing (WES) was performed on blood and tumor samples to identify pathogenic germline and somatic mutations in DNA repair genes. Primary objective was to determine response rate based on germline or somatic mutation status of DNA repair genes. **Results:** Between July 2018 to May 2019, 23 patients were enrolled, 15 pleural and 8 peritoneal MM [14 male; median age 63 (range 41-75 years); median number of prior treatments 3 (range 1-5)]. Median olaparib cycles received was 4 (2-21). WES to identify pathogenic mutations in the germline and tumor was performed in 23 and 17 patients respectively. Four patients had germline *BAP1*, 1 germline *MRE11A*, and 5 had somatic *BAP1* mutations. Of 22 evaluable patients, 1(4%) had partial response (PR), 17 (77%) had stable disease at 6 weeks and 4 (18%) had progressive disease. Patient with PR had a germline mutation in *MRE11A*. Median progression free survival (PFS) and overall survival (OS) for all patients was 3.4 months (95% CI: 2.7 – 4.8 months) and 8.1 months (95% CI: 4.5 months – not estimable) respectively. Median PFS of germline *BAP1* mutant patients (n = 4) was 2.3 months (95% CI: 1.3 – 3.6 months) compared to 4.1 months (95% CI: 2.7 – 5.5 months) for *BAP1*wild type patients (n = 18;P = 0.026). Median OS was 4.6 months (95% CI: 3.1 – 4.9 months) for patients with germline *BAP1* mutation versus not reached for those without germline *BAP1* mutation (P = 0.0058). The most common side effects of olaparib were anemia (16%), lymphopenia (24%), nausea (14%), and increased creatinine (9%). **Conclusions:** Olaparib has limited anti-tumor activity in previously treated MM patients including those with germline or somatic *BAP1* mutations. Presence of germline *BAP1* mutations was associated with decreased PFS and OS. Clinical trial information: NCT03531840. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

9055 Poster Session (Board #248), Fri, 8:00 AM-11:00 AM

Phase I study of TRC102 in combination with cisplatin and pemetrexed in patients with advanced solid tumors/Phase II study of TRC102 with pemetrexed in patients with mesothelioma refractory to pemetrexed and cisplatin or carboplatin. *First Author: Marianna Koczywas, Department of Medical Oncology and Therapeutics Research, City of Hope, Duarte, CA*

Background: Treatment options remain limited in malignant pleural mesothelioma refractory to pemetrexed +/- platinum. TRC102 (methoxyamine hydrochloride) is a novel biochemical inhibitor of the BER pathway. Available data support the hypothesis that TRC102 bound DNA is a substrate for topoisomerase II, which cleaves TRC102-bound DNA sites to produce strand breaks in cancer cells that cause cellular apoptosis and enhance the cytotoxic effects of chemotherapy. **Methods:** This was a parallel cohort trial of a Phase I of TRC102 in combination with cisplatin (CDDP) and pemetrexed in patients with advanced solid tumors (Arm A) and a Phase II of TRC102 with pemetrexed in patients with mesothelioma refractory to platinum and pemetrexed (Arm B). **Results:** In Arm A dose escalation, 16 pts (11M/5F) were treated; 9 evaluable through 3 TRC102 dose levels (50, 75, and 100 mg/day, PO), with CDDP 60 mg/m^2 and pemetrexed 500 mg/m^2 (levels 1- 3); and 5 evaluable at TRC102 100 mg/day PO, CDDP 75 mg/m^2, pemetrexed 500 mg/m^2 (level 4). Cycles were every 21 days. There were no DLT's, establishing level 4 as the RP2D. The only grade 4 treatment-related AE was thrombocytopenia on cycle 22 (level 2). Cycle 1 grade 3 AEs were 1 hypophosphatemia (level 1) and 1 leukopenia (level 2). There were 3 PRs (all parotid salivary gland tumors). Median PFS (95%CI) = 7.1% (1.4 – 15.5) mos. Arm B was designed as the first stage of a two stage Gehan design trial of patients with mesothelioma who had progressed on or recurred within 6 months of pemetrexed + platinum frontline treatment. 14 pts were treated with TRC102 50 mg/day D1-4 and pemetrexed 500 mg/m^2 every 21 days. There were 2 PRs (both in epithelioid cancer of which 1 was confirmed), meeting the pre-specified criteria for continued interest ($>$ 0/14). mPFS (95% CI) was 4.3 (1.4 - 6.8) mos. 8 pts had stable disease for at least 1 cycle (4 stable at cycles 6, 9, 10 and 12). There were 1 grade 4 neutropenia and 5 grade 3 AE's (1 each – anemia, neutropenia, leukopenia, fatigue, hyponatremia). **Conclusions:** TRC102 in combination with CDDP and pemetrexed exhibited antitumor activity, particularly in salivary gland tumors, and a tolerable safety profile at the doses tested. The combination of TRC102 and pemetrexed demonstrated activity in malignant mesothelioma that progressed on prior pemetrexed. Additional studies are warranted to confirm preliminary signals of activity. Clinical trial information: NCT02535312. Research Sponsor: U.S. National Institutes of Health.

9056 Poster Session (Board #249), Fri, 8:00 AM-11:00 AM

Genomic landscape and immune phenotype of malignant pleural mesothelioma. *First Author: Meera Patel, Wayne State University/Karmanos Cancer Institute, Detroit, MI*

Background: Malignant pleural mesothelioma (MPM) is a relatively uncommon malignancy with poor prognosis and no major therapeutic breakthroughs over the past decade. Better understanding of the genomic landscape and distribution of immune biomarkers in this disease has the potential to enable development of novel therapies. **Methods:** We analyzed molecular profiles of 222 MPM tumors using next-generation sequencing of 592 genes utilizing Caris Life Sciences platform. Genes were grouped into pathways: DNA damage repair (DDR) (*ATM, BRCA2, BRIP1, BAP1, CHEK2, ERCC2, FANCA/D2/E/L, MLH1, MSH6, MUTYH, NBN, PMS2, RAD50/51B, WRN*), cell cycle regulation including *TP53* (*RB1,CCNE1, CDKN2A, CCND1, CCND3, CDKN1B*), chromatin remodeling (CR) (*ARID2, ASXL1, DNMT3A, EP300, EZH2, KDM6A, KMT2C, KMT2D, NSD3, PBRM1, SMARCB1/A4, SETD2*), RAS/MAPK (*KRAS, MAP2K1, NF1, NF2*), and PI3K/AKT (*AKT, PIK3CA, PIK3R1/R2, PTEN, RICTOR, TSC1, TSC2, ZNF703*). Tumor mutational burden (TMB), PD-L1 expression (SP142 IHC, tumor staining), and MSI/MMR were analyzed. Seventy-two cases also had whole transcriptome sequencing data. Differences in alterations were compared for age, gender, and pathways. **Results:** Median age of patients (pts) was 72 yr (range, 37-90), 73% were male. Gene pathway alterations were seen in 81% of cases. DDR, specifically homologous recombination (HR), was the most commonly mutated pathway (36.9%), followed by RAS (25.2%) and CR (18.9%). Genes mutated in ≥5% of cases included *BAP1* (26.3%), *NF2* (23.5%), *TP53* (15.5%), *SETD2* (10.2%). PD-L1 was high (≥50% tumor cells positive) in 11.4% (n = 24), intermediate (1-49%) in 31.4% (n = 66), and negative (< 1%) in 57.1% (n = 120) pts. TMB was high (≥10 mutations/Mb) in 9.6% of tumors (n = 20). None of the tumors were dMMR/MSI-H. HR gene *BAP1* and CR gene *SETD2* mutations trended to be more prevalent in pts ≥70 yo (p = 0.02). CR trended to be more commonly mutated in females (p = 0.02). No other significant differences were found in specific gene/pathway alterations, PD-L1 expression, or TMB in the context of age and gender. Distribution of PD-L1 expression was not different among various pathways. No highly recurrent, targetable fusion isoforms were seen among the 85 identified (mean 1.1 fusions/tumor), which have not yet been characterized for pathogenicity. **Conclusions:** The majority of MPM tumors harbor alteration in one of the key cellular pathways. HR pathway mutations are the most common. The majority of tumors were PD-L1 negative and carry low TMB indicating low immunogenicity. No age and gender specific differences exist except for *BAP1* and *SETD2* mutations. Research Sponsor: None.

9057 Poster Session (Board #250), Fri, 8:00 AM-11:00 AM

MiST1: A phase IIa trial of rucaparib in patients harbouring BAP1/BRCA1 deficient relapsed malignant mesothelioma. *First Author: Dean Anthony Fennell, University Hospitals of Leicester, Leicester, United Kingdom*

Background: Malignant Mesothelioma (MM) remains an incurable cancer lacking effective treatments in the relapsed setting. Personalised therapy is still in its infancy. Homologous recombination (HR) deficiency associated with BRCA1 mutation has been shown to predict sensitivity to inhibition of poly-ADP ribose. In MM, BRCA1 associated protein 1 carboxy-terminal hydrolase (BAP1) is frequently mutated. It regulates both HR, and BRCA1 expression which is lost in 38% of mesotheliomas. Mesothelioma Stratified Therapy 1 (MiST1) was designed to test the hypothesis that BAP1/BRCA1 negative mesotheliomas would exhibit defective HR and exhibit sensitivity to PARP inhibition. **Methods:** MiST1 was a single centre, open label single arm phase IIa design with prospective molecular stratification; cytoplasmic/negative *BAP1* or *BRCA1* deficient MM was deemed eligible. Treatment was 600mg BD rucaparib (R) PO daily every 28 days for 6 cycles or until disease progression, unacceptable toxicity, withdrawal or death. Primary outcome was disease control rate at 12 weeks (DCR12w); secondary outcomes safety and toxicity profile, objective response rate (ORR) and DCR at 24 weeks (DCR24w). The null hypothesis states the true DCR12w is less than or equal to 25% and was tested against a one-sided alternative hypothesis that the DCR12w will be equal to or greater than 50%. **Results:** Between February 2019 and June 2019, 26 patients (pts) were eligible and consented to MiST1, median age 65.5 years, 85% are male and 15% female. Of these pts 15% had an ECOG performance status (PS) of 0 and 85% had an ECOG PS of 1. Molecular eligibility was 89% for BAP1 alone, 50% BRCA1 alone, and 39% BAP1+BRCA1. Primary tumour site was thoracic (96%) and subtype epithelioid (81%). DCR12w was 57.7% (95% CI, 36.9 - 76.7), DCR24w was 23.1% (95% CI, 9.0 – 43.7) and ORR was 11.5% (95%CI, 2.5 – 30.2). R was well tolerated with 9% (15/166) grade (G) 3/4 toxicities seen in 10 pts (38%), with no G5 toxicities. The most common adverse events were nausea occurring in 18 pts (69%), fatigue in 14 pts (54%), and decreased appetite in 10 pts (38%). Six cycles of R was received by 8 pts (30.8%). Dose reductions occurred in 9 pts (n = 8; 1 dose and n = 1; 2 doses). Dose delays occurred in 14 pts. **Conclusions:** MiST1 using the PARP inhibitor R met its primary endpoint of disease control rate at 12 weeks, showing promising efficacy with manageable toxicity. HR deficiency mutation signature enrichment is being investigated to refine the identification of responders to PARP inhibition. PARP inhibition warrants further investigation in MM. Clinical trial information: NCT03654833. Research Sponsor: British Lung Foundation, Pharmaceutical/Biotech Company.

9058 Poster Session (Board #251), Fri, 8:00 AM-11:00 AM

Safety and efficacy of tazemetostat, an enhancer of zeste-homolog 2 inhibitor, in patients with relapsed or refractory malignant mesothelioma. *First Author: Marjorie Glass Zauderer, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Breast cancer gene 1 (BRCA1)-associated protein 1 (BAP1), a nuclear deubiquitinase, is commonly inactivated in malignant mesothelioma. Preclinical data showed that BAP1 inactivation sensitizes mesothelial cells to inhibition of enhancer of zeste-homolog 2 (EZH2), a methyltransferase implicated as an oncogenic driver in this tumor. This study evaluated the safety and efficacy of tazemetostat (TAZ), a potent and selective EZH2 inhibitor, in relapsed/refractory (R/R) malignant mesothelioma with BAP1-inactivation. **Methods:** EZH-203 (NCT02860286) was a 2-part, open-label, phase 2 study that assessed the pharmacokinetics (PK), safety, and efficacy of TAZ in pts with R/R malignant mesothelioma. In part 1, pts received TAZ 800 mg QD on day 1 (D1) and 800 mg BID, beginning day 2 of cycle 1 (C1). In part 2, pts received 800 mg of TAZ BID on D1 of C1. A two-stage Green-Dahlberg design was used for part 2. Primary endpoints were PK profiling of TAZ in all pts (part 1), and disease control rate (DCR) at week 12 in pts with BAP1-deficient R/R malignant mesothelioma (part 2). Secondary endpoints included safety, overall response rate (ORR), progression-free survival, overall survival, and duration of response (DOR). **Results:** The study enrolled 74 pts with R/R malignant mesothelioma, 70 pts (95%) were centrally confirmed to be BAP1-deficient. Median prior lines of therapy were 2 (range, 1-9). Observed clinical data in the presence of CYP3A4 inhibitors and inducers suggest a low DDI potential of TAZ. The 12 week DCR was 47% (n = 35). The ORR per RECIST version 1.1 was 3% [complete response: 0%; partial response (PR): 3% (n = 2)]. Of the 2 patients with PR, 1 had a DOR of 21 weeks and the other is ongoing (15.3 weeks at data cut off). 47 pts (64%) and 21 pts (28%) had stable disease (SD) and progressive disease, respectively. Overall, 91% pts discontinued, either due to disease progression (n = 65), death (n = 5), or treatment discontinuation (n = 1). Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in ≤5% of patients, most commonly anemia (5%) and dyspnea (4%). No pts discontinued due to TEAEs. There were no treatment related deaths. **Conclusions:** Based on disease control rate and stable disease, TAZ showed antitumor activity in pts with BAP1-deficient R/R malignant mesothelioma. TAZ monotherapy was generally well-tolerated. The current data support further clinical evaluation of TAZ in these pts. Furthermore, this trial presents an optimal paradigm for drug development in molecularly-enriched cohorts in mesothelioma. Clinical trial information: NCT02860286. Research Sponsor: Epizyme, Inc.

9059 Poster Session (Board #252), Fri, 8:00 AM-11:00 AM

Peritoneal mesotheliomas characterized by less cell-cycle alterations and more *TRAF7* alterations than malignant pleural mesotheliomas. *First Author: Michael Offin, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: While peritoneal mesotheliomas (PM) are clinically distinct from malignant pleural mesotheliomas (MPM) it is unknown if genetic alterations reflect these differences. Here we report the molecular alterations and clinicopathologic characteristics of a prospectively collected PM cohort as compared to MPM. **Methods:** Patients with PM (n = 59) and targeted next generation sequencing (NGS; MSK-IMPACT) from January 2014 to January 2019 were assessed and followed through February 2020. Germline variants were analyzed in consented patients. NGS was compared to patients with MPM (n = 194) assessed in the same time interval. **Results:** Median age at diagnosis was 61 (range: 20-77), 56% were women (n = 33), and 92% had epithelioid histology (n = 54). 66% had ascites (n = 39) and 24% developed extra-abdominal metastases (n = 14; including lung, pleura, and mediastinum). 68% (n = 40) underwent surgical debulking and 80% (n = 47) had infusional therapy (median lines: 3) including platinum/pemetrexed (n = 38), EPIC (n = 22), HIPEC (n = 15), and immunotherapy (n = 16). The median overall survival (OS) from diagnosis was 5.4 years (median follow up 3.5 years). The median tumor mutation burden (TMB) was 1.8 mut/Mb (range: 0-14.9) in PM vs 2.0 mut/Mb (range: 0-31.5) in MPM (p = 0.049). More patients with PM had *TRAF7* alterations than in MPM (5/59 vs 3/194; p = 0.02) while fewer had *CDKN2A*/*CDKN2B* (4 vs 55; p = 0.0004). All patients with TRAF7 altered PM had well-differentiated papillary epithelioid histology. There was no difference in the prevalence of other common alterations such as *BAP1* (32 vs 98; p = 0.66), *NF2* (12 vs 55, p = 0.24), *SETD2* (11 vs 24; p = 0.28), and *TP53* (9 vs 28; p = 0.84) in PM vs MPM respectively. Patients with *BAP1*-altered PM had shorter OS (4.6 vs 9.8 years; HR 2.6, 95% CI 1.1-6.4; p = 0.04) while *TRAF7*-altered PM had improved OS (not reached vs 4.8 years; HR 0.3, 95% CI 0.1-0.9; p = 0.04) compared to wild type. 13% (4/30) of patients with PM had pathogenic variants on germline NGS (*POT1* I78T, *MUTYH* R109Y, *BAP1* E402*, *APC* I1037K). **Conclusions:** NGS confirms the distinct biology of PM compared to MPM. Specifically, the former shows fewer cell cycle (*CDKN2*) alterations compared to MPM. In contrast to MPM, *BAP1* alteration was associated with shorter survival. As previously described, we found enrichment of *TRAF7* in well differentiated papillary epithelioid PM associated with improved survival but notably some *TRAF7* alterations were identified in poorly differentiated MPM. Consistent with other reports, the prevalence of germline alterations was 13%. Research Sponsor: National Cancer Institute of the National Institutes of Health (T32 CA009207, P30 CA008748).

9060 Poster Session (Board #253), Fri, 8:00 AM-11:00 AM

Role of immunotherapy in stage IV large cell neuroendocrine carcinoma of the lung. *First Author: Takefumi Komiya, Parkview Cancer Institute, Fort Wayne, IN*

Background: Despite approvals of immune checkpoint inhibitors in both small cell and non-small cell lung cancers, role of immunotherapy in large cell neuroendocrine carcinoma (LCNEC) in lung is undefined. **Methods:** Using National Cancer Database (NCDB), Stage IV LCNEC cases diagnosed in 2014-2016 with at least 30-day follow up were analyzed. Clinical demographics included age (20-69 vs. 70+), sex (male vs. female), race (whites vs. others), insurance (uninsured vs. others), institution (academic vs. others), Charlson-Deyo score (0-1 vs. 2-3), brain metastasis (Yes vs. No), liver metastasis (Yes vs. No). Information regarding cancer treatment was limited to first course of therapy, including surgery for primary lesion (Yes vs. No), radiation (Yes vs. No), chemotherapy (Yes vs. No), and immunotherapy (Yes vs. No). Survival analysis was performed using Kaplan-Meier curves and Log-rank tests. Cox proportional hazard model was used for multivariate analyses. A two-sided p-value < 0.05 was considered as significant. **Results:** Among 661 eligible cases, 37 patients were treated with immunotherapy. No significant association between use of immunotherapy and clinical demographics was observed except for use of chemotherapy ($p = 0.0008$). Chemotherapy was administered in 34 (92%) and 406 (65%) of cases in immunotherapy and non-immunotherapy groups, respectively. Use of immunotherapy was associated with improved overall survival (Log-rank $p = 0.0168$). Landmark analysis in the immunotherapy group showed 12 and 18-month survival of 34.0% and 29.1%, respectively, as compared with 24.1% and 15.0% in the non-immunotherapy group Multivariate analysis demonstrated that female sex, presence of liver metastases, surgery, use of chemotherapy and immunotherapy (HR = 0.64, $p = 0.0164$) had significantly improved survival. Propensity score matching in overall survival showed a nonsignificant trend ($p = 0.0733$) in favor of immunotherapy group. **Conclusions:** This retrospective study using one of the largest cancer databases suggests that use of immunotherapy may improve survival of LCNEC patients. Prospective studies are warranted for further validation. Research Sponsor: None.

9061 Poster Session (Board #254), Fri, 8:00 AM-11:00 AM

Carboplatin versus cisplatin for the treatment of extensive-stage small cell lung cancer (SCLC): A National VA Database analysis. *First Author: Ibrahim Azar, Karmanos Cancer Institute, Detroit, MI*

Background: Current standard of care first line treatment for extensive stage SCLC includes combination of platinum-etoposide doublet with an immune checkpoint inhibitor. Carboplatin is preferred over cisplatin in the extensive stage disease because of its favorable toxicity profile. Data comparing the efficacy of carboplatin with cisplatin in the metastatic setting are limited. **Methods:** Data from the National VA Cancer Cube database were compiled. Only pathologically confirmed cases of extensive stage SCLC that received platinum-based multiagent chemotherapy were included. Interval-censored Weibull and Cox proportional hazard regression models were used to estimate median overall survival (OS) and hazard ratio (HR), respectively. Two survival curves were compared by a Wald test. **Results:** Overall, 2600 SCLC cases were studied: 1968 received carboplatin-based therapy (Carbo-SCLC) while 632 received cisplatin-based therapy (Cis-SCLC). Median OS of Carbo-SCLC and Cis-SCLC was 0.71 years (95% CI 0.68-0.75) versus 0.70 years (95% CI 0.64-0.76), respectively (HR = 0.99; 95% CI 0.90-1.10; $p = 0.90$). Median OS of patients with ECOG-PS of 0, 1, 2 and 3 was similar for Carbo-SCLC and Cis-SCLC. HR of death for Carbo-SCLC compared to Cis-SCLC stratified by performance status were: ECOG-PS 0: 1.04 (95% CI 0.78-1.38; $p = 0.80$); ECOG-PS 1: 0.87 (95% CI 0.71-1.06; $p = 0.17$); ECOG-PS 2: 0.92 (95% CI 0.69-1.24; $p = 0.6$); ECOG- PS 3: 1.13 (95% CI 0.66-1.92; $p = 0.66$). Multivariable regression analysis accounting for age and ECOG-PS shows a HR of 0.92 (95% CI 0.80-1.05; $p = 0.24$). **Conclusions:** Cisplatin-based chemotherapy was not associated with a survival advantage over carboplatin-based chemotherapy in extensive-stage SCLC., including in patients with robust performance status and young patients. The findings from this large dataset along with the favorable toxicity profile of carboplatin support its use as the platinum agent of choice in extensive stage SCLC. Research Sponsor: None.

9062 Poster Session (Board #255), Fri, 8:00 AM-11:00 AM

Correlation of decreased expression of PD-L1 on circulating tumor cells and clinical benefit in SCLC Patients treated with RRx-001, a CD47 down-regulator, in a phase II trial. *First Author: Corey Carter, EpicentRx, Torrey Pines, CA*

Background: In a Phase 2 trial called QUADRUPLE THREAT (QT) (NCT02489903), where 2nd line+ small cell lung cancer (SCLC) patients were treated with RRx-001 and a platinum doublet, the programmed death-ligand 1 (PD-L1) status of circulating tumor cells (CTCs) in 14 patient samples was evaluated. **Methods:** 26 consented patients received weekly RRx-001 4 mg followed by a reintroduced platinum doublet; epithelial cell adhesion molecule (EPCAM+) CTCs from 10 ml of blood on two consecutive timepoints cycle 1 day 1 and cycle 3 day 8 (cycle duration = 1 week) were detected by EpCAM-based immunomagnetic capture and flow cytometric analysis. CTCs were further characterized for protein expression of PD-L1. Tumor response was classified as partial or complete response based on the response evaluation criteria in solid tumors (RECISTv1.1) measured every 6 weeks. **Results:** The analyzed clinical data set comprised 14 RECIST-evaluable patients. 50% were females (7/14) and the median age (years) at baseline was 64.5 (Min = 48.5, Max = 84.2, SD = 10.3). The logistic model McFadden goodness of fit score (0 to 100) is 0.477, which is a strong correlation value. The logistic model analyzing the association of CTC PD-L1 expression at two timepoints and response had an approximate 92.8% accuracy in its prediction of clinical benefit (SD/PR/CR). Accuracy is defined in the standard way as 1- (False positive rate + False negative rate). The estimated ROC displayed in Figure 1 suggests a ROC AUC of 0.93 (95% CI: 0.78, 0.99), an excellent measure of performance. **Conclusions:** Reduction of PD-L1 expression was correlated with good clinical outcome after RRx-001 + platinum doublet treatment. PD-L1 expression reduction in favor of RRx-001 RECIST clinical benefit was clinically significant as compared to non-responders with progressive disease (PD). In the ongoing SCLC Phase 3 study called REPLATINUM (NCT03699956), analyses are planned to correlate response and survival with expression of CD47 and PD-L1 on CTCs. Clinical trial information: NCT02489903. Research Sponsor: EpicentRx.

9063 Poster Session (Board #256), Fri, 8:00 AM-11:00 AM

Effect of anlotinib in advanced small cell lung cancer (SCLC) patients relapsed within three months after second-line treatment: A subgroup analysis from a randomized, double-blind phase II trial (ALTER 1202). *First Author: Jianhua Shi, Linyi Cancer Hospital, Linyi, China*

Background: Anlotinib had significantly improved progress-free survival (PFS) and overall survival (OS) of advanced small cell lung cancer (SCLC) patients received at least two lines chemotherapy in the ALTER 1202 trial. Here, we reported the effect of anlotinib in advance SCLC patients relapsed within 3 months after second-line treatment. **Methods:** The ALTER 1202 was a randomized, double-blind phase 2 trial including patients with advanced SCLC that received at least two previous lines of chemotherapy. Eligible patients were randomized in a 2:1 ratio to receive either anlotinib or placebo until tumor progression or unacceptable toxicity. The subgroup analysis assessed the effect of anlotinib in patients relapsed within 3 months after second-line treatment. The primary outcome was PFS. The secondary outcomes were OS, objective response rate (ORR), disease control rate (DCR) and safety. This trial was registered with ClinicalTrials.gov, number NCT03059797. **Results:** In the ALTER1202 trial, 67 patients in anlotinib group and 34 patients in placebo group relapsed within 3 months after second-line treatment. Among them, the median PFS was 3.98 months (95% confidence interval [CI], 2.79 to 4.24) with anlotinib versus 0.72 months (95% CI, 0.69 to 0.82) with placebo (hazard ratio [HR], 0.14; 95% CI, 0.08 to 0.26; $P < 0.0001$). Meanwhile, anlotinib significantly prolonged OS compared with placebo (7.29 months [95% CI, 6.51 to 10.51] versus 4.37 months [95% CI, 2.33 to 6.47]; HR, 0.42 [95% CI, 0.23 to 0.74]; $P = 0.0059$) in patients relapsed within 3 months after second-line treatment. ORR was 4.48% (3 PR) for anlotinib and 2.94% (1 PR) for placebo ($P = 0.708$). DCR was 73.13% for anlotinib and 11.76% for placebo ($P < 0.0001$). The most common adverse events were hypertension (38.81%), anorexia (28.36%), fatigue (22.39%) and Elevation of alanine aminotransferase (17.91%). **Conclusions:** Anlotinib improved PFS and OS in advanced SCLC patients relapsed within 3 months after second-line treatment and was well tolerated. Research Sponsor: None.

9064 Poster Session (Board #257), Fri, 8:00 AM-11:00 AM

Phase II study of gedatolisib for small-cell lung cancer (SCLC) patients (pts) with genetic alterations in PI3K/AKT/mTOR pathway based on a large-scale nationwide genomic screening network in Japan (EAGLE-PAT/LC-SCRUM-Japan). *First Author: Hibiki Udagawa, National Cancer Center Hospital East, Kashiwa, Japan*

Background: Development of targeted therapy for SCLC based on a large-scale genomic screening is an innovative challenge. Gedatolisib is a highly potent dual inhibitor of PI3K/mTOR and is expected to have an effect for tumors with PI3K/AKT/mTOR pathway alterations. SCLC harboring this pathway alterations is rare. Thus, we conducted a phase II study based on a nationwide genomic screening network in Japan (LC-SCRUM-Japan) to develop novel targeted therapies. **Methods:** SCLC pts with targetable genetic alterations were screened at 154 institutions in Japan. A multicenter, single-arm phase II study was conducted to evaluate the efficacy and safety of gedatolisib in advanced SCLC pts with genetic alterations in the PI3K/AKT/mTOR pathway. The primary endpoint was objective response rate (ORR). The planned sample size was 19 (threshold and expected ORR of 20% and 50%, one-sided alpha of 5%, and power of 80%). **Results:** 930 SCLC pts were screened from July 2015 to January 2020. Targetable genetic alterations were identified in 148 pts (16%), including 53 PI3K/AKT/mTOR (6%), 81 MYC family (9%), 10 EGFR (1%) and 15 KRAS (2%). A total of 12 pts with genetic alterations in the PI3K/AKT/mTOR pathway (5 PIK3CA, 6 PTEN, and 1 AKT1 mutation) were enrolled in the phase II study. The median age was 67 years (range 58-79), 7 pts were male and 5 pts received 2 or more prior chemotherapy (range 1-4). The ORR was 0% and disease control rate was 25%. The median progression-free survival (PFS) was 0.9 months (95% CI, 0.4 to 3.0). The median overall survival was 5.8 months (95% CI, 1.1 to NR). Treatment-related G3 adverse events (hypertension, hypoalbuminemia, oral mucositis, ALT increased and creatinine increased) were observed in 4 pts. One patient with PTEN I8fs mutation had a long duration of stable disease (PFS; 6.7 months). **Conclusions:** This Large-scale nationwide genomic screening network was effective to identify rare targetable genetic alterations and had a potential role to develop targeted therapies in SCLC. This phase II study didn't show promising clinical benefit of gedatolisib for advanced SCLC pts with genetic alterations in the PI3K/AKT/mTOR pathway. The safety profile of gedatolisib was similar to that reported previously. Clinical trial information: UMIN000020585. Research Sponsor: Japan Agency for Medical Research and Development.

9065 Poster Session (Board #258), Fri, 8:00 AM-11:00 AM

Preliminary efficacy data of platinum-pretreated small cell lung cancer (SCLC) cohort of NCI 9881 study: A phase II study of cediranib in combination with olaparib in advanced solid tumors. *First Author: Joseph W. Kim, Yale Cancer Center, Yale School of Medicine, New Haven, CT*

Background: Cediranib, a pan-vascular endothelial growth factor receptor tyrosine kinase inhibitor, suppresses expression of *BRCA1, BRCA2*, and *RAD51* and increases sensitivity of tumors to poly-(ADP-ribose) polymerase (PARP) inhibitors *in vitro*. Olaparib, a PARP inhibitor, demonstrated clinical efficacy in patients with advanced solid tumors carrying a germline *BRCA* mutation. We therefore tested the anti-tumor activity of cediranib and olaparib combination in patients (pts) with advanced solid tumors. Here, we report the data from the SCLC cohort. **Methods:** This multi-institutional, two-stage, phase 2 study enrolled pts with metastatic SCLC previously treated with a minimum of one prior line of platinum-based chemotherapy in advanced setting. Patients were treated with cediranib 30mg po daily plus olaparib 200mg po BID until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) by RECIST v1.1. Baseline tumor biopsies were obtained for biomarker analyses. **Results:** Baseline characteristics of the 25 pts enrolled are summarized below. The overall ORR rate was 28% (95% CI: 0.104,0.456). Median duration of response was 3.8 months (mos). Six of 8 pts had an objective response lasting longer than 3 mos up to 10.3 months. Disease control rate (# of pts with CR, PR or SD / # evaluable pts) was 88% (95% CI: 0.75,1.01). Median progression free survival was 4.1 mos (95% CI: 2.3, 6.2). Median OS was 5.5 mos (95% CI: 3.4, NA). Grade 3/4 adverse events (G3/4 AEs), irrespective of attribution, occurred in 14 of 25 (56%). G3/4 AEs occurring in $>$ 10% of pts were hypertension (21%), fatigue (17%) and weight loss (13%). **Conclusions:** The cediranib/olaparib combination resulted in promising clinical activity with ORR of 28% in biomarker-unselected pts with platinum-pretreated SCLC. The regimen required prompt initiation of antihypertensives, but AEs were overall manageable. Analyses of mutation status in homologous recombination DNA repair genes are going and will be correlated with clinical activity. Clinical trial information: NCT02498613. Research Sponsor: U.S. National Institutes of Health.

Median (range)	SCLC (n = 25)
Age	67, (46-79)
# of prior therapies	2 (1-5)
Platinum-sensitive disease (> 90 days interval to start subsequent therapy)	80%
Prior immunotherapy (IO)	52%
Interval from the last dose IO to start of study drugs, in days	97, (31-651)

9066 Poster Session (Board #259), Fri, 8:00 AM-11:00 AM

The efficacy and safety profile of anlotinib with etoposide plus cisplatin/carboplatin in treatment-naive extensive-stage small cell lung cancer(SCLC) patients: Results from a phase II single-arm trial. *First Author: Pengbo Deng, Department of Respiratory Medicine, Xiangya Hospital, Central South University, Changsha, China*

Background: Combination of etoposide and cisplatin/carboplatin is the most commonly used initial chemoptherapy regiment in extensive-stage small cell lung cancer. A meta-analysis released that, there is no significant difference was observed in Objective response rate(ORR), progression-free survival (PFS), or overall survival(OS) in patients(pts) receiving cisplatin-base versus carboplatin-based regimens. We performed a single-arm phase II trial to determine if maintain of single-agent anlotinib, an oral VEGFR, FGFR, PDGFR and c-Kit tyrosine kinase inhibitor, after 4-6 cycles of anlotinib + etoposide + cisplatin/carboplatin would improve PFS and ORR. **Methods:** SCLC pts (18~70 yrs, extensive-stage SCLC, no prior systematic chemo/ICI therapy) received anlotinib(12mg QD from day 1 to 14 of a 21-day cycle) +etoposide(100mg/m^2, d1~3 of 21-day cycle)+ cisplatin(75-80mg/m^2,Q3W)/ carboplatin(AUC = 5~6,Q3W) for 4~6 cycles, and anlotinib maintenance. The dual-primary endpoint were PFS and ORR. **Results:** Between Oct.2018 to Dec.2019, 27 pts enrolled and included in the efficacy and safety analysis: age: median 62 (range:44-71); male 93%; cisplatin/ carboplatin/ both 11%/78%/11%; 37%(10/27) of pts required chemotherapy dose modification only, and the other 30% (8/27) of pts required anlotinib+ chemotherapy dose modification.The median PFS was 9.61 months (95%CI:7.80-11.42). ORR was 77.78% (21/27), disease control rate (DCR) was 96.30% (26/27).Toxicities≥grade 3 included: neutropenia 22%, leukopenia 11%, hand-foot syndrome 15%, nausea 4%, mucositis 4%, edema 4%, anorexia 4%, xerostomia 4% and fatigue 4%; there were no grade 5 toxicities. **Conclusions:** Combined treatment with anlotinib plus etoposide and cisplatin/carboplatin for treatment-naive extensive-stage SCLC was well tolerated with promising PFS and ORR to date but showed no new risk for AEs. Based on these encouraging results, phase III trial of anlotinib plus etoposide and cisplatin/carboplatin for treatment-naive SCLC has been warranted. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

9067 Poster Session (Board #260), Fri, 8:00 AM-11:00 AM

Early ctDNA response assessment for prediction of platinum sensitivity in small cell lung cancer. *First Author: Yonina R. Murciano-Goroff, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Small cell lung cancer (SCLC) is an aggressive disease, characterized by inevitable chemotherapy resistance and rapid progression. We hypothesized that circulating tumor DNA (ctDNA) analysis can rapidly identify sensitivity to platinum-based therapy. **Methods:** Patients with SCLC at Memorial Sloan Kettering Cancer Center underwent serial plasma collections, including prior to the start of treatment and prior to Cycle 2 Day 1 of therapy (C2D1). Tumor mutations were identified from pre-treatment biopsies by MSK-IMPACT and/or pre-treatment plasma by CAncer Personalized Profiling by deep Sequencing (CAPP-Seq). Median variant allele fraction (VAF) of all mutations was monitored on subsequent blood draws using CAPP-Seq. Progression free survival (PFS) was measured from the time of first pre-treatment blood draw. **Results:** Plasma was collected from 19 patients treated with carboplatin and etoposide, including three who received concurrent atezolizumab. Seven were female, and mean age was 64.5 years. ctDNA was detected in 17 patients (89%), including in the two patients in our series with limited stage disease. The most common mutations were in *TP53* and *RB1* in 14 and 6 patients, respectively. Fourteen patients had available plasma at C2D1. At baseline prior to treatment, median VAF did not differ significantly between radiologic responders and non-responders (9.4% versus 30.3%, p = 0.35). After one cycle of chemotherapy, the VAF percent decrease was significantly more in responders versus non-responders (-96.9% versus -10.3%, p $<$ 0.001). Median VAF was therefore significantly lower by C2D1 in patients who responded compared to non-responders (0.51% versus 27.2%, p = 0.02). Those who ultimately responded to therapy all had a $>$ 2 fold decrease in VAF by C2D1. With a median follow-up of 180 days, PFS was significantly longer in patients with $>$ 2 fold decrease in VAF by C2D1 (6.4 versus 1.9 months, log rank p $<$ 0.001). **Conclusions:** A 2-fold decrease in plasma VAF by C2D1 predicted platinum-sensitivity in SCLC and was associated with longer PFS. ctDNA may permit early assessment of benefit and expedite alternative treatment options for those without significant decrease in median VAF after one cycle of therapy. Research Sponsor: U.S. National Institutes of Health, Philanthropy from patients.

9068 Poster Session (Board #261), Fri, 8:00 AM-11:00 AM

First-line durvalumab plus platinum-etoposide in extensive-stage (ES)-SCLC (CASPIAN): Impact of brain metastases on treatment patterns and outcomes. *First Author: Yuanbin Chen, Cancer & Hematology Centers of Western Michigan, Grand Rapids, MI*

Background: In the Phase 3, randomized, open-label CASPIAN study, first-line durvalumab (D) added to etoposide plus either cisplatin or carboplatin (EP) significantly improved OS vs EP alone (HR 0.73 [95% CI 0.59–0.91]; p = 0.0047) in pts with ES-SCLC at the planned interim analysis. Here we describe treatment patterns and outcomes for pts according to brain metastases. **Methods:** Treatment-naïve pts (WHO PS 0/1) with ES-SCLC received 4 cycles of D 1500 mg + EP q3w followed by maintenance D 1500 mg q4w until disease progression (PD) or up to 6 cycles of EP q3w and optional prophylactic cranial irradiation (PCI; investigator's discretion). Pts with either asymptomatic or treated and stable brain metastases were eligible. Brain imaging was suggested for pts with suspected brain metastases, but was not mandated at screening or during treatment. The primary endpoint was OS. Analysis of OS and PFS in pt subgroups with and without brain metastases was prespecified. Other analyses in these subgroups were post hoc. Data cutoff: Mar 11, 2019. **Results:** At baseline, 28 (10.4%) of 268 pts in the D + EP arm and 27 (10.0%) of 269 pts in the EP arm had known brain metastases; of these, only 3 pts (~11% of those with baseline brain metastases) in each arm received radiotherapy (RT) to the brain prior to study entry. D + EP consistently improved OS vs EP in pts with or without known brain metastases at baseline (HR 0.69 [95% CI 0.35–1.31] and 0.74 [0.59–0.93], respectively); PFS was also consistently improved with D + EP regardless of the presence or not of baseline brain metastases (HR 0.73 [0.42–1.29] and 0.78 [0.64–0.95]). Among pts without known brain metastases at baseline, similar proportions developed new brain metastases at first PD in the D + EP (20/240; 8.3%) and EP arms (23/242; 9.5%), despite 19 (7.9%) pts in the EP arm having received PCI. Overall, 48 of 268 (17.9%) and 49 of 269 (18.2%) pts in the D + EP and EP arms received RT to the brain subsequent to study treatment; rates remained similar across the D + EP and EP arms regardless of baseline brain metastases (11 of 28 [39.3%] and 11 of 27 [40.7%] pts with known baseline brain metastases, compared to 37 of 240 [15.4%] and 38 of 242 [15.7%] pts without known baseline brain metastases). **Conclusions:** In CASPIAN, OS and PFS outcomes were improved with D + EP vs EP regardless of baseline brain metastases, consistent with the ITT analyses. Rates of new brain metastases at first PD were similar between arms, although PCI was permitted only in the control arm. Rates of subsequent RT to the brain were also similar in both arms. Clinical trial information: NCT03043872. Research Sponsor: AstraZeneca.

9069 Poster Session (Board #262), Fri, 8:00 AM-11:00 AM

RESILIENT part I, an open-label, safety run-in of liposomal irinotecan in adults with small cell lung cancer (SCLC) who have progressed with platinum-based first-line (1L) therapy: Subgroup analyses by platinum sensitivity. *First Author: David R. Spigel, Sarah Cannon Research Institute, Nashville, TN*

Background: Most patients with extensive SCLC develop drug resistance to platinum-based 1L therapy or discontinue for other reasons, and second-line (2L) therapies are limited. RESILIENT (NCT03088813) is a two-part phase 2/3 study assessing the safety, tolerability and efficacy of 2L liposomal irinotecan monotherapy in adults with SCLC who progressed with platinum-based 1L therapy. Preliminary data from RESILIENT part 1 (cut-off May 8 2019; ≥ 12 weeks follow-up) showed that liposomal irinotecan 70 mg/m^2 free base every 2 weeks was generally well tolerated and had encouraging antitumor activity (Paz-Ares *et al*. WCLC 2019 OA03.03). Objective response rate (ORR; secondary endpoint) was 44% (11/25). Here we report efficacy analyses in *post hoc* subgroups by platinum sensitivity. **Methods:** RESILIENT part 1 was an open-label, single-arm study comprising dose-finding and dose-expansion phases. Eligible patients were aged ≥ 18 y, with an ECOG performance status score of 0/1 and adequate organ function; a single line of prior immunotherapy was allowed. Participants received liposomal irinotecan 70 mg/m^2 or 85 mg/m^2 free base every 2 weeks, with tumor assessments every 6 weeks (RECIST v1.1). Analyses were undertaken for the dose-finding phase recommended dose (RD) in subgroups of platinum-resistant/sensitive patients (with/without progression within 90 days from completion of 1L therapy). **Results:** During dose finding, 5 patients received liposomal irinotecan 85 mg/m^2 (deemed not tolerable; dose-limiting toxicity) and 12 received 70 mg/m^2 (deemed tolerable; RD for dose-expansion phase in which 13 more patients were included). Analyses included all 25 patients receiving the RD (mean exposure, 13.95 weeks [median 14.86; SD 7.222]). In the platinum-sensitive subgroup (33.3% men; median age 62.0 y) ORR was 53.3% (8/15) and 12-week disease control rate (DCR12wks) was 60% (9/15); in the platinum-resistant subgroup (50% men, median age 58.0 y) both ORR and DCR12wks were 30% (3/10). Overall and progression-free survival (secondary endpoints) are not yet mature. **Conclusions:** ORR and DCR12wks were numerically higher in platinum-sensitive than in platinum-resistant patients with SCLC who had progressed with platinum-based 1L therapy before receiving 2L liposomal irinotecan 70 mg/m^2 in this phase 2 study. RESILIENT part 2, an ongoing, phase 3, randomized controlled trial vs topotecan, will provide further data. Clinical trial information: NCT03088813. Research Sponsor: Ipsen.

9071 Poster Session (Board #264), Fri, 8:00 AM-11:00 AM

The impact of adjuvant therapy for non-metastatic thymic carcinoma: An analysis of the surveillance, epidemiology, and end results (SEER) database. *First Author: Richard Lee O'Neal, University of Kentucky, Markey Cancer Center, Greenville, KY*

Background: Thymic Carcinoma is a rare malignancy with an aggressive clinical course. While the importance of surgery in the non-metastatic setting has been well defined, the optimal role of radiation and/or systemic therapy in this setting remains controversial. This study utilized the Surveillance, Epidemiology, and End Results (SEER) database to investigate the impact of adjuvant therapy on overall survival in patients with thymic carcinoma. **Methods:** We identified adults in the SEER database with thymic carcinoma diagnosed between 1989 to 2015 for analysis. As the primary treatment for non-metastatic thymic carcinoma is surgery, we excluded patients who did not have surgery as a component of their treatment Patients were categorized into Masaoka-Koga stage groups (I-IIa, IIb, III, and IV). Kaplan-Meier estimates of 10-year OS and multivariate Cox proportional hazards regression analyses were performed. **Results:** 515 patients met the inclusion criteria, of which 125 were stage I-IIa, 46 were stage IIb, 191 were stage III, and 143 were stage IV. A multivariate analysis was performed, adjusting for age, sex, race, and tumor size. When compared to surgery, no statistical improvement in survival was seen with adjuvant radiation or chemotherapy in stage I-IIa or IIb thymic carcinoma. In stage III disease, standard of care surgery was compared with adjuvant radiation (hazard ratio 0.69 (95% confidence interval 0.29 – 1.63], p = 0.39), adjuvant chemotherapy (hazard ratio [HR] 0.84 [95% confidence interval 0.28 – 2.53], p = 0.76), and adjuvant chemo-radiotherapy (HR 0.40 [0.18 – 0.93], p = 0.03). On Kaplan-Meier analysis, triple therapy (surgery + chemo-radiotherapy) was also associated with a marked improvement in 10-year overall survival at 55.3%, compared to 39.8%, 23.9%, and 20.8% (adjuvant radiation, adjuvant chemotherapy, and surgery alone, respectively). **Conclusions:** This study finds that in stage III thymic carcinoma, surgery followed by chemo-radiotherapy is associated with improved overall survival compared to single or dual-modality treatments. Because of the rarity of this disease, there are no large randomized studies evaluating the most appropriate treatment modalities, therefore this data may assist with clinical decision making in non-metastatic thymic carcinoma. Research Sponsor: None.

9072 Poster Session (Board #265), Fri, 8:00 AM-11:00 AM

Treatment strategies for thymic carcinoma in a real-life setting: Insights from the rythmic network. *First Author: Nicolas Girard, Institut Curie, Institut du Thorax Curie-Montsouris, Paris, France*

Background: Thymic carcinomas are an aggressive and difficult to treat subset of thymic epithelial tumors (TETs) that represent a heterogeneous group of rare intrathoracic malignancies. Most of the current knowledge and guidelines tumors rely on surgically-oriented databases focusing on early-stage disease, and small prospective, single-arm trials conducted in metastatic thymic carcinomas, mostly in a refractory, late-line setting. "Réseau tumeurs THYMiques et Cancer" (RYTHMIC) is the nationwide network for TETs in France. The management of any patient has to be systematically discussed on a real-time basis at a national multidisciplinary tumor board; a database is hosted by the French Thoracic Cancer Intergroup (IFCT). **Methods:** We took advantage of the RYTHMIC prospective database to describe baseline characteristics, analyze treatment strategies, and provide landmark outcomes in a cohort of consecutive patients with thymic carcinoma. The inclusion period was January 2012 to April 2017. **Results:** A total of 213 patients were analyzed. Overall, 60 (28%) patients were considered as surgical candidates upfront, 91 (43%) received primary chemotherapy, and 62 (29%) received exclusive chemotherapy. Median OS was 49.2 months (IC95%: 34.8-63.6); OS was significantly longer in patients with a lower stage at diagnosis ($p < 0.001$), who were operated on upfront, as opposed to patients who received primary or exclusive chemotherapy ($p < 0.001$). Surgery, conducted upfront or after primary chemotherapy, was significantly associated with more prolonged OS ($p < 0.001$); complete resection and postoperative radiotherapy were also predictors of better outcome (p = 0.018 and p = 0.081, respectively). Exclusive chemotherapy was delivered to 62 patients with advanced disease, who all received platinum-based regimen as first-line treatment; PAC regimen was delivered to 66% of patients. Best objective response to first-line chemotherapy was partial response in 33 (53%) patients. Median PFS was 8.0 months (IC95%: 5.0-11.1). Median OS was 32.9 months (IC95%: 20.6-45.1). Response to first-line chemotherapy and squamous histology were the only significant predictors of OS (p = 0.002 and p = 0.040, respectively). **Conclusions:** Our cohort is the first to analyze in depth outcomes and treatment strategies in a prospective cohort of consecutive patients with thymic carcinoma. While we confirm the major prognostic impact of surgery, our data highlight the need for optimized multidisciplinary management and innovative therapies as the survival of patients remains limited. Research Sponsor: None.

9073 Poster Session (Board #266), Fri, 8:00 AM-11:00 AM

Prevalence of autoimmune diseases in thymic epithelial tumors (TET) insights from RYTHMIC. *First Author: Jose Carlos Benitez, Gustave Roussy, Villejuif, Paris, YT, France*

Background: TET are associated with autoimmune disorders (AID) in up to 30% of patients (pts). However, there have been wide variations in the reported prevalence of AID in TET pts in small single-center series. RYTHMIC (Réseau tumeurs THYMiques et Cancer) is a French network mandated to systematically discuss every case of TET. We aimed to describe the prevalence of AID in a large French population. **Methods:** RYTHMIC database, hosted by IFCT (Intergroupe Francophone de Cancérologie Thoracique), prospectively includes all consecutive pts with a diagnosis of TET discussed in French national or regional tumor boards. We analyzed epidemiologic, clinical and pathological characteristics of pts with TET's related AID. **Results:** From January 2012 to December 2019, 2909 pts were included in the database. The mean age at diagnosis of TET was 54 and 52% were male. In the overall population, Masaoka Koga stages were well balanced with 12.6% (n = 187) stage I, 8.8% (n = 131) stage IIa, 8.4% (n = 124) stage IIb, 11.1% (n = 164) stage III and 8.5% (n = 125) stage IV. There were 364 (12.5%) events of AID in 302 pts. 62 pts (17%) had more than 1 AID. Among the events, 236 were myasthenia gravis (MG) (64.8%), 19 Hypogammaglobulinemia syndrome (5.2%), 15 pure red cell aplasia (4.1%), 18 thyroiditis (4.9%) and 16 systemic erythematous lupus (4.4%). Diagnosis of AID was mostly done at tumor diagnosis (n = 239, 65.7%) but some patient had AID diagnosed before diagnosis (n = 67, 18.4%) or during follow up (n = 32, 8.8%). Among pts presenting AID, B2 was the most common subtype (n = 133, 36.5%). The incidence of AID per subtype was as follow: A (n = 10/81, 12.3%), AB (n = 48/225, 21.3%), B1 (n = 35/130, 26.9%), B2 (n = 133/295, 45.0%), B3 (n = 46/113, 40.7%), thymic carcinoma (n = 16/275, 5.8%). **Conclusions:** The prevalence of AID in pts with TET was 12.5%, $>$ 40% in B2 and B3 subtypes. Diagnosis of AID can be delayed compared to the diagnosis of TET. Immunotherapy indication should be carefully assessed in pts with TET other than thymic carcinoma. Research Sponsor: None.

9074 Poster Session (Board #267), Fri, 8:00 AM-11:00 AM

Low-dose oral etoposide is an active option for patients with heavily pretreated thymic epithelial tumors. *First Author: Margaret Ottaviano, Department of Clinical Medicine and Surgery, University Federico II of Naples, Naples, Italy*

Background: Platinum based regimens are used in the first line setting for advanced Thymic Epithelial Tumors (TETs). Angiogenesis plays an important role in TETs: VEGF is overexpressed in TETs, and associated with aggressiveness and advanced stage. Etoposide inhibits angiogenesis *in vitro* and *in vivo* by decreasing VEGF production and microvessel density. The aim of this study is to assess the activity of metronomic oral etoposide, with identification of circulating predictive and pharmacodynamics biomarkers. **Methods:** Patients with advanced platinum pretreated TET referred from 2014 to 2019 at Rare Tumors Reference Center of Naples, were prospectively enrolled in this study. Oral etoposide 50 mg daily for 3 weeks on and 1 week off every 28 days, has been delivered until progression of disease, complete response or unacceptable toxicity. Response rate (RR), progression free survival (PFS), toxicity and ratio between time to etoposide progression (TTPe) and time to previous best treatment progression (TTPp) were evaluated. Serum samples were prospectively obtained from ten patients with simultaneously radiological assessment. cfDNA quantification was assessed using Qubit Fluorometric Quantitation. **Results:** 21 patients were enrolled: median age 59 years range (41 - 88); 70% male, 60% T (4 B1, 3 B2, 4 B3, 1 B1-B2); 40% had TC. A median of 5 (range 1-9) prior therapy regimens had been administered. Median follow-up since etoposide was 5 years (range 0.5-5). Obtaining an overall response rate of 85%, 3 patients achieved complete response and 15 partial response. Median PFS was 16 months [95%CI 3-60] with respectively a median PFS of 12 for T (95%CI 3-38) and 19 for TC (95%CI 6-60). No grade 3-4 related events occurred, G1-2 myelotoxicity has been registered in 20% of patients. Therapy is still ongoing for 15 patients and all are still alive. Median TTPe was 16 months, TTPp was 9 months and TTPe / TTPp ratio equal to 1.7. The median cfDNA of 8 responder patients, before starting therapy, was 2.2 ng/μl (0.178-5.24), dropping dramatically at radiological response to 0.5 ng/μl (0.323-2.56). 2 out of 3 non-responder patients had a median baseline value of 2.49 ng/μl, increasing to 4.6 ng/μl at progression. Variation of circulating VEGF correlates with radiological response. **Conclusions:** Taking into account that other antiangiogenic drugs, showing some activity in second and further lines treatment, are very expensive and associated with several side effects, we suggest that low dose oral etoposide might become the preferred treatment option in heavily pretreated TETs. Research Sponsor: CRCTR (Reference Rare Tumors Center of Campania Region).

TPS9075 Poster Session (Board #268), Fri, 8:00 AM-11:00 AM

CANOPY-A: A phase III, multicenter, randomized, double-blind, placebo-controlled trial evaluating canakinumab as adjuvant therapy in patients (pts) with completely resected non-small cell lung cancer (NSCLC). *First Author: Edward B. Garon, David Geffen School of Medicine, University of California/TRIO-US Network, Los Angeles, CA*

Background: In the CANTOS study, canakinumab (selective IL-1β inhibitor) treatment was associated with reduced incidence and mortality from NSCLC in pts with stable post-myocardial infarction with elevated high-sensitivity C-reactive protein (hs-CRP) levels. In CANOPY-A study, we investigate the therapeutic role of canakinumab in NSCLC. **Methods:** The CANOPY-A study (NCT03447769) is evaluating the efficacy and safety of canakinumab as adjuvant therapy in adult pts with completely resected NSCLC. Pts with AJCC/UICC v.8 stages II–IIIA and IIIB (T $>$ 5 cm, N2), any histology, completely resected (R0) NSCLC who completed adjuvant cisplatin-based chemotherapy ($\geq$2 cycles) and radiotherapy (if applicable) are eligible. Pts must not have had prior neoadjuvant chemotherapy or radiotherapy. Pts (~1500) are randomized 1:1 to receive canakinumab (200 mg Q3W, SC) or placebo (Q3W, SC) for 18 cycles or until disease recurrence as determined by investigator, unacceptable toxicity, treatment discontinuation at the discretion of the investigator or patient, start of a new antineoplastic therapy, death, or loss to follow-up. Randomization is stratified by AJCC/UICC v.8 stage (IIA vs IIB vs IIIA vs IIIB with T $>$ 5 cm, N2 disease), tumor histology (squamous vs non-squamous), and region (western Europe and North America vs eastern Asia vs rest of the world). Primary objective: disease-free survival (DFS) per local investigator assessment. Secondary objectives: overall survival (OS), lung cancer specific survival, safety, pharmacokinetics, immunogenicity, and patient reported outcomes. Adult pts with stage IIA–IIIA, IIIB (N2 disease only) NSCLC who are candidates for complete resection surgery (and therefore prospective candidates for the main study) will be asked to participate in a biomarker sub-study to understand how resection may impact biomarkers involved in the IL-1β inflammatory pathway and mutations present in blood. In the sub-study, the levels of hs-CRP, other cytokines, and additional biomarkers in blood will be assessed at pre- and post-surgery (endpoint: summary statistics of hs-CRP and other pharmacodynamics [PD] biomarkers). For pts who will enroll in the main study, possible associations between pre- and post-surgery biomarker levels with canakinumab efficacy will be assessed (endpoint: DFS and OS by hs-CRP and other PD biomarkers). The CANOPY-A study is currently enrolling. As of Jan 13, 2020, there are 307 study locations. Clinical trial information: NCT03447769. Research Sponsor: Novartis.

TPS9076 Poster Session (Board #269), Fri, 8:00 AM-11:00 AM

Checkmate 77T: A phase III trial of neoadjuvant nivolumab (NIVO) plus chemotherapy (chemo) followed by adjuvant nivo in resectable early-stage NSCLC. *First Author: Tina Cascone, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Although surgery for early NSCLC is potentially curative, 5-year overall survival (OS) rates for patients with stage IIA–IIIB disease are historically $<$ 50%, representing a population of high unmet need. Conventional neoadjuvant or adjuvant chemo provides only a 5% absolute improvement in OS at 5 years. A rational approach to improve survival in these patients is to eradicate micrometastatic disease and potentially induce anti-tumor immunity to minimize the risk of relapse with peri-operative regimens including NIVO, a fully human anti–programmed death receptor-1 antibody. Early phase trials indicate that NIVO-based regimens have the potential to deepen pathological responses and extend survival in this setting (Reuss JE et al. Poster presentation at ASCO 2019. Abstract 8524; Cascone T et al. Oral presentation at ASCO 2019. Abstract 8504; Provencio M et al. Oral presentation at WCLC 2019. Abstract OA13.05). Data from the phase 2 single-arm NADIM trial (NCT03081689) demonstrated the highly encouraging major pathological response (MPR) rate of 83% with neoadjuvant NIVO plus chemo followed by adjuvant NIVO in patients with resectable stage IIIA NSCLC (Provencio M et al. Oral presentation at WCLC 2019. Abstract OA13.05). These results require validation in a large randomized controlled study. CheckMate 77T (NCT04025879) is a phase 3, randomized, double-blind trial evaluating neoadjuvant NIVO plus chemo followed by adjuvant NIVO in resectable early stage NSCLC. **Methods:** Approximately 452 patients aged $\geq$ 18 years with resectable stage IIA–IIIB (T3N2 only) NSCLC, ECOG performance status 0–1, and available lung tumor tissue will be enrolled at 113 sites in North America, South America, Europe, Asia, and Australia. Patients with *EGFR/ALK* mutations, brain metastasis, prior systemic anti-cancer treatment or radiotherapy, and autoimmune disease are excluded. Patients will be randomized to receive neoadjuvant NIVO plus carboplatin- or cisplatin-based doublet chemo followed by surgery and adjuvant NIVO, or neoadjuvant placebo plus carboplatin- or cisplatin-based doublet chemo followed by surgery and adjuvant placebo. The primary endpoint is event-free survival, assessed by blinded independent central review. Secondary endpoints include OS, pathological complete response and MPR assessed by blind independent pathological review, safety and tolerability. The start date was September 2019. The estimated primary completion date is May 2023. Clinical trial information: NCT04025879. Research Sponsor: Bristol-Myers Squibb.

TPS9077 **Poster Session (Board #270), Fri, 8:00 AM-11:00 AM**

ALCHEMIST: Adjuvant targeted therapy or immunotherapy for high-risk resected NSCLC. *First Author: Jacob Sands, Lahey Hospital and Medical Center, Boston, MA*

Background: ALCHEMIST (Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial) is a clinical trial platform of the National Cancer Institute that offers biomarker analysis for high-risk resected non-small cell lung cancer (NSCLC) to support randomized trials of novel adjuvant therapies within the National Clinical Trials Network (NCTN). EA5142, a trial of adjuvant nivolumab for patients (pts) without EGFR / ALK alterations, has completed enrollment. Given the survival benefit seen with 1st-line chemo-immunotherapy (chemo-IO) for advanced NSCLC without EGFR / ALK alterations, there was compelling rationale for the launch of a trial offering concurrent immunotherapy with adjuvant chemo. Here we report updated enrollment to ALCHEMIST as of Jan 14, 2020. **Methods:** ALCHEMIST includes a screening trial (A151216, 5362 registered) that enrolls pts with completely resected clinical stage IB ($\geq$4 cm)–IIIA (per AJCC 7) NSCLC. Tissue and blood are collected, biomarker testing includes EGFR sequencing, ALK FISH and PD-L1 IHC. 733 active sites are enrolling across the NCTN. Pts with EGFR mutations may enroll to adjuvant erlotinib vs observation (A081105, 352 randomized); those with ALK fusions may enroll to adjuvant crizotinib vs observation (E4512, 99 randomized). A trial offering adjuvant nivolumab vs observation regardless of PD-L1 status (EA5142, 935 randomized) recently completed enrollment. To support ongoing investigation of adjuvant immunotherapy, ALCHEMIST is adding A081801 (opens spring 2020). Pts will be randomized to one of 3 arms: chemo-IO with pembrolizumab during and after chemo vs sequential chemo followed by pembrolizumab vs chemo alone. Pts with pathological N2 nodes are eligible and can undergo postoperative radiotherapy after completing chemo. Pts are eligible if enrolled to A151216, negative for EGFR and ALK alterations, and with PD-L1 testing completed (required for stratification). Local testing for EGFR, ALK and PD-L1 will be accepted for enrollment; central testing will not delay randomization. Pts may not have received any therapy except surgery for the lung cancer and must be age $>$18, Eastern Cooperative Oncology Group performance status 0-1, have no active autoimmune disease requiring systemic treatment within 2 years, must not be pregnant or nursing, have no active second malignancy within 3 years and meet standard organ function values. By building off the ongoing ALCHEMIST platform, we hope to facilitate rapid enrollment to A081801 across participating NCTN sites. Clinical trial information: NCT02194738. Research Sponsor: U.S. National Institutes of Health.

TPS9078 **Poster Session (Board #271), Fri, 8:00 AM-11:00 AM**

Trial in progress: Neoadjuvant immune checkpoint blockade in resectable malignant pleural mesothelioma. *First Author: Joshua E. Reuss, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

Background: While the role of surgery in limited-stage (stage I-III) malignant pleural mesothelioma (MPM) is controversial, many centers have adopted an aggressive tri-modality approach incorporating (neo)adjuvant chemotherapy, surgical resection and radiotherapy. Despite this, most patients relapse and die from their disease. Immune checkpoint blockade (ICB) has shown promise in advanced MPM, but the mechanisms of response and resistance remain elusive. Improving the mechanistic understanding of ICB in MPM while concurrently optimizing the treatment strategy for limited-stage MPM are two urgent unmet needs. This multicenter multi-arm phase I/II study seeks to evaluate the safety and feasibility of neoadjuvant ICB in resectable MPM, incorporating novel genomic and immunologic analyses to deliver mechanistic insight into the biology of ICB in MPM. **Methods:** Patients with surgically resectable stage I-III treatment-naïve epithelioid or biphasic MPM receive neoadjuvant treatment with nivolumab every 2 weeks for 3 doses with or without 1 dose of ipilimumab (arm A: nivolumab monotherapy; arm B: nivolumab + ipilimumab). After macroscopic complete resection, patients receive optional investigator-choice adjuvant chemotherapy +/- radiation. Following this, patients will receive up to 1 year of adjuvant nivolumab. Feasibility and safety are co-primary endpoints of this study with feasibility defined by a delay in surgery of $\leq$24 days from the preplanned surgical date and safety defined by adverse events according to CTCAE v5.0. Bayesian-designed stopping rules have been implemented for feasibility and safety. Secondary endpoints include assessment of pathologic response and radiographic response using RECIST 1.1 for MPM. Correlative analyses will be performed on tissue specimens obtained pre- and post-ICB, as well as blood obtained pre, during, and post-ICB. Key correlates include multiplex immunofluorescence and longitudinal ctDNA assessment. Whole exome sequencing, T-cell receptor sequencing, and the MANAFEST functional neoantigen assay will be utilized to identify neoantigen-specific T-cell clonotypes and track these clonotypes temporally (during/post ICB) and spatially (across immune compartments). Single-cell RNA sequencing will be used to characterize the functionality of expanded T-cell clonotypes. Accrual to arm B will commence following complete accrual to arm A with a planned total enrollment of 30 patients. This study is open with 1 patient enrolled at the time of submission. Clinical trial information: NCT03918252. Research Sponsor: Bristol Meyers Squibb.

TPS9079 **Poster Session (Board #272), Fri, 8:00 AM-11:00 AM**

A phase III randomized trial of pleurectomy/decortication plus chemotherapy with or without adjuvant hemithoracic intensity-modulated pleural radiation therapy (IMPRINT) for malignant pleural mesothelioma (MPM) (NRG LU-006). *First Author: Andreas Rimner, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Pleurectomy/Decortication (P/D) with neoadjuvant or adjuvant chemotherapy has become a common lung-sparing surgical approach for MPM. Adjuvant hemithoracic IMPRINT was developed at Memorial Sloan Kettering Cancer Center and safe in a multi-institutional phase II study, with promising survival outcomes. The National Cancer Institute (NCI) sponsored this phase III randomized cooperative group trial to test the efficacy of this lung-sparing trimodality approach for resectable MPM. **Methods:** Patients with newly diagnosed MPM amenable to P/D are enrolled and undergo P/D followed by adjuvant platinum/pemetrexed (preferred) or neoadjuvant chemotherapy followed by P/D. Patients are stratified by histologic subtype, resection status (R0/1 vs. R2), and center patient volume ($\leq$10 vs. $>$ 10 P/Ds per year). Within 8 weeks after completion of the second modality patients are randomized 1:1 to undergo hemithoracic IMPRINT vs. no further therapy. All IMPRINT contours and treatment plans will be centrally reviewed. A contouring atlas and treatment planning constraints for target structures and organs at risk including acceptable and unacceptable variations and deviations were developed. Photon and proton therapy are permitted. The primary endpoint of the study is overall survival. Secondary endpoints include local failure-free, distant-metastases-free and progression-free survival, treatment-related toxicities (CTCAE v5.0) and change in quality-of-life (EORTC QLQ-C30 mean score changes at 9 months post randomization). The target accrual is 150 patients. This study was activated on January 29, 2020. Over 20 institutions have already committed to opening the study which is open to all National Clinical Trials Network (NCTN) sites. Treatment planning guidelines and helpful hints for photon and proton therapy will be presented. Conclusions: NRG LU-006 (clinicaltrials.gov: NCT04158141) is open to accrual. This is the first NRG Oncology randomized phase III trial on MPM and evaluates the use of IMPRINT following lung-sparing P/D and chemotherapy. This project was supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology SDMC), U24CA180803 (IROC) from the National Cancer Institute (NCI). Clinical trial information: NCT04158141. Research Sponsor: U.S. National Institutes of Health.

TPS9080 **Poster Session (Board #273), Fri, 8:00 AM-11:00 AM**

Phase I study of AMG 757, a half-life extended bispecific T-cell engager (HLE BiTE immune therapy) targeting DLL3, in patients with small cell lung cancer (SCLC). *First Author: Taofeek Kunle Owonikoko, Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA*

Background: SCLC is an aggressive neuroendocrine tumor with poor prognosis and few treatment options. Delta-like ligand 3 (DLL3) is an inhibitory Notch ligand that is highly expressed on the surface of most SCLC tumors but minimally expressed in normal tissues. As such, DLL3 may be a promising therapeutic target. AMG 757 is an HLE BiTE immune therapy designed to redirect cytotoxic T cells to cancer cells by binding to DLL3 on cancer cells and CD3 on T cells, resulting in T cell activation and expansion and T cell-dependent killing of tumor cells. In addition to its direct antitumor effect, BiTE immune therapy can inflame the tumor microenvironment. Combining AMG 757 with a PD-1 pathway inhibitor may lead to increased antitumor activity by enabling sustained T cell-dependent killing of tumor cells. **Methods:** NCT03319940 is an open-label, ascending, multiple-dose, phase 1 study evaluating AMG 757 as monotherapy; the protocol was recently amended to also evaluate AMG 757 in combination with pembrolizumab. The study will include a dose exploration (monotherapy and combination) followed by a dose expansion (monotherapy). Key eligibility criteria: adult patients with relapsed/refractory SCLC whose disease progressed or recurred after at least 1 platinum-based chemotherapy regimen, ECOG performance status 0–2, at least 2 measurable lesions per modified RECIST 1.1, no untreated or symptomatic brain metastases, and adequate organ function. Primary objectives are to evaluate safety/tolerability and determine the maximum tolerated dose or recommended phase 2 dose of AMG 757 as monotherapy and in combination with pembrolizumab. Secondary objectives are to characterize pharmacokinetics and evaluate preliminary antitumor activity; exploratory objectives are to assess immunogenicity and changes in biomarkers in blood and tumor tissue. In the dose exploration phase, dose escalation/de-escalation decisions will be guided by a Bayesian logistic regression model; backfill enrollment at dose levels deemed safe and tolerable will be allowed. The study is open and recruiting patients. Clinical trial information: NCT03319940. Research Sponsor: Amgen Inc.

TPS9081 **Poster Session (Board #274), Fri, 8:00 AM-11:00 AM**

RESILIENT part II: an open-label, randomized, phase III study of liposomal irinotecan injection in patients with small-cell lung cancer who have progressed with platinum-based first-line therapy. *First Author: Luis G. Paz-Ares, Hospital Universitario 12 de Octubre, Madrid, Spain*

Background: Although small cell lung cancer (SCLC) is often sensitive to established first-line therapies, many patients relapse and develop drug resistance, and second-line therapies are limited. RESILIENT (NCT03088813) is a two-part phase 2/3 study assessing the safety, tolerability, and efficacy of liposomal irinotecan monotherapy in patients with SCLC who progressed with platinum-based first-line therapy. Preliminary data from the dose-ranging part of the study (part 1) showed that liposomal irinotecan 70 mg/m^2 administered every 2 weeks was well tolerated and had promising antitumor activity (Paz-Ares *et al.* ASCO 2019; poster 318). Here, we present the design of the second, larger part of the study, which will evaluate the efficacy and safety of liposomal irinotecan versus topotecan in the same patient population. **Methods:** Part 2 of RESILIENT is a phase 3, open-label study with a planned sample size of 450. Patients are randomly allocated 1:1 to intravenous liposomal irinotecan or intravenous topotecan. Liposomal irinotecan is administered every 2 weeks at 70 mg/m^2 (free-base equivalent) and topotecan is administered for 5 consecutive days every 3 weeks at 1.5 mg/m^2. As of January 2020, 80 patients have been enrolled in part 2 of the trial. Tumor assessments are performed using the Response Evaluation Criteria in Solid Tumors version 1.1 and the Response Assessment in Neuro-oncology criteria for CNS lesions; symptom improvement is measured using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30. Safety assessments include monitoring for adverse events. The primary endpoint is overall survival (OS) and secondary endpoints are progression-free survival (PFS), objective response rate, and proportion of patients reporting symptom improvement. Patients will continue study treatment until disease progression, unacceptable toxicity or study withdrawal and will then be followed for survival until death or study end (when all patients have died, withdrawn consent or are lost to follow-up). Clinical trial information: NCT03088813. Research Sponsor: Ipsen.

TPS9082 **Poster Session (Board #275), Fri, 8:00 AM-11:00 AM**

NRG Oncology/Alliance LU005: A phase II/III randomized clinical trial of chemoradiation versus chemoradiation plus atezolizumab in limited stage small cell lung cancer. *First Author: Helen J. Ross, Mayo Clinic Arizona, Phoenix, AZ*

Background: Limited stage small cell lung cancer (LS-SCLC) is treated with standard of care platinum/etoposide (EP) and thoracic radiation therapy (TRT) with curative intent, however the majority of patients are not cured and median overall survival is approximately 30 months. Addition of atezolizumab to chemotherapy in extensive stage SCLC has improved progression free and overall survival in a non-curative setting leading to hope that addition of an immune checkpoint inhibitor to standard chemoradiotherapy could benefit LS-SCLC patients. LU005 is a randomized phase II/III trial of standard concurrent chemoradiation with or without atezolizumab for patients with LS-SCLC. **Methods:** Patients are randomly assigned in a 1:1 ratio to standard EP chemotherapy with concurrent TRT (45 Gy BID or 66 Gy QD) with or without atezolizumab beginning concurrently with TRT, and continued every 3 weeks for up to 12 months. Eligible patients have LS-SCLC, PS 0-2, adequate organ function, no concerning comorbidities (including no active autoimmune disease) and are eligible for TRT. Patients are randomized prior to their second cycle of EP and thoracic radiation begins with the second overall cycle of chemotherapy (first cycle of study therapy) in both treatment arms. Prophylactic cranial radiation (PCI) is recommended for patients who respond to treatment. The phase II/III primary endpoints are progression free (PFS) and overall survival (OS) respectively. Secondary endpoints include objective response rates, local and distant disease control, and quality of life/patient reported outcomes assessment. Translational science component includes blood and tissue based immune related assays. This study activated in May 2019. 50 of 506 planned patients have been accrued as of 2/1/2020. Supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology SDMC), U23CA180803 (IROC) from the National Cancer Institute (NCI) and Genentech. *Authors Ross and Higgins are co-first authors and contributed equally to this work. Clinical trial information: NCT03811002. Research Sponsor: U.S. National Institutes of Health.

TPS9083 **Poster Session (Board #276), Fri, 8:00 AM-11:00 AM**

A phase III trial-in-progress called REPLATINUM that compares RRx-001 + a platinum doublet to a platinum doublet in third-line or beyond small cell lung cancer. *First Author: Daniel Morgensztern, Washington University School of Medicine in St. Louis, St. Louis, MO*

Background: Despite several recent checkpoint inhibitor approvals extensive stage small cell lung cancer (SCLC) is associated with a poor prognosis and remains an area of high unmet need. RRx-001 is a first-in-class, minimally toxic small molecule immunotherapeutic that inhibits c-Myc, downregulates the antiphagocytic checkpoint, CD47, repolarizes tumor associated macrophages (TAM) from protumor M2 to antitumor M1 and resensitizes to previously active first line therapies. On the basis of favorable results from a Phase 2 trial called QUADRUPLE THREAT (NCT02489903) in combination with a platinum doublet in later line SCLC, a Phase 3 trial called REPLATINUM was started in 3rd line or beyond SCLC in Q4 2019. Enrollment is ongoing. **Methods:** This US-based, open-label, randomized, phase 3 study (NCT03777657) compares RRx-001 4mg + a platinum doublet (carboplatin or cisplatin + etoposide) versus a platinum doublet for pts with 3rd line or beyond SCLC that have previously received a checkpoint inhibitor. Approximately 120 pts from 25 centers will be randomized 1:1 to receive RRx-001 4 mg in combination with a platinum doublet vs. a platinum doublet. The platinum doublet will be administered on both arms for up to 4 cycles; on the RRx-001 arm only patients with stable disease or better are eligible to continue on RRx-001 4 mg + carboplatin AUC 2-4 maintenance therapy. If radiologic progression occurs on the control arm prior to the 4th cycle, patients are eligible to crossover to the RRx-001 treatment arm. PFS is the primary endpoint. Secondary endpoints include OS and ORR. Exploratory endpoints include c-Myc, CD-47 and PD-L1 on circulating tumor cells and SIRP-alpha expression on circulating monocytes. Clinical trial information: NCT03777657. Research Sponsor: EpicentRx.

TPS9084 **Poster Session (Board #277), Fri, 8:00 AM-11:00 AM**

A phase Ib/II study of niraparib plus temozolomide plus atezolizumab versus atezolizumab as maintenance therapy in extensive-stage small cell lung cancer (TRIO-US L-06). *First Author: Amy Lauren Cummings, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA*

Background: Maintenance therapy is a promising therapeutic approach for extensive-stage small cell lung cancer (ES-SCLC), especially in light of IMpower 133 (Horn NEJM 2018). SCLC models of poly (ADP-ribose) polymerase (PARP) protein 1 and 2 inhibition suggested synergy with temozolomide (TMZ) (Wainberg AACR 2016). Combining PARP inhibition and TMZ with atezolizumab after first-line therapy for ES-SCLC may improve disease control. **Methods:** This is a phase 1b/2, randomized, open-label study of TMZ plus niraparib, a PARP inhibitor, with atezolizumab versus atezolizumab as maintenance therapy in adult patients with ES-SCLC after completion of platinum-based first-line chemotherapy. The primary outcome for phase 1b is the RP2D of TMZ in combination with niraparib, and for phase 2, progression-free survival (PFS). Secondary endpoints include safety, objective response rate, and overall survival. Exploratory endpoints include adverse events and patient-reported outcomes, including health-related quality of life. Phase 1b participants are required to have an advanced and incurable solid malignancy. Part one of phase 1b includes an accelerated lead-in of 12 participants treated in cohorts of 6 with an initial dose level of niraparib 200 mg po daily in 28-day cycles and low-dose TMZ 40 mg po daily on days 1-5 of each cycle. Part two includes a safety lead-in of 6 patients receiving standard-of-care atezolizumab, to which R2PD niraparib and TMZ will be added. For phase 2, participants are required to have ES-SCLC with a complete response or partial response per RECIST 1.1 following 4 to 6 cycles of platinum-based chemotherapy and ability to proceed to randomization within 7 weeks after day 1 of the last cycle of prior chemotherapy. Prophylactic WBRT is allowed prior to study. 52 participants will be stratified by a history of brain metastases and randomized 1:1 to atezolizumab with or without RP2D niraparib plus TMZ. There will be no crossover between arms. To date, cohort 1 had two DLTs. Enrollment to dose level -1 and an intermediate dose have been completed without a DLT. The atezolizumab safety lead-in begins enrollment in March 2020. Clinical trial information: NCT03830918. Research Sponsor: TESARO/GSK.

9500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Nivolumab + ipilimumab versus platinum-doublet chemotherapy as first-line treatment for advanced non-small cell lung cancer: Three-year update from CheckMate 227 Part 1. *First Author: Suresh S. Ramalingam, Winship Cancer Institute, Emory University, Atlanta, GA*

Background: In the phase 3 CheckMate 227 Part 1 (NCT02477826; minimum follow-up, 29.3 mo), 1L NIVO + IPI significantly improved overall survival (OS) vs chemo in treatment-naive patients (pts) with aNSCLC and tumor PD-L1 expression ≥ 1% (primary analysis) or < 1% (pre-specified descriptive analysis). Here we report data with 3-y minimum follow-up. **Methods:** Pts with stage IV / recurrent NSCLC and PD-L1 ≥ 1% (n = 1189) were randomized 1:1:1 to NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W), NIVO (240 mg Q2W) alone, or chemo. Pts with PD-L1 < 1% (n = 550) were randomized to NIVO + IPI, NIVO (360 mg Q3W) + chemo, or chemo. Primary endpoint was OS with NIVO + IPI vs chemo in pts with PD-L1 ≥ 1%. An exploratory analysis of OS in pts by response status (CR/PR, SD, progressive disease [PD]) at 6 mo was conducted. **Results:** After a median follow-up of 43.1 mo (database lock, 28 Feb 2020), pts with PD-L1 ≥ 1% continued to derive OS benefit from NIVO + IPI vs chemo (HR: 0.79; 95% CI, 0.67–0.93); 3-y OS rates were 33% (NIVO + IPI), 29% (NIVO), and 22% (chemo). At 3 y, 18% of pts with PD-L1 ≥ 1% treated with NIVO + IPI remained progression-free vs 12% with NIVO and 4% with chemo; 38% of confirmed responders remained in response in the NIVO + IPI arm at 3 y vs 32% in the NIVO arm and 4% in the chemo arm. In pts with PD-L1 < 1%, OS HR for NIVO + IPI vs chemo was 0.64 (95% CI, 0.51–0.81); 3-y OS rates were 34% (NIVO + IPI), 20% (NIVO + chemo), and 15% (chemo); 13%, 8%, and 2% of pts remained progression-free; and 34%, 15%, and 0% of confirmed responders remained in response, respectively. Pts with PD-L1 ≥ 1% with either CR/PR at 6 mo had longer subsequent OS with NIVO + IPI vs chemo; pts with SD or PD at 6 mo had generally similar subsequent OS between treatments (Table); results in PD-L1 < 1% pts will be presented. Any-grade / grade 3–4 treatment-related AEs were observed in 77% / 33% of all pts treated with NIVO + IPI, and 82% / 36% with chemo. **Conclusions:** With 3 y minimum follow-up, NIVO + IPI continued to provide durable and long-term OS benefits vs chemo for pts in 1L aNSCLC. Pts with PD-L1 ≥ 1% who achieved CR/PR at 6 mo had marked OS benefit with NIVO + IPI vs chemo. No new safety signals were identified for NIVO + IPI. Clinical trial information: NCT02477826. Research Sponsor: Bristol-Myers Squibb and Ono Pharmaceutical.

Landmark analysis of OS by response status at 6 mo in pts with PD-L1 ≥ 1% (NIVO + IPI vs chemo).

Pts alive at 6 mo	Response status at 6 mo, %	Post-landmark 1-y OS rate, %	Post-landmark 2-y OS rate, %	Post-landmark 3-y OS rate, %
NIVO + IPI (n = 295) vs Chemo (n = 306)	CR or PR, 39 vs 25 SD, 14 vs 18 PD, 46 vs 58	90 vs 73 69 vs 54 44 vs 47	76 vs 51 45 vs 38 22 vs 25	70 vs 39 34 vs 33 19 vs 17

9501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx) for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA. *First Author: Martin Reck, Department of Thoracic Oncology, Airway Research Center North, German Center for Lung Research, LungClinic, Grosshansdorf, Germany*

Background: NIVO + IPI was shown to improve overall survival (OS) and durability of response vs chemo in 1L advanced NSCLC in CheckMate 227 Part 1, regardless of PD-L1 expression. We hypothesized that a limited course of chemo combined with NIVO + IPI could provide rapid disease control while building on the durable OS benefit seen with dual PD-1 and CTLA-4 inhibition. CheckMate 9LA (NCT03215706) is a phase 3 randomized study evaluating NIVO + IPI + 2 cycles chemo vs chemo in 1L stage IV/recurrent NSCLC. **Methods:** Adults with tx-naive, histologically confirmed stage IV/recurrent NSCLC, ECOG performance status 0–1, and no known sensitizing *EGFR/ALK* alterations were randomized 1:1 to NIVO 360 mg Q3W + IPI 1 mg/kg Q6W + chemo (2 cycles) (n = 361) or chemo (4 cycles) alone (n = 358), stratified by PD-L1 (< 1% vs ≥ 1%), sex, and histology (squamous vs non-squamous). Chemo was based on histology. Pts with non-squamous NSCLC in the chemo-only arm could receive optional pemetrexed maintenance. Pts were treated with immunotherapy until disease progression, unacceptable toxicity, or for 2 y. The primary endpoint was OS; the interim analysis using Lan–DeMets alpha spending function with O'Brien–Fleming boundary was planned at ~80% information fraction (ie, after observing ~322 total events). Secondary endpoints included progression-free survival (PFS) and objective response rate (ORR) by blinded independent central review, and efficacy by PD-L1 subgroups. Exploratory endpoints included safety/tolerability. **Results:** Baseline characteristics were balanced across arms. At a preplanned interim analysis (minimum follow-up 8.1 mo), OS was significantly prolonged with NIVO + IPI + chemo vs chemo (HR 0.69, 96.71% CI: 0.55–0.87; $P = 0.0006$); statistically significant improvements in PFS and ORR were seen. With longer follow-up (minimum 12.7 mo), NIVO + IPI + chemo vs chemo continued to provide longer OS; median 15.6 vs 10.9 mo (HR 0.66, 95% CI: 0.55–0.80); 1-y OS rates were 63 vs 47%. Clinical benefit was consistent across all efficacy measures in key subgroups including by PD-L1 and histology. Grade 3–4 tx-related adverse events were reported in 47 vs 38% of pts in the NIVO + IPI + chemo vs chemo arms, respectively. **Conclusions:** CheckMate 9LA met its primary endpoint: a statistically significant improvement in OS was observed with NIVO + NSCLC-optimized IPI + a limited course of chemo vs chemo (4 cycles) in 1L advanced NSCLC. No new safety signals were reported. Clinical trial information: NCT03215706. Research Sponsor: Bristol-Myers Squibb and Ono Pharmaceutical.

9502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

CCTG BR.34: A randomized trial of durvalumab and tremelimumab +/- platinum-based chemotherapy in patients with metastatic (Stage IV) squamous or nonsquamous non-small cell lung cancer (NSCLC). *First Author: Natasha B. Leighl, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: First-line therapy for advanced NSCLC includes PD-1 checkpoint inhibitor (ICI) monotherapy, and in combination with chemotherapy. Combination ICI have also demonstrated better survival compared to chemotherapy (CM-227). In CCTG BR.34, we compared overall survival (OS) in patients with advanced NSCLC receiving first-line durvalumab plus tremelimumab (DT) with or without platinum doublet chemotherapy (CT). **Methods:** This international, open-label, randomized trial accrued 301 participants from Canada and Australia, with stage IV NSCLC, *EGFR/ALK* wildtype, ECOG PS 0/1. Patients were randomized to DT for 4 cycles or DT+CT (pemetrexed- or gemcitabine-platinum), with ongoing D or D + pemetrexed (non-squamous) maintenance until disease progression. Stratification factors included histology, stage IVA v. IVB and smoking status. The primary endpoint was OS; secondary endpoints included progression-free survival (PFS), objective response rate (ORR = CR + PR) and adverse events (AEs). **Results:** At a median follow up of 16.6 months, no significant difference in OS was seen between the two treatment arms, with a median OS of 16.6 months with DT+CT v. 14.1 months with DT, (estimated HR 0.88, 90% CI 0.67-1.16). PFS was significantly improved in the DT+CT arm (stratified HR 0.67, 95% CI 0.52-0.88; medians 7.7 v. 3.2 months). ORR was higher in the DT+CT arm, 28% v. 14%, (odds ratio 2.1, p=0.001). Preplanned subgroup analysis demonstrated no significant differences in treatment outcomes by plasma TMB (<20 v. ≥20 mut/Mb, Guardant OMNI), age, sex, or smoking status. There was a trend to improved OS with DT+CT in the subgroup with PD-L1 TPS≥50%, (HR 0.64, 95% CI 0.40-1.04, p=0.07). Plasma TMB<20 mut/Mb was associated with shorter survival in both treatment groups (HR 1.99, 95% 1.3-3.1). Toxicity was greater in the DT+CT arm, with grade≥3 adverse events in 82% v. 70%, (p=0.02), most commonly dyspnea, nausea and cough. The incidence of immune-related adverse events was similar between arms (colitis 11%, pneumonitis 6%, endocrinopathy 21%). Grade 5 events occurred in 2.7%, (5 with DT+CT, 3 with DT). **Conclusions:** The addition of CT to first-line DT did not improve OS in advanced NSCLC. CT+DT improved ORR and PFS, and was associated with greater toxicity. No differential effects were seen by PD-L1 TPS nor bTMB. These data suggest that adding chemotherapy to ICI may be beneficial in those with PD-L1 TPS >=50%, and warrant further analysis in independent datasets. Clinical trial information: NCT03057106. Research Sponsor: Canadian Cancer Society Research Institute, Pharmaceutical/Biotech Company.

9503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Primary analysis of a randomized, double-blind, phase II study of the anti-TIGIT antibody tiragolumab (tira) plus atezolizumab (atezo) versus placebo plus atezo as first-line (1L) treatment in patients with PD-L1-selected NSCLC (CITYSCAPE). *First Author: Delvys Rodriguez-Abreu, Hospital Universitario Insular de Gran Canaria, Las Palmas De Gran Canaria, Spain*

Background: The immunomodulatory receptor TIGIT is a novel inhibitory immune checkpoint present on activated T cells and NK cells in multiple cancers, including NSCLC. In a phase I study (GO30103), co-inhibition of TIGIT and PD-L1 signaling with tira plus atezo in CIT-naïve PD-L1 positive NSCLC potentially improved overall response rates (ORR) compared to historical ORR with PD-L1/PD-1 inhibitors. We conducted this phase II trial to confirm the efficacy and safety of tira plus atezo (TA) compared to placebo plus atezo (PA) in 1L NSCLC (GO40290, NCT NCT03563716). **Methods:** This prospective, randomized, double-blind, placebo-controlled trial enrolled patients (pts) with chemotherapy-naïve PD-L1+ (TPS ≥ 1% by 22C3 IHC pharmDx Dako assay) locally advanced or metastatic NSCLC with measurable disease, ECOG PS 0-1, and without *EGFR* or *ALK* alterations. Pts were randomized 1:1 to TA (tira 600 mg IV plus atezo 1200 mg IV) or PA (placebo plus atezo 1200 mg IV) on day 1 of every 3-week cycle. Stratification factors were PD-L1 status (TPS ≥ 50% vs TPS 1-49%), histology, and tobacco history. Co-primary endpoints were investigator assessed ORR and PFS, and additional endpoints were duration of response (DOR), OS, and safety. Exploratory endpoints were the effect of PD-L1 status on ORR and PFS. **Results:** 135 pts were randomized to PA (n = 68) or TA (n = 67). At primary analysis (30 Jun 2019), TA improved ORR and median PFS (mPFS) compared to PA, with median follow-up of 5.9 mo. In the safety population (68 in PA, 67 in TA), treatment-related AEs (TRAEs) occurred in 72% (PA) and 80.6% (TA); Grade ≥3 TRAEs occurred in 19.1% (PA) and 14.9% (TA). AEs leading to treatment withdrawal occurred in 10.3% (PA) and 7.5% (TA). Clinical trial information: NCT03563716. With an additional six months of follow-up since the primary analysis (2 Dec 2019, median follow-up of 10.9 mo), improvement in ORR and mPFS was maintained in ITT for TA (37.3% [25.0, 49.6] and 5.6 mo [4.2, 10.4]) vs PA (20.6% [10.2, 30.9] and 3.9 mo [2.7, 4.5]). The safety profile remained tolerable. **Conclusions:** Treatment with TA compared to PA showed clinically meaningful improvement in ORR and PFS in ITT. The safety profile of TA was similar to PA. Research Sponsor: Genentech, Inc.

	ITT	
	PA	**TA**
n	68	67
ORR % (95% CI)	16.2 (6.7, 25.7)	31.3 (19.5, 43.2)
Odds ratio (95% CI)	2.57 (1.07, 6.14)*	
mPFS, months (95% CI)	3.6 (2.7, 4.4)	5.4 (4.2, NE)
HR (95% CI)	0.57 (0.37, 0.90)*	

*stratified

9504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer (NSCLC): Interim results of DESTINY-Lung01. *First Author: Egbert F. Smit, Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and topoisomerase I inhibitor payload. In a phase I trial, patients (pts) with HER2-mutated NSCLC who received T-DXd had a confirmed objective response rate (ORR) of 72.7% (8/11) (Tsurutani et al, WCLC 2018). DESTINY-Lung01 (NCT03505710) is an ongoing, multicenter, phase II study of T-DXd in pts with non-squamous NSCLC overexpressing HER2 or containing a HER2-activating mutation. We report data for the cohort with HER2 mutations after a median follow-up of 8.0 mo (range, 1.4-14.2 mo). **Methods:** Pts were treated with T-DXd 6.4 mg/kg every 3 weeks. The primary endpoint was confirmed ORR (complete response [CR] + partial response [PR]) by ICR. Additional endpoints were disease control rate (DCR; CR + PR + stable disease), duration of response (DOR), progression-free survival (PFS), and safety. **Results:** At data cutoff (25 Nov 2019), 42 pts (64.3% female) had received T-DXd. Median age was 63.0 years (range, 34-83 years; $<$ 65 y, 59.5%); 45.2% had central nervous system metastases; ECOG performance status was 0 in 23.8% of pts and 1 in 76.2%. HER2 mutations were predominantly in the kinase domain (90.5%). Most pts (90.5%) had prior platinum-based chemotherapy and 54.8% had anti–PD-1 or –PD-L1 treatment; median number of prior treatment lines was 2 (range, 1-6). Median treatment duration was 7.75 mo (range, 0.7-14.3 mo); 45.2% of pts remained on treatment. Confirmed ORR by ICR among the 42 pts was 61.9% (95% CI, 45.6%-76.4%); median DOR was not reached at data cutoff; 16 of 26 responders remained on treatment at data cutoff; DCR was 90.5% (95% CI, 77.4%-97.3%); estimated median PFS was 14.0 mo (95% CI, 6.4-14.0 mo). All pts (42/42) had treatment-emergent adverse events (TEAEs); 64.3% were grade $\geq$ 3 (52.4% drug-related), including decreased neutrophil count (26.2%) and anemia (16.7%). There were 5 cases (11.9%) of drug-related interstitial lung disease (ILD) as adjudicated by an independent committee (all grade 2, no grade $\geq$ 3) and 1 case of grade 1 ILD is pending adjudication. TEAEs led to dose interruption in 25 pts (59.5%), dose reduction in 16 pts (38.1%), and treatment discontinuation in 10 pts (23.8%). **Conclusions:** T-DXd demonstrated promising clinical activity with high ORR and durable responses in pts with HER2-mutated NSCLC. The safety profile was generally consistent with previously reported studies. Clinical trial information: NCT03505710. Research Sponsor: Daiichi Sankyo, Inc.

9505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Efficacy and safety of the antibody-drug conjugate (ADC) SAR408701 in patients (pts) with non-squamous non-small cell lung cancer (NSQ NSCLC) expressing carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5). *First Author: Anas Gazzah, Department of Drug Development (DITEP), Gustave Roussy, Villejuif Cedex, France*

Background: We report updated safety and efficacy of DM4-conjugated anti-CEACAM5 ADC from the expansion part of the first-in-human study (NCT02187848; Gazzah A et al. J Clin Oncol. 2019;37:15, 9072) in 92 NSQ NSCLC pts. **Methods:** CEACAM5 expression was assessed by immunohistochemistry on archived tumor samples. Two cohorts of pts have been analyzed: moderate and high expressors, with CEACAM5 expression at $\geq$2+ intensity between $\geq$1% to $<$ 50% and $\geq$50% of the tumor cell population, respectively. SAR408701 was administered at 100 mg/m^2 IV every 2 weeks. Tumor assessments were done every 4 cycles (8 weeks). Primary endpoint was overall response rate (ORR). **Results:** As of January 2020, 92 pts were treated: 28 moderate and 64 high expressors, with median age 62.5 years (31–91; 42.4% of pts $\geq$65), 51.1% male, 71.7% ECOG PS $\geq$1; median of 3 prior treatments (1–10 lines) for advanced disease, including anti-tubulin agents (60.9%) and anti-PD1/PD-L1 (75%). In the moderate expressor cohort, 2 confirmed partial responses (PR) were observed (ORR 7.1%). In the high expressor cohort, 13 pts had confirmed PRs (ORR 20.3% [95% confidence interval 12.27%–31.71%]); 27 (42.2%) had stable disease; ORR of 17.8% was observed in 45 pts who had prior anti-PD1/PD-L1. Pts had a median of 7 (1–49) cycles; median relative dose intensity was 0.98. Six pts discontinued due to treatment-emergent adverse events (TEAEs). Most frequent TEAEs (all grades) were asthenia (38.0%), keratopathy/keratitis (38.0%), peripheral neuropathy (26.1%), dyspnea (23.9%), and diarrhea (22.8%). 31 pts had dose modification due to a TEAE, including dose reduction for keratopathy/keratitis in 10 pts. Hematological toxicity included leukopenia (14.4%), neutropenia (4.4%), and thrombocytopenia (13.3%). Grade $\geq$3 TEAEs occurred in 47.8% of pts and were assessed as drug-related in 15.2%. **Conclusions:** SAR408701 shows promising antitumor activity in heavily pretreated advanced NSQ NSCLC pts with high CEACAM5 expression. SAR408701 was well tolerated, with minimal hematological toxicity compared to conventional chemotherapy; keratopathy was reversible and manageable with dose modification. These data support the activity of SAR408701 in NSQ NSCLC CEACAM5 high expressors. A phase 3 trial evaluating the activity of CEACAM5-DM4 ADC monotherapy in comparison with docetaxel in NSQ NSCLC CEACAM5 high expressors after failure of standard first line chemotherapy and anti-PD1/PD-L1 is underway. Clinical trial information: NCT02187848. Research Sponsor: Sanofi.

9506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

NEJ026: Final overall survival analysis of bevacizumab plus erlotinib treatment for NSCLC patients harboring activating EGFR-mutations. *First Author: Makoto Maemondo, Iwate Medical University, Morioka, Japan*

Background: In NEJ026, a phase III trial comparing bevacizumab plus erlotinib (BE) to erlotinib monotherapy (E) for EGFR-mutated non-small-cell lung cancer (NSCLC), we demonstrated the progression-free survival (PFS) of BE was significantly superior to E (Saito et al. Lancet Oncol. 2019 May;20(5):625-635.). However overall survival analysis were immature at the cutoff date. **Methods:** Chemotherapy-naïve pts with advanced non-squamous NSCLC harboring EGFR-mutation were randomly assigned to receive either combination with erlotinib (150 mg daily) plus bevacizumab (15 mg/kg iv q3w) or erlotinib (150 mg daily). The primary endpoint was PFS. Secondary endpoints were OS, RR, safety, and QoL. **Results:** The 226 pts were assigned to BE (n=112) and E (n=114). For the follow-up OS analysis, the data cut-off date was 30 November 2019. Median follow up time was 39.2 months. Median OS was 50.7 months (95% CI, 37.3 months to not reached) with BE and 46.2 months (95% CI, 38.2 months to not reached) with E (hazard ratio, 1.00; 95% CI, 0.68 to 1.48). Twenty-nine patients (25.9%) in BE and twenty-six patients (23.2%) in E were treated by osimertinib as second line treatment. The median survival time between enrollment and progressive disease of second-line treatment (median PFS2) was 28.6 months (95% CI, 22.1 months to 35.9) with BE and 24.3 months (95% CI, 20.4 months to 29.1 months) with E (hazard ratio, 0.80; 95% CI, 0.59 to 1.10). In both arms, the median OS of patients with osimertinib second-line treatment were longer than other second-line chemotherapy groups [50.7 months (95% CI, 38.0 months to 50.7 months) vs 40.1 months (95% CI, 29.5 months to not reached), (hazard ratio, 0.645; 95% CI, 0.40 to 1.03), respectively. **Conclusion:** The additional effect of bevacizumab on erlotinib monotherapy for NSCLC with EGFR mutations gradually decreased in the order of PFS2 and survival, with no significant differences. Clinical trial information: UMIN000017069. Research Sponsor: Chugai Pharmaceutical.

9507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Concurrent osimertinib plus gefitinib for first-line treatment of EGFR-mutated non-small cell lung cancer (NSCLC). *First Author: Julia K Rotow, Dana-Farber Cancer Institute, Boston, MA*

Background: First-line treatment with an EGFR tyrosine kinase inhibitor (TKI) is standard of care for patients (pts) with *EGFR*-mutated NSCLC. The EGFR TKI osimertinib is active against the acquired gefitinib-resistant mutation *EGFR* T790M, as is gefitinib against the osimertinib-resistant *EGFR* C797S. Preclinical evidence suggests dual EGFR inhibition with gefitinib + osimertinib may delay emergence of acquired resistance. **Methods:** This ongoing phase I/II study enrolled pts with stage IV *EGFR*-mutated (L858R or del19) NSCLC, without prior therapy for metastatic disease. Treatment in dose escalation (n = 6): concurrent osimertinib 40 mg or 80 mg + gefitinib 250 mg daily. In dose expansion (n = 21): osimertinib + gefitinib at the maximum tolerated dose (MTD). Prior to protocol amendment 6 pts received alternating monthly cycles of TKI monotherapy and were excluded from this analysis. The primary endpoints in the dose escalation and expansion phases were, respectively, identification of the MTD and feasibility, defined as receipt of combination therapy for $\geq$ 6 four-week cycles. Secondary endpoints included overall response rate (ORR), survival outcomes, plasma *EGFR* mutation clearance (cell free DNA by droplet digital PCR (ddPCR)), and mechanisms of acquired resistance. **Results:** From May 2017 to July 2019 27 pts were enrolled and evaluable for the primary endpoints. The MTD was osimertinib 80 mg plus gefitinib 250 mg orally daily. In feasibility analysis, 81.5% completed $\geq$6 cycles combination therapy (1 pt discontinued for progression, 4 for toxicity). The ORR was 85.2% (95% CI 67.5%-94.1%). Best response: 85.2% partial response, 14.8% stable disease. The most common treatment-related adverse effects (TRAEs) (% any grade, % grade 3) were rash (96.3%, 3.7%), diarrhea (85.2%, 11.1%) and dry skin (70.4%, 0%). Plasma ddPCR (n = 25 pts) detected the driver *EGFR* mutation at baseline in 68% of pts. In these pts, plasma *EGFR* cleared to undetectable at 2 weeks treatment in 82.4%. At 14.8 months median follow up the median progression free survival was not yet reached. **Conclusions:** Combination therapy with osimertinib and gefitinib is tolerable for first-line treatment of *EGFR*-mutated NSCLC and resulted in rapid plasma clearance of the *EGFR* mutation. The observed ORR is consistent with previously reported first-line response rates to osimertinib. Analysis of survival outcomes and acquired resistance mechanisms are pending data maturity and will facilitate understanding of the role of first-line dual EGFR TKI therapy for this pt population. Clinical trial information: NCT03122717. Research Sponsor: AstraZeneca, U.S. National Institutes of Health.

9508 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

First-line tyrosine kinase inhibitor with or without aggressive upfront local radiation therapy in patients with EGFRm oligometastatic non-small cell lung cancer: Interim results of a randomized phase III, open-label clinical trial (SINDAS) (NCT02893332). *First Author: Xiaoshan Wang, Cancer Center Hospital of University of Electronic Science and Technology of China and Sichuan Provincial People's Hospital, Chengdu, China*

Background: The effectiveness of aggressive local therapy for oligometastatic non-small-cell lung cancer (NSCLC) is unknown. This multi-institutional, randomized, open label, phase III clinical trial was performed to assess upfront stereotactic radiotherapy to all sites at diagnoses in previously untreated EGFRm oligometastatic non-small-cell lung cancer on progression-free survival and overall survival. **Methods:** The study was conducted at five centers located in different provinces of China.Eligible participants had pathologically confirmed adenocarcinoma, gene sequencing confirmed EGFRm, stage IV, five or fewer metastatic disease lesions, an ECOG performance status score of ≤ 2, systemic therapy naive, and no brain disease before randomization.Participants were randomized to receive either first-line tyrosine kinase inhibitor (TKI) treatment alone or up front stereotactic radiotherapy to all sites of disease along with TKI treatment.The primary endpoint was progression-free survival and the secondary endpoint was overall survival. **Results:** From January 2016 to January 2019, 133 participants were enrolled, including 65 (48.8%) in the TKI arm who received standard of care TKI alone and 68 (51.1%) in the stereotactic radiotherapy sites at diagnosis arm who received stereotactic radiotherapy and TKI.At a median follow-up of 19.6 months (IQR 9.4 - 41.0), the median progression-free survival for tyrosine kinase inhibitor alone was 12.5 months, and for tyrosine kinase inhibitor and stereotactic radiotherapy was 20.20months, respectively (HR 0.6188 [95% CI 0.3949-0.9697], log rank $P < .001$). The median overall survival in the TKI alone arm was 17.40 months, and for TKI and stereotactic radiotherapy arm was 25.50 months, respectively (HR 0.6824 [95% CI 0. 4654-1.001], log rank $P < .001$). Adverse events were similar between groups, with no grade 5 or deaths due to treatment. Grade 3/4 adverse events with or without radiotherapy included pneumonitis (7.3% vs. 2.9%; $P > .05$) and esophagitis (4.4%vs. 3.0% $P > .05$). **Conclusions:** Upfront stereotactic radiotherapy to sites at diagnosis along with first line TKI improved both progression-free survival and overall survival significantly compared with TKI alone. This finding suggests aggressive local therapy to sites at diagnosis should be explored further in large cohort phase III trials as a standard treatment option in this clinical scenario. Clinical trial information: NCT02893332. Research Sponsor: National scienceand technology bureau [grant numbers 3035031263], Other Foundation.

9509 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Capmatinib in patients with high-level *MET*-amplified advanced non–small cell lung cancer (NSCLC): results from the phase 2 GEOMETRY mono-1 study. *First Author: Juergen Wolf, Center for Integrated Oncology, University Hospital Cologne, Cologne, Germany*

Background: In the ongoing, multicohort, phase 2 GEOMETRY mono-1 study, capmatinib (INC280) has shown efficacy in *METex14*–mutated NSCLC patients (pts) who were pretreated (cohort 4) or treatment (tx)-naïve (cohort 5b). Here, we report the efficacy and safety of capmatinib in pts with high-level *MET*-amplified (gene copy number [GCN] $\geq$10) advanced NSCLC who were either pretreated with 1 or 2 prior lines of systemic therapy (cohort 1a) or tx-naïve (cohort 5a). **Methods:** Adult pts ($\geq$18 years), ECOG PS 0–1 who had *ALK* and *EGFR* wt, stage IIIB/IV (any histology) *MET*-amplified NSCLC with GCN$\geq$10 received capmatinib 400 mg twice daily (fasting). Primary and key secondary endpoints were overall response rate (ORR) and duration of response (DOR), respectively, by blinded independent review committee (BIRC) assessment per RECIST v1.1. Other secondary endpoints included investigator-assessed ORR, DOR, disease control rate (DCR), progression-free survival (PFS, BIRC and investigator assessment), overall survival, and safety. **Results:** As of Jan 06, 2020, 84 pts were evaluable for efficacy (cohort 1a [2nd/3rd line], 69 pts; Cohort 5a [1st line], 15 pts). Tx was ongoing for 3 pts in cohort 1a, none in cohort 5a. Per BIRC assessment in cohorts 1a and 5a, respectively, ORR was 29% and 40%, median DOR was 8.31 months (mo, 20 responders, 95% CI: 4.17–15.44) and 7.54 mo (6 responders, 95% CI: 2.56–14.26), and median PFS was 4.07 (95% CI: 2.86–4.83) and 4.17 (95% CI: 1.45–6.87) mo. Investigator assessment was in line with BIRC assessment (Table). The most common adverse events across all cohorts ($\geq$25%, all grades, N = 364) were peripheral edema (51.1%), nausea (44.8%) and vomiting (28.0%). Data for biomarker analysis and pts with brain metastasis will be presented at the ASCO 2020 meeting. **Conclusion:** Capmatinib has demonstrated activity in the subset of pts with high-level *MET*-amplified (GCN$\geq$10) NSCLC, with a higher response rate in tx-naïve pts. Safety profile remains favorable and similar to previous reports of capmatinib. Clinical trial information: NCT02414139. Research Sponsor: Novartis Pharmaceuticals.

	Cohort 1a (2/3L) N = 69		Cohort 5a (1L) N = 15	
	BIRC	**Investigator**	**BIRC**	**Investigator**
ORR, % (95% CI)	29 (18.7–41.2)	27.5 (17.5–39.6)	40 (16.3–67.7)	40 (16.3–67.7)
DCR, % (95% CI)	71.0 (58.8–81.3)	60.9 (48.4–72.4)	66.7 (38.4–88.2)	73.3 (44.9–92.2)
Median PFS, mo (95% CI)	4.07 (2.86–4.83)	4.14 (2.79–5.52)	4.17 (1.45–6.87)	2.76 (1.45–6.87)
Median DOR, mo (95% CI)	**N = 20** 8.31 (4.17–15.44)	**N = 19** 6.80 (4.21–20.73)	**N = 6** 7.54 (2.56–14.26)	**N = 6** 9.66 (4.01–17.08)

9510 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Safety and preliminary clinical activity of the MET antibody mixture, Sym015 in advanced non-small cell lung cancer (NSCLC) patients with MET amplification/exon 14 deletion ($MET^{Amp/Ex14\Delta}$). *First Author: D. Ross Camidge, Medical Oncology Department, University of Colorado, Aurora, CO*

Background: Sym015, a mixture of 2 humanized antibodies, triggers MET degradation by a unique mechanism with superior specificity compared to tyrosine kinase inhibitors (TKIs). The Sym015-01 phase (P)1a trial met, the primary objective of identifying the recommended P2 dose (RP2D) as 18 mg/kg on cycle 1 day 1 followed by 12 mg/kg Q2W. The P2a was expanded to enroll $MET^{Amp/Ex14\Delta}$ NSCLC patients (pts) based on preliminary efficacy findings. Here we present interim safety (n = 45) and efficacy (NSCLC cohort, n = 20) results from P2a. **Methods:** The expansion NSCLC Cohort enrolled pts with $MET^{Ex14\Delta}$ (n = 12) or MET^{Amp} (n = 8 defined as $>$ 5 *MET* copies by NGS or *MET*/CEP7 ratio $>$ 2.2 updated to $\geq$3.0 by *in situ* hybridization; including 1 with $MET^{Amp+Ex14\Delta}$). Tumor *MET* status was confirmed centrally and longitudinal ctDNA was analyzed by Guardant360. **Results:** By January 2020, 45 pts (median age 61.7 years) have been treated in P2a. Median duration of exposure (DoE) was 3.8 months (m) (n = 45; range 0.4+ to 22 m). Treatment emergent adverse events occurred in 93%, treatment related AEs (TRAE) in 42.2% and TRAE $\geq$G3 in 13.3% pts. No pts discontinued or died due to TRAE. The most common TRAE in $\geq$10% pts were fatigue (13.3%) and peripheral edema (11.1%). Of 20 NSCLC pts, 5 had confirmed PR (ORR 25%; 2/8 MET^{Amp} and 3/12 $MET^{Ex14\Delta}$); 11 had SD (DCR 80%; 6/8 MET^{Amp} and 5/12 $MET^{Ex14\Delta}$); 2 had PD (2/12 $MET^{Ex14\Delta}$); and 2 were not evaluable. 10 NSCLC pts were MET TKI naive (7 MET^{Amp} and 3 $MET^{Ex14\Delta}$) and had 50% ORR and 100% DCR (5 PR and 5 SD; DoR range 1 to 18.3 m; DoE 1.5 to 22 m); 10 NSCLC pts were prior MET TKI treated (9 $MET^{Ex14\Delta}$ and 1 $MET^{Amp+Ex14\Delta}$) with DCR 60%, (6 SD; DoE 0.4-9.6 m). Median PFS was 5.5 m overall (95% CI 3.5-9.7 m). Median PFS for MET TKI naive and MET TKI pre-treated NSCLC pts was 6.5 m (95% CI 3.4-21.9 m) and 5.4 m (95% CI 1.2-9.7 m) respectively. Median OS was not reached for overall or for prior MET TKI subgroups. 89% $MET^{Ex14\Delta}$ tumor tissue to blood concordance (8/9 NSCLC pts) was observed. **Conclusions:** Sym015 was well-tolerated at the RP2D with a response rate similar to MET TKI in MET-treatment naïve $MET^{Amp/Ex14\Delta}$ NSCLC and seems to delay disease progression in MET TKI pretreated NSCLC pts. Combination with MET TKI to delay or prevent resistance should be further explored. Clinical trial information: NCT02648724. Research Sponsor: Symphogen A/S.

9511 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Characterization of 1,387 NSCLCs with MET exon 14 (METex14) skipping alterations (SA) and potential acquired resistance (AR) mechanisms. *First Author: Mark M. Awad, Massachusetts General Hospital, Cambridge, MA*

Background: *MET*ex14 SA are oncogenic drivers in NSCLC. Due to the numerous sites around ex14 that bind the spliceosome complex, many variations can result in deleterious alterations (alts). We present a comprehensive overview of these ex14 SA across 1,387 NSCLCs and characterized potential AR mechanisms. **Methods:** Hybrid-capture based comprehensive genomic profiling (CGP) was performed on samples from 60,495 NSCLC patients (pts). A scoring system was applied leveraging our large database of samples with METex14 SA to optimize accurate reporting of these variants. Paired samples were collected $\geq$ 60 days apart (median 462). **Results:** 1,393 *MET*ex14 SA were identified in samples (1,278 tissue, 109 circulating tumor DNA (ctDNA)) from 1,387 NSCLC pts (2.3%) spanning multiple functional sites: donor (42%), acceptor (4.7%), poly-pyrimidine tract (15%), acceptor and poly-pyrimidine tract (13%), D1010 (23%), Y1003 (2.1%), and whole exon deletions (0.3%). 6 samples (5 tissue, 1 ctDNA) harbored 2 *MET*ex14 SA, each including a mutation (mut) at the donor or acceptor site. *MDM2* and *CDK4* amplifications (amps) co-occurred in 32% and 19% of *MET*ex14 samples, respectively, but were more common with polypyrimidine tract (37% and 23%) vs donor site (32%, p = 0.07 and 18%, p = 0.07) alts. *MET* co-amp was present in 12% of cases and frequency did not significantly differ by functional site. 66 (4.8%) cases (57 tissue, 9 ctDNA) had known NSCLC co-drivers, including *KRAS* (68%) and *EGFR* (14%) mut, a subset of which may represent AR. Paired samples with a *MET*ex14 SA in the 1st sample were available for 36 pts. The *MET*ex14 SA was detected in the 2nd sample for 32 pts, excluding 3 with low ctDNA. 22/36 (61%) had reportable acquired alts detected including 9 with $\geq$1 acquired *MET* muts [D1228X (4), Y1230X (3), Y1003F (1), D1228A/E/H + L1195V (1)] and 3 with acquired *MET* amp. Other acquired alts included *ERBB2* amp and mut (1 each), *EGFR* ex19ins (1), *KRAS* amp (1), *PIK3CA* mut (1), *AKT2* amp (1) and others with unknown functional significance. Potential AR alts were present with primary *MET*ex14 SA spanning all functional sites. **Conclusions:** In a dataset of $>$ 60,000 advanced NSCLCs, *MET*ex14 SA were present in 2.3% of cases, and represented 6 major subtypes. Among paired cases, potential AR mechanisms included secondary *MET* alts (33%), and acquired alts in *EGFR*, *ERBB2*, *KRAS*, and PI3K pathways. Acquired alts were independent of the type of *MET*ex14 SA. Characterizing common co-occuring may be critical for predicting responses to MET inhibitors and informing rational combination strategies. Research Sponsor: Foundation Medicine.

9512 Poster Discussion Session; Displayed in Poster Session (Board #278), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Amivantamab (JNJ-61186372), an anti-EGFR-MET bispecific antibody, in patients with EGFR exon 20 insertion (exon20ins)-mutated non-small cell lung cancer (NSCLC). *First Author: Keunchil Park, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

Background: EGFR exon20ins-mutated NSCLC is generally refractory to EGFR tyrosine kinase inhibitors (TKIs) and is associated with poor prognosis. Amivantamab (JNJ-61186372) is a novel, fully human anti-EGFR-MET bispecific antibody whose mechanism of action can target both EGFR- and MET-driven disease and has shown monotherapy activity in patients (pts) with diverse EGFR mutant disease characterized by EGFR C797S, T790M, exon20ins, and MET amplification. We present preliminary results of pts with advanced NSCLC harboring exon20ins mutations from CHRYSALIS, an ongoing phase 1 study of amivantamab (NCT02609776). **Methods:** This study comprises a dose escalation phase in pts with advanced NSCLC and a dose expansion phase in pts with EGFR- and MET-mutated disease. This analysis includes all enrolled pts with exon20ins disease who received the recommended phase 2 dose (RP2D) of 1050 mg (1400 mg, pts ≥80 kg) amivantamab. Response was assessed by investigator per RECIST v1.1. **Results:** As of 30 Oct 2019, 50 pts with exon20ins mutations had received amivantamab at the RP2D. 39/50 pts were response-evaluable and had ≥2 disease assessments or had discontinued therapy prior to the assessment period; among these pts, 29 had prior platinum-based chemotherapy (PBCT). Median age for response-evaluable pts was 61 y (40–78), 51% were female, and median prior lines was 1 (0–7). In the 50 pts harboring exon20ins mutations treated at the RP2D, the most common adverse events (AEs) reported were rash (72%), infusion related reaction (60%), and paronychia (34%). Additional EGFR-related AEs included stomatitis (16%), pruritus (14%), and diarrhea (6%). Grade ≥3 AEs were reported in 36% of pts; 6% were treatment-related. One grade 3 diarrhea and no grade ≥3 rash was reported. Among the 39 response-evaluable pts, with a median follow-up of 4 months (1–26), the overall response rate (≥partial response [PR]) was 36% (95% CI, 21–53), and 41% (95% CI, 24–61) for the 29 pts who had prior PBCT. The clinical benefit rate (≥PR or stable disease ≥11 weeks) was 67% for response-evaluable pts and 72% for pts who had prior PBCT. Among all 14 responders, median duration of response was 10 months (1–16), with ongoing responses in 9 pts at data cutoff. Median progression-free survival was 8.3 months (95% CI, 3.0–14.8) for response-evaluable pts and 8.6 months (95% CI, 3.7–14.8) for pts who had prior PBCT. **Conclusions:** Amivantamab demonstrates robust and durable antitumor activity in pts with exon20ins disease, with a manageable safety profile. Clinical trial information: NCT02609776. Research Sponsor: Janssen Research & Development, LLC.

9513 Poster Discussion Session; Displayed in Poster Session (Board #279), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

ECOG-ACRIN 5162: A phase II study of osimertinib 160 mg in NSCLC with EGFR exon 20 insertions. *First Author: Zofia Piotrowska, Massachusetts General Hospital Cancer Center, Boston, MA*

Background: EGFR exon 20 insertions (ins20), which comprise 4-10% of EGFR-mutant NSCLC, are generally refractory to first- and second-generation EGFR TKIs. While the clinical activity of the third-generation EGFR TKI osimertinib against EGFR ins20 is unknown, preclinical studies suggest its favorable therapeutic window may allow for inhibition of EGFR isn20 at clinically-achievable doses (Hirano, Oncotarget 2015). We report the results of EA5162, a single-arm, phase II study of osimertinib 160 mg in NSCLC pts with EGFR ins20 (NCT03191149). **Methods:** Pts with advanced NSCLC with an EGFR ins20 mutation identified by any local, CLIA-certified tissue assay were treated with osimertinib 160 mg daily until progression, intolerable toxicity or withdrawal. At least one prior line of therapy was required; stable, asymptomatic brain metastases were allowed. The primary endpoint was objective response rate (ORR). Secondary endpoints included safety, progression-free survival (PFS) and overall survival. The estimated sample size was 19 patients. **Results:** 21 pts were enrolled between 4/2018 and 7/2019 (median age 65; 15 female, 6 male; median 2 prior therapies); 1 patient did not meet eligibility criteria due to laboratory studies obtained 1 day out of window. As of 1/21/20, 6 pts remain on treatment. Among the 20 eligible pts, the best response was PR in 4 pts and CR in one pt, for a confirmed ORR of 25%; 12 (60%) pts had SD. The median PFS was 9.7 months (95% CI, 4.07, NA), median duration of response (DOR) was 5.7 months (95% CI, 4.73, NA.) Grade > 3 treatment-related adverse events (TRAE) observed in > 1 pt included anemia (n=2), fatigue (n=2), prolonged QT interval (n=2.) One pt had grade 4 respiratory failure, there were no grade 5 TRAEs. One pt discontinued study treatment due to grade 3 anemia. **Conclusions:** Osimertinib 160mg daily is well-tolerated and showed clinical activity in EGFR ins20-mutant NSCLC with a response rate of 25%, disease control rate of 85%, and mPFS of 9.7 months. The adverse events with osimertinib 160 mg QD in this cohort were consistent with other reports of this regimen; grade 3 rash and diarrhea were not observed. Clinical trial information: NCT03191149. Research Sponsor: U.S. National Institutes of Health.

9514 Poster Discussion Session; Displayed in Poster Session (Board #280), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Poziotinib shows activity and durability of responses in subgroups of previously treated EGFR exon 20 NSCLC patients. *First Author: Xiuning Le, Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Treatment of non-small cell lung cancer (NSCLC) with EGFR exon 20 mutations is an unmet medical need. Poziotinib is a potent tyrosine kinase inhibitor (TKI) of EGFR and HER2 exon 20 insertion mutants. We evaluated the efficacy and safety of poziotinib in previously treated NSCLC patients with EGFR exon 20 insertion mutations in an independent cohort of a multi-cohort, multi-center Phase 2 study (*ZENITH20-1*). **Methods:** *ZENITH20-1* study enrolled pts with advanced NSCLC with an EGFR exon 20 insertion identified on local tissue testing who had received at least one prior line of therapy. Poziotinib (16 mg) was administered orally QD, allowing dose reductions for AEs, with follow up for 24 months. The primary endpoint was objective response rate (ORR), evaluated centrally by RECIST v1.1. Secondary endpoints included disease control rate (DCR), duration of response (DOR), progression-free survival (PFS) and safety. Efficacy was also evaluated by specific exon 20 insertions and prior lines of therapy. **Results:** 115 patients with a median age of 61 years (33-83) were enrolled. Patients had a median of 2 prior lines of therapy (range, 1-9.) The median relative dose intensity was 72% (7-100%) with 65% having dose reductions. The ORR in the as-treated population was 14.8% (95% CI 8.9 - 22.6%), and the DCR was 68.7% (95% CI 59.4 - 77.0%) with a median DoR of 7.4 months. 65% patients had tumor size reductions and the median PFS was 4.2 months. In the evaluable population (n = 88), the ORR was 19.3% and the unconfirmed ORR was 25%. Responses were predominantly observed in insertions between residues M766 to D770 of exon 20 (8/44; 18.2%). Responses were observed in patients with 2 lines (14%); ≥3 lines of therapy (16.2%). The most common treatment-related Grade ≥3 AEs were rash (28%), diarrhea (26%), stomatitis (9%) and paronychia (6%). The incidence of treatment-related pneumonitis was 4%, however some cases may have been confounded by prior checkpoint inhibitors as first line treatment. **Conclusions:** Although the ORR primary endpoint was not met, poziotinib induced tumor reduction in the majority of patients with durable responses, including the heavily pre-treated population. Responses were more common in patients with insertions between M766 to D770 of EGFR exon 20. The safety profile was overall consistent with other 2nd generation EGFR TKIs. Evaluation of these subgroups with refined dosing and improved toxicity management to maintain continuous treatment is warranted to assess the potential of poziotinib in Exon20 related tumors. Clinical trial information: NCT03318939. Research Sponsor: Spectrum Pharmaceuticals, Inc.

9515 Poster Discussion Session; Displayed in Poster Session (Board #281), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Registrational dataset from the phase I/II ARROW trial of pralsetinib (BLU-667) in patients (pts) with advanced RET fusion+ non-small cell lung cancer (NSCLC). *First Author: Justin F. Gainor, Massachusetts General Hospital, Boston, MA*

Background: Pralsetinib is an investigational, highly potent, selective RET kinase inhibitor targeting oncogenic RET alterations. We provide the registrational dataset for pts with RET fusion+ NSCLC with and without prior treatment from the global ARROW study. **Methods:** ARROW (75 sites in 11 countries; NCT03037385) consists of a phase I dose escalation to establish recommended phase II dose (400 mg once daily [QD] orally) and phase II expansion cohorts defined by tumor type and/or RET alteration. Primary objectives were overall response rate (ORR; blinded independent central review per RECIST v1.1) and safety. Efficacy analyses are shown for response-evaluable pts (REP) with RET fusion+ NSCLC who initiated 400 mg QD pralsetinib by July 11 2019 and safety for all pts (regardless of diagnosis) treated with 400 mg QD. **Results:** As of November 18 2019, 354 pts with advanced solid tumors had received pralsetinib at starting dose of 400 mg QD with median follow-up 8.8 months. ORR, disease control rate (DCR), and % of pts with tumor size reduction are shown in the table for pts with metastatic RET fusion+ NSCLC (n=116; 72% KIF5B; 16% CCDC6; 12% other/fusion present but type unknown) and with prior platinum treatment (n=80) or without prior systemic treatment (n=26). ORR was similar regardless of RET fusion partner, prior therapies, or central nervous system involvement. Overall there were 7 (6%) complete responses, 4 (5%) in prior platinum pts and 3 (12%) in treatment naïve pts; median time to response overall was 1.8 months and median duration of response (DOR) was not reached (95% CI, 11.3–NR). In the safety population (n=354), most treatment-related adverse events (TRAEs) were grade 1-2, and included increased aspartate aminotransferase (31%), anemia (22%), increased alanine aminotransferase (21%), constipation (21%) and hypertension (20%). 4% of pts in the safety population (all tumor types) discontinued due to TRAEs. **Conclusions:** Updated, registrational, centrally reviewed data demonstrate that pralsetinib has rapid, potent, and durable clinical activity in pts with advanced RET fusion+ NSCLC regardless of RET fusion genotype or prior therapies, and QD oral dosing is well-tolerated. Clinical trial information: NCT03037385. Research Sponsor: Blueprint Medicines Inc.

	Overall (n=116[a])	Prior platinum treatment (n=80)	No prior systemic treatment (n=26)
ORR, % (95% CI)	65 (55–73)[b]	61 (50–72)[b]	73 (52–88)
DCR, % (95% CI)	93 (87–97)	95 (88–99)	88 (70–98)
Tumor size reduction, % of pts	96	95	100

[a]Including n=10 with prior non-platinum treatment
[b]Including n=2 with partial response pending confirmation

9516 Poster Discussion Session; Displayed in Poster Session (Board #282), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Intracranial activity of selpercatinib (LOXO-292) in RET fusion-positive non-small cell lung cancer (NSCLC) patients on the LIBRETTO-001 trial. *First Author: Vivek Subbiah, Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Patients with RET fusion-positive NSCLC have an ~50% lifetime prevalence of developing central nervous system (CNS) metastases. Selpercatinib is a highly selective oral RET inhibitor with CNS penetration. Its intracranial antitumor activity was previously demonstrated in an orthotopic RET fusion-positive preclinical model. The activity of selpercatinib in RET fusion-positive NSCLC patients with CNS metastases was evaluated as a prespecified subgroup analysis in LIBRETTO-001, a registrational phase 1/2 trial (NCT03157128). **Methods:** This global (89 sites, 16 countries) trial enrolled patients with advanced RET-altered solid tumors, including patients with RET fusion-positive advanced NSCLC with baseline CNS metastases. The selpercatinib recommended phase 2 dose was 160 mg twice daily, dosed orally in 28-day cycles. CNS metastases were assessed by MRI/CT scan at baseline, then every 8 weeks for 1 year, and every 12 weeks thereafter. The primary endpoint for this analysis was intracranial objective response rate (ORR, confirmed; RECIST v1.1) as assessed by independent review committee (IRC). Secondary endpoints included intracranial duration of response (DoR) by IRC. To be included in the efficacy analysis, patients were required to have adequate follow-up time (opportunity for ≥6 months follow-up from the first dose). Analyses were based on 17Jun2019 data cutoff date. **Results:** 79 patients with RET fusion-positive NSCLC and baseline CNS metastases were enrolled. Per IRC, 22 of 79 patients had measurable (≥10 mm) CNS disease; 14 of the 22 patients had adequate follow-up time for analysis. This efficacy-evaluable population had a median age of 64 yrs (range 43-80), ECOG PS 0/1 = 21% / 79%, and all had prior systemic therapy. 5 of the 14 patients received prior intracranial radiotherapy; all radiotherapy was completed > 2 months prior to selpercatinib. The intracranial ORR in the 14 patients was 93% (n = 13; 95% CI = 66.1 – 99.8), including 2 complete responses (14%) and 11 partial responses (79%). The median intracranial DoR was 10.1 months (95% CI = 6.7 – NE), with CNS progression events (n = 5) or death (n = 1) reported in 6 of 13 responders. The remaining responders (n = 7) were ongoing and censored. Presentation will include updated IRC data as of 16Dec2019. **Conclusions:** Selpercatinib had marked intracranial anti-tumor activity in RET fusion-positive NSCLC patients with CNS metastases. Tumor responses were durable, independently-confirmed, and observed in patients with prior systemic chemotherapy. Clinical trial information: NCT03157128. Research Sponsor: Loxo Oncology, a wholly owned subsidiary of Eli Lilly and Company.

9517 Poster Discussion Session; Displayed in Poster Session (Board #283), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Correlation of baseline molecular and clinical variables with ALK inhibitor efficacy in ALTA-1L. *First Author: D. Ross Camidge, Division of Medical Oncology, University of Colorado, Anschutz Medical Campus, Aurora, CO*

Background: Efficacy of ALK TKIs in patients (pts) with *ALK*+ non-small cell lung cancer (NSCLC) varies. We evaluated the impact of *EML4-ALK* fusion variants and other baseline (BL) molecular and clinical variables on clinical efficacy of brigatinib (BRG) vs crizotinib (CRZ) as first ALK TKI therapy in pts with *ALK*+ NSCLC in the phase 3 ALTA-1L (NCT02737501) trial. **Methods:** Plasma samples were collected at screening for molecular genetic analysis of *ALK* and other genes implicated in NSCLC by next-generation sequencing. Exploratory analyses were performed to identify associations of clinical outcomes with oncogenic alterations including *ALK* fusion variants and *TP53* status. **Results:** 124 BL samples were collected from 136 BRG-treated pts and 127 from 137 CRZ-treated pts. Pts with plasma samples were representative of the intent-to-treat population. BL *ALK* fusion detection rate was 52% (65/124) and 54% (68/127) in the BRG and CRZ arms, respectively, of which 83% (54/65) and 93% (63/68) were *EML4-ALK* fusions. In pts with detectable *EML4-ALK* fusions, the three predominant *EML4-ALK* fusion variants (V1, V2, V3) were equally distributed between arms; V1 and V3 were most prevalent (BRG/CRZ: V1, 42%/47%; V3, 42%/33%) but V1 was more frequent than V3 in pts without BL brain metastasis (47% vs 36%) or prior chemotherapy (45% vs 35%). Gender and age did not impact variant type. BRG showed higher ORR and improved mPFS vs CRZ in all variant subgroups; pts with V3 had poorer PFS compared with V1 and V2 regardless of treatment (Table). In pts with V3, BRG showed significantly improved PFS (HR=0.273, 95% CI 0.125, 0.597) and higher ORR (84% vs 67%) vs CRZ. *TP53* mutation was detected in 30% (37/124) of pts in BRG arm and 26% (33/127) in CRZ arm. In pts with detectable *ALK* fusion, *TP53* mutation showed poorer PFS in both arms than nonmutant/undetected cases (Table). BRG had better ORR and PFS vs CRZ in pts regardless of *TP53* mutation status. Additional analyses of BL variables are ongoing. **Conclusions:** *EML4-ALK* fusion variant 3 and *TP53* mutation were identified as poor prognosis biomarkers in *ALK*+ NSCLC. BRG demonstrated better efficacy than CRZ as first-line therapy in pts regardless of *EML4-ALK* fusion variant and *TP53* mutation status. These findings may help define areas of greatest unmet need. Clinical trial information: NCT02737501. Research Sponsor: ARIAD Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

Efficacy by *EML4-ALK* variant and *TP53* status.

	BRG	CRZ
***EML4-ALK* variant**		
V1, n	25	30
ORR, %	84	73
mPFS, mo	NR	13
V2, n	6	6
ORR, %	83	50
mPFS, mo	16	11
V3, n	25	21
ORR, %	84	67
mPFS, mo	16	7
***TP53* status[a]**		
Not detected, n	43	44
ORR, %	91	68
mPFS, mo	24	11
Mutant, n	24	24
ORR, %	79	63
mPFS, mo	8	7

NR, not reached [a]*TP53* status assessed only in pts with *ALK* fusions detected.

9518 Poster Discussion Session; Displayed in Poster Session (Board #284), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Updated overall survival (OS) and safety data from the randomized, phase III ALEX study of alectinib (ALC) versus crizotinib (CRZ) in untreated advanced *ALK*+ NSCLC. *First Author: Solange Peters, Lausanne University Hospital (CHUV), Lausanne University, Lausanne, Switzerland*

Background: Final, mature PFS from the global phase III ALEX study (NCT02075840) of ALC vs CRZ in untreated, advanced/metastatic *ALK*+ NSCLC have been previously published: ALC 34.8 months (m) (95% CI 17.7–NR) vs CRZ 10.9 m (95% CI 9.1–12.9), (HR 0.43, 95% CI 0.32–0.58). We report 5-year OS and updated safety data from ALEX with a further 12 m follow-up (FU) (cutoff date: Nov 29, 2019). **Methods:** Patients (pts) with stage IIIB/IV *ALK*+ NSCLC (by central IHC), ECOG PS 0–2 and no prior systemic therapy for advanced NSCLC were randomized 1:1 to ALC 600 mg BID (n = 152) or CRZ 250 mg BID (n = 151). Asymptomatic CNS metastases (mets) at baseline (BL) were allowed. OS was a secondary endpoint, and no formal statistical testing was planned. **Results:** Median duration of FU: 48.2 m with ALC vs 23.3 m with CRZ. OS data remain immature (events: 37%; stratified HR 0.67 [95% CI 0.46–0.98]); median OS with CRZ was 57.4 m (95% CI 34.6–not estimable [NE]) vs NE with ALC. The 5-year survival rate was 62.5% (95% CI 54.3–70.8) with ALC vs 45.5% (95% CI 33.6–57.4) with CRZ (Table). In pts with CNS mets at BL the OS HR was 0.58 (95% CI 0.34–1.00) and 0.76 (95% CI 0.45–1.26) in pts without CNS mets at BL. The OS benefit of ALC vs CRZ was generally consistent across all subgroups. Considering the longer treatment duration for ALC (28.1 m) vs the previous analysis (27.7 m), the safety profile of ALC remains consistent; no new safety signals were observed. With ALC, 35% of pts remain on study treatment vs 9% of pts remaining on CRZ. In pts with ≥1 known post-progression treatment (ALC: 32.2%; CRZ: 45.7%), lorlatinib was the most common ALK TKI received after first-line ALC (7.2%), compared with ceritinib after first-line CRZ (15.2%). **Conclusions:** This is the first global randomized study of a 2nd generation ALK TKI to demonstrate a clinically meaningful improvement in OS vs CRZ in *ALK*+ NSCLC (5-year survival rate: 62.5%, ALC vs 45.5%, CRZ); longer FU is required as OS data remain immature. Clinical trial information: NCT02075840. Research Sponsor: F. Hoffman-La Roche Ltd.

	ALC (n = 152)	CRZ (n = 151)	
Survival rate, % (95% CI) [No. pts at risk]			Difference, % (95% CI)
Year 1	84.3 (78.4–90.2) [120]	82.5 (76.2–88.9) [104]	-1.8 (-10.4–6.9)
Year 2	72.5 (65.1–79.9) [94]	65.3 (57.0–73.6) [73]	-7.2 (-18.3–3.9)
Year 3	67.0 (59.1–74.8) [81]	57.0 (48.2–65.9) [60]	-9.9 (-21.8–1.9)
Year 4	65.3 (57.3–73.3) [77]	51.2 (42.1–60.3) [48]	-14.1 (-26.2– -2.0)
Year 5	62.5 (54.3–70.8) [8]	45.5 (33.6–57.4) [3]	-17.0 (-31.5– -2.5)
Safety event, n (%) [median treatment duration: 28.1 m ALC; 10.8 m CRZ]			
AEs leading to discontinuation	22 (14.5)	22 (14.6)	
AEs leading to dose reduction	31 (20.4)	30 (19.9)	

9519 Poster Discussion Session; Displayed in Poster Session (Board #285), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II study of savolitinib in patients (pts) with pulmonary sarcomatoid carcinoma (PSC) and other types of non-small cell lung cancer (NSCLC) harboring MET exon 14 skipping mutations (METex14+). *First Author: Shun Lu, Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China*

Background: There are unmet medical needs for pts with METex14+ NSCLC. PSC is a rare type of NSCLC with high incidence of MET exon 14 mutations and poor prognosis. Savolitinib (AZD6094, HMPL-504, volitinib) is a highly selective oral MET tyrosine kinase inhibitor, and its anti-tumor activity has been shown in combination with osimertinib in pts with EGFR-mutant, MET-amplified NSCLC (Yu H, et al. 2019 AACR, Abstract CT032). **Methods:** This was a multicenter, multi-cohort, single-arm phase II study (NCT02897479) to evaluate the efficacy, safety, and pharmacokinetics of savolitinib in pts with unresectable or metastatic METex14+ PSC and other NSCLC. MET mutation was tested or retrospectively confirmed by central laboratory. Savolitinib was taken orally, once daily (QD) (600mg for weight ≥50kg or 400mg weight < 50kg) until disease progression or intolerable toxicity. Tumor was evaluated every 6 weeks during the 1st year and every 12 weeks thereafter. The primary endpoint was independent review committee (IRC) assessed objective response rate (ORR) (RECIST version 1.1). Here we report the results of one cohort of prior MET-treatment naïve patients. **Results:** As of October 31, 2019, 593 pts were pre-screened/screened, 87 identified with METex14+ and 70 treated. Among treated pts, median age was 68.7 years (range 51.7-85.0), 58.6% pts were male, 92.9% stage IV, 60.0% previously treated, 57.1% with adenocarcinoma, 35.7% with PSC and the rest with other pathological types. Sixty-one pts were efficacy evaluable by IRC assessment (N = 61) (including pts who had at least one measurable lesion at baseline and had ≥1 scheduled post-baseline tumor assessment or evidence of any post-baseline radiological disease progression): ORR was 47.5% (95% CI: 34.6%, 60.7%), disease control rate 93.4% (95% CI: 84.1%, 98.2%) and median duration of response not reached yet. The median progression-free survival was 6.8 months (95% CI 4.2, 13.8) among all treated pts. Efficacy results were consistent with investigators'assessments. The most common (≥20%) treatment-related adverse events (TRAEs) were peripheral edema, nausea, increased AST/ALT, vomiting and hypoalbuminemia. The incidence of ≥ grade 3 TRAEs was 41.4%. TRAEs leading to treatment discontinuation occurred in 14.3% pts, among which liver injury and hypersensitivity were most common (each 2.9%). **Conclusions:** Savolitinib demonstrated promising anti-tumor activity and acceptable tolerability in METex14+ NSCLC pts. Clinical trial information: NCT02897479. Research Sponsor: Hutchison MediPharma Limited.

9520 Poster Discussion Session; Displayed in Poster Session (Board #286), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Capmatinib in patients with *METex14*-mutated or high-level *MET*-amplified advanced non–small-cell lung cancer (NSCLC): results from cohort 6 of the phase 2 GEOMETRY mono-1 study. *First Author: Harry J.M. Groen, University of Groningen and University Medical Center Groningen, Groningen, Netherlands*

Background: Capmatinib (INC280) has shown promising efficacy in patients (pts) with *MET* exon 14 (*METex14*)–mutated NSCLC who were pretreated (cohort 4) or treatment (tx)-naïve (cohort 5b) in the ongoing, multicohort, phase 2 GEOMETRY mono-1 study. We report the results for pts enrolled in the expansion cohort 6 with either high-level *MET* amplification (gene copy number [GCN] ≥10) or *METex14* mutation (any *MET* GCN) whose disease progressed on 1 prior line of systemic therapy. **Methods:** Adult pts (≥18 years), ECOG PS 0–1 who had *ALK* and *EGFR* wt, stage IIIB/IV NSCLC (any histology) received capmatinib tablets 400 mg twice daily (with or without food). Key efficacy endpoints were overall response rate (ORR) and duration of response (DOR) by blinded independent review committee (BIRC) per RECIST v1.1. Other secondary endpoints included investigator-assessed ORR, DOR, disease control rate (DCR), progression-free survival (PFS; BIRC and investigator assessment) and safety. **Results:** As of Jan 6, 2020, 34 NSCLC pts with *METex14* mutation (n = 31) or high-level *MET* amplification (n = 3) were included in this analysis. Tx was ongoing for 38.2% of pts. In *METex14*-mutated NSCLC pts, per BIRC assessment: ORR was 48.4%, median DOR was 6.93 months (mo, not yet mature, 95% CI: 4.17–NE) and median PFS was 8.11 mo (not yet mature, 95% CI: 4.17–9.86). Investigator-assessed responses were similar to BIRC assessment (Table). Only 3 pts with high-level *MET* amplification were included in this cohort due to challenges in enrollment. All 3 pts had stable disease per BIRC assessment and were on treatment for 48, 85 and 97 days. Most common AEs (≥25%, all grades, N = 34) were peripheral edema (64.7%), nausea (35.3%), fatigue (29.4%), back pain (26.5%) and vomiting (26.5%). Data for pts with brain metastasis will be presented at the ASCO 2020 meeting. **Conclusions:** Capmatinib was confirmed to be efficacious in 2nd line, *METex14*-mutated NSCLC pts. This is the first cohort where capmatinib has been administered without fasting restriction and data confirm the favorable safety profile. Clinical trial information: NCT02414139. Research Sponsor: Novartis Pharmaceuticals.

	Cohort 6 (2L, *METex14*-mutated) N = 31	
	BIRC	**Investigator**
ORR, % (95% CI)	48.4 (30.2–66.9)	41.9 (24.5–60.9)
DCR, % (95% CI)	90.3 (74.2–98.0)	90.3 (74.2–98.0)
Median PFS, mo (95% CI)	8.11 (4.17–9.86)	6.9 (5.55–NE)
Median DOR, mo (95% CI)	**N = 15** 6.93 (4.17–NE)	**N = 13** 8.18 (4.17–NE)

9521 Poster Discussion Session; Displayed in Poster Session (Board #287), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Evaluation of blood TMB (bTMB) in KEYNOTE-189: Pembrolizumab (pembro) plus chemotherapy (chemo) with pemetrexed and platinum versus placebo plus chemo as first-line therapy for metastatic nonsquamous NSCLC. *First Author: Marina Chiara Garassino, Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: In a previous analysis of KEYNOTE-189 (NCT02578680), we showed that tissue TMB (tTMB) assessed by whole-exome sequencing was not significantly associated with efficacy in either arm and that pembro + chemo improved outcomes vs placebo + chemo in both the tTMB ≥175 and tTMB < 175 mut/exome subgroups. Here, we explored the association of bTMB with efficacy in KEYNOTE-189. **Methods:** 616 patients (pts) were randomized 2:1 to pembro + chemo or placebo + chemo. bTMB was assessed in cfDNA using the Guardant Health Omni assay. Association of bTMB (continuous square root transformed) with outcomes in each arm was assessed using Cox proportional hazards models (OS, PFS) and logistic regression (ORR) adjusted for ECOG PS; statistical significance was determined at the 0.05 level without multiplicity adjustment. The clinical utility of bTMB on outcomes was assessed using the cutoff that most closely approximated the 175 mut/exome tTMB cutoff as determined by AUROC analysis. Data cutoff was 21 Sep 2018. **Results:** 235 (38%) treated pts had evaluable tTMB and bTMB: 160 in the pembro + chemo arm and 75 in the placebo + chemo arm. bTMB as a continuous variable was not significantly associated with OS or ORR for pembro + chemo (one-sided P = .229 and .051) or placebo + chemo (two-sided P = .641 and .069); bTMB was significantly associated with PFS in the pembro + chemo arm (one-sided P = .015) but not the placebo + chemo arm (two-sided P = .058). bTMB and tTMB scores were moderately correlated (r = .61). The bTMB cutoff that most closely approximated tTMB 175 mut/exome was 15 mut/Mb (AUROC 0.81, 95% CI 0.75-0.86). 178 (76%) pts had concordant bTMB and tTMB results—101 low and 77 high by both—whereas 57 (24%) had discordant results—21 high bTMB but low tTMB, 36 low bTMB but high tTMB. Pembro + chemo improved OS, PFS, and ORR vs placebo + chemo for bTMB ≥15 and < 15 mut/exome (Table). **Conclusions:** Similar to previous findings based on tTMB, bTMB has limited clinical utility in the setting of pembro with pemetrexed and platinum given as first-line therapy for metastatic nonsquamous NSCLC. Clinical trial information: NCT02578680. Research Sponsor: Merck & Co., Inc., Kenilworth, NJ, USA.

	bTMB ≥15 mut/Mb		bTMB < 15 mut/Mb	
	Pembro + Chemo n = 70	**Placebo + Chemo n = 28**	**Pembro + Chemo n = 90**	**Placebo + Chemo n = 47**
Median OS (95% CI), mo	20.4 (17.4-NE)	9.7 (7.6-NE)	17.7 (12.2-NE)	8.0 (6.5-18.8)
HR (95% CI), OS	0.61 (0.36-1.06)		0.64 (0.41-0.99)	
Median PFS (95% CI), mo	8.3 (4.9-14.1)	4.7 (2.8-5.5)	7.0 (6.2-9.7)	4.7 (4.0-5.3)
HR (95% CI), PFS	0.35 (0.21-0.57)		0.50 (0.34-0.73)	
ORR, % (95% CI)	49 (36-61)	11 (2-28)	40 (30-51)	19 (9-33)

9523 Poster Discussion Session; Displayed in Poster Session (Board #289), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Prevalence and association of *ARID1A* with driver alterations and immune checkpoint inhibitor (ICPi) biomarkers in cell-free circulating tumor DNA (ctDNA) from 27,000 non-small cell lung cancer (NSCLC) patients. *First Author: David R. Gandara, University of California Davis Comprehensive Cancer Center, Sacramento, CA*

Background: Recent data suggest that the tumor suppressor gene *ARID1A* is associated with high anti-tumor immunity and may have value as a predictive biomarker for response to ICPi therapy in NSCLC. We examined *ARID1A* alterations detected in ctDNA from a large cohort of advanced NSCLC patients using a commercially available liquid biopsy assay and explored associations of *ARID1A* with lung cancer driver alterations and other putative ICPi mutational biomarkers. **Methods:** Consecutive samples from stage IIIB/IV NSCLC patients tested from March 2016 - August 2019 using a 73- to 74-gene targeted next-generation sequencing ctDNA assay (Guardant360) were queried. Testing included analysis of single nucleotide variants, insertions/deletions, fusions, and amplifications (*KEAP1* not tested). Mutation frequencies were compared using Fisher's exact test, with variants of uncertain significance and synonymous variants excluded. **Results:** Of 27,776 NSCLC patients with >1 ctDNA alteration detected, 1,094 (3.9%) had >1 functional *ARID1A* (f*ARID1A*) mutation. f*ARID1A* mutations were significantly more common in patients with squamous histology compared to adenocarcinoma (5.1% vs 3.8%, p = 0.0007). There were significantly fewer *EGFR* exon 19 deletion mutations (4.9% vs 11.1%; p < 0.0001) and *EGFR* L858R mutations (4.0% vs 7.0%; p < 0.0001), and significantly more *BRAF* V600E alterations (2.2% vs 1.4%; p = 0.0338) in patients with f*ARID1A*. There was no significant difference in the frequency of *ALK* and *ROS1* fusions, nor *STK11* mutations between patients with and without f*ARID1A* (8.0% vs 6.8%; p = 0.126). Activating *KRAS* mutations were significantly more frequent in patients with f*ARID1A* (31.1% vs 19.4%; p < 0.0001), including *KRAS* G12C (10.9% vs 7.0%; p < 0.0001). **Conclusions:** These data provide a mutational landscape for f*ARID1A* mutations in NSCLC. f*ARID1A* was associated with significant differences in the frequency of multiple lung cancer driver alterations, of particular interest in the *EGFR*-mutated cohort, where ICPi efficacy is low. The frequency of *STK11* mutations, a possible negative predictor of ICPi efficacy, was not significantly different. *KRAS* mutations were significantly more frequent in patients with f*ARID1A*, notable given recent data reporting that *KRAS* mutations, particularly *KRAS* G12C, may be a positive predictor of ICPi response in NSCLC. Determination of ICPi efficacy in patients with f*ARID1A* is in-process. Research Sponsor: None.

9524 Poster Session (Board #290), Fri, 8:00 AM-11:00 AM

PREDICT1: An observational study for identifying blood biomarkers associated with clinical benefit from carboplatin and pemetrexed (CbP) treatment in patients with non-squamous (NS) non-small cell lung cancer (NSCLC) (CJLSG1201). *First Author: Tetsunari Hase, Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan*

Background: At present, platinum-doublet chemotherapy or in combination with an immune check point inhibitor are standard treatment for patients with metastatic or recurrent NSCLC which lacks somatic gene alterations. Although CbP is one of the commonly used treatment options for NS-NSCLC, its clinical utility is limited due to lack of optimal biomarkers. **Methods:** Chemotherapy-naïve patients with pathologically proven advanced or recurrent NS-NSCLC received carboplatin (area under the curve = 5-6, at investigator's discretion) plus pemetrexed (500 mg/m2) every 3 weeks followed by maintenance pemetrexed until disease progression. Blood samples were collected before treatment for proteomic analysis using mass spectrometry (MS). A classifier was constructed based on both an objective response assessed by radiologist independent of attending physicians in accordance with RECIST v1.1 and expression profiles of protein in a training cohort. The constructed classifier was then assessed with a validation cohort evaluating prediction accuracy of good responder, progression free survival (PFS) and overall survival (OS). **Results:** Of 244 patients with NS-NSCLC in a training cohort, proteomic profiles in blood from 96 patients who responded or progressed after treatment with CbP were analyzed to develop a classifier based on weighted voting. Details of the classifier will be presented at the 2020 ASCO Annual Meeting. The classifier was then applied to validation cohort (n = 94), and we successfully identified patients who benefit from the treatment (55 in good MS group) or not (39 in poor MS group). The objective response rate of the good MS group was significantly higher than that of the poor MS group (30.9% vs. 5.1%; p = 0.0018). The good MS group showed a significantly improved survival compared to the poor MS group (median PFS, 6.0 m vs. 2.3 m; hazard ratio [HR], 0.15; 95% confidence interval [CI], 0.09-0.27; p < 0.001; median OS, 25.7 m vs. 5.1 m; HR, 0.18; 95% CI, 0.1-0.34; p < 0.001). **Conclusions:** In the present study, we successfully developed and validated a predictive classifier using proteomic analyses with blood samples collected from patients before treatment with CbP, suggesting the clinical utility of the classifier in selecting NS-NSCLC patients for treatment with CbP. Clinical trial information: UMIN000008476. Research Sponsor: Japan Agency for Medical Research and Development.

9525 Poster Session (Board #291), Fri, 8:00 AM-11:00 AM

Comprehensive modeling of longitudinal circulating tumor DNA dynamics to predict clinical response to first-line immunotherapy and chemo-immunotherapy in advanced non-small cell lung cancer. *First Author: Joseph Christopher Murray, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins School of Medicine, Baltimore, MD*

Background: First-line immunotherapy (IO) and chemo-immunotherapy (chemo-IO) are approved for PD-L1-expressing advanced non-small cell lung cancer (NSCLC), but PD-L1 expression does not reliably predict therapeutic response. Therefore, accurate on-therapy response assessment is needed to guide clinical decision-making. Conventional radiographic imaging is the gold-standard, but may not capture the nature and timing of an immune-mediated response. We investigated whether comprehensive longitudinal circulating tumor DNA (ctDNA) dynamics could enhance prediction of clinical response. **Methods:** We conducted targeted error correction sequencing (TEC-Seq) of longitudinal plasma specimens and matched white blood cells (WBCs) in patients with NSCLC treated with first-line IO or chemo-IO. Plasma ctDNA variants were identified by filtering out clonal hematopoiesis (CH) and germline (GL) variants found in matched WBCs. Clinical and pathological data, including PD-L1 tumor proportion score (TPS), and imaging response by RECIST1.1 were assessed. ctDNA dynamics were modeled to predict durable clinical benefit (at 6 months), progression-free survival (PFS), and overall survival (OS). **Results:** A total of 143 longitudinal plasma and 24 white blood cell samples underwent TEC-Seq for 31 patients with NSCLC treated with IO (n = 17) or chemo-IO (n = 14). ctDNA variants were found in 77% (n = 24) of patients after filtering out CH and GL variants, which comprised 53% (n = 196 of 373) of all variants. Molecular response, signified by elimination of ctDNA variants, was detected in 32% (n = 10) of patients and associated with improved PFS (p = 0.0004, log rank) and OS (p = 0.017, log rank). Time to molecular response was shorter than time to best RECIST response (median 3 vs. 7.71 weeks, p = 0.048, Mann-Whitney U test). A logistic regression model incorporating molecular response, recrudescence, or emergence of new variants predicted durable clinical benefit (sensitivity 84%, specificity 76%, AUC 0.88) better than PD-L1 TPS (AUC 0.67, p = 0.046, bootstrap method). **Conclusions:** Comprehensive modeling of ctDNA variant dynamics predicts clinical outcome independent of PD-L1 status in patients with advanced NSCLC treated with first-line IO or chemo-IO. Verification of bona fide ctDNA variants by matched WBC sequencing is essential. Molecular response can be identified earlier than imaging response and could enable on-therapy decision-making to alter clinical outcomes. Research Sponsor: NCI R01 CA121113, Emerson Collective, LUNGevity Foundation, The V Foundation, Swim Across America.

9526 Poster Session (Board #292), Fri, 8:00 AM-11:00 AM

Targeted DNA sequencing analysis to reveal genetic diversity and androgen-receptor alteration in advanced EGFR mutant lung adenocarcinoma. *First Author: Wei Wu, University of California, San Francisco, San Francisco, CA*

Background: Lung cancer remains the leading cause of death from cancer around the world. Several oncogenic drivers have been identified from large cancer genome projects focused mainly on profiling early-stage lung cancers. Targeted therapies have been developed for specific activated driver gene mutations and are used in advanced-stage patients. For instance, advanced EGFR mutant lung cancer is primarily treated with EGFR tyrosine receptor inhibitors (TKIs). However, resistance remains an obstacle to durable anti-tumor control. We hypothesize that concurrent genetic alterations co-exiting with EGFR driver mutations contribute to the failure of EGFR TKI therapy. **Methods:** To understand the complexity and diversity of genetic alterations present in EGFR mutant advanced lung cancers, we utilized 660 EGFR mutant advanced lung adenocarcinomas samples with targeted DNA sequencing from Foundation Medicine, 394 cases from MSK-IMPACT dataset, along with TCGA lung cancer data. We performed systematic co-mutation analysis, molecular simulation, functional annotation and pathway enrichment analysis. **Results:** We updated mutational profiling on EGFR gene with hotspots at exon 18, 19, 20 and 21. Among them, EGFR L858R, exon19 deletion, T790M and G719A are top ranking alleles among EGFR mutations. Interestingly, a subset (n = 26 cases) of EGFR T790M mutations parallel with other EGFR mutations, which could affect the TKI binding pocket as inferred by molecular simulations. Furthermore, in advanced lung cancer EGFR mutations co-occurred with known oncogenic mutations in KRAS, MET, NF-1, MAP2K1, ERBB2, and ALK/ROS-1/RET fusions. Functional annotation suggests that concurrent mutated genes and copy number alterations in advanced EGFR mutant lung cancer were enriched in signatures of epigenetic modifiers, genome instability, WNT signaling, and RNA splicing. Compared to early stage TCGA-lung adenocarcinomas, Cell cycle, DNA repair, WNT signaling and androgen receptor-mediated signaling pathways are predominantly altered in advanced EGFR mutant lung cancers. **Conclusions:** We characterized the genetic landscape of advanced EGFR-mutant lung adenocarcinomas and further dissected concurrent mutated genes with EGFR driver mutations. Our findings provide a rational for polytherapy roadmap for testing in advanced EGFR-mutant lung cancer. Research Sponsor: U.S. National Institutes of Health.

9527 Poster Session (Board #293), Fri, 8:00 AM-11:00 AM

RELAY study of erlotinib (ERL) + ramucirumab (RAM) or placebo (PL) in *EGFR*-mutated metastatic non-small cell lung cancer (NSCLC): Biomarker analysis using circulating tumor DNA (ctDNA) in Japanese patients (pts). *First Author: Kazuto Nishio, Department of Genome Biology, Kindai University Faculty of Medicine, Osaka, Japan*

Background: The phase III RELAY study (NCT02411448) showed significantly improved progression-free survival (PFS) for RAM+ERL vs PL+ERL in 449 pts with previously untreated *EGFR* mutation-positive metastatic NSCLC (median PFS 19.4 vs 12.4 mo, HR 0.591 [95% CI 0.461–0.760], p<.0001). To understand baseline genetic mutations and treatment-emergent (TE) resistance mechanisms, this exploratory liquid biopsy substudy examined biomarkers in ctDNA from participating Japanese pts by next-generation sequencing (NGS) and droplet digital PCR (ddPCR). **Methods:** Plasma samples were collected at baseline, during treatment (Cycle 4, 13, and every 6 cycles to Cycle 53) and post-study treatment discontinuation (30-day follow-up [30d FU]). Mutations were assessed at baseline and 30d FU by NGS (Ion AmpliSeq Colon and Lung Cancer panel). *EGFR* mutations and *MET* and *ERBB2* copy number (CN) were assessed at all time points by ddPCR. Baseline markers were analyzed in pts with any detectable baseline mutation (to confirm ctDNA presence; NGS N=84, ddPCR N=74). TE mutations were analyzed in pts with any detectable mutation at baseline and 30d FU (NGS N=26, ddPCR N=28). Among these pts, 81% and 57% for NGS and ddPCR, respectively, had progressed by 30d FU. **Results:** By plasma NGS, baseline *EGFR* activating mutations (exon 19 deletion or exon 21 [L858R] mutation) were detected in 83.3% of pts. Common co-occurring baseline mutations were *TP53* (42.9%), *PTEN* (7.1%) and *KRAS* (6.0%). Baseline *TP53* mutation rate was higher in men vs women (p=.02). No difference in PFS was detected by baseline *TP53* status (interaction predictive p=.45, prognostic p=.33). TE mutations were detected in *EGFR* (including T790M), *FGFR3*, *KRAS* and *TP53*. Slightly higher rates of TE *KRAS* (p=.03) and *TP53* (p=.07) mutations were detected in RAM+ERL than in PL+ERL. TE total *EGFR* mutations (p=.65) or TE T790M (p=.69) did not differ by arm. By ddPCR, baseline *EGFR* activating mutations were detected in all pts. T790M was detected at baseline in 2/37 pts/arm (5.4%) and was TE in 6/11 (55%) RAM+ERL pts and 7/17 (41%) PL+ERL pts. There was a trend (p=.054) for greater *ERBB2* CN in RAM+ERL vs PL+ERL at Cycle 4. *MET* CN decreased slightly at Cycle 4 in both arms (significant in PL+ERL, p=.003). Biomarker levels by ddPCR across all time points will be presented. **Conclusions:** Though limited by sample size and likely inconsistent tumor shedding, this exploratory study identified potential differences in *TP53*, *KRAS*, *ERBB2* and *MET* by demographics, treatment and/or time. Clinical trial information: NCT02411448. Research Sponsor: Eli Lilly and Company.

9528 Poster Session (Board #294), Fri, 8:00 AM-11:00 AM

Exon-16-skipping *ERBB2* (*ERBB2*ΔEx16) as a novel resistance mechanism against EGFR tyrosine kinase inhibitors in non-small cell lung cancer (NSCLC). *First Author: Xin Zhao, Department of Respiratory and Critical Care Medicine, Jiangsu Province Hospital, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China*

Background: In addition to *ERBB2* amplification/protein overexpression, activating *ERBB2* alterations have been increasingly discovered in diverse human cancers with varying incidence. *ERBB2*ΔEx16 is an alternatively spliced isoform of *ERBB2*, lacking the entire exon 16 which encodes a small extracellular domain. *ERBB2*ΔEx16 was recently reported to lead to oncogenic activation of ERBB2 and osimertinib resistance in *EGFR* T790M+ non-small cell lung cancer (NSCLC). **Methods:** A total of 38,680 Chinese cancer patients whose tumor specimen or circulating cell-free DNA underwent genomic profiling by targeted next-generation sequencing of cancer-related genes were retrospectively reviewed. Clinicopathological features and treatment history of *ERBB2*ΔEx16+ patients were evaluated. RNA sequencing was performed to validate the presence of exon-16-skipping *ERBB2* at the transcriptional level. **Results:** A total of eighteen *ERBB2*ΔEx16+ patients (11 NSCLC, 2 colorectal cancer, 2 gastric cancer, and 3 others) were identified (0.047%, 18/38,680). *ERBB2* exon 16 skipping may result from large fragment deletion spanning the whole or partial region of exon 16 (72.2%, 13/18), base substitution at the splice acceptor site (16.7%, 3/18) and deletion of the splice donor site (11.1%, 2/18). *ERBB2* exon 16 skipping, including large fragment deletion and splice site deletion, was validated at the RNA level by RNA sequencing in 3 patients with available samples. Co-occurrence of *ERBB2* amplification and *ERBB2* mutations were found in 83.3% (15/18) and 50% (9/18) of cases, respectively. Concurrent copy number variations were prevalent in *CDK12* (55.6%, 10/18), *CDKN2B* (44.4%, 8/18), *NKX2.1* (38.9%, 7/18) and *PTPRD* (33.3%, 6/18). Among the 11 cases of *ERBB2*ΔEx16+ NSCLC, 9 had coexisting activating *EGFR* mutations (exon 19 deletions, exon 21 L858R) and received prior treatment with EGFR tyrosine kinase inhibitors (TKIs), with 2 harboring acquired *EGFR* T790M mutation and 1 *EGFR* copy number gain. Further analysis of the matched pretreatment samples in 3 *EGFR*-mutated NSCLC patients confirmed that *ERBB2*ΔEx16 was acquired during EGFR TKI therapy. In the 7 cases of other cancers, 4 to 31 non-*ERBB2* mutations were identified in each sample, with *TP53* being the most frequently mutated gene. **Conclusions:** Our data suggest that *ERBB2*ΔEx16 may be a general mechanism of EGFR TKI resistance in a subset of *EGFR*-mutated NSCLC patients, in addition to being an oncogenic driver as reported in some solid malignancies including colorectal, gastric and ovarian cancers. Research Sponsor: None.

9529 Poster Session (Board #295), Fri, 8:00 AM-11:00 AM

A model comparing the value of broad next-gen sequencing (NGS)-based testing to single gene testing (SGT) in patients with nonsquamous non-small cell lung cancer (NSCLC) in the United States. *First Author: Nathan A. Pennell, Cleveland Clinic Foundation, Cleveland, OH*

Background: Patients (pts) with nonsquamous (ns) NSCLC should be tested for actionable driver oncogenes (ADOs), and highly effective treatments (tx) may be available for these pts. Although EGFR and ALK single gene testing (SGT) is relatively common (>80%) in the US, testing for less common ADOs is rare. Unidentified pts with ADOs have survival comparable to pts without alterations. We interrogate plausible testing configurations and discuss their implications for the US population. **Methods:** Simulation was used to evaluate various levels of testing with SGT or NGS on the basis of life years gained (LYG) as well as cost per LYG. Expected prevalence of ADOs among nsNSCLC pts as well as the survival distribution of pts in the presence versus absence of an ADO tx strategy were calibrated based on current literature. Survival duration for each simulated pt was generated from Weibull distributions fit to statistical estimates of median and 5-year survival. With appropriate match between ADO and targeted tx, the Weibull distribution offered a median additional 2 years of life. ADOs included in NGS: EGFR, ALK, ROS1, BRAF, RET, MET, NTRK. SGT: EGFR and ALK. **Results:** Each incremental 10% increase in NGS instead of SGT produces 2630 additional LYG and a cost savings per LYG between -$49 to -$109. At the current 80% testing rate, replacing SGT with NGS would result in an additional 21,019 LYG with reduced cost per LYG of -$599. Increasing testing from 80% to 100% of eligible pts would increase LYG by 15,017 over the current state. If 100% of eligible pts were tested with NGS and every identified pt received tx, the cost per LYG of this strategy would be $16,641.57. **Conclusions:** In a hypothetical model where highly effective tx is available to all identified pts with ADOs, broad NGS testing compared to SGT for EGFR/ALK leads to large gains in life years at reduced cost per LYG compared to SGT, supporting universal NGS testing of all advanced nsNSCLC pts. Conversely, lower levels of testing or only testing for common ADOs (as is the current state) result in large numbers of pts being unidentified and not experiencing these benefits. Research Sponsor: None.

Eligible nsNSCLC pts for testing in US annually.	89,000
Estimated pts with ADOs (EGFR/ALK/ROS1/BRAF/RET/MET/NTRK)	26,300
CMS reimbursement for NGS	$627.50
CMS reimbursement for SGTs (EGFR+ALK)	$732.30
Cost of treatment for 2 years	$10K/year = $20,000
Estimated median and 5-year survival of pt with ADO with highly-effective tx	39 months and 25%
Estimated median and 5-year survival of pt with ADO who goes unidentified	14 months and 5%

9530 Poster Session (Board #296), Fri, 8:00 AM-11:00 AM

Impact of SWI/SNF complex mutations in patients with non-small cell lung cancer (NSCLC) treated with immune checkpoint inhibitors: Immuno-oncology biomarker study in LC-SCRUM-Japan (LC-SCRUM-IBIS). *First Author: Kiyotaka Yoh, National Cancer Center Hospital East, Kashiwa, Japan*

Background: The SWI/SNF chromatin remodeling complex is reported to be involved in sensitivity and resistance to immune checkpoint inhibitor (ICI). However, their role in non-small cell lung cancer (NSCLC) remains unclear. We examined the relationship between SWI/SNF complex mutations and clinical outcomes of ICI in patients with NSCLC. **Methods:** Of 1017 lung cancer patients enrolled in LC-SCRUM-IBIS, 350 patients were analyzable for whole-exome sequencing (WES). WES data were used to analyze the presence of mutations in 29 major subunits of the SWI/SNF complexes. ARID1A and SMARCA4 mutations were also evaluated in a targeted NGS panel (Oncomine comprehensive assay, OCA). PD-L1 expression by 22C3, tissue tumor mutational burden (tTMB) by WES, STK11 and KEAP1 mutations by WES or OCA were also assessed. Durable clinical benefit (DCB) including CR, PR and SD > 6 mos to ICI, progression-free survival (PFS) and overall survival (OS) were compared in status of each of SWI/SNF complex mutations and other factors. **Results:** At least one mutation in any subunits of the SWI/SNF complex was present in 28% of NSCLC patients. The most common mutated subcomplexes were SMARCA4 (12%), BAF (7%: ARID1A, 4%), non-canonical BAF (3%), PBAF (3%), and SMARCA2 (2%). Of 101 NSCLC patients treated with PD-1/PD-L1 inhibitors, SMARCA4 mutations tended to be associated with lower DCB (16 vs 31%) and shorter median PFS (1.9 vs 3.6 m) and OS (7.4 vs 18.1m). Patients with ARID1A mutations tended to have better clinical outcomes (DCB, 40 vs 28%) compared to those without mutations. No significant associations were found between PD-L1 expression and SMARCA4 or ARID1A mutations. Patients with STK11/KEAP1 mutations had lower rate of PD-L1 expression (TPS > 50%) (18% vs 48%, $P = 0.03$) and worse clinical outcomes (DCB, 6 vs 33%) compared to those without mutations. There was no significant association between a tTMB status and clinical outcome. **Conclusions:** SMARCA4 and ARID1A mutations appear to affect clinical outcomes of ICI in NSCLC patients. These findings indicate that SWI/SNF complex mutations may serve as a predictive biomarker for ICI in NSCLC patients. Research Sponsor: AstraZeneca, Bristol-Myers Squibb, Chugai, Ono.

9531 Poster Session (Board #297), Fri, 8:00 AM-11:00 AM

Identification and in silico structural insights of rare recurrent *EGFR* mutations as resistance mechanisms to osimertinib in *EGFR*-mutated lung cancer. *First Author: N/a Zhoutong, Department of Medical Oncology, Changzhou Cancer Hospital of Soochow University, Changzhou, China*

Background: Inevitable progression on 3rd-generation EGFR-tyrosine kinase inhibitor (TKI) osimertinib of *EGFR*-mutated lung cancer patients represents a great challenge in clinic. Previous studies have revealed that one-third of the resistant mechanisms are due to acquired *EGFR* secondary mutations, mainly on C797, L718 and L792 residues. Our study aims to gain insights into novel mechanisms of acquired resistance to osimertinib. **Methods:** We performed genomic profiling on a total of 1,058 *EGFR*-mutated lung cancer patients with progressed disease on osimertinib, and a cohort of 1,803 patients who received only 1st-generation EGFR TKIs upon progression. Recurrent *EGFR* mutations with a significant enrichment in the osimertinib group were identified. We further established and applied molecular dynamic simulation-based computational model of the mutant EGFR protein to predict its sensitivity to osimertinib. **Results:** As expected, compared with 1st-TKIs alone group, *EGFR* mutations, including C797S/G (22.1% vs. 0.5%), L718Q/V (6.2% vs. 0.3%), L792F/H (4.4% vs. 0.3%), were significantly more enriched in the osimertinib cohort. Our computational model has also successfully predicted their sensitivities to osimertinib: WT (-35.19 kcal/mol) > L792F (-34.10 kcal/mol) > L718Q (-30.33kcal/mol) > C797S (-28.02 kcal/mol), which are consistent with our previous *in vitro* validations. Importantly, a total of 14 low-frequency *EGFR* mutations were exclusively observed in the osimertinib group, seven of which, including *EGFR* G796S(n = 6), V802F(n = 3), T725M(n = 2), Q791L/H(n = 2), P794S/R(n = 2), were predicted to dramatically reduce the binding affinity of osimertinib to EGFR. Of note, analysis of the pretreatment samples of two patients supported that *EGFR* V802F and Q791L/H were acquired during osimertinib treatment. Interestingly, *EGFR* G796S was predicted to be sensitive to gefitinib, suggesting the possibility of administration of gefitinib in patients with acquired *EGFR* G796S to first-line osimertinib treatment. Further *in vitro* functional validations are currently ongoing. **Conclusions:** Our study represents the largest *EGFR*-mutated lung cancer cohort so far to investigate osimertinib resistance in a real-world setting, and has uncovered a list of recurrent low-frequency *EGFR* mutations that may confer acquired resistance to osimertinib. Our *in silico* structural model was proved to be powerful and robust in the prediction of osimertinib sensitivity of EGFR mutants. Research Sponsor: None.

9532 Poster Session (Board #298), Fri, 8:00 AM-11:00 AM

Residual circulating tumor DNA (ctDNA) after two months of therapy to predict progression-free and overall survival in patients treated on S1403 with afatinib +/- cetuximab. *First Author: Philip C. Mack, Icahn School of Medicine at Mount Sinai, New York, NY*

Background: ctDNA from patient plasma has demonstrated diagnostic utility in non-small cell lung cancer (NSCLC). Longitudinal changes in mutant allele frequency (MAF) have great potential to refine clinical management on targeted therapies. **Methods:** S1403 was a first-line phase II study of afatinib w or w/o cetuximab in pts with EGFR-mutant NSCLC. Between March, 2015 and April, 2018, 174 pts were randomized with 168 determined to be eligible. The study closed early due to futility. Plasma specimens were prospectively collected at baseline, Cycle 3 Day 1 (C3D1; 8 weeks) and at progression, and processed for batch analysis of ctDNA by next-generation sequencing (Guardant 360). A complete case analysis approach was used. The Kaplan-Meier method was used to estimate survival distributions, a Cox model to estimate hazard ratios and confidence bounds, and the log-rank test to compare distributions. A landmark analysis was used to assess predictive value of ctDNA clearance at C3D1. **Results:** 104 patients (62%) had analyzable baseline plasma specimens available, with *EGFR* mutations detected in 83 (80%). PFS was significantly shorter for pts with *EGFR* ctDNA positivity at baseline (p = 0.03) (Table) compared to those with no detectable ctDNA, likely a prognostic effect. Kinetic changes in ctDNA MAFs were analyzed in 79 pts with matching baseline and C3D1 specimens. Of 62 cases with detectable ctDNA at baseline, 68% (42/62) became undetectable at C3D1 ("ctDNA clearance"); ctDNA clearance relative to residual ctDNA was associated with significantly longer PFS (p = 0.00001) and OS (0.003) (Table). To date, 29 pts had matching *at-progression* samples. T790M mutations were observed at progression in 6/29 (24%) cases. Other putative emergent resistance factors include: a *TACC3-FGFR3* and an *EML4-ALK* fusion, *MET* exon 14 skipping, multiple *MET* amplifications and *NF1* frameshift mutations. **Conclusions:** Clearance of *EGFR* ctDNA after 60 days of therapy was associated with a substantial and statistically significant improvement in subsequent PFS and OS. Incorporation of ctDNA kinetics into routine clinical care represents a promising platform to identify patients with inferior outcomes on TKIs and detect targetable emergent resistance mechanisms. Research Sponsor: Boehringer Ingelheim; Eli Lilly, U.S. National Institutes of Health.

Baseline				
	Detectable	**Not-detectable**	**HR**	**p-value**
PFS	10.2 (7.3-13.5)	14.7 (10.1-NR)	1.80 (0.29-2.01)	**0.03**
OS	30.2 (25-NR)	NR	2.10 (0.82-5.39)	**0.10**
Landmark				
	Clearance at C3D1	**Residual at C3D1**	**HR**	**p-value**
PFS	15.1	2.8	0.24 (0.13-0.44)	**0.00001**
OS	27.2	15.0	0.30 (0.14-0.66)	**0.003**

9533 Poster Session (Board #299), Fri, 8:00 AM-11:00 AM

Effect of performance status on survival with pembrolizumab monotherapy in advanced non-small cell lung cancer (NSCLC). *First Author: Kartik Sehgal, Beth Israel Deaconess Medical Center, Boston, MA*

Background: Pembrolizumab (P) is now widely used as standard of care (SOC) in advanced NSCLC. We sought to identify prognostic factors influencing survival with it in a real-world setting. **Methods:** We conducted a retrospective cohort study of with advanced NSCLC patients who initiated treatment with SOC P monotherapy at our center from 2/11/16 to 10/15/19 (data cutoff 1/15/20). Patient demographic, clinicopathologic, therapeutic and outcomes data were extracted. Survival time was defined from start of P. Cox proportional hazards and logistic regression were utilized. **Results:** Of 74 patients with median follow up of 83.9 weeks, 30 (40.5%) were alive at cutoff. Patient characteristics at start of therapy were: 36 (48.6%) female, median age 68.5 yr (range 33-87), 10 (13.5%) with symptomatic brain metastases; 54 (72.9%) treatment-naïve, 29 (39.2%) with ECOG performance status (PS) ≥2. Tumor characteristics were: 53 (71.6%) with PD-L1 tumor proportion score (TPS) ≥50%, median PD-L1 TPS 75% (range 1-100), tumor mutational burden (TMB) tested in only 37 (50%) patients, median TMB 8 mut/mB (range 1-62). Any grade immune-related adverse events (irAE) occurred in 33 (44.6%) patients, while 16 (21.6%) received systemic steroids. Median survival was 43.3 wks (95% CI 29-104.1). Multivariable regression showed ECOG PS of ≥2 as the strongest risk factor for death (Table). We next evaluated differences in characteristics of patients who were alive vs dead within 12 wks of starting P, by which initial response assessments are completed in routine practice. ECOG PS was the only significantly different baseline variable, even after multivariable adjustment (p = 0.002). **Conclusions:** ECOG PS of ≥2 is a poor prognostic risk factor associated with P monotherapy in advanced NSCLC. Though comprising a clinically significant subset of patients in real-world, they were not included in landmark trials (KEYNOTE-024 & 042). Prospective evaluation is warranted. Research Sponsor: U.S. National Institutes of Health.

	Univariate Hazard ratio for death (95% CI)	p	Multivariable Hazard ratio for death (95% CI)	p
ECOG PS ≥2 / 0-1	3.72 (1.99 – 6.95)	< 0.001	3.63 (1.80 – 7.31)	< 0.001
Any grade irAE, No / Yes	3.36 (1.72 – 6.58)	< 0.001	3.16 (1.59 – 6.28)	0.001
Symptomatic brain metastases, Yes / No	1.83 (0.84 – 3.9)	0.13	1.70 (0.74 – 3.95)	0.21
Age	1.02 (0.99 – 1.06)	0.11	1.01 (0.97 – 1.04)	0.78
PD-L1 TPS	0.99 (0.99 – 1.01)	0.56	1.01 (0.99 – 1.02)	0.25
Ever smoker, No / Yes	1.78 (0.75 – 4.26)	0.19		
Prior therapy / Treatment-naïve	1.02 (0.52 – 1.99)	0.96		
TMB (limited availability)	0.91 (0.83 – 0.99)	0.04		
Systemic steroids for irAE, No / Yes	1.19 (0.59 – 2.42)	0.63		

9534 Poster Session (Board #300), Fri, 8:00 AM-11:00 AM

Distinct genomic instability landscape of lung adenocarcinoma associated with treatment and metastasis. *First Author: Chuanxin Wu, Department of Medical Oncology, Cancer hospital of Guangzhou Medical University, Guangzhou, China*

Background: Lung adenocarcinoma (LUAD) is the most common subtype of non-small cell lung cancer (NSCLC). Genomic instability, defined as genome-wide copy number alterations, is a key pathogenic signature which occurs at the early stage of most cancers and is associated with an increased risk of recurrence or death. We examined the pattern of genomic instability in primary and metastatic LUAD. **Methods:** We performed deep targeted sequencing (425 genes) of 3395 tissue samples and whole exome sequencing (WES) of 60 tissue samples from LUAD patients. Whole-genome doubling (WGD) and arm level aneuploidy were analyzed to uncover correlation with clinical phenotypes and other genomic alterations including driver mutations, tumor mutation burden (TMB), and microsatellite instability (MSI). **Results:** Overall, targeted sequencing revealed that WGD occurred in 64.33% LUAD samples, which was comparable with WES results. Compared to primary site, metastasis exhibited higher proportion of WGD (1.14 fold). Specifically, liver metastasis has the highest WGD percentage among metastasis sites (~87.5%; 1.40 fold increase compared to primary). Interestingly, patients who received tyrosine kinase inhibitors (TKI) had higher frequency of WGD than patients without TKI treatment. In addition, TMB was higher in WGD^+ patients but MSI status was not significantly different between groups. Arm-level aneuploidy was prevalent in this cohort. The most common amplification events were 7p gain (62%), 5p gain (54%), and 8q gain (53%); top deletion events were 19p loss (47%), 15q loss (42%), and 10 q loss (41%). Patients with EGFR or TP53 mutation were more likely to have aneuploidy compared to wildtypes. Subgroup analysis showed distinct patterns of aneuploidy among metastasis sites, suggesting organ-specific alterations. Evolution analysis showed 7p gain was an early event common in primary tumor whereas metastatic tumor had multiple distinct evolutionary trajectories following 7p gain. Several copy number signatures were associated with specific TKI and chemotherapies. For example, TKI-naïve tumors lacked 7p gain but had 19p loss as the most common alteration. **Conclusions:** The genomic landscape of LUAD was characterized by widespread large-scale copy number alterations including WGD and chromosomal aneuploidy. Metastasis had elevated level of aneuploidy compared to primary tumors which were specific to metastatic site. Copy number signature associated with different treatments may contribute to distinct long-term survival and side effects among patients. Research Sponsor: None.

9535 Poster Session (Board #301), Fri, 8:00 AM-11:00 AM

Prediction of the molecular status in non-small cell lung cancer based on metastatic pattern: A free webtool powered by artificial intelligence. *First Author: Benjamin Besse, Gustave Roussy Université Paris Sud, Villejuif, France*

Background: Molecular characterization of metastatic lung adenocarcinomas is mandatory but might be hampered by the quantity of tissue, restricted access to molecular platforms or limited economical resources. Our aim was to develop a tool supported by the hypothesis that radiological patterns of pts could help predict the rate of positivity of the most common oncogenic drivers. **Methods:** We defined an algorithm based on a molecularly defined cohort of 656 pts with stage IV lung adenocarcinoma. Two radiologists centrally reviewed the baseline imaging. Clinical data were retrospectively collected. There were 135 *EGFR* mutations, 81 *ALK* fusions, 47 *BRAF* mutations, 141 *KRAS* mutations, and 146 pan-negative tumors for these 4 oncogenic drivers. Univariate correlation analyses were performed to define an algorithm predicting the molecular testing positivity based on the metastatic pattern. Subsequently, an online tool was developed. This study was approved by our institutional review board. **Results:** Metastatic patterns correlated with the genomic drivers when compared to the pan-negative group. In the *EGFR* group, pleural metastases were more frequent (32% vs. 20%; p = 0.021), whereas adrenal and node metastases less frequent (6% vs.23%; p < 0.001 and 11% vs. 23% respectively; p = 0.011). In the *ALK* group, there were more brain and lung metastases (respectively 42% vs. 29%; p = 0.043 and 37% vs. 24% respectively; p = 0.037). In the *BRAF* group, pleural and pericardial metastases were more common (47% vs. 20%; p < 0.001 and 11% vs. 3% respectively; p = 0.04) and bone metastases less common (21% vs. 42%; p = 0.011). Lymphangitis was more frequent in *EGFR*, *ALK* and *BRAF* groups (6%, 7% and 15% vs. 1%; p = 0,016, p = 0,009 and p < 0,001 respectively). A free online access to the algorithm is now available after registration at http//tactic-ct.fr. Physicians enter age, sex, smoking status and the sites of metastases at diagnosis (present/absent/unknown). A mutation score is calculated, reflecting the % of chance to find an oncogenic driver. On the website, contributors can also enter new cases and an artificial intelligence will refine the algorithm and expand the number of oncogenic drivers. **Conclusions:** Our free access tool allows establishing a hierarchy in the molecular testing based on simple clinical and radiological information. Continual learning from new cases entered in the database will increase the sensitivity of the tool. This tool might save time, tumor tissue, economical resources and accelerate access to personalized treatment. Research Sponsor: Digital Tech Year program of CentraleSupélec, University Paris-Saclay.

9536 Poster Session (Board #302), Fri, 8:00 AM-11:00 AM

Interaction between CAF and CD8+ T cells in non-small cell lung cancer affects prognosis and efficacy of immunotherapy. *First Author: Xinlong Zheng, Fujian University of Traditional Chinese Medicine, Fuzhou, China*

Background: Cancer-related fibroblasts (CAFs) are important components of the tumor microenvironment (TME) and play a key role in tumor progression. There is growing evidence that CAF levels in tumors are highly correlated with treatment response and prognosis. However, the effect of CAFs on immunotherapy response remains unknown. **Methods:** RNA-seq and clinical data were downloaded from TCGA and GEO. The SVA package *ComBat* function was used to remove batch effects. The ssGSEA algorithm was used to assess the level of cell infiltration in each sample. OS (overall survival) and DFS (disease free survival) were analyzed using the Kaplan–Meier method. GO enrichment analysis was used to assess the biological processes of subgroup differential genes. The Tumor Immune Dysfunction and Exclusion (TIDE) algorithm and subclass mapping were used to predict the clinical response to immune checkpoint blockade. **Results:** We evaluated the infiltration abundance of 24 types of immune cells and fibroblasts in 1768 NSCLC samples and found that almost all IMFRs (immune cells / fibroblasts) are beneficial to the prognosis. This phenomenon is called "CAFs-mediated immune resistance pattern (CMIRP)". We evaluated the infiltration abundance of 24 types of immune cells and fibroblasts in 1768 NSCLC samples and found that almost all IMFRs (immune cells / fibroblasts) are beneficial to the prognosis. This phenomenon is called "CAFs-mediated immune resistance pattern (CMIRP)". The prognosis according to CD8+ T cells was not strong, but CD8+ T cells / fibroblasts (CFR) were significant protective prognostic factors [n = 1588; hazard ratio (HR), 0.66; 95% confidence interval (CI), 0.56–0.78; P < 0.001]. Multivariate analysis revealed that the CFR was an independent prognostic biomarker. The TCGA pan-cancer cohort confirmed the widespread presence of CMIRP in cancer. We further defined the CFR high and CFR low subgroups. CFR high samples were enriched with immune activation pathways including T cell activation, cytolysis, and antigen presentation, while CFR low was associated with immunosuppression including activation of transforming growth factor β, epithelial-mesenchymal transition, and angiogenesis pathways. Finally, we combined TIDE and submap to speculate that CFR is a potential prognostic marker of immunotherapy for NSCLC. **Conclusions:** We proposed the term "CMIRP" to shed light on a more accurate assessment of immune status. CFR is a potential marker for prognosis and predictive efficacy of immunotherapy in NSCLC. Research Sponsor: None.

9537 Poster Session (Board #303), Fri, 8:00 AM-11:00 AM

Brigatinib in Japanese ALK positive NSCLC patients previously treated with ALK tyrosine kinase inhibitors: J-ALTA. *First Author: Tatsuya Yoshida, Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan*

Background: Brigatinib is an ALK inhibitor with demonstrated activity against ALK resistance mutations. To evaluate efficacy and safety in Japanese patients with ALK-positive non-small cell lung cancer (NSCLC), a prospective, single-arm, phase 2 study was conducted. We report the efficacy and safety of brigatinib in patients who have progressed on alectinib with or without prior crizotinib and of those who previously received up to two ALK tyrosine kinase inhibitors (TKIs) with or without prior chemotherapy. **Methods:** A safety evaluation lead-in was followed by an expansion stage of an ALK TKI-naïve and two ALK TKI-refractory cohorts. The refractory cohorts included patients with stage IIIB, IIIC, or IV NSCLC with ALK rearrangements. This report describes efficacy results from the post-alectinib patients in the expansion cohort and safety results from all refractory patients. The primary endpoint was confirmed objective response rate (ORR) assessed by IRC, secondary endpoints included duration of response (DoR), progression-free survival (PFS), disease control rate (DCR), and intracranial ORR (iORR). Brigatinib was administered at 180 mg QD with 90 mg QD lead-in for the first 7 days, and efficacy was evaluated every 8 weeks. **Results:** A total of 72 patients were enrolled in 28 sites, including a cohort of 47 patients with prior alectinib, with/without crizotinib between January 2018 and September 2019. The primary analysis of brigatinib in this cohort (data cut-off date 26 September 2019) demonstrated an IRC-assessed, confirmed ORR of 30% and a median DoR of 6.1 months. The median PFS was 7.3 months. Clinically meaningful intracranial efficacy was also observed (see table). Grade ≥3 TEAEs included blood creatine phosphokinase increase (18.1%), lipase increase (13.9%), hypertension (11.1%), amylase increase (4.2%), and pneumonitis (1.4%). Brigatinib also showed anti-tumor activity in patients with refractory secondary mutations in the ALK kinase domain, including G1202R, I1171N, V1180L, and L1196M. **Conclusions:** Brigatinib showed clinically meaningful efficacy in Japanese patients refractory to prior alectinib (first line or post crizotinib), regardless of prior chemotherapy. The safety profile of brigatinib was consistent with prior studies and no new safety findings were identified. Clinical trial information: NCT03410108. Research Sponsor: Takeda Pharmaceutical Company Ltd.

Endpoint	Value, 95% CI
ORR	30.6%, 16.530, 44.165
DCR	78.7%, 64.336, 89.297
DoR, median	6.1 months, 3.8, not reached
PFS, median	7.3 months, 3.7, not reached
iORR	25.0%, 3.185, 65.086

9538 Poster Session (Board #304), Fri, 8:00 AM-11:00 AM

Early pulmonary function changes associated with brigatinib initiation. *First Author: Terry L. Ng, Division of Medical Oncology, University of Colorado, Anschutz Medical Campus, Aurora, CO*

Background: Phase I-III studies reported symptomatic pulmonary toxicity within the first week of initiating brigatinib in 6% patients post-crizotinib and 3% in TKI naive patients with standard dosing (90mg QD for 7 days then 180mg QD as tolerated). A prospective observational study of pulmonary function testing (PFT) on initiating brigatinib was conducted. **Methods:** Patients PS≤2, with resting O2 sats on RA ≥90% and Hg ≥10 g/dL, without significant heart/lung disease or steroid use initiating brigatinib 90 mg QD were eligible. PFT with DLCO, Borg dyspnea and 6-minute walk tests were performed at baseline (prior to brigatinib), and on day 2 (D2), 8 (D8), and 15 (D15) of brigatinib. D15 analyses were initially as clinically indicated but became mandatory if DLCO had not returned to baseline by D8. Peripheral blood was collected at baseline, D2 and D8 for CyTOF analysis. The primary endpoint was the incidence of Early Onset Pulmonary Events (EOPEs), defined as a DLCO reduction of ≥ 20% from baseline. An interim analysis was performed on the first 10 patients due to a higher than expected incidence of DLCO reduction. **Results:** D2 and D8 measurements were captured in all 10 patients, D15 in 7 patients. Ninety percent (9/10) of patients experienced DLCO reduction with nadir occurring on D2 in 4/9 and on D8 in 5/9 patients. Median DLCO nadir was −13.33% from baseline (range: −34.44 to −5.00). Three patients (30%) met EOPE criteria, all on D8, all without symptoms. Brigatinib was not held and all 10 patients escalated to 180mg on D8. Despite continued dosing, 4/9 patients recovered DLCO to baseline or above by D15 (2/3 EOPEs cases), 2/9 recovered above nadir but below baseline by D15 (1/3 EOPE case), and 3/9 did not have improvement from nadir values but no D15 assessment was performed. Dyspnea and 6-minute walk test did not correlate with DLCO changes. Patients who experienced an EOPE had significantly higher levels of activated neutrophils (pERKhi) at baseline. On the day of the EOPE event, patients who met EOPE criteria had significantly higher levels of activated neutrophils and fewer activated CD4+ effector memory T cells. **Conclusions:** Modest DLCO reduction occurred in 90% (9/10) patients during the first 8 days of brigatinib-dosing without associated symptoms. When rechecked on D15, DLCO improved in 100% patients (6/6) despite continued dosing and standard dose escalation at D8. Patients unlikely to tolerate even this modest, short-lived change should consider shallower step-up dosing or alternative drugs. CyTOF analysis suggests levels of pretreatment neutrophils may be a biomarker for developing EOPEs. Clinical trial information: NCT03389399. Research Sponsor: Takeda Oncology.

9539 Poster Session (Board #305), Fri, 8:00 AM-11:00 AM

PD-L1 tumor proportion score and clinical benefit from first-line pembrolizumab in patients with advanced nonsquamous versus squamous non-small cell lung cancer (NSCLC). *First Author: Deborah Blythe Doroshow, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY*

Background: The predictive value of PD-L1 tumor proportion score (TPS) on NSCLC tumor cells as a biomarker for response to PD-(L)1 inhibitors is well established. However, its histology specific value in advanced (a) squamous (Sq) versus nonsquamous (NS) cancers remains unclear. Here, we used real world data to assess the differential value of PD-L1 TPS as a predictive biomarker for overall survival (OS) after first-line pembrolizumab (P) in patients (pts) with Sq versus NS NSCLC. **Methods:** Inclusion criteria for this analysis of the Flatiron Health EHR-derived de-identified database required that pts were diagnosed with aNSCLC, tested for PD-L1 TPS and received a numerical result, had no alteration in *EGFR*, *ALK*, or *ROS*, and received first-line, single agent P. The primary endpoint was overall survival (OS) from the first dose of P in patients with TPS ≥ 50% (H) compared to patients with TPS < 50% (L). Due to the violation of the proportional hazards assumption, a generalized gamma model of OS was used, adjusting for demographic variables and estimated median OS and their confidence intervals with the bootstrap method. The PD-L1-histology interaction was examined by comparing the differences in median OS (H vs. L) between Sq and NS patients. **Results:** Of 1560 pts with NSCLC treated from 1/2011 – 5/2019, 1055 had NS and 405 Sq. No meaningful differences in age, gender, or smoking history were seen between PD-L1 H and L pts with either histology. Among NS pts, H had significantly longer OS than L, with unadjusted hazard ratio (HR) of 0.71 (95% CI: 0.53 - 0.94; p = 0.018). Among Sq pts, H was not associated with longer OS than L, with unadjusted HR 0.89 (95% CI: 0.64 - 1.25; p = 0.514). Based on the generalized gamma model, PD-L1 H in Sq patients was associated with a 0.19 year improvement in median OS (95% CI: -0.22-0.49, P = 0.283), whereas PD-L1 H in the NS group was associated with a 0.70 year improvement in OS (95% CI: 0.34-1.05, P < 0.001). The median improvements between the Sq and NS patients were significantly different (P = 0.034), after adjusting for demographic variables. **Conclusions:** PD-L1 TPS of ≥ 50% predicted longer OS in pts with NS NSCLC treated with first-line P compared to pts whose tumors had a TPS of < 50%. However, no relationship between PD-L1 TPS and OS after first-line P was seen in patients with Sq NSCLC. These data suggest that PD-L1 may not be an appropriate predictive biomarker for checkpoint inhibitor use in NSCLC with squamous histology. Research Sponsor: None.

9540 Poster Session (Board #306), Fri, 8:00 AM-11:00 AM

SRC-homology 2 domain-containing phosphatase 2 (SHP2) in epidermal growth factor receptor (EGFR)-mutant lung adenocarcinoma (LUAD). *First Author: Rafael Rosell, Catalan Institute of Oncology, Barcelona, Spain*

Background: Epidermal growth factor (EGFR)-mutant lung adenocarcinomas (LUADs) display impaired phosphorylation of extracellular signal-regulated kinase (ERK) and SRC-homology 2 domain-containing phosphatase 2 (SHP2) in comparison with EGFR wild-type LUADs. However, the function of SHP2 in early EGFR-mutant LUADs and EGFR wild-type LUADs has not been reported. We posit that SHP2 mRNA expression could be a predictive marker in resected EGFR-mutant LUADs versus EGFR wild-type patients (pts). **Methods:** We examined 267 resected LUADs from Japan and Spain. mRNA expression levels of AXL, MET, CDCP1, STAT3, YAP1 and SHP2 were analyzed by quantitative reverse transcriptase polymerase chain reaction (PCR). EGFR mutant cell lines were investigated for their activity of SHP2. **Results:** Among the 267 enrolled pts, 100 (37.3%) were EGFR-mutant LUADs. Five-year recurrence-free survival (RFS) and overall survival (OS) were lower for EGFR-mutant LUADs with high SHP2 mRNA levels (hazard ratio = 1.83 and 2.28, respectively. p = 0.03 and p = 0.04). However, SHP2 was not associated with RFS nor OS in the 167 wild-type EGFR LUADs. In EGFR-mutant cells, RMC-4550 (SHP2 inhibitor) plus erlotinib showed synergism via inhibition of AKT (S473) and ERK1/2 (T202/Y204). While erlotinib translocates SHP2 (Y542) into the nucleus, either RMC-4550 alone, or in combination with erlotinib, relocalizes SHP2 into the cytoplasm membrane, limiting AKT and ERK activation. **Conclusions:** High SHP2 mRNA is related to shorter RFS and OS in EGFR-mutant LUADs, but not in EGFR wild-type LUADs. The findings indicate that the addition of SHP2 inhibitors could improve adjuvant therapy in EGFR-mutant LUADs. Research Sponsor: None.

9541 Poster Session (Board #307), Fri, 8:00 AM-11:00 AM

An FDA analysis of the association of tumor growth rate and overall and progression-free survival in metastatic non-small cell lung cancer (NSCLC) patients. *First Author: Yutao Gong, U.S. Food and Drug Administration, Silver Spring, MD*

Background: Previous studies have suggested that tumor growth rate (g), estimated using prostate-specific antigen values, is associated with overall survival (OS) in prostate cancer (Wilkerson, 2016). We performed a retrospective pooled analysis in non-small cell lung cancer (NSCLC) to investigate the extent to which g values estimated using radiological tumor measurements in clinical trials are associated with survival. **Methods:** We identified 24 randomized clinical trials submitted to FDA between 2013 and 2019 investigating either immune checkpoint inhibitor (ICI) or targeted therapy (TT) in pts with metastatic NSCLC. Of 9934 patients (pts) enrolled, 5532 pts (2401, 1189, and 1942 pts treated with ICI, TT, and chemotherapy respectively) had sufficient data to derive a valid g. The g was evaluated by both type and line of therapy. Pts were then grouped according to quartiles of g, with Q1 being the lowest. We calculated OS and progression-free survival (PFS) for each group via the Kaplan-Meier method, and used the Cox model for group comparison. **Results:** Median g was 9.7E-4, 1.4E-3, and 2.2E-3/day, and median OS was 34.2, 21.3, and 15.3 months (mo), in pts treated with TT, ICI, and chemotherapy, respectively, regardless of lines of therapy. When treated with the same type of therapy, pts receiving 2nd line therapy had a higher median g than those receiving 1st line. The median survival and log-rank hazard ratios for pts treated with 1st line ICI monotherapy are shown in the Table. **Conclusions:** TT is associated with the lowest median g, followed by ICI, and then chemotherapy, perhaps due to patient selection, better inherent biology/natural history, or favorable results of TT on selected tumors. Regardless, we found that g is inversely associated with survival, across treatment types. This relationship is also observed in pts treated with the same type and line of therapy (for example, 1st line ICI), where Q1 has the longest survival, followed by Q2, Q3, and then Q4. In summary, our exploratory analysis suggests that g derived from radiological tumor measurements in NSCLC may relate to survival. Prospective studies are needed to evaluate if g might be an earlier endpoint compared to classical response criteria. Research Sponsor: None.

		OS		PFS	
	N	Median (mo)	Hazard Ratio	Median (mo)	Hazard Ratio
Q1	110	NR (NR, NR)	1	32.5 (21.5, NR)	1
Q2	109	26.1 (22.9, NR)	1.8 (1.1, 3.1)	13.1 (10.4, 18.7)	2.3 (1.6, 3.4)
Q3	109	16.7 (13.5, 22.4)	4.6 (2.8, 7.3)	6.1 (4.2, 7.1)	6.6 (4.5, 9.8)
Q4	109	8.7 (7.2, 12.9)	6.8 (4.3, 10.7)	3.4 (2.1, 4.1)	11.0 (7.2, 16.9)

*NR = Not Reached

9542 Poster Session (Board #308), Fri, 8:00 AM-11:00 AM

ctDNA levels before treatment predict survival in non-small cell lung cancer patients treated with a tyrosine kinase inhibitor. *First Author: Mariano Provencio-Pulla, Department of Medical Oncology, University Hospital Puerta de Hierro-Majadahonda, Madrid, Spain*

Background: Currently there is an intense debate concerning therapeutic strategies in EGFR positive NSCLC patients with advance disease. Osimertinib is superior to standard EGFR Tyrosine Kinase Inhibitors (TKIs) as first line treatment. However, it is yet unclear whether this option is superior to sequential treatment of a 1st or 2nd generation TKI followed by osimertinib. In order to clarify this issue it is important to identify which patients are at high risk of progression disease. **Methods:** This is a prospective, multicentre, cross-sectional study promoted by Spanish Lung Cancer Group. 698 plasma samples from 196 advanced NSCLC patients with tumors harboring an EGFR activating mutation and treated with a first line TKI (afatinib, gefitinib, erlotinib or osimertinib) were analyzed. Plasma samples were prospectively collected before treatment (T0), after 3 months of treatment (T3), after 6 months of treatment (T6) and at first disease progression. EGFR mutations were analyzed by dPCR. Multivariate Cox proportional hazards analysis was used to determine the significance of ctDNA in the prediction of prognosis. **Results:** The median follow up was 19.8 months. At baseline patients with plasma EGFR sensitizing mutations at allele frequency (AF) $\geq$ 10% had worse OS and PFS than patients in which the opposite occurred (HR = 1.86; 95 %CI: 1.09-3.17, and HR = 1.65; 95 %CI: 1.07-2.58, respectively). Noteworthy, median OS and PFS time were 18.6 and 8.8 months respectively, in patients with plasma AF$\geq$10% before treatment initiation compared to 37.9 and 12.4 months for patients with plasma AF $<$ 10%. Similar results were obtained when a cutoff of AF$\geq$ 5% was used (HR = 1.73; 95%CI: 1.02-2.94 for OS, and HR = 1.72; 95%CI: 1.13-2.61 for PFS). Patients who remained ctDNA-positive after 3 months of treatment exhibited also poorer outcomes (HR = 3.24; 95%CI: 1.77-5.94 for OS, and HR = 3.1; 95%CI: 1.91-5.03 for PFS). In the same way, detectable levels of ctDNA after 6 months of treatment predicted shorter OS and PFS (HR = 3.3; 95%CI: 1.53-7.13 and HR = 2.62; 95%CI: 1.62-4.25, respectively). **Conclusions:** ctDNA levels significantly predict survival. Moreover, ctDNA levels before treatment initiation can be useful to assess patient's progression risk which is not possible to assess otherwise facilitating treatment decision making. Research Sponsor: Boehringer Ingelheim.

9543 Poster Session (Board #309), Fri, 8:00 AM-11:00 AM

Racial diversity of genomic alterations in lung adenocarcinomas. *First Author: Huashan Shi, Mayo Clinic, Jacksonville, FL*

Background: Lung cancer is the leading cause of cancer related death in the United States in all racial groups. However, the overall death rate from lung cancer is different among white, black and Asian. Although differences in socioeconomic status and treatments received might be the contributing factors, the biology, particularly genomic alteration of cancer might also have an important impact. To date, the differences of genomic alterations among all racial patients are poorly understood. **Methods:** The American Association for Cancer Research (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE, version 7.0) database was analyzed. A total of 8908 patients with lung adenocarcinoma (LUAD) were identified. Among them, 5652 patients who had comprehensive sequencing results (gene panel $\geq$ 275) were selected for further analysis. Patients with unknown race, undefined and Pacific Island (only 3 patients) were excluded. Finally, 5360 patients were included in the study. The prevalence and distribution of genomic alteration cross all racial groups were analyzed. **Results:** Overall 5951 samples from 5360 patients were collected (85.7% white, 7.9% Asian, 4.7% black, 0.2% Native American and 1.4% other). Most patients have only one sample. The median mutation counts in white, black, Asian, Native American and others are 7, 6, 5, 5, 7 respectively (Kruskal–Wallis test, $P<$ 0.001). Asian have significantly higher rates of insertion and deletions than other races (14.8% of Asian versus 9.8% of white, 10.7% of black, 10.4% of Native American, 11.1% of other; Pearson's chi-square test, $<$0.001). TP53, EGFR, KRAS and STK11 are the most frequent alterations in white, black and other. EGFR, TP53, KRAS and APC are the most frequent alterations in Asian. STK11 mutations are rare in both Asian and Native American. Native Americans have more alterations of LRP1B, ARID2 and ATM, although the patients' number remains small. ATM and KEAP1 mutations are also common in white and black. EGFR is the highest discrepancy gene in racial distribution. 78.9% Asian, 47.7% black, 36.4% of native American had EGFR alteration in comparison to 29.6% in white (Fisher's exact test, $P < 0.001$). KRAS is the second highest discrepancy gene in racial distribution. 11.6% Asian, 26.3% black, 27.3% of Native American had KRAS alteration in comparison to 36.1% in white (Fisher's exact test, $P<$ 0.001). **Conclusions:** Our study demonstrated the potential diversity of genomic alterations across all racial groups with potential impact on therapeutic decisions. Research Sponsor: Paul Calabresi Career Development Award for Clinical Oncology (K12) - National Cancer Institute Awardee: Yanyan Lou.

9544 Poster Session (Board #310), Fri, 8:00 AM-11:00 AM

Characterization of KRAS mutations (mt) in non-small cell lung cancer (NSCLC). *First Author: Stephen V. Liu, Georgetown University, Washington, DC*

Background: KRAS is the most commonly mutated oncogene in NSCLC and the development of direct KRAS inhibitors has renewed interest in this molecular subtype. However, there are several different KRAS mts, representing unique biology and different prognostic and therapeutic impact. A more comprehensive understanding of the genomic landscape relative to each KRAS mt subset will help guide therapeutic development. **Methods:** Molecular profiles of 17,113 NSCLC specimens were obtained using next-generation sequencing of 592 genes (Caris Life Sciences) and classified based on presence and types of KRAS mt. Incidence of KRAS mts was noted across the cohort and by histology. Co-occurring genomic alterations, tumor mutational burden (TMB) and PD-L1 IHC (22C3, TPS score) were analyzed by KRAS mt type. **Results:** Across the entire cohort, 4706 (27%) of samples harbored a KRAS mt (Table). The most common was G12C (40%), followed by G12V (19%) and G12D (15%). The prevalence of KRAS mt was 37.2% among adenocarcinoma and only 4.4% in squamous. High TMB, defined by $>$ 10 mts/Mb, varied across the different KRAS mt types, most common in G13X (68.3%) and least common in G12D (43.2%). PD-L1 expression also varied. G12C was the most likely to be PD-L1 positive, with 65.5% TPS $>$ 1%, and the most likely to be PD-L1 high, with 41.3% TPS $>$ 50%. STK11 was mutated in 8.6% of KRAS wild type NSCLC but more frequently noted in every KRAS subtype, with the highest rate in G13X (36.2%) and the lowest in G12D(14.2%). TP53 mts were more frequent in KRAS wild type NSCLC (73.6%), with the highest rate among KRAS mutants at 55.4% (G12other) and the lowest at 36.8% (Q61X). NF1 was noted to be mutated in 21.4% of KRAS G13X cases, while all other KRAS mts had a lower frequency of NF1 mts than KRAS wild type (11.5%). **Conclusions:** KRAS mts are relatively common in lung adenocarcinoma and KRAS G12C is the most common variant. The different KRAS mts have different co-occurring mutations and a different genomic landscape. KRAS G12C was associated with the highest rate of PD-L1 expression. The clinical relevance of these differences in the context of therapeutic intervention warrants investigation. Research Sponsor: None.

	KRAS WT	KRAS G12C	KRAS G12V	KRAS G12D	KRAS G13X	KRAS Q61X	KRAS G12A	KRAS G12other
Incidence	12407	1882	915	684	327	313	298	210
TMB > 10 mut/Mb	50.1%	58.1%	55.3%	43.2%	68.3%	51.2%	52.3%	65.0%
PDL1 > 1%	52.1%	65.5%	58.2%	62.7%	57.7%	62.6%	61.5%	56.4%
PDL1 > 50%	25.9%	41.3%	35.2%	35.3%	35.0%	36.7%	36.3%	28.2%
STK11 mutant	8.6%	23.0%	23.6%	14.2%	36.2%	26.2%	23.4%	29.2%
KEAP1 mutant	4.2%	6.3%	5.7%	3.7%	13.1%	5.1%	6.0%	5.7%
TP53 mutant	73.6%	48.9%	46.0%	44.0%	52.8%	36.8%	43.1%	55.4%

9545 Poster Session (Board #311), Fri, 8:00 AM-11:00 AM

Real-world performance of blood-based host immune profiling in first-line immunotherapy treatment in advanced-stage non-small cell lung cancer. *First Author: R. Brian Mitchell, Virginia Cancer Inst, Midlothian, VA*

Background: Immune checkpoint inhibition (ICI) has improved outcomes for many treatment-naïve advanced non-small cell lung cancer (NSCLC) patients. However, better biomarkers are needed to predict patient response and guide treatment decisions considering added toxicity and higher cost of combination treatments. A prospectively designed, observational study assessed the ability of a clinically validated, blood-based, host immune classifier (HIC) to predict ICI therapy outcomes. **Methods:** The study (NCT03289780) includes 33 US sites having enrolled over 3,000 NSCLC patients at any stage and line of therapy. All enrolled patients are tested and designated HIC-Hot (HIC-H) or HIC-Cold (HIC-C) prior to therapy initiation. An interim analysis of secondary and exploratory endpoints was performed after 12- 18 months (mo) follow-up with the first 2,000 enrolled patients. We report the overall survival (OS) of HIC-defined subgroups comprising advanced stage (IIIB and higher) NSCLC patients treated with first-line regimens (284 ICI containing treatments, 877 total first-line patients). **Results:** In a real-world clinical setting, OS of advanced stage NSCLC treatment-naïve patients receiving platinum-based chemotherapy (n = 392) did not differ significantly from patients receiving any type of ICI containing regimen (n = 284); 11.7 mo vs. 14.4 mo; hazard ratio (HR) = 0.94 [95% confidence interval (CI): 0.76–1.17], p = 0.59. HIC-H patients experienced longer survival than HIC-C across multiple regimens, including ICI. For all ICI, median OS (mOS) was not reached for HIC-H (n = 196, CI: 15.4 mo–undefined) vs. 5.0 mo (n = 88, CI: 2.9 mo–6.4 mo) for HIC-C patients (HR = 0.38 [CI: 0.27–0.53], p $<$ 0.0001). Similar results were seen in the ICI only (16.8 mo vs. 2.8 mo; n = 117, HR = 0.36 [CI: 0.22–0.58], p $<$ 0.0001) and ICI/chemotherapy combination subgroups (unreached vs. 6.4 mo; n = 161, HR = 0.41 [CI: 0.26–0.67], p = 0.0003). In the PD-L1 high cohort (PD-L1 $\geq$50%), mOS for HIC-H was not reached (n = 81, CI: 13.9 mo–undefined) vs. 3.9 mo (n = 41, CI: 2.1 mo–7.8 mo) for HIC-C (HR: 0.39 [CI: 0.24-0.66], p = 0.0003). HIC results were independent of PD-L1 score (p = 0.81) and remained predictive of OS in first-line ICI-treated patients when adjusted for PD-L1 and other covariates by multivariate analysis (HR = 0.40 [CI: 0.28-0.58], p $<$ 0.0001). **Conclusions:** Blood-based host immune profiling may provide clinically meaningful information for selecting NSCLC patients for two common ICI containing regimens independent of and complementary to PD-L1 score. Research Sponsor: Biodesix, Inc.

9546 Poster Session (Board #312), Fri, 8:00 AM-11:00 AM

Tumor antigen expression and survival of patients with previously treated advanced non-small cell lung cancer (NSCLC) receiving viagenpumatucel-L (HS-110) plus nivolumab. *First Author: Daniel Morgensztern, Washington University School of Medicine in St. Louis, St. Louis, MO*

Background: Viagenpumatucel-L (HS-110) is an allogeneic cellular vaccine derived from a human lung adenocarcinoma cell line transfected with gp96-Ig fusion protein. Gp96-Ig functions as an antigen chaperone for dendritic cell activation and direct CD8+T cell expansion via cross presentation. DURGA is a multi-cohort study evaluating HS-110 plus anti-PD-1 mAbs in patients (pts) with advanced NSCLC. We report on Cohort A, which enrolled previously-treated pts who had not received an anti-PD(L)1 prior to study entry. **Methods:** Primary objectives were safety and objective response rate (ORR). Overall Survival (OS) was a secondary endpoint. Pts received 1 X 10^7 HS-110 cells intradermally every week for 18 wks and nivolumab until tumor progression. To determine cancer testis antigen (CTA) overexpression from baseline pt tumor samples, hybrid-capture RNA-seq libraries were prepared from macrodissected formalin fixed paraffin embedded tumor tissue and sequenced on an Illumina NovaSeq 6000. Gene-level transcripts were quantified using the Salmon software package. **Results:** 47 pts were enrolled into Cohort A. ORR and clinical benefit rate (CR + PR + SD) were 21% and 43%, respectively, with a 17.2 month median duration of response. Median OS was 28.7 months (mos), with a median follow up of 15.7 mos. One and 2-year survival were 57% and 36%, respectively. A prespecified exploratory analysis of CTA expression level in baseline pt tumor tissue was performed. 50% of pts shared at least 8 of the 39 total antigens overexpressed by HS110. Although there was no difference in ORR between these groups, mOS was higher in pts with tumors that shared $\geq$ 8 antigens with HS-110 (not reached (NR) [95%CI: 10.3 mos, NR] vs 6.7 mos [95%CI: 1.4 mos, NR]), p = 0.028. Pts whose tumors expressed the ZNF492 antigen also had improved OS (NR [95%CI: 11.6 mos, NR] vs 7.2 mos [95%CI: 1.6 mos, NR]), p = 0.03. All pts experienced at least one adverse event (AE), and the most common AEs were fatigue (28%), arthralgia (19%) and cough (17%). There were 2 grade 5 AEs not related to treatment. **Conclusions:** The combination of HS-110 and nivolumab appears safe and well tolerated. OS was improved in pts whose tumors express $\geq$ 8 shared antigens with HS110, as well as in those who specifically expressed ZNF492. Further exploration of antigen expression as a predictor for treatment outcome with HS110 plus nivolumab is ongoing. Clinical trial information: NCT02439450. Research Sponsor: Heat Biologics.

9547 Poster Session (Board #313), Fri, 8:00 AM-11:00 AM

Circulating and tumor-associated neutrophil subtypes discriminate hyper-progressive disease (HPD) from conventional progression (PD) upon immune checkpoint inhibitors (ICI) in advanced non-small cell lung cancer (NSCLC) patients (pts) and in vivo models. *First Author: Roberto Ferrara, Medical OnIstituto Nazionale Dei Tumori di Milano, Milan, Italy*

Background: HPD occurs in $\simeq$10-25% of NSCLC pts upon single-agent ICI and correlates with poor prognosis. High circulating neutrophil count and neutrophils/lymphocytes ratio have been associated with shorter survival and HPD in NSCLC pts. In mouse lung cancer models, interleukin-17 (IL-17) promoted tumour growth upon ICI increasing intratumoral neutrophils. The role of specific circulating and/or tumour-associated neutrophils in driving HPD is currently unknown. **Methods:** NSCLC pts treated with single agent ICI were assessed for HPD and circulating neutrophils' phenotype. Conventional PD was defined by RECIST 1.1. HPD required 3 tumour assessments (2 before ICI, 1 upon ICI) and was defined as delta tumour growth rate (TGR) (TGR upon ICI – TGR before ICI) $>$ 50% and/or TGR ratio (TGR upon ICI/ TGR before ICI) $\geq$2. Correlations with continuous variables were performed by Mann-Whitney test. Circulating low density neutrophils (LDNs) subtypes were assessed by flow cytometry (FC) on peripheral blood mononuclear cells (PBMCs) from fresh blood samples. LDNs were defined as $CD66b^+CD15^+$ cells among $CD11b^+$ PBMCs. Immature subtypes were defined as $CD10^-$ and $CD10^-CD16^-$ LDNs. The occurrence of HPD upon anti-PD-1 treatment was tested in C57BL/6 immune competent mice bearing Lewis Lung Carcinoma and treated with anti-murine PD-1. Tumour associated neutrophils' phenotype was assessed by FC. **Results:** Of 52 NSCLC, 65% were $>$ 65 years, 83% had stage IV, 25% PD-L1 on tumour cells $\geq$50%, 67% received 1st line ICI. PD and HPD occurred in 21 (40%) and 5 (10%) pts, respectively. Before ICI start, HPD pts had higher circulating immature neutrophils measured as median percentage of $CD10^-$ LDNs [41.9 (min 26.7; max 83.5) vs 10.1 (min 0.69; max 79.3), p = 0.01] and of $CD16^-$ cells among $CD10^-$ LDNs [93 (min 89.5; max 98.4) vs 86.3 (min 24.2; max 99), p = 0.03] compared to conventional PD pts. PD and HPD occurred in 17 (71%) and 3 (12.5%) of 24 immune competent mice treated with anti-murine PD-1. The median percentage of IL-17^+ tumour associated neutrophils ($Gr1^{high}Ly6C^{low}$) was significantly higher in HPD compared to PD mice [0.25 (min 0.14; max 0.63) vs 0.06 (min 0.02; max 0.32), p = 0.02]. **Conclusions:** Circulating immature ($CD10^-$ and $CD10^-$ $CD16^-$) LDNs and IL-17^+ tumour associated neutrophils discriminate HPD from conventional PD upon ICI in NSCLC pts and in vivo models, respectively. Functional characterization of specific neutrophil subsets is ongoing. Research Sponsor: IASLC Young Investigator Award 2019 and ASCO Merit Award 2019.

9548 Poster Session (Board #314), Fri, 8:00 AM-11:00 AM

Radiotherapy to augment pembrolizumab responses and outcomes in metastatic non-small cell lung cancer: Pooled analysis of two randomized trials. *First Author: James William Welsh, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: In metastatic non-small cell lung cancer (mNSCLC), the clinical trials NCT02492568 and NCT02444741 are the only known randomized comparisons of pembrolizumab alone versus pembrolizumab combined with radiation therapy (RT). When the trials were analyzed individually, some potential benefit was observed in the combination therapy group, but the relatively small sample size of each trial limited the detection of potential differences in response rates and outcomes. Hence, we perform a pooled analysis of these two randomized trials to validate and explore whether RT improves mNSCLC patient responses to immunotherapy. **Methods:** This was a pooled analysis of two randomized trials (NCT02492568 and NCT02444741) of pembrolizumab with or without RT for mNSCLC. Endpoints included the out-of-field overall response rate (ORR) and disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and subgroup analysis of the different RT schemes. **Results:** In all, 131 patients were analyzed (n = 66 pembrolizumab; n = 65 pembrolizumab/RT (iRT)). ORR was 21% in the pembrolizumab arm vs. 38% in the iRT arm (p = 0.01); DCR was 53% in the pembrolizumab arm vs. 67% in the iRT arm (p = 0.0009); PFS was 4.4 m vs 8.3 m (p = 0.046); and OS was 9.2 m vs 19.2 m (HR 0.66; p = 0.040). Ablative RT (24Gy/3 fractions and 50Gy/4 fractions) had better ORRs of 48% and 54%, respectively, compared to 18% for non-ablative RT (45Gy/15 fractions) and 20% for pembrolizumab alone (p $<$ 0.05, respectively). **Conclusions:** The addition of RT to immunotherapy significantly increased the ORR of unirradiated lesions and was additionally associated with significant improvements in PFS and OS. Ablative RT was associated with response rates significantly higher than those of non-ablative RT, possibly due to a detrimental effect of non-ablative RT on ALC. These hypothesis-generating findings require dedicated, large-volume, and randomized studies for corroboration. Clinical trial information: NCT02492568 and NCT02444741. Research Sponsor: Merck Sharp & Dohme.

9549 Poster Session (Board #315), Fri, 8:00 AM-11:00 AM

Long-term responders to PD-1 blockade in patients with advanced non-small cell lung cancer (NSCLC). *First Author: Jia Luo, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Long-term response – the plateau of the survival curve – is the transcendent benefit from PD-1 blockade. However, only a subset of responses achieve substantial durability. The frequency, characteristics, and predictors of long-term responders (LTR) to PD-1 blockade are not well known and may differ from short-term responders (STR). **Methods:** Patients with advanced NSCLC treated with anti-PD-1/PD-L1 therapy from two institutions (MSK and DFCI) were examined. Responses were assessed by RECIST. LTR was defined as PR/CR lasting $\geq$ 24 months. STR was defined as PR/CR lasting $<$ 12 months. Comparisons were also made to patients with progressive disease (PD). PD-L1 expression was assessed by IHC. TMB was assessed by targeted NGS; high TMB was defined as $\geq$ median of the cohort. A subset had detailed molecular profiling by MSK-IMPACT. Fisher's exact and Mann-Whitney U tests were used to compare features, and the log-rank test was used to compare survival. **Results:** Of 2318 patients (MSK n = 1536, DFCI n = 782), 126 (5.4%, 95% CI 4.6-6.4%) achieved LTR, with similar rates in both cohorts. STR occurred in 139 (6%). Overall survival was longer in LTR compared to STR (median NR vs 19.6 months, HR 0.07, $p <$ 0.001). LTR had deeper responses compared to STR (median best overall response -69% vs -46%, $p < 0.001$). Patients with LTR were younger ($<$ 65 years old) and had increased TMB ($\geq$ median mut/Mb) compared to both STR and PD ($p = 0.006$, $p = 0.03$; $p < 0.001$, $p < 0.001$). The rate of LTR was enriched among patients with both high TMB/high PD-L1 compared to those with low TMB/low PD-L1 (9% vs 1%, OR 9.2, $p < 0.001$), while STR was similar in both groups (7% vs 6%). 2% of patients with sensitizing EGFR mutations (n = 243) achieved LTR. Loss of function variants in ARID1A (14% vs 2%), PTEN (8% vs 0%), and KEAP1 (12% vs 2%) were enriched in LTR compared to STR ($p < 0.05$ for each). Among patients with KRAS mutations, the rate of LTR was higher in those with co-mutation with TP53 compared to STK11 (11% vs 2%, $p = 0.01$). **Conclusions:** Long-term response (LTR, ongoing response $\geq$ 24 months) to PD-1 blockade is an uncommon but profound clinical outcome in metastatic lung cancers. Younger age and high TMB correlate with LTR; the combination of high TMB/high PD-L1 enriches for LTR but not STR. Features predicting long term response may be distinct from those predicting initial response. Research Sponsor: T32-CA009207, NIH-T32, Investigational Cancer Therapeutics Training Program Grant.

9552 Poster Session (Board #318), Fri, 8:00 AM-11:00 AM

Comparative efficacy of chemoimmunotherapy versus immunotherapy alone in the front-line treatment of advanced non-small cell lung cancer: A systematic review and network meta-analysis. *First Author: Ranjan Pathak, Section of Medical Oncology, Yale School of Medicine, New Haven, CT*

Background: Immune checkpoint inhibitors (ICI) and combination chemotherapy (chemo) plus ICI (Chemo-ICI) have been shown in RCTs to have improved OS compared to chemo in the 1L treatment of advanced NSCLC. However, the benefit of chemo-ICI compared with ICI alone is unknown. **Methods:** Systematic review using MEDLINE, Embase and Cochrane CENTRAL was done to identify relevant studies up to December 2019. Phase 3 RCTs that evaluated the efficacy of 1L ICI or chemo-ICI and reported outcomes stratified by PD-L1 status ($<$1%, 1-49%, $\geq$50%) were included. ICI was defined as single-agent PD-1 axis inhibitor or dual checkpoint blockade with PD-1 axis inhibitor plus CTLA-4 inhibitor. Comparison for PD-L1$<$1% included chemo-ICI vs ipi/nivo and for PD-L1 1-49% and PD-L1$>$50% included chemo-ICI vs ipi/nivo or single-agent ICI. OS, PFS, and ORR were extracted. Network meta-analysis (NMA) was done in Bayesian random-effects regression models. **Results:** Ten phase 3 RCTs (7971 screened) involving 7,218 patients assigned to ICI (pembro or atezo or ipi/nivo) or chemo-ICI (platinum-doublet + atezo, pembro, or nivo) were included. In PD-L1 $<$1% patients, NMA comparing chemo-ICI with ipi/nivo failed to show a statistically significant difference in OS, PFS or ORR. In PD-L1 1-49% patients, there was no significant difference between chemo-ICI vs ICI in OS or ORR; PFS could not be analyzed due to lack of available data. In PD-L1 $>$50% patients, chemo-ICI was associated with improved PFS and ORR compared to ICI alone, but without any OS difference (Table). **Conclusions:** Although the addition of chemo to ICI appears to improve ORR and PFS in PD-L1 $\geq$50% patients when compared to ICI alone, chemo-ICI does not confer an OS benefit in the 1L treatment of NSCLC patients regardless of PD-L1 status. Prospective trials comparing chemo-ICI, ICI monotherapy, and combination ICI are needed to confirm these findings. OS, PFS and ORR with chemo-ICI vs ICI. Research Sponsor: None.

PD-L1 status	Comparison	OS (HR, 95% CrI)	PFS	ORR (OR, 95% CrI)
PD-L1 <1%	Chemo-ICI vs ipi/nivo	1.23 (0.74-1.99)	0.94 (0.53-1.60)	1.38 (0.40-5.05)
PD-L1 1-49%	Chemo-ICI vs ICI overall	0.83 (0.44-1.50)	NA	2.40 (0.66-9.10)
	Chemo-ICI vs ipi/nivo	0.82 (0.34-1.92)	NA	NA
	Chemo-ICI vs ICI monotherapy	0.84 (0.34-2.00)	NA	2.30 (0.65-8.20)
PD-L1 ≥50%	Chemo-ICI vs ICI overall	0.92 (0.66-1.30)	0.64 (0.47-0.88)	2.10 (1.20-3.50)
	Chemo-ICI vs ipi/nivo	0.88 (0.53-1.49)	0.66 (0.39-1.15)	2.27 (0.91-5.31)
	Chemo-ICI vs ICI monotherapy	0.95 (0.64-1.40)	0.63 (0.44-0.96)	2.00 (1.10-3.80)

9553 Poster Session (Board #319), Fri, 8:00 AM-11:00 AM

Clinical performance of a comprehensive novel liquid biopsy test for identifying non-small cell lung cancer (NSCLC) patients for treatment with osimertinib. *First Author: Jhanelle Elaine Gray, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Genotyping is required to identify cancer patients (pts) eligible for targeted therapy; however, many do not receive biomarker testing, in part due to limitations associated with tissue-only genotyping practices and the growing list of biomarkers recommended to be tested. Liquid biopsy overcomes many of these limitations but is not yet fully adopted. We report here the clinical performance of a comprehensive liquid biopsy test based on next generation sequencing (NGS) of circulating tumor DNA (ctDNA) for the identification of NSCLC patients with *EGFR* exon 19 deletions (ex19del) or L858R mutations (*EGFR*m) or *EGFR* T790M, eligible for treatment with osimertinib. **Methods:** 441 (79%) of 556 pts randomized in FLAURA (NCT02296125; first-line osimertinib vs comparator EGFR TKI in *EGFR*m NSCLC) and 300 (72%) of 419 pts from AURA3 (NCT012151981; osimertinib vs chemotherapy in NSCLC pts with T790M at progression on EGFR TKI) were retrospectively tested with Guardant360 (G360), a 74-gene ctDNA NGS assay assessing single nucleotide variants, insertion-deletions, amplifications, and fusions in genes relevant to targeted therapy selection as well as microsatellite instability. Progression-free survival (PFS) of pts with *EGFR*m or T790M detected by G360 was compared to pts detected by the cobas EGFR Mutation Test (cobas) using tissue or plasma with an unadjusted cox model. **Results:** Treatment with osimertinib was associated with a significant PFS benefit relative to control therapy in NSCLC pts with *EGFR*m (FLAURA) and T790M (AURA3) detected using G360 (Table). Observed clinical benefit for pts with *EGFR*m or T790M detected by G360 was similar to that for pts with *EGFR*m or T790M identified by cobas using tissue or plasma specimens. **Conclusions:** This analysis demonstrates that G360 accurately identifies pts for osimertinib therapy while simultaneously providing comprehensive genotyping for other therapeutic molecular targets. The application of NGS liquid biopsy has the potential to increase rates of pts genotyped and access to precision medicine. Research Sponsor: AstraZeneca.

Pivotal study (*EGFR* mutations)	PFS Hazard Ratio (95% CI)	p-value
FLAURA (ex19del/L858R)		
G360	0.42 (0.31, 0.55)	< 0.0001
cobas plasma	0.45 (0.35, 0.58)	< 0.0001
cobas tissue	0.43 (0.34, 0.54)	< 0.001
AURA3 (T790M)		
G360	0.39 (0.28, 0.57)	< 0.0001
cobas plasma	0.42 (0.28, 0.62)	< 0.0001
cobas tissue	0.37 (0.29, 0.48)	< 0.0001

9554 Poster Session (Board #320), Fri, 8:00 AM-11:00 AM

Phase III study of tislelizumab plus chemotherapy vs chemotherapy alone as first-line (1L) treatment for advanced squamous non-small cell lung cancer (sq NSCLC). *First Author: Jie Wang, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China*

Background: Tislelizumab is an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis. Tislelizumab in combination with chemotherapy has demonstrated a manageable tolerability profile and preliminary efficacy as 1L treatment for NSCLC. **Methods:** In this open-label phase 3 study (NCT03594747), Chinese pts with histologically confirmed stage IIIB or IV sq NSCLC were randomized (1:1:1) to receive IV Q3W: tislelizumab (200 mg, D1) + paclitaxel (P; 175 mg/m^2, D1) and carboplatin (carb; AUC 5, D1) (*Arm A*); tislelizumab + *nab*-P (100 mg/m^2; D1, 8, and 15) and carb (AUC 5, D1) (*Arm B*); or P (175 mg/m^2, D1) and carb (AUC 5, D1) (*Arm C*). Chemotherapy was administered for 4-6 cycles followed by tislelizumab. Patients were stratified by tumor stage and PD-L1 expression. The primary endpoint, PFS per RECIST v1.1, was assessed by Independent Review Committee; key secondary endpoints included OS, ORR, DoR, and safety/tolerability. **Results:** Across 360 pts, median PFS was significantly improved with tislelizumab plus chemotherapy (*Arms A* and *B*) compared with chemotherapy alone (*Arm C*) (Table). As of 6 Dec 2019, ORRs were higher and median DoRs were longer in *Arms A* and *B* vs *Arm C*. Across all arms, median OS was not reached and median number of treatment cycles were comparable. Adverse events (AEs) leading to discontinuation of any treatment were reported in 12.5%, 29.7%, and 15.4% of pts in *Arms A*, *B*, and *C*, respectively. The most commonly reported grade $\geq$3 AEs were hematologic in nature (eg, neutropenia) and consistent with known chemotherapy AEs. Serious treatment-related AEs (TRAEs) were reported in 72 pts (37.5% [*A*]; 38.9% [*B*]; 23.6% [*C*]); TRAEs leading to death were reported in 6 pts (n=1 [*A*]; n=2 [*B*]; n=3 [*C*]), none of which were solely attributed to tislelizumab. **Conclusions:** As 1L treatment for advanced sq NSCLC, addition of tislelizumab to P/carb or *nab*-P/carb chemotherapy significantly improved PFS and showed higher ORR and longer DoR than chemotherapy alone. The safety profile is in line with the known profiles of tislelizumab, chemotherapy, and underlying NSCLC; no new safety signals were identified with addition of tislelizumab to chemotherapy. Clinical trial information: NCT03594747. Research Sponsor: BeiGene, Ltd.

	Arm A (n=120)	*Arm B* (n=119)	*Arm C* (n=121)
Median PFS, mo (95% CI)	7.6 (6.0-9.8)	7.6 (5.8-11.0)	5.5 (4.2-5.7)
Stratified HR (95% CI)	0.52 (0.4-0.7)	0.48 (0.3-0.7)	NA
***P*-value**	0.0001	<0.0001	
ORR, % (95% CI)	72.5 (63.6, 80.3)	74.8 (66.0, 82.3)	49.6 (40.4, 58.8)
Median DoR, (95% CI)	8.2 (5.0, NE)	8.6 (6.3, NE)	4.2 (2.8, 4.9)

9556 Poster Session (Board #322), Fri, 8:00 AM-11:00 AM

Primary efficacy and biomarker analyses from the VISION study of tepotinib in patients (pts) with non-small cell lung cancer (NSCLC) with *MET*ex14 skipping. *First Author: Xiuning Le, Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Preliminary tepotinib data showed durable activity in pts with NSCLC with *MET*ex14 skipping prospectively identified by liquid (L+) or tissue (T+) biopsy. Having met target enrollment of ≥60 L+ pts & ≥60 T+ pts, we report primary data. **Methods:** VISION Cohort A enrolled pts with advanced *EGFR/ALK* wt, *MET*ex14 skipping NSCLC (asymptomatic brain metastases [BM] allowed), who received oral tepotinib 500 mg QD. On-study treatment decisions were based on investigator assessment (INV) of response. Primary endpoint was objective response rate (ORR) by independent review committee (IRC) analyzed in 3 primary ITT sets: L+ and/or T+, L+, T+. 2ary endpoints included ORR by INV, duration of response (DOR), disease control rate (DCR), PFS, OS, & safety. Preplanned analyses were performed in pts with BM at baseline (BL). BL/on-treatment ctDNA plasma samples (L+) were analyzed using a 73-gene NGS panel (Guardant360). Deep molecular responses (MR), defined as > 75% depletion of *MET*ex14, were compared with objective responses (OR). **Results:** By data cut-off (1 Oct 19) 151 pts received tepotinib (safety set); 99 L+/T+, 66 L+, 60 T+ pts comprised the 3 ITT sets with ≥6-month [m] allowed-up. Across treatment lines (n = 44 1L, n = 55 ≥2L), primary ORR & mPFS [95% CI] in 99 L+/T+ pts were 43% [34–54] & 8.6 m [6.9–11.0] by IRC and 56% [45–66] & 9.5 m [6.7–13.5] by INV. ORR was similar in L+ or T+ pts (table) or in T+L− pts (n = 25): 40% [21–61] by IRC and 48% [28–69] by INV. Only 2 pts were T−L+. Outcomes were also comparable in pts with BM (n = 11): IRC ORR 55% [23–83] & mPFS 10.9 m [8.0–ne]. 34/51 pts (67%) with matched BL/on-treatment L+ samples had deep MR strongly associated with clinical response: 32/34 pts (94%) with MR had disease control (INV), including 29/34 pts (85%) with OR; 2/34 pts had progressive disease. Further biomarker data will be presented. Grade ≥3 treatment-related adverse events (TRAEs) were reported by 37/151 pts (25%). 13 pts (9%) discontinued due to TRAEs. **Conclusions:** Tepotinib is a promising targeted therapy with durable clinical activity and manageable toxicity in pts with *MET*ex14 skipping NSCLC L+ or T+, including pts with BM. High ORR & DCR in pts with ctDNA molecular responses support that MET inhibition in *MET*ex14+ tumor cells can lead to clinical benefit. Clinical trial information: NCT02864992. Research Sponsor: Merck KGaA.

	L+		T+	
	66		60	
N	**IRC**	**INV**	**IRC**	**INV**
[95% CI]				
ORR %	44 [32–57]	56 [43–68]	47 [34–60]	62 [48–74]
mDOR m	11.1 [8.3–ne]	16.4 [7.3–21.5]	12.4 [9.7–ne]	16.4 [7.0–21.5]
DCR %	64 [51–75]	70 [57–80]	70 [57–81]	78 [66–88]
mPFS m	8.5 [5.1–11.0]	8.5 [5.6–11.2]	11.0 [7.8–17.1]	12.2 [6.3–17.7]
Immature mOS m	19.1 [9.5–ne]		19.7 [12.8–ne]	

9557 Poster Session (Board #323), Fri, 8:00 AM-11:00 AM

Genetic profiling and the response to RET inhibitors in RET fusion positive non-small cell lung cancer (NSCLC) identified by international genomic screening project (LC-SCRUM-Asia). *First Author: Kaname Nosaki, National Cancer Center Hospital East, Kashiwa, Japan*

Background: *RET* fusions are targetable oncogenic drivers in 1 – 2 % of NSCLC, yet no RET inhibitors are approved. Selective RET inhibitors, such as LOXO-292 and BLU-667, are currently in development. The impact of co-occurring mutation on outcome in RET-TKI therapy remains largely unknown. **Methods:** In an international genome screening project in Asia (LC-SCRUM-Asia), 161 cancer-related genes have been analyzed by a next-generation sequencing (NGS) system, Oncomine™ Comprehensive Assay. The therapeutic efficacy and survival of *RET* fusion+ NSCLC were evaluated using a large-scale clinicogenomic database in the LC-SCRUM-Japan. **Results:** From Feb 2013 to Dec 2019, a total of 7177 patients with non-squamous NSCLC were enrolled. *RET* fusion were detected in 167 patients (2.3 %). Median age was 61 years (range: 29 - 85), 60 % were female, 61 % were never-smokers, 99 % had adenocarcinoma, and 78 % had stage IIIB/IV disease. Based on our database, the median overall survival was 37 months. 62 patients received RET inhibitor therapy. *RET* fusions was identified by NGS assay (KIF5B-RET: 75, CCDC6-RET: 30, Others: 2) in 107 patients. Co-occurring genomic alterations were detected in 62 (58 %) patients, the median number of co-mutations was 1 (range 0 - 4). The most common co-occurring mutations in tumor involved *TP53* (31; 29 %), *STK11* (6; 6 %), *CDKN2A* (5; 5 %) and *TSC2* (5; 5 %). In 23 patients treated with RET inhibitor (unapproved drugs), there was a strong association between co-occurring mutation and time to treatment discontinuation (TTD) in RET inhibitor therapy; HR 2.75 (95%CI 1.71 - 15.6, P = 0.0096). **Conclusions:** *RET* rearrangements continue to represent a rare but high unmet need disease. Co-occurring mutation was significantly associated with shorter TTD. Our data is the largest cohort of advanced-stage *RET* fusion+ NSCLC profiled by NGS to date. Co-occurring mutation should be evaluated in the development of novel targeted therapies for *RET* fusion+ NSCLC. Research Sponsor: None.

9558 Poster Session (Board #324), Fri, 8:00 AM-11:00 AM

Two-year follow-up of bintrafusp alfa, a bifunctional fusion protein targeting TGF-β and PD-L1, for second-line (2L) treatment of non-small cell lung cancer (NSCLC). *First Author: Byoung Chul Cho, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea*

Background: Bintrafusp alfa (M7824) is a first-in-class bifunctional fusion protein composed of the extracellular domain of the TGF-βRII receptor (a TGF-β "trap") fused to a human IgG1 mAb blocking PD-L1. Interim analysis of a global phase 1 study (NCT02517398) found an objective response rate (ORR) of 27.5% and a manageable safety profile in patients with NSCLC who received bintrafusp alfa 1200 mg in the 2L setting; median overall survival (OS) was not reached. Here we present the longest efficacy and safety follow-up in a cohort receiving bintrafusp alfa. **Methods:** Patients with advanced NSCLC unselected for PD-L1 expression level who progressed after first-line standard treatment (no prior immunotherapy) were randomized to receive bintrafusp alfa 500 or 1200 mg (n = 40 each) Q2W until disease progression, unacceptable toxicity or trial withdrawal. The primary objective was best overall response (BOR) per RECIST 1.1; secondary and exploratory objectives include safety and OS, respectively. **Results:** As of October 15, 2019, a total of 40 patients received bintrafusp alfa at the recommended phase 2 dose of 1200 mg Q2W for a median of 17 (range, 2-136) weeks, with a median follow-up of 128 weeks; 18 patients were still alive, 3 patients had an ongoing response, and 1 patient remained on treatment. Results for the 1200 mg dose cohort showed an ORR of 27.5%, and a median duration of response of 18 months. The 18- and 24-month progression-free survival and OS rates were 18.4% and 11.0%, and 49.7% and 39.7%, respectively. Duration of response rates at 18 and 24 months were 42.4% and 21.2%, respectively. Median OS in patients with positive (≥1%) PD-L1 expression was 21.7 months; 6 of 7 patients with high (≥80% with Ab clone 73-10, which is equivalent to ≥50% with 22C3) PD-L1 expression were still alive. The overall safety profile has remained consistent since the interim analysis, with no new safety signals or deaths and 1 additional treatment-related discontinuation (blood alkaline phosphatase increased). **Conclusions:** After two years of follow-up, bintrafusp alfa continues to show manageable safety with durable responses and encouraging long-term survival, especially in patients with high PD-L1 expression. A study evaluating bintrafusp alfa vs pembrolizumab as first-line treatment for NSCLC is ongoing in patients with high PD-L1 expression (NCT03631706). Clinical trial information: NCT02517398. Research Sponsor: Merck KGaA, Darmstadt, Germany, Pharmaceutical/Biotech Company.

9560 Poster Session (Board #326), Fri, 8:00 AM-11:00 AM

Nivolumab (NIVO) plus ipilimumab (IPI) with two cycles of chemotherapy (chemo) in first-line metastatic non-small cell lung cancer (NSCLC): CheckMate 568 Part 2. *First Author: Justin F. Gainor, Massachusetts General Hospital, Boston, MA*

Background: In Part 1 of the phase II CheckMate 568 study (NCT02659059), NIVO + IPI was active and tolerable in patients (pts) with advanced NSCLC. The addition of chemo to dual immune checkpoint inhibitor therapy may further improve initial disease control. We report results from Part 2 of CheckMate 568, which evaluates NIVO + IPI combined with 2 cycles of chemo in pts with advanced treatment-naive NSCLC. **Methods:** Adult pts with untreated stage IV NSCLC received NIVO 360 mg Q3W + IPI 1 mg/kg Q6W combined with 2 cycles of histology-based platinum-doublet chemo, followed by NIVO + IPI without chemo until disease progression/unacceptable toxicity for ≤ 2 years. The primary endpoints were dose-limiting toxicity (DLT) within the first 9 weeks and safety/tolerability. Treatment was considered safe if ≤ 25% of at least 22 evaluable pts had a DLT. DLTs included but were not limited to: uncontrolled grade 3 non-skin treatment-related adverse events (TRAEs), grade 4 TRAEs, grade 2 treatment-related pneumonitis not resolved within 14 days, and treatment-related hepatic function abnormalities. **Results:** In total, 36 pts received treatment; 97% of pts completed 2 cycles of chemo combined with NIVO + IPI. Three pts discontinued IPI while continuing NIVO. Minimum follow-up was 14.9 months. Only 1 (3%) pt experienced a DLT (transient, asymptomatic grade 3 AST and ALT elevation) within the first 9 weeks. The elevation occurred on cycle 1, day 21 and resolved 2 weeks later with discontinuation of IPI, delay of NIVO, and treatment with prednisone; chemo was continued throughout and NIVO was restarted thereafter without recurrent toxicity. Grade 3–4 TRAEs occurred in 21 (58%) pts. Eight (22%) pts experienced a TRAE leading to discontinuation, most commonly colitis, encephalopathy, pneumonitis, and arthralgia (each in 2 [6%] pts); these events occurred outside of the 9-week window for DLT assessment. The most common select TRAEs (defined as AEs of potential immunologic causes) were skin related (18 [50%] pts); the most common grade 3–4 select TRAEs were endocrine (3 [8%] pts), skin related, gastrointestinal, and pulmonary (each in 2 [6%] pts). No treatment-related deaths occurred. Updated safety in addition to efficacy data will be presented. **Conclusions:** In pts with untreated advanced NSCLC, the addition of 2 cycles of platinum-doublet chemo to NIVO + tumor-optimized IPI was tolerable. No unexpected safety signals were observed. Clinical trial information: NCT02659059. Research Sponsor: Bristol-Myers Squibb.

9561 Poster Session (Board #327), Fri, 8:00 AM-11:00 AM

Soluble BTN2A1 as a potential predictive biomarker of immune checkpoint inhibitor efficacy in advanced non-small cell lung cancer (NSCLC). *First Author: Philippe Rochigneux, Institut Paoli-Calmettes, CRCM U1068, Marseille, France*

Background: Medical treatment of lung cancer has irreversibly changed since the development of immune checkpoint inhibitors (ICI). However, immune biomarkers of efficacy are still lacking. Preliminary data in leukemia and pancreatic cancer showed that soluble immune checkpoints are associated with a reduced overall survival (OS). This led us to explore the prognostic and predictive value of soluble immune checkpoints in non-small cell lung cancer (NSCLC) patients treated with chemotherapy or ICI. **Methods:** We analyzed 90 advanced NSCLC patients. The pilot cohort (Rennes University Hospital, France), included 48 patients treated with platinum doublets (n = 33) or ICI (n = 15) (LOC/11-16 protocol). The confirmation cohort (Paoli-Calmettes Institute) included 42 patients treated with ICI (nivolumab or pembrolizumab) in a longitudinal prospective setting (Immunosup trial, NCT03595813). In both cohorts, enzyme-linked immunosorbent assays (ELISA) were performed in baseline plasma samples for soluble forms of PD-1, PD-L1, global BTN3, BTLA, BTN3-A1 and BTN2A1. Soluble ICI levels were linked to clinical data using Kaplan-Meier, log-rank and Cox proportional-hazards models. Cut-points were determined using maxstat package for survival, R software R 3.6.2. **Results:** Five soluble immune checkpoints correlated and clustered together in unsupervised analysis (PD-1, PD-L1, global BTN3, BTLA, BTN3-A1), but were not associated with ICI efficacy. In patients treated with ICI, in the pilot and confirmation cohort, a high baseline plasmatic concentration of soluble BTN2A1 was significantly associated with an improved OS (confirmation cohort with a BTN2A1 cut-point of 3.55 ng/ml: HR = 0.30, 95%CI = 0.12-0.74, p = 0.0057, median OS in $BTN2A1^{low}$ = 7.6 months and median OS in $BTN2A1^{hi}$ = 19.5 months). On the contrary, in patients treated with chemotherapy, soluble BTN2A1 concentration was not associated with overall survival. **Conclusions:** In advanced NSCLC patients, a high baseline plasmatic concentration of soluble BTN2A1 was correlated with improved outcomes for ICI, but not for chemotherapy, suggesting that baseline soluble BTN2A1 level is a potential predictive biomarker of ICI efficacy. Additional studies are ongoing to confirm this finding. Research Sponsor: Institut Paoli Calmettes and Rennes University Hospital.

9562 Poster Session (Board #328), Fri, 8:00 AM-11:00 AM

A phase Ib study of abemaciclib in combination with pembrolizumab for patients (pts) with stage IV Kirsten rat sarcoma mutant (KRAS-mut) or squamous non-small cell lung cancer (NSCLC) (NCT02779751): Interim results. *First Author: Jean-Louis Pujol, Centre Hospitalier Universitaire, Maladies Respiratoires, Montpellier, France*

Background: Abemaciclib is an orally administered, selective small molecule cyclin-dependent kinase 4 and 6 inhibitor. In preclinical models, abemaciclib induced intratumor immune inflammation and synergized with PD-1 blockade to enhance antitumor efficacy in anti-PD-L1 refractory disease. Here, we report the safety and antitumor activity of abemaciclib plus the approved NSCLC treatment pembrolizumab in 2 cohorts for pts with nonsquamous and squamous NSCLC. **Methods:** Eligible pts for this non-randomized, open-label, multicohort, phase 1b study were either chemotherapy-naive with ≥ 1% tumor cell (TC) PD-L1 staining, *KRAS*-mut nonsquamous NSCLC (Cohort A) or had a squamous subtype and received ≤ 1 prior platinum-containing chemotherapy regimen (Cohort B) for metastatic NSCLC. Primary endpoint was safety; secondary objectives included objective response rate (ORR), progression-free survival (PFS), and overall survival (OS). **Results:** Twenty-five pts with NSCLC were enrolled in each cohort. Most pts (68%) in Cohort B had received 1 prior line of chemotherapy. Safety profiles observed in both cohorts were largely consistent with previous reports for abemaciclib and pembrolizumab monotherapy. Grades 3/4 AEs in Cohorts A and B, respectively, included ALT increase (6 pts [24%]/ 0 pts), diarrhea (3 pts [12%]/ 0 pts), neutropenia (3 pts [12%]/ 0 pts), and pneumonitis (3 pts [12%]/ 1 pt [4%]). Six pts in Cohort A (24%) and 2 pts in Cohort B (8%) had a confirmed partial response for a disease control rate (CR+PR+SD) of 52% and 64%, respectively. In Cohort A, the ORR in pts with strong (≥50% TC) PD-L1 staining (n = 13) was 31% vs. 17% in pts with weak (1-49% TC) PD-L1 expression (n = 12). Median PFS and OS were 7.6 months (95% CI: 1.6, NR) and 22.0 months (95% CI: 9.9, NR) in Cohort A and 3.3 months (95% CI: 1.4, 5.2) and 6.0 months (95% CI: 3.7, 13.1) in Cohort B, respectively. **Conclusions:** Abemaciclib plus pembrolizumab resulted in a numerical higher rate of transaminase elevations and pneumonitis. Antitumor activity was remarkable in the *KRAS*-mut nonsquamous NSCLC but not noticeably higher as compared to historical data for pembrolizumab monotherapy. Clinical trial information: NCT02779751. Research Sponsor: Eli Lilly and Company.

9563 Poster Session (Board #329), Fri, 8:00 AM-11:00 AM

Randomized phase II study of pembrolizumab (P) alone versus pegilodecakin (PEG) in combination with P as first-line (1L) therapy in patients (pts) with stage IV non-small cell lung cancer (NSCLC) with high PD-L1 expression (CYPRESS 1). *First Author: David R. Spigel, Sarah Cannon Research Institute, Nashville, TN*

Background: Pembrolizumab (P) is an immune checkpoint inhibitor (CPI) approved to treat 1L advanced NSCLC pts with high PD-L1 expression. PEG + CPI has demonstrated promising efficacy in NSCLC pts in a phase I trial (IVY; NCT02009449; Naing et al., 2019 *Lancet Oncol*), providing rationale for this randomized phase II trial (CYPRESS 1; NCT03382899). **Methods:** CYPRESS 1 was an open label phase II trial, for treatment-naïve, ECOG 0-1, PD-L1 high (22C3 clone TPS ≥ 50%), Stage IV NSCLC pts, without known EGFR/ALK mutations. Pts were randomized 1:1 to arm P (received 200mg IV on day 1 of a 21-day cycle) v. arm PEG+P (received P as above + PEG daily of 0.8 mg if weight ≤80kg and 1.6mg if weight> 80 kg up to 35 cycles in each arm). Pts were stratified by tumor histology and must have no prior history of cancer or prior CPI therapy. Primary endpoint was ORR (per RECIST v1.1 by investigator) Secondary endpoints included PFS, OS, and safety. Exploratory endpoints included ORR and PFS by blinded independent central review (BICR). Immune activation biomarkers (baseline and change from baseline) were assessed by serum immunoassay, IHC, and sequencing. **Results:** As of Dec 6, 2019, 101 pts were randomized to PEG+P (n=51) or P (n=50). Median follow-up time was 10.0 months (95% CI [8.4, 11.1]). Results for PEG+P versus P were: ORR per investigator was 47% v. 44% (p=0.76), ORR per BICR was 53% v. 46%(p=0.78), mPFS per investigator was 6.3 v. 6.1 months with HR = 0.94 (95% CI [0.54, 1.63];p=0.82), mPFS per BICR was 6.4 v. 7.2 months with HR = 1.10 (95%CI [0.62, 1.96]; p=0.74), and mOS was 16.3 months v. not reached with HR = 1.36 (95% CI [0.66, 2.77]; p-value=0.40). Gr ≥3 treatment related adverse events (TRAEs) were 62% for PEG+P versus 19% for P. Gr ≥3 TRAEs with ≥10% incidence included anemia (20% vs. 0%) and thrombocytopenia (12% vs. 2%). Biomarker data on immunostimulatory signals of the IL-10R pathway will be included. **Conclusions:** Adding PEG to P did not lead to improvement in ORR, PFS, or OS, in 1L advanced NSCLC with high PD-L1 expression. PEG+P arm demonstrated expected safety profile but overall higher toxicity compared to pembrolizumab alone. Clinical trial information: NCT03382899. Research Sponsor: Eli Lilly and Company.

9564 Poster Session (Board #330), Fri, 8:00 AM-11:00 AM

RELAY+: Exploratory study of ramucirumab plus gefitinib in untreated patients (pts) with *epidermal growth factor receptor* (*EGFR*)-mutated metastatic non-small cell lung cancer (NSCLC). *First Author: Makoto Nishio, Thoracic Medical Oncology, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan*

Background: The phase III randomized part of the RELAY study (Part B; RELAY; NCT02411448) showed a significant improvement in progression-free survival (PFS) for ramucirumab (RAM) plus erlotinib (ERL) vs placebo plus ERL in 449 untreated pts with *EGFR*-mutated metastatic NSCLC (median PFS: 19.4 vs 12.4 months; stratified hazard ratio: 0.59, 95% CI: 0.46–0.76, p<0.0001; 1-year PFS rate: 71.9% vs 50.7%). Here we report initial results from RELAY+ (additional cohort of RELAY; Part C), an open-label, single-arm, exploratory study evaluating RAM plus gefitinib (GEF) in East Asian pts. **Methods:** Previously untreated East Asian pts with metastatic NSCLC and *EGFR* exon 19 deletions (Ex19del) or exon 21 substitution mutation (Ex21.L858R) received RAM (10 mg/kg Q2W) plus GEF (250 mg/day) until disease progression or unacceptable toxicity. The 1-year PFS rate (primary endpoint, assuming a 1-year PFS rate of 55% for RAM+GEF), tumor response, biomarkers, and safety were assessed. *EGFR* T790M status (baseline/30-day follow-up) was assessed in liquid biopsy samples by Guardant360 NGS. **Results:** In total, 82 pts were enrolled (Japan: 68; Taiwan: 8; Korea: 6); 65.9% were female, 65.9% were never-smokers, and 43.9% had Ex19del. With median follow-up of 13.8 months (range: 2.6–20.2; censoring rate: 58.5%), the overall 1-year PFS rate (95% CI) was 65.0% (52.4–75.1), 67.2% (48.6–80.3) in pts with Ex19del (n=36), and 63.4% (45.0–77.1) in pts with Ex21.L858R (n=46). The objective response rate was 70.7% (95% CI: 59.6–80.3), disease control rate was 98.8% (95% CI: 93.4–100.0), and duration of response was immature at this point in time with a censoring rate of 56.9% where the median point estimate was 13.6 months (95% CI: 11.1–18.2). Post-progression *EGFR* T790M was seen in 7 of 9 (78%; 95% CI: 45.3–93.7) pts with 30-day follow-up NGS results in which *EGFR* activating mutation was detected. Grade ≥3 treatment-emergent adverse events reported in >5% of pts were ALT increased (23.2%), hypertension (22.0%), and AST increased (12.2%). **Conclusions:** With a 1-year PFS rate of 65.0%, the primary endpoint of RELAY+ was met. The efficacy of RAM+GEF in RELAY+ was similar to that of RAM+ERL in RELAY, and the safety profile of the combination was similar to that of the individual drugs. Clinical trial information: NCT02411448. Research Sponsor: Eli Lilly and Company.

9566 Poster Session (Board #332), Fri, 8:00 AM-11:00 AM

Phase Ib study of BI 836880, a VEGF/Ang2-blocking nanobody, in combination with BI 754091, an anti-PD-1 antibody: Initial results in patients (pts) with advanced non-small cell lung cancer (NSCLC). *First Author: Nicolas Girard, Institut Curie, Institut du Thorax Curie-Montsouris, Paris, France*

Background: Preclinical studies show that combining anti-VEGF/Ang2 with anti-PD-1 therapy promotes an immunopermissive state supportive of T-cell-mediated tumor cell destruction. BI 836880 is a humanized bispecific nanobody that targets VEGF and Ang2, and BI 754091 is an anti-PD-1 antibody. Each has shown manageable safety and preliminary activity as monotherapy. Here, we report initial results from a Phase Ib study assessing BI 836880 in combination with BI 754091. **Methods:** In Part 1 (dose escalation), pts with locally advanced or metastatic (m) non-squamous NSCLC who progressed during/after completion of ≥2 cycles of platinum-based chemotherapy (CT) ± a checkpoint inhibitor (CPI) were enrolled. Pts received BI 836880 (cohorts of 360, 500 and 720 mg intravenously [iv] 3-weekly [q3w]) plus fixed-dose BI 754091 (240 mg iv q3w). Dose escalation was guided by Bayesian logistic regression models with overdose control. Primary endpoint in Part 1 was maximum tolerated dose (MTD)/recommended phase 2 dose (RP2D), based on dose-limiting toxicities (DLTs) in Cycle 1. Initial safety and efficacy results of Part 1 are reported here. Part 2 will assess safety and efficacy in 6 expansion cohorts: mNSCLC after CPI monotherapy; mNSCLC after CT + CPI; mSCLC after CT ± CPI; immunotherapy-resistant m-melanoma; recurrent glioblastoma after 1st-line CT; and hepatocellular carcinoma after prior sorafenib or lenvatinib ± subsequent CPI. **Results:** 12 pts received BI 836880 plus BI 754091 (8 male; median age 59.5 years; 8 had received prior CPI). 4 pts remain on treatment (including 1 treated for 15 cycles). 1 pt had a DLT during Cycle 1 (360 mg; G3 pulmonary embolism). All pts experienced an adverse event (AE; any-cause; safety data cut-off Nov 2019), most commonly (all%/G3%) hypertension (58/25), vomiting (42/0), nausea (33/0), and asthenia (33/0). Hypertension was transient. No G4 AEs were reported; one G5 AE occurred (general physical health deterioration). 5 pts had immune-related AEs (G2 hypothyroidism in 2 pts; G2 pruritus, G1 papular rash, and G2 vomiting). To date (Jan 2020), 2 pts have achieved partial response; 1 pt (500 mg dose; CPI-naïve) had 58% target lesion reduction, and 1 (720 mg; prior CPI) had 35% target lesion reduction. 8 pts had stable disease. **Conclusions:** MTD/RP2D was BI 836880 720 mg plus BI 754091 240 mg q3w. The combination had a manageable safety profile, and preliminary anti-tumor activity was observed. Expansion cohorts are ongoing. Equal contribution: JA and BH Clinical trial information: NCT03468426. Research Sponsor: Boehringer Ingelheim.

9567 Poster Session (Board #333), Fri, 8:00 AM-11:00 AM

Phase II randomized trial of first-line pembrolizumab and vorinostat in patients with metastatic NSCLC (mNSCLC). *First Author: Andreas Nicholas Saltos, Department of Thoracic Oncology, Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Histone deacetylase inhibitors may enhance tumor immunogenicity through various mechanisms including induced expression of T cell chemokines. A previous phase I trial demonstrated the combination of pembrolizumab (P) with vorinostat (V) in mNSCLC was well tolerated with signals of activity in ICI-pretreated pts. We initiated a randomized trial in the first-line setting with the primary objective to determine if the combination had superior ORR compared to pembrolizumab monotherapy. **Methods:** Pts with treatment-naïve mNSCLC and PD-L1 expression ≥ 1% were eligible. Pts were randomized open-label 1:1 to receive P 200 mg IV q3 wk as monotherapy [Arm A] or P 200 mg IV q3 wk plus V 400 mg PO daily [Arm B]. The primary endpoint was overall response rate (ORR). Secondary endpoints included DOR, PFS and OS. Tumor biopsies were collected both pre- and on-treatment (day 15-21) for analysis of CD8+ TIL, scored using a 0-3 scale in tumor beds. Here we report results after a preplanned interim analysis for efficacy, with accrual ongoing to a planned total of 39 patients per arm. **Results:** Between 7/2017 – 1/2019, 49 pts were enrolled, with 47 pts evaluable for response (24 in Arm A and 23 in Arm B). Median age was 69 (range 47 - 87), 49% female, ECOG PS 0/1 in 11%/89%. PD-L1 TPS was ≥50% in 13/24 (54%) of pts in Arm A, and in 13/23 (57%) of pts in Arm B. The most common TRAEs in Arm A included diarrhea (13%), fatigue (8%), and pruritus (8%). 3 pts in Arm A experienced grade ≥ 3 irAEs (including 1 each of grade 3 hepatitis, pneumonitis, and rash). The most common TRAEs in Arm B included anorexia (43%), fatigue (43%), nausea (35%) and increased creatinine (35%). 1 pt in Arm B experienced grade ≥ 3 irAE (1 grade 3 pneumonitis). Pre-treatment CD8+ TIL were not significantly different between Arm A and Arm B (p = 0.85) with the majority of tumors in both arms having a low TIL score of 1 (65% Arm A and 73.7% Arm B). A significant increase from pre-treatment to on-treatment TIL scores was seen in both Arm A (p = 0.001) and Arm B (p = 0.002). The ORR in Arm B pts with low pre-treatment TIL (score = 1) pts was substantially higher (66.7%) than in Arm A (33.3%), suggesting the combination may be especially beneficial against low TIL tumors. **Conclusions:** The combination arm had a considerably higher ORR compared to pembrolizumab monotherapy, with a manageable toxicity profile. The combination of pembrolizumab plus vorinostat in mNSCLC warrants further investigation. Clinical trial information: NCT02638090. Research Sponsor: Merck, Other Government Agency.

Best response:	Arm A N = 24	Arm B N = 23	P value
PR	6 (25%)	11 (48%)	p = 0.135
SD	8 (33%)	10 (43%)	
PD	10 (42%)	2 (9%)	
DCR	14 (58%)	21 (91%)	p = 0.017

9568 Poster Session (Board #334), Fri, 8:00 AM-11:00 AM

Outcomes to first-line pembrolizumab in patients with PD-L1-high (≥50%) non-small-cell lung cancer and a poor performance status. *First Author: Joao Victor Machado Alessi, Hospital Sírio-Libanês, São Paulo, Brazil*

Background: Patients with non-small cell lung cancer (NSCLC) and a poor Eastern Cooperative Oncology Group performance status (ECOG PS) have been excluded from immunotherapy clinical trials. We sought to evaluate clinical outcomes to first-line pembrolizumab in patients with advanced NSCLC, a PD-L1 tumor proportion score (TPS) of ≥50%, and an ECOG PS of 2. **Methods:** We performed a multicenter retrospective analysis of patients with metastatic NSCLC and a PD-L1 tumor proportion score (TPS) of ≥50% (negative for genomic alterations in *EGFR* and *ALK*) who received treatment with first-line commercial pembrolizumab. Clinical outcomes were compared in patients based on ECOG PS. **Results:** Among 234 patients, 83.3% (N = 195) had an ECOG PS of 0 or 1, and 16.7% (N = 39) had an ECOG PS of 2. The baseline clinicopathological characteristics were balanced between the ECOG PS 0-1 vs 2 groups in terms of age, sex, tobacco use, histology, *KRAS* mutation status, presence of other potentially targetable driver mutations (*BRAF*, *MET*, *HER2*, *RET*), history of central nervous system (CNS) disease, and PD-L1 TPS distribution. Compared to patients with an ECOG PS of 0-1, patients with an ECOG PS of 2 had a significantly lower objective response rate (ORR 43.1% vs 25.6%; P = 0.04), a numerically shorter median progression free survival (mPFS 6.6 months vs 4.0 months; P = 0.09), and a significantly shorter median overall survival (mOS 20.3 months vs 7.4 months; P < 0.001). Upon disease progression, patients with an ECOG PS of 2 were significantly less likely to receive second-line systemic therapy compared to patients with an ECOG PS of 0-1 (55.5% vs 14.3%, P < 0.001). **Conclusions:** Although a subset of patients with an ECOG PS of 2 can respond first-line pembrolizumab, clinical outcomes in this population are poor, and use of second-line systemic therapy is infrequent. Research Sponsor: None.

9569 Poster Session (Board #335), Fri, 8:00 AM-11:00 AM

Angiogenesis inhibitor plus erlotinib versus erlotinib alone as first-line for advanced non-small cell lung-cancer harboring EGFR mutation. *First Author: Thierry Landre, UCOG-HUPSSD-APHP, Paris, France*

Background: Erlotinib is indicated in first line treatment for patients with Non-Small-Cell-Lung cancer (NSCLC) harbouring EGFR mutation. Addition of anti-VEGF in combination with erlotinib in this setting is controversial. **Methods:** We performed a meta-analysis of randomized trials comparing VEGF inhibitor plus erlotinib with erlotinib alone in first line treatment for advanced NSCLC harbouring EGFR mutation. The outcomes included overall survival (OS), progression-free survival (PFS) objective response rate (ORR), and median duration of response (DOR). A fixed-effect model was used. **Results:** Four studies evaluated bevacizumab + erlotinib (ARTEMIS, NEJ026, J025667, Stinchcombe et al), and one study evaluated ramucirumab + erlotinib (RELAY). These five eligible studies included 1230 non-squamous NSCLC patients (654 with Ex19del and 568 with Leu858Arg);. Most of the patients were women (63%), Asian (85%) and non-smokers (60%), with a median age of 64 years. The combination (anti-VEGF + erlotinib) was significantly associated with improvement of PFS (hazards ratio [HR]: 0.59, 95%CI: 0.51-0.69, p < 0.00001). Improvement in PFS was seen across all subgroups analyzed. Interim analysis of OS (HR: 0.90, 95%CI; 0.68-1.19, p = 0.45) and ORR (odds ratio [OR], 1.19, 0.91-1.55, p = 0.21) were not statistically significant. DOR was statistically longer with combination (p < 0.005). **Conclusions:** For patients with untreated advanced NSCLC with EGFR mutation, the anti-VEGF combination with erlotinib, compared with erlotinib alone, is associated with significantly improved PFS and DOR, but mature data for OS are needed to confirm the benefit of this strategy. Research Sponsor: None.

9570 Poster Session (Board #336), Fri, 8:00 AM-11:00 AM

Osimertinib in non-small cell lung cancer (NSCLC) with atypical EGFR activating mutations: A retrospective multicenter study. *First Author: Jingran Ji, University of California Davis Comprehensive Cancer Center, Sacramento, CA*

Background: Osimertinib (osi) is a 3rd generation EGFR tyrosine kinase inhibitor (TKI) approved for first line (1L) treatment of metastatic NSCLC harboring EGFR Exon 19 del and L858R (representing > 80% of EGFR activating mutations) or in NSCLC with $EGFR^{T790M}$ (the most common resistance mutation to 1st or 2nd generation TKI). However, it has not been well-studied in EGFR-mutant NSCLC harboring less common EGFR activating mutations such as G719X, L861Q, S768I, and exon 20 insertion (ins), among others. **Methods:** We conducted a multi-institution, retrospective study approved on institutional IRB protocols in a series of patients (pts.) with metastatic NSCLC treated with osi who harbored at least one atypical EGFR mutation, excluding those with concurrent L858R, Exon 19 del, or T790M. Kaplan-Meier analyses were generated with SPSS, v25 (IBM Corp., USA). Response was assessed by RECIST 1.1 in evaluable pts. Time on osi was employed as a surrogate endpoint for clinical benefit in this retrospective analysis. **Results:** Fifty-one NSCLC pts with uncommon EGFR mutations were identified among six US institutions. Pt characteristics: 72.5% women, median age 65 yo (44-83 yo), 82.3% ECOG PS 0-1, 43.1% never smoker, 100% lung adenocarcinoma, 58.8% Caucasian, 25.5% Asian, 3.9% Black, 2.0% Hispanic, and 9.8% Other. The most frequent mutations were L861Q (35.3%, N = 18), G719X (27.5%, N = 14), and Exon 20 ins (15.7%, N = 8). Osi was used in the 1L setting in 39.2% (N = 20). Median time on osi was 7.1 months (mo.) in the overall cohort (95% CI, 5.4 to 8.8 mo.) and 8.9 mo. (95% CI, 7.0 to 10.8 mo.) in pts receiving 1L osi. Patients harboring G719X (N = 4) and L861Q (N = 10) mutations had a median time on 1L osimertinib of 5.8 mo. and 19.3 mo., respectively. One patient's tumor had an EGFR exon 19 ins and was on 1L osi with a partial response for 16.8 months. Two patients with Exon 20 ins were on 1L osi for 9.3 mo. and 8 mo., respectively. **Conclusions:** In this largest known clinically annotated dataset of patients with atypical EGFR-mutations treated with osi, activity was noted, though 1L clinical benefit on osi appears lower in this multicenter US cohort than in E19del or L858R. These results are comparable to the recently published prospective phase II trial (*Cho et al*, 2019) conducted in Korea. Patients with L861Q and Exon 19 insertion appeared to benefit the most from osi in this time on treatment retrospective analysis. More detailed analysis of this cohort is planned and further prospective studies are warranted to determine clinical benefit of osi amongst diverse atypical EGFR-mutations. Research Sponsor: None.

9571 Poster Session (Board #337), Fri, 8:00 AM-11:00 AM

Intracranial anti-tumor activity of lazertinib in patients with advanced NSCLC who progressed after prior EGFR TKI therapy: Data from a phase I/II study. *First Author: Sang-We Kim, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea*

Background: Lazertinib (YH25448) is a highly mutant-selective, irreversible 3rd-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) that targets the activating EGFR mutations (Del19 and L858R), as well as the T790M mutation, while sparing wild type. Brain metastasis (BM) are common in patients (pts) with advanced NSCLC. Lazertinib showed a high blood-brain barrier penetration profile in pre-clinical studies. We report intracranial response data in pts with advanced NSCLC from a Phase I/II study of lazertinib (NCT03046992). **Methods:** Pts with advanced NSCLC, who had progressed after prior EGFR-TKI therapy, were enrolled in an open-label, multicenter, phase I/II study with dose-escalation, dose-expansion and dose-extension phases. Brain MRI was done in all pts at baseline. Pts with asymptomatic BM were eligible for enrollment. Intracranial anti-tumor activity of lazertinib was analysed in pts with BM present on baseline brain scan. Pre-defined intracranial endpoints included objective intracranial response rate (OIRR) and intracranial progression-free survival (IPFS) by independent central review (ICR). The brain metastasis full analysis population included pts with measurable and/or non-measurable BM lesion present on baseline brain scan; the brain metastasis population evaluable for response included only pts with measurable BM lesion. **Results:** As of 30 Sep 2019, a total of 181 pts received at least one dose of lazertinib 20-320 mg across 7 dose levels. Of those, 64 pts (56% female, median age 63, 86% T790M mutation positive by central testing) were included in the brain metastasis full analysis population; Intracranial disease control rate (IDCR) was 90.6% (58/64; 95% CI 83.5, 97.8) and median IPFS was not reached (95% CI 14.0, NR). In the brain metastasis population evaluable for response, a total of 22 pts were included; OIRR and IDCR were 54.5% (12/22; 95% CI 33.7, 75.4) and 90.9% (20/22; 95% CI 78.9, 100), respectively. In 13 pts (7.2%) out of 181 pts, brain was the first site of disease progression by existing and/or new lesions. **Conclusions:** Lazertinib demonstrated clinically meaningful activity against BM, aligned with preclinical data. Clinical trial information: NCT03046992. Research Sponsor: Yuhan Corporation, Other Government Agency.

9572 Poster Session (Board #338), Fri, 8:00 AM-11:00 AM

Efficacy and safety of lazertinib 240 mg as the clinical dose in patients with EGFR T790M mutant NSCLC: Data from a phase I/II study. *First Author: Ki Hyeong Lee, Division of Medical Oncology, Department of Medicine, Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, South Korea*

Background: Lazertinib (YH25448) is a highly mutant-selective, irreversible 3rd-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) that targets the activating EGFR mutations (Del19 and L858R), as well as the T790M mutation, while sparing wild type. We report the efficacy and safety results of lazertinib 240 mg as recommended phase 2 dose (RP2D) from a phase I/II study of lazertinib (NCT03046992). **Methods:** Patients (pts) with advanced NSCLC, who had progressed after prior EGFR-TKI therapy were enrolled in an open-label, multicenter, phase I/II study with dose-escalation (20-320 mg), dose-expansion (40-240 mg) and dose-extension phases. Pts were assessed for safety, tolerability, pharmacokinetics and efficacy. For dose-expansion and extension phases, tumors had to be T790M mutation-positive (T790M+). Of all 78 pts assigned to lazertinib 240 mg dose level across all phases, 76 pts with centrally confirmed T790M+ were included for efficacy analysis. **Results:** As of 30 Sep 2019, a total of 78 pts (49% female, median age 62) received at least one dose of lazertinib 240 mg. The median duration of follow-up was 9.6 months and 44 pts were ongoing at data cut-off. Of 78 pts, 76 pts with centrally confirmed T790M+ showed the objective response rate (ORR) 57.9% (95% CI 46.8, 69.0), the disease control rate (DCR) 89.5% (95% CI 82.6, 96.4), the median progression-free survival (PFS) 11.0 months (95% CI 5.6, 16.4) and the median duration of response (DoR) 13.8 months (95% CI 9.6, NR) by independent central review (ICR), respectively. Two pts (3%) experienced a confirmed complete response. The investigator-assessed ORR, DCR, median PFS and median DoR were 72.4% (95% CI 62.3, 82.4), 94.7% (95% CI 89.7, 99.8), 13.2 months (95% CI 9.6, not reached) and 11.8 months (95% CI 8.4, not reached), respectively. The most common treatment-emergent adverse events (TEAEs) at the 240 mg dose regardless of its causality were rash (35%), pruritus (33%) and paraesthesia (32%), which were mostly mild (Grade ≥3 rash: 1%; no Grade ≥3 pruritus or paraesthesia). TEAEs leading to dose reduction and dose discontinuation were observed in 13% (10/78) and 8% (4/78), respectively. Drug related TEAEs of grade ≥3 were observed in 6% (5/78). **Conclusions:** Lazertinib 240 mg has a favorable safety profile, and exhibits promising anti-tumor activity in pts with EGFR T790M+ NSCLC. Clinical trial information: NCT03046992. Research Sponsor: Yuhan Corporation, Other Government Agency.

9573 Poster Session (Board #339), Fri, 8:00 AM-11:00 AM

Study of anlotinib combined with icotinib as the first-line treatment in non-small cell lung cancer (NSCLC) patients harboring activating EGFR mutations (ALTER-L004). *First Author: Dingzhi Huang, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China*

Background: Anti-angiogenic monoclonal antibodies plus EGFR TKIs have previously shown to prolong PFS in patients with EGFR-mutated NSCLC (JO25567 and NEJ026). Unlike bevacizumab, anlotinib is more convenient with orally administered and can inhibit more targets. Monotherapy using anlotinib has significantly prolonged median PFS and OS compared with the placebo values for third-line treatment or beyond in advanced NSCLC. We conducted a study to investigate the activity of anlotinb combined with icotinib, an oral EGFR TKI. **Methods:** This is a prospective, single-arm, multicenter clinical trial. Patients with locally advanced and/or metastatic IIIB, IIIC or IV non-squamous NSCLC are enrolled. Patients with EGFR exon 19 deletion and/or exon 21 L858R mutation who have not received prior therapies are eligible. The regimen consists of anlotinib (12 mg p.o, qd, day 1 to 14 every 21-day cycle) and icotinib (125mg p.o, tid). The primary endpoint is PFS. Secondary endpoints are OS, ORR, DCR and safety. **Results:** Between Jul 2018 and Dec 2019, 35 patients were enrolled in five centers and treated with anlotinb and icotinib. At data cutoff (Jan 7, 2020), patients were followed up for a median of 6.01 months.32 tumors were analyzed with 30 evaluable. Preliminary efficacy results: ORR was 59% (0 CR, 19 PR), DCR was 88% (0 CR, 19 PR, 9 SD). 26 patients are still receiving treatment and the longest exposure was 14 cycles. 10 (67%) of 15 patients with exon 19 deletions and 9 (53%) of 17 patients with L858R mutations achieved an objective response. 18 patients harbored aberrations in additional oncogenic drivers (PIK3CA or AKT1) and/or tumor suppressors (TP53, RB1, and PTEN) with an ORR of 72%. Upon analyses, AEs were observed in 97% (34/35) of patients. No Gr 5 AEs were reported. The most common Grade 3 AEs were hypertension (6 [17%]), hypertriglyceridemia (2 [6%]), diarrhea (1 [3%]), hyperuricemia (1 [3%]), hand and foot skin reaction (1 [3%]), asthenia (1 [3%]), and acute coronary syndrome (1 [3%]). Hypertriglyceridemia was the only grade 4 AE (2 [6%]). Three patients had to adjust treatment dosage. **Conclusions:** The strategy of anlotinib plus icotinib showed encouraging efficacy for previously untreated, EGFR-mutated advanced NSCLC patients. The combination was well tolerated and the AEs were manageable. The follow-up time is not sufficient and the PFS and OS outcomes need further evaluation. Clinical trial information: NCT03736837. Research Sponsor: None.

9574 Poster Session (Board #340), Fri, 8:00 AM-11:00 AM

Nazartinib (EGF816) in patients with treatment-naïve *EGFR*-mutant non-small cell lung cancer (NSCLC): Updated phase II results. *First Author: Daniel Shao-Weng Tan, National Cancer Centre Singapore, Singapore, Singapore*

Background: Prior data from a phase I/II study showed durable responses, including efficacy in brain lesions, and a tolerable safety profile with nazartinib in treatment (tx)-naïve patients (pts) with *EGFR*-mutant (mut), locally advanced (adv)/metastatic NSCLC. Here we report updated phase II results, including overall survival (OS). **Methods:** Tx-naïve adult pts with activating *EGFR*-mut (L858R or ex19del), stage IIIB/IV adv NSCLC with neurologically stable and controlled brain metastasis (BM) received oral nazartinib 150 mg once daily (continuous schedule). Primary endpoint: overall response rate (ORR) by BIRC per RECIST v1.1; secondary endpoints: disease control rate (DCR), duration of response (DOR), time to response, progression-free survival (PFS), OS, and safety. **Results:** At data cut-off (Nov 1, 2019), 45 pts were enrolled (median [range] age: 64 [28–83] years; 26 pts [58%] ECOG PS 1; 18 pts [40%] had baseline BM). *EGFR* mutations: 56% ex19del, 40% L858R, 4% other. 26/45 pts (58%) discontinued tx, with the primary reason being progressive disease in 19 pts (42%); 2 pts (4%) discontinued tx due to AEs. Median (range) follow-up for OS: 25 (0–33) months (mo); and for PFS: 17 (0–33) mo. ORR by BIRC: 69%; median PFS by BIRC: 18 mo; median OS was NE and at 33 mo, 56% of pts were alive (Table). BIRC results by baseline BM are shown in the Table. Median (range) duration of exposure: 24 (0–34) mo. Most frequent AEs (≥20% all grade, all causality): diarrhea (47%), maculopapular rash (38%), pyrexia (29%), cough and stomatitis (27% each), decreased appetite and pruritus (24% each), and dermatitis acneiform (22%). Most frequent grade 3/4 AEs (≥10%, all causality): maculopapular rash (5 pts [11%]; all grade 3) and increased lipase (5 pts [11%]; 1 pt with grade 4; no clinical pancreatitis AE was observed). **Conclusions:** After additional follow-up, median OS was still not reached and the safety profile was manageable. Nazartinib is a promising 3rd generation EGFR TKI for tx-naïve pts with adv *EGFR*-mut NSCLC, including pts with baseline BM. Clinical trial information: NCT02108964. Research Sponsor: Novartis Pharmaceuticals.

	BM – Yes N=18	BM – No N=27	All Pts N=45
ORR, n (%) (95% CI)	12 (67) (41–87)	19 (70) (50–86)	31 (69) (53–82)
DCR, n (%) (95% CI)	18 (100) (82–100)	23 (85) (66–96)	41 (91) (79–98)
Median DOR, mo (95% CI)	15 (9–25)	NE (15–NE)	25 (14–NE)
Events, n (%)	9 (75)	6 (32)	15 (48)
24-mo rate, % (95% CI)	33 (10–59)	65 (38–83)	52 (33–68)
Median PFS, mo (95% CI)	17 (11–21)	NE (15–NE)	18 (15–NE)
Events, n (%)	12 (67)	12 (44)	24 (53)
24-mo rate, % (95% CI)	27 (8–50)	51 (30–69)	42 (26–56)
Median OS, mo (95% CI)			NE (23–NE)
Events, n (%)			15 (33)
33-mo rate, % (95% CI)			56 (33–74)

9575 Poster Session (Board #341), Fri, 8:00 AM-11:00 AM

Tepotinib in patients (pts) with NSCLC with *MET* exon 14 (*MET*ex14) skipping: Health-related quality of life (HRQoL). *First Author: Paul K. Paik, Thoracic Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: In the phase II VISION study (NCT02864992) tepotinib had promising efficacy (response rate of 40–50% & median duration of response >1 y) and tolerable safety in pts with advanced NSCLC with *MET*ex14 skipping (3–4% of NSCLC), who are typically elderly with poor prognosis. Pt reported outcomes (PROs) of HRQoL are described here. **Methods:** Pts with advanced NSCLC positive for *MET*ex14 skipping by tissue or liquid biopsy received oral tepotinib 500 mg once daily; PROs were assessed using QLQ-LC13 (lung cancer symptoms), EORTC QLQ-C30 (Global health status [GHS] & 5 functional scales), and EQ-5D-5L (VAS). Questionnaires were completed at baseline (BL) and every 6 weeks (Wk); results were scored from 0–100 (minimal clinically important difference [MCID] ≥10 points). Mean change from BL was analyzed at Wk 12 (predefined analyses). **Results:** By 19 Jul 19 cut-off, 130 pts across treatment lines were enrolled (median age 74.2 y), with PROs available for 129. Questionnaire completion rates were 90.1% at Wk 12. Symptom burden at BL was moderate for advanced NSCLC; mean change from BL for PROs are shown in the table (better functioning: lower QLQ-LC13 or higher QLQ-C30 scores). For the QLQ-LC13 symptoms, mean changes from BL indicated a meaningful improvement in coughing, with a median time to improvement (2.8 months) paralleling the onset of objective response (within first 3 months), and a numerical improvement in dyspnea (–2.3 at Wk 12) and chest pain (–4.2 at Wk 12). QLQ-C30 values remained stable over treatment as did EQ-5D-5L scores (higher=better): mean (standard deviation, SD) change from BL score (60 [20.4]) was 6 (18.6) at Wk 6 and 5 (20.9) at Wk 12. **Conclusions:** In this first analysis of PROs in pts with advanced NSCLC with *MET*ex14 skipping with a moderate symptom burden, treatment with tepotinib led to a clinically meaningful improvement in coughing symptoms, while maintaining HRQoL. Coupled with the efficacy and safety profile, the predefined HRQoL analysis from the VISION study supports tepotinib as a promising treatment option for this elderly population with *MET*ex14+ NSCLC. Clinical trial information: NCT02864992. Research Sponsor: Merck KGaA.

			Mean change (SD):	
MCID: ≥10 points		**BL mean (SD)**	**Wk 6**	**Wk 12**
QLQ-LC13	Cough	36.0 (29.6)	–14.2 (28.6)	–11.6 (32.3)
	Dyspnea	31.4 (25.2)	–4.0 (15.5)	–2.3 (19.9)
	Chest pain	19.8 (27.7)	–8.4 (20.6)	–4.2 (25.0)
QLQ-C30	GHS	53.2 (24.4)	10.0 (21.6)	6.7 (20.5)
	Functional scales			
	Physical	31.0 (24.6)	–2.1 (16.4)	–0.3 (16.7)
	Role	34.5 (32.1)	–3.8 (25.5)	–4.8 (29.6)
	Cognitive	20.1 (23.7)	–2.0 (17.5)	1.3 (22.7)
	Emotional	30.0 (24.0)	–6.4 (19.9)	–7.1 (20.3)
	Social	27.7 (30.1)	–8.4 (24.9)	–3.7 (27.2)

9576 Poster Session (Board #342), Fri, 8:00 AM-11:00 AM

Lung-MAP (SWOG S1400): Design, implementation, and lessons learned from a biomarker-driven master protocol (BDMP) for previously-treated squamous lung cancer (sqNSCLC). *First Author: Mary Weber Redman, Fred Hutchinson Cancer Research Center, Seattle, WA*

Background: S1400, a BDMP, was designed to address an unmet need in sqNSCLC, run within the National Clinical Trials Network of the National Cancer Institute using a public-private partnership (PPP). The goal of was to establish an infrastructure for biomarker-screening and rapid evaluation of targeted therapies in biomarker-defined groups leading to regulatory approval. **Methods:** S1400 included a screening part using the FoundationOne assay and a clinical trial part with biomarker-driven studies (BDS) and "non-match" studies (NMS) for patients not eligible for any BDS. Patients could be screened (SaP) at progression or pre-screened (PreS). **Results:** Between June 2014 and January 2019, 1864 patients enrolled (711 PreS, 1079 SaP), 1674 with biomarker results, and 653 registered to a study with 217 to BDS and 436 to NMS. Six BDS and 3 NMS were initiated in small subsets with all BDS and 2 NMS completed within 2-3 years (see Table). Completed BDS have not demonstrated activity with 0-2 responses. On S1400I, Nivolumab and ipilimumab did not improve survival. Response with durvalumab (S1400A) was 16%. **Conclusions:** Lung-MAP met its goal to quickly answer targeted and other novel therapy questions in rare sqNSCLC subpopulations, answering questions that likely would not have been otherwise feasible, thereby demonstrating value. Activated just prior to the success of PD-(L)1 therapies in sqNSCLC, the trial had to undergo major design changes. Lessons learned include the need to update based on new science and that the PPP collaboration was essential to success. Lung-MAP continues now with new BDS and NMS in all NSCLC as of January 2019. Clinical trial information: NCT02154490. Research Sponsor: U.S. National Institutes of Health, Public-private partnership through Foundation for the NIH.

Clinical studies.

	Biomarker/Population	Therapy	Design	N	Endpoint	Open Date, Duration
S1400A	Immune-checkpoint inhibitor naive (ICIN)	Durvalumab	Single arm phase 2 (SAP2)	116	Response by RECIST 1.1 (R)	6/14 18 months(mths)
S1400B	PI3KCA	Taselisib	SAP2	26	R	6/14 30 mths
S1400C	Cell Cycle Gene Alterations	Palbociclib	SAP2	36	R	6/14 27 mths
S1400D	FGFR	AZD4547	SAP2	27	R	6/14 28 mths
S1400E	c-MET by IHC	Rilotumumab + Erlotinib versus (v) Erlotinib	Phase 2/3	9	R	6/14 5 mths
S1400F	NMS, PD-(L)1 exposed	Durvalumab + Tremelimumab	SAP2	30 acquired ICI resistant (AR) 36 primary ICI resistant (PR)	R	AR: 10/17 25 mths PR: 10/17 On-going
S1400G	Homologous recombinant repair deficiency genes	Talazoparib	SAP2	51	R	2/17 17 mths
S1400I	NMS ICIN	Nivolumab + Ipilimumab v. Nivolumab	Phase 3	275	Overall survival	12/15 28 mths
S1400K	c-MET by IHC	ABBV-399	SAP2	28	R	2/18 10 mths

9577 Poster Session (Board #343), Fri, 8:00 AM-11:00 AM

Clinicopathologic characteristics and immunotherapy outcomes in SMARCA4-mutant (mut) non-small cell lung cancer (NSCLC). *First Author: Joao Victor Machado Alessi, Dana-Farber Cancer Institute, Boston, MA*

Background: The catalytic unit of the SWI/SNF chromatin remodeling complex is encoded by the SMARCA4 gene, which is mutated in ~10% of NSCLCs. We sought to characterize the clinicopathologic characteristics and outcomes to immune checkpoint inhibition in SMARCA4-mutant NSCLC. **Methods:** We collected clinicopathologic and genomic data from patients with NSCLC that had undergone targeted next generation sequencing (NGS) by OncoPanel at the Dana-Farber Cancer Institute. SMARCA4 frameshift, nonsense, and splice-site mutations were considered pathogenic, as were missense mutations if predicted to be pathogenic by Mutation Assessor and Polyphen-2. Clinical outcomes to immune checkpoint inhibition among SMARCA4-mutant NSCLCs were retrospectively assessed. **Results:** Of 2690 patients with NSCLC, 8% (N = 211) harbored SMARCA4 mutations. Clinicopathological characteristics were balanced between SMARCA4 mut and SMARCA4 wild-type (wt) in terms of age, histology, and PD-L1 expression. We observed a male predominance (P = 0.03), greater use of tobacco (P < 0.001), a higher tumor mutational burden (TMB) (P < 0.001), a higher prevalence of advanced disease (P < 0.001), and a lower prevalence of concurrent targetable driver mutations (P < 0.001) in SMARCA4mut vs SMARCA4wt NSCLCs. Among 513 patients with nonsquamous NSCLC who received immune checkpoint inhibitors, 11% (N = 57) harbored SMARCA4 mutations. From the start of immunotherapy, we observed no difference in overall response rate (ORR 21.5% vs 19.3%; P = 0.3), median progression free survival (mPFS 3.2 months vs 2.1 months; P = 0.4), or median overall survival (mOS 12.0 months vs 8.2 months; P = 0.09) in SMARCA4wt vs SMARCA4mut NSCLC, respectively. However, among KRASmut NSCLC, a concurrent SMARCA4 mut conferred a significantly lower ORR (23.1% vs 0.0%; P = 0.02), a significantly shorter mPFS (4.8 months vs 1.7 month; HR: 0.31 [95% CI: 0.15-0.61]; P < 0.001), and a significantly shorter mOS (15.6 months vs 2.7 months; HR: 0.25 [95%CI: 0.12-0.49]; P < 0.001). The deleterious effect of SMARCA4 mut on immunotherapy outcomes in KRAS mut NSCLC was maintained when controlling for concurrent STK11 mut. **Conclusions:** SMARCA4 mutations define a genomic subset of NSCLC with unique clinicopathologic characteristics, and confer worse outcomes to immunotherapy in KRAS mut NSCLC. Research Sponsor: None.

9578 Poster Session (Board #344), Fri, 8:00 AM-11:00 AM

***FOXO3* polymorphisms were correlated with gefitinib-induced hepatotoxicity in patients with non-small cell lung cancer.** *First Author: Shaoxing Guan, Laboratory of Drug Metabolism and Pharmacokinetics, School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, China*

Background: Drug-induced liver injury (DILI) is one of the most safety concern in drug development and clinical therapy. Severe hepatotoxicity of gefitinib often leads to acute/chronic liver injury, drug discontinuation and further treatment failure, however, the mechanism of gefitinib-induced hepatotoxicity remains unclear. *AKT1/FOXO3* regulates expression of genes involved in multiple biological/pathological processes in liver cells, including apoptosis, oxidative stress, and cell-cycle transition, as well as expression of autophagy-related (Atg) genes. Therefore, we investigated the correlation between single nucleotide polymorphisms (SNP) in *AKT1/FOXO3* and gefitinib-induced hepatotoxicity in patients with advanced non-small cell lung cancer (NSCLC). **Methods:** A total of 172 advanced NSCLC patients with activating *EGFR* mutations were enrolled and administered with gefitinib 250mg daily. 22 tag SNPs in *AKT1/FOXO3* were selected by Heploview 4.2 and sequenced by Agena MassARRAY System. The associations between polymorphisms of *AKT1/FOXO3* and gefitinib-induced hepatotoxicity were analyzed by Chi square test. This study was approved by the ethical committee of Sun Yat-Sen University Cancer Center. **Results:** *FOXO3* rs4946935 and *FOXO3* rs75544369 were found to be associated with gefitinib-induced hepatotoxicity in NSCLC patients. *FOXO3* rs4946935 AA carriers have higher risk of developing gefitinib-induced hepatotoxicity than those with *FOXO3* rs4946935 AG/GG. ($P = 0.018$, OR = 12.414, 95%CI (1.53-100.711)). Patients with *FOXO3* rs75544369 GA have higher risk of developing hepatotoxicity with *P* of 0.0002 (OR = 5.241, CI%(1.85-14.851)), or developing severe hepatotoxicity with *P* of 0.033 (OR = 2.963, 95%CI (1.090-8.059)), than those with *FOXO3* rs75544369 GG. **Conclusions:** *FOXO3* rs4946935 and *FOXO3* rs75544369 are predictive biomarkers for gefitinib-induced hepatotoxicity in NSCLC patients. The mechanism underlying the association between *FOXO3* polymorphisms and gefitinib-induced hepatotoxicity are worth investigating in further studies. Clinical trial information: NCT01994057. Research Sponsor: National Natural Science Foundation of China.

9579 Poster Session (Board #345), Fri, 8:00 AM-11:00 AM

Is checkpoint inhibitor pneumonitis underreported in patients with advanced non-small cell lung cancer (NSCLC) on PD-1 inhibitor monotherapy? *First Author: Benjamin Oren Spieler, University of Miami Miller School of Medicine, Miami, FL*

Background: For patients with advanced non-small cell lung cancer (NSCLC), immunotherapy (ImT) has led to improvements in survival and quality of life. Checkpoint inhibitor pneumonitis (CIP) is an uncommon but sometimes life-threatening adverse event. While CIP is a diagnosis of exclusion, many oncologists believe the incidence of CIP is underreported. Radiomics, an image analysis technique that can extract imperceptible information from radiographic images, has been incorporated into predictive models for many cancers. Recent studies suggest that radiomic analysis of pre-ImT imaging can predict CIP. We hypothesized that for patients with advanced NSCLC treated with Nivolumab monotherapy, the rate of CIP is underreported and radiomics features can identify CIP that was clinically misclassified. **Methods:** From an IRB-approved database (DB) of 159 patients with advanced NSCLC treated with Nivolumab, chart review identified 8 patients diagnosed with CIP of any grade (5%). 42 additional patients from the same DB without diagnosis of CIP were randomly selected for analysis. For all 50 patients, uninvolved lung in the last pre-ImT CT imaging study was segmented, delineated, and analyzed for radiomics features associated with CIP. A logistic regression model incorporating radiomics assigned a CIP probability score to every patient. **Results:** Six radiomics features correlated with CIP (*p*-values range from 0.02 to 0.03). Each feature had an AUC of ~0.79 (range 0.789 to 0.794) showing large effect size, with odds ratios greater than 3.50 (4 features) or less than 0.3 (2 features). The radiomics-based probability model assigned 7/42 patients (17.5%) without clinical diagnosis of CIP a greater than 50% probability of CIP. Chart review revealed that 6/7 "misclassified" patients exhibited symptoms or radiographic features highly suggestive of CIP within 5 months of initial immunotherapy treatment. These indications originally had been attributed to disease progression, overshadowed by more severe symptoms or simply mislabeled (e.g. a case of recall pneumonitis was described as "radiation pneumonitis"). **Conclusions:** For patients with advanced NSCLC treated with nivolumab, the incidence of checkpoint-inhibitor pneumonitis (CIP) is underreported and radiomics features can help identify CIP that has been clinically misclassified. Future directions include expansion of this study across the full database, correlation of radiomics features with blood biomarkers, and the inclusion of tumor burden as an additional covariate in the analysis. Research Sponsor: None.

9580 Poster Session (Board #346), Fri, 8:00 AM-11:00 AM

Indirect comparison of TAK-788 vs real-world data outcomes in refractory non-small cell lung cancer (NSCLC) with *EGFR* exon 20 insertions. *First Author: Leora Horn, Vanderbilt-Ingram Cancer Center, Nashville, TN*

Background: Currently approved epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) are ineffective in patients (pts) with *EGFR* exon 20 insertion NSCLC. TAK-788 is an EGFR TKI with potent and selective preclinical inhibitory activity against *EGFR* exon 20 insertions, and has demonstrated preliminary efficacy in a single-arm phase 1/2 clinical trial (NCT02716116). We performed an indirect comparison of real-world outcomes with clinical trial data for this subset of pts to determine whether TAK-788 provides superior efficacy over standard treatment options. **Methods:** We compared efficacy in pts with refractory NSCLC with *EGFR* exon 20 insertions treated with TAK-788 160 mg qd (1–7 prior lines) from the ongoing clinical trial (data cut Mar 1, 2019) vs real-world data (RWD) in the second-line setting from the US Flatiron Health electronic health record–derived database (Jan 2011–Jun 2018). This analysis was conducted using an unadjusted data set, as well as by applying propensity score modeling with inverse probability of treatment weighting (IPTW) to adjust for group differences in key baseline characteristics. Progression-free survival (PFS) and objective response rate (ORR) were compared between groups. **Results:** A total of 99 pts were included, n=28 TAK-788 and n=71 RWD; mean age 62/65 y; male 25%/46%; Asian 18%/10%; former smoker 39%/45%; brain metastases 43%/34%. In the RWD, there was no consistent regimen for second-line treatment (including 29.6% immuno-oncologic agents, 25.4% EGFR TKI, 10% docetaxel). Baseline characteristics were comparable after weighting. PFS and ORR showed statistically significant improvements with TAK-788 vs RWD (Table). Specifically, after weighting, median PFS for TAK-788 vs RWD is 7.3 vs 3.5 mo, and ORR is 43% vs 13%. **Conclusions:** Despite a more heavily pretreated pt population, the efficacy of TAK-788 in pts with refractory NSCLC with *EGFR* exon 20 insertions appears better than other second-line treatment options used in the real-world setting. Clinical trial information: NCT02716116. Research Sponsor: Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

	TAK-788 (n=28)	RWD Unweighted (n=71)	RWD Weighted (n=71)
PFS[a] median, mo (95% CI)	7.3 (4.4, NE)	3.7 (2.6, 5.9)	3.5 (2.3, 5.9)
HR (95% CI)		0.50 (0.27, 0.92)	0.44[b] (0.22, 0.91)
Log-rank *P*		0.0235	0.0098
ORR, % (95% CI)	43 (25, 63)	14 (7, 24)	13 (0.4, 25)
Rate difference, % (95% CI)		29 (9, 49)	30 (8, 52)
OR (95% CI)		4.58 (1.68, 12.48)	5.14[c] (1.35, 19.65)
P		0.0030	0.0167

[a]Per investigator RECIST 1.1 for TAK-788 and clinician-reported tumor growth for RWD. [b]Cox regression model with IPTW. [c]Logistic regression model with IPTW. HR, hazard ratio; NE, not estimable; OR, odds ratio.

9581 Poster Session (Board #347), Fri, 8:00 AM-11:00 AM

SPRING: A Worldwide Innovative Network (WIN) Consortium phase I study of triple therapy (avelumab, axitinib, and palbociclib) in advanced non-small cell lung cancer (NSCLC) with genomic and transcriptomic correlates. *First Author: Benjamin Maurice Solomon, Avera Cancer Institute, Sioux Falls, SD*

Background: The Worldwide Innovative Network (WIN) Consortium has developed the Simplified Interventional Mapping System (SIMS) algorithm in order to predict treatment response by comparing tumor and normal tissue biopsies on both genomic and transcriptomic platforms. SPRING is the first trial to assess a SIMS-based tri-therapy regimen in advanced non-small cell lung cancer (NSCLC). **Methods:** Patients with advanced NSCLC (no *EGFR* or *ALK* alterations; no *ROS1* alterations if tested; PD-L1 unrestricted; $\leq$2 prior therapy lines) were treated with avelumab, axitinib, and palbociclib (3+3 dose escalation design). Tumor and normal endobronchial mucosal biopsies were obtained on all patients for retrospective SIMS algorithm validation. **Results:** Fifteen patients were treated: 6 at dose level 1 (DL1); 6, dose level 2 (DL2); 3, dose level 3 (DL3). Three dose-limiting toxicities (DLTs) at least possibly drug-related occurred: 1 DLT at DL2 (Grade 3 (G3) infusion reaction); 2 patients with DLTs at DL3 (1 with G3 hand/foot syndrome and G3 fatigue and 1 with G5 respiratory failure). Among 14 evaluable patients, the partial response (PR) rate was 28.6% (4/14 patients including 2/6 patients at DL1; two PRs in patients who failed prior pembrolizumab; two PRs in patients with PD-L1 $<$ 1%). The maximum tolerated dose was avelumab 10 mg/kg IV q2weeks, axitinib 5 mg PO BID continuous, palbociclib 75 mg PO daily on days 8-28 of a 28 day cycle (DL2). DL2 was above the recommended phase II dose (RP2D), since 5/6 patients treated at DL2 required later treatment delays and/or dose reductions, mostly due to neutropenia. To further evaluate DL1, 3 patients were added to this cohort (total of 6). Since no DLTs were seen at DL1, and 5 of 6 patients did not require dose reduction, DL1 (avelumab 10 mg/kg IV q2weeks, axitinib 3 mg PO BID continuous, palbociclib 75 mg PO daily on days 8-28 of a 28 day cycle) is the RP2D. **Conclusions:** The RP2D was determined to be dose level 1. This triplet showed antitumor activity in patients with NSCLC, including those progressing on prior pembrolizumab. SIMS algorithm correlates of response are being assessed. Clinical trial information: NCT03386929. Research Sponsor: ARC Foundation for cancer research, Villejuif, France, Pharmaceutical/Biotech Company.

9582 Poster Session (Board #348), Fri, 8:00 AM-11:00 AM

Final analysis of KEYNOTE-189: Pemetrexed-platinum chemotherapy (chemo) with or without pembrolizumab (pembro) in patients (pts) with previously untreated metastatic nonsquamous non-small cell lung cancer (NSCLC). *First Author: Delvys Rodriguez-Abreu, Complejo Hospitalario Universitario Insular Materno-Infantil de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas De Gran Canaria, Spain*

Background: The phase III KEYNOTE-189 study (NCT02578680), showed significant improvements in OS and PFS with pembro + chemo vs placebo + chemo in pts with previously untreated metastatic nonsquamous NSCLC without sensitizing *EGFR/ALK* mutations. We report the protocol-specified final analysis of KEYNOTE-189. **Methods:** Pts were randomized 2:1 to receive 35 cycles of pembro 200 mg Q3W (n = 410) or placebo Q3W (n = 206) plus 4 cycles of pemetrexed (pem) and carboplatin/cisplatin followed by maintenance pem. Pts in the placebo + chemo arm could crossover to pembro upon PD. PFS and OS were primary endpoints; ORR was a secondary endpoint. PFS2 (time from randomization to objective tumor progression on next-line treatment/death), was an exploratory endpoint. **Results:** At data cutoff (May 20, 2019), median (range) time from randomization to data cutoff was 31.0 (26.5–38.8) mo. 17 pts in the pembro + chemo arm and 1 pt in the placebo + chemo arm were receiving initially assigned treatment; 84 pts crossed over to pembro. Median (95% CI) OS (22.0 [19.5–24.5] vs 10.6 [8.7–13.6] mo; HR 0.56 [95% CI, 0.46–0.69]) and PFS (9.0 [8.1–10.4] vs 4.9 [4.7–5.5] mo; HR 0.49 [95% CI, 0.41–0.59]) were longer with pembro + chemo vs placebo + chemo (Table). The 2-y OS rate was 45.7% vs 27.3% and the 2-y PFS rate was 22.0% vs 3.4%. ORR was 48.3% with pembro + chemo vs 19.9% with placebo + chemo. 56 pts in the pembro + chemo arm completed 35 cycles of pembro among whom ORR was 85.7% (4 CR, 44 PR, 8 SD) and median OS was not reached. 292 (72.1%) pts in the pembro + chemo arm and 135 (66.8%) pts in the placebo + chemo arm had grade 3–5 AEs. **Conclusions:** Pembro + chemo continued to show improved outcomes in OS, PFS, ORR and PFS2 compared with placebo + chemo, with manageable toxicity. These findings support first-line pembro + chemo in pts with previously untreated metastatic nonsquamous NSCLC. Clinical trial information: NCT02578680. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

HR (95% CI)	All pts N = 616	PD-L1 TPS ≥50% n = 202	PD-L1 TPS 1-49% n = 186	PD-L1 TPS < 1% n = 190
OS	0.56 (0.46–0.69)	0.59 (0.40–0.86)	0.66 (0.46–0.96)	0.51 (0.36–0.71)
PFS	0.49 (0.41–0.59)	0.35 (0.25–0.49)	0.53 (0.38–0.74)	0.67 (0.49–0.93)
PFS2	0.50 (0.41–0.61)	0.52 (0.36–0.75)	0.57 (0.40–0.81)	0.47 (0.33–0.66)

9583 Poster Session (Board #349), Fri, 8:00 AM-11:00 AM

A phase Ib study of a novel c-MET, AXL and VEGFR-2 inhibitor ningetinib and gefitinib combination therapy in Chinese EGFR-TKI resistant NSCLC with T790M negative. *First Author: Hongyun Zhao, Department of Medical Oncology, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Sun Yat-sen University, Guangzhou, China*

Background: Ningetinib is a novel tyrosine kinase inhibitor, targeted at c-Met, Axl, VEGFR-2, Mer and Flt3. This phase Ib trial (NCT03758287) evaluated the safety, determined the recommended phase II dose (RP2D), and further explored the pharmacokinetic and efficacy of Ningetinib + Gefitinib in EGFR-TKIs acquired resistant NSCLC patients (pts) with T790M negative. **Methods:** Chinese Pts with advanced or metastatic NSCLC, acquired resistant to at least one EGFR-TKI, T790M negative were enrolled. Pts received Ningetinib 30, 40, 60 mg + Gefitinib 250mg orally once daily in dose-escalation (n = 12) by a Fibonacci 3+3 design. Expansion phase (n = 74, enrollment is ongoing) started at tolerated dosage. Safety, RP2D were primary endpoints; PK, antitumor activity were secondary endpoints. Non-mandatory tumor samples at baseline were collected for exploratory objectives. **Results:** Totally, 86 eligible pts were enrolled between Nov 2016 and Dec 2019, and received treatment (Ningetinib 30 mg, n = 36; 40 mg, n = 46; 60 mg, n = 4), with median age 56.7 years, 36% with baseline brain metastasis, 66%/33%/1% prior 1/2/3 lines EGFR-TKI treatment, respectively. Treatment-related adverse events (TRAEs) occurred in 82 (95%) pts, grade 3/4 in 32 pts (37%). Most common TRAEs (≥30%) were myocardial enzyme elevation (all grade 74.4%; grade 3-4 0%), transaminase elevation (73.3%; 2.3%), skin rash (60.5%; 3.5%), albuminuria (44.2%; 0%), coagulation abnormalities (mostly asymptomatic Fbp decrease; 37.2%; 15.1%), diarrhea (33.7%; 2.3%) and hypertension (32.6%; 11.6%). Two Dose limited toxicities were observed at 60 mg dosage (both were grade 3 Fbg decrease), RP2D was decided at 40 mg. Of 84 efficacy evaluable pts, ORR was 19.1% (16 PR), DCR was 91.7% (61 SD, 7 PD). Totally, 65 (75.6%) progression events occurred at data cut-off (9 Jan 2020), the median PFS for all pts was 4.4 months (95%CI 3.7-4.6). No PFS differences were found between pts grouped by 3rd TKIs history or brain metastasis. C-Met gene amplification by FISH was conducted in 72 pts (83.7%). Pts with higher gene copy number (GCN) responded better in treatment, ORR in the GCN ≥6 (n = 11), GCN ≥5 (n = 16) and GCN ≥3 (n = 37) subgroups was 36.4%, 25.0% and 21.6% respectively. **Conclusions:** Ningetinib was well tolerated at 30 mg and 40 mg dosage with Gefitinib 250 mg, the RP2D for Ningetinb was 40 mg. This combination therapy showed promising anti-tumor activity in prior EGFR-TKIs acquired resistant NSCLC pts with T790M negative. C-Met GCN was the potential efficacy biomarker. Clinical trial information: NCT03758287. Research Sponsor: HEC R&D Center, Sunshine Lake Pharma Co., Ltd.

9584 Poster Session (Board #350), Fri, 8:00 AM-11:00 AM

Genomic characterization of metastatic lung cancers. *First Author: Hui Yu, Department of Medical Oncology, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China*

Background: Lung carcinomas are most often diagnosed at stage IV, with metastases, which contribute to 90% of deaths of patients. Enormous efforts have been made in previous studies in seek of underlying mechanisms and treatments that prevent or cure metastases. However, few comprehensive conclusions have been drawn on organ-specific genomic landscapes and molecular dependencies of lung cancer metastases, largely due to limited sample sizes. **Methods:** We employed massive targeted next generation sequencing (NGS) with a panel covering 425 cancer-related genes on 10409 samples from 8619 patients with lung cancer, including 8479 from primary tumors and 1930 from metastases to the brain, liver, pleura, bones, and lymph nodes. We investigated single nucleotide variants (SNVs), copy number variants (CNVs), structural variations (SVs), mutational signatures, and other genomic characteristics at all primary and metastatic sites. With data of primary-metastatic tumor pairs, we also examined genomic evolutionary patterns. **Results:** Our data revealed that metastases harbored more instable and complicated genomes. Most SNVs (5/6), CNVs (41/47), and SVs (2/3) that showed significant differences of prevalence between primary tumors (PTs) and metastases (MTs) were MT-enriched. Among them, we identified a novel MT-enriched event, *PTK2* amplification (2.33 folds), as well as known ones including mutations of *TP53*, *ARID1A*, and *BRCA1* (1.23, 1.74, and 2.29 folds), and amplifications of *MYC*, *RICTOR*, and *EGFR* (2.04, 2.15, and 1.59 folds). In addition, almost all actionable CNV alterations (6/7) showed higher frequencies in MTs. *ALK* fusions and *EGFR* mutations, which indicate distinct target therapies, exhibited opposite preference in MTs and PTs, respectively. We also identified MT site-specificity of alterations, such as *NF2*, *TSC2*, and *LRP1B* mutations enriched in the brain, *BRAF* and *GNAS* mutations absent in the liver, and APOBEC-associated mutational signatures enriched in lymph nodes. Moreover, we unraveled organ-specific patterns of genomic evolutionary trajectories in metastatic diseases. **Conclusions:** The genomic profile and evolutionary pattern of metastatic lung cancer differed from that of primary tumors. The identification of site-specific characteristics that may have empowered directional metastasis, such as *NF2*, *TSC2*, and *LRP1B* mutations in the brain and APOBEC-associated mutational signatures in lymph nodes, may guide personalized disease management, design of clinical trials, and/or discovery of therapeutic targets for metastatic lung cancer at different body regions. Research Sponsor: None.

9585 Poster Session (Board #351), Fri, 8:00 AM-11:00 AM

A phase I, dose-escalation and expansion study of TQ-B3139, a novel ALK TKI, in Chinese ALK or ROS1 positive advanced non-small cell lung cancer (NSCLC). *First Author: Yuxiang Ma, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: TQ-B3139 is a novel ALK inhibitor with activity 3-7 folds higher than Crizotinib against a broad range of ALK mutations. This phase I study (NCT03099330) is to investigate the safety, and determine the recommended phase II dose (RP2D), and pharmacokinetic (PK), clinical efficacy of TQ-B3139 in Chinese NSCLC patients. **Methods:** Patients with advanced NSCLC and failed at least one systemic anti-cancer treatment were enrolled. TQ-B3139 was administered orally from 50mg~100mg qd and 200, 300, 400, 500, 600 and 800mg bid, using a PK-guided modified Fibonacci 3+3 dose escalation design. The dose-escalation evaluated patients in 28-day cycles, dose limited toxicities (DLTs) was observed at first cycle. Dose-expansion phase started at dose level which objective response occurs. Treatment was continued until disease progression, death or unacceptable toxicity. **Results:** Between July 2017 and May 2019, totally 63 patients (59 ALK+, 4 ROS1+) were enrolled. Sixteen patients had prior ALK inhibitor therapy (11 Crizotinib, 5 Ensartinib), and 23 (36.5%) with baseline brain metastasis. Totally, 62 (98.4%) patients experienced treatment-related adverse events (TRAEs), grade 3-4 TRAEs were observed in 21 (33.3%) patients. One DLT occurred in the 800mg bid dose cohort (grade 3 nausea and vomiting). Top 3 common TRAEs were nausea (all grade 87.3%; grade 3-4 3.2%), diarrhea (84.1%, 6.4%), transaminase elevation (65.1%, 4.8%). AUC and C_{trough} at steady state increased proportionally from 200mg to 600mg bid. Absorption saturation was observed in 800mg bid. Base on the safety and PK results, PR2D was decided at 600mg bid. Overall ORR was 73.0% (2 CR, 44 PR); DCR was 85.7% (8 SD). Objective response was observed from dose level 200mg bid cohort, ORR and DCR at ≥200mg bid was 78.0% and 89.8%. For ALK TKI-naïve and -resistant patients, the ORR was 78.7% (37/47) and 56.3% (9/16) respectively. For patients with measurable baseline brain metastasis, the ORR for brain lesions was 80.0% (8/10). At data cut-off (23 Jan 2020), 32 events (50.8%) occurred, the median PFS for all patients was 12.1 months (95%CI 8.5-15.6), for patients at ≥200mg bid dose was 12.2 months. The median PFS was not reached for -naive patients (6 months PFS rate 74.5%, 95%CI 68.1-80.9), and 5.6months (95%CI 1.6-9.5) for ALK TKI-resistant patients. **Conclusions:** TQ-B3139 was well tolerated in Chinese NSCLC patients with high antitumor activity. RP2D was established at 600mg bid. A randomized phase III trial of TQ-B3139 versus Crizotinib in advanced ALK-TKI naïve NSCLC patients is underway. Clinical trial information: NCT03099330. Research Sponsor: CHIA TAI TIANQING PHARMACEUTICAL GROUP CO., LTD.

9586 Poster Session (Board #352), Fri, 8:00 AM-11:00 AM

High-dose osimertinib for CNS progression in EGFR+ non-small cell lung cancer (NSCLC): A multi-institutional experience. *First Author: Andrew Piper-Vallillo, Beth Israel Deaconess Medical Center, Boston, MA*

Background: High-dose osimertinib 160 mg QD (osi160) has activity in osi-naïve, EGFR+ NSCLC pts with CNS or leptomeningeal disease (LMD) per the BLOOM trial, but the role of dose-escalation for CNS progression (PD) and/or LMD that develops while on 80 mg QD (osi80) is unclear. We describe here our multi-institutional experience with osi160. **Methods:** 105 pts from 8 institutions with advanced EGFR+ NSCLC treated with osi160 were retrospectively reviewed. To assess the CNS efficacy of dose escalation for CNS PD, we focused on pts who escalated from osi80 to osi160 for CNS PD without the addition of chemo and/or RT during dose escalation (cohort A, 24 pts). We also examined osi escalation for CNS PD while receiving chemo and/or RT (cohort B, 34 pts) and those who started on osi160 for CNS PD as the initial osi dose without overlapping therapies (cohort C, 11 pts). Radiographic responses were clinically assessed via chart review of scan reports. Kaplan-Meier analysis was used for time-to-event endpoints. We defined median duration of CNS disease control (MedDurCNSCon) on osi160 as time from the start of osi160 to CNS PD or discontinuation of osi160. **Results:** Among the 105 pts, 69 (26M, 43F; median age 57) EGFR+ NSCLC pts (29 del19, 31 L858R, 9 other) received osi160 for CNS PD between 10/2013 and 1/2020. Median lines of therapy pre-osi was 1 (range 0-8). While all 69 pts had CNS PD at the start of osi160, 61 (90%) had isolated CNS/LMD PD, without systemic PD. In cohort A, osi160 monotherapy had a MedDurCNSCon of 3.8 mos (95% CI, 1.7 – 5.8). Cohort A pts with isolated LMD (11) had MedDurCNSCon 5.8 mos (95% CI, 1.7 – 9) while those with parenchymal mets only (11) had MedDurCNSCon of 2 mos (95% CI, 1 - 4.9). In cohort B, osi160 in combination with RT (22) and/or chemo (14), had a MedDurCNSCon of 5.1 mos (95% CI, 3.1 – 6.5). In cohort C, osi160 monotherapy had a MedDurCNSCon of 4.2 mos (95% CI, 1.6 – NA). Pts on osi160 had no severe or life-threatening side effects. **Conclusions:** In this real-world cohort of EGFR+ NSCLC pts with CNS and/or LMD PD on osi80, dose escalation to 160 provided modest benefit with median 3.8 mos added CNS disease control. Dose escalation appeared more effective in pts with LMD versus parenchymal disease (MedDurCNSCon of 5.8 vs 2 mos). Treatment intensification with osi escalation plus RT and/or chemo appeared to confer about 1 month additional CNS disease control (power for comparison limited). Osi naïve pts started at 160 for CNS PD derived similar benefit. While limited by small numbers and retrospective design, this study suggests we need improved strategies to optimally manage CNS PD arising on osi80. Research Sponsor: None.

9587 Poster Session (Board #353), Fri, 8:00 AM-11:00 AM

IMpower150: Exploratory analysis of brain metastases development. *First Author: Federico Cappuzzo, Azienda Unità Sanitaria Locale della Romagna, Ravenna, Italy*

Background: In the global phase III IMpower150 study (NCT02366143), atezolizumab (atezo) + bevacizumab (bev) + chemo (carboplatin + paclitaxel [CP] (ABCP) showed significant improvements in PFS and OS vs BCP in patients with chemotherapy-naive metastatic NSCLC (Socinski et al. *N Engl J Med* 2018). Because bev has been shown to delay or prevent brain metastases progression in NSCLC (Fu et al. *J Chemother* 2016; Ilhan-Mutlu et al. *Mol Can Ther* 2016), exploratory analyses were conducted to assess the development of brain metastases in patients treated with ABCP, BCP and atezo + CP (ACP) in IMpower150. **Methods:** A total of 1202 patients (intention-to-treat [ITT] population) were randomized 1:1:1 to receive ABCP, ACP or BCP. Doses were given every 3 weeks: atezo 1200 mg, bev 15 mg/kg, carboplatin AUC 6 mg/mL/min and paclitaxel 200 mg/m^2. Co-primary endpoints were investigator-assessed PFS and OS in ITT–wild-type (no *EGFR* or *ALK* alterations) patients. Exploratory analyses included the rate and time to development (TTD) of new brain metastases in the ITT population, regardless of the presence of baseline brain metastases, as well as safety. Brain scans were performed as clinically indicated, and analyses were based on investigator assessments. **Results:** With a minimum follow-up of 32.4 months in the ITT population (data cutoff: September 13, 2019), 100 patients had developed brain metastases, with the highest rate of new brain lesions seen in the ACP (11.9%) vs the ABCP (7.0%) and BCP (6.0%) arms (table). Median TTD was not reached in any arm; a trend toward delayed TTD was seen in the ABCP vs BCP arm (HR, 0.68 [95% CI: 0.39, 1.19]). Among patients with and without brain metastases, 17 (35.4%) and 155 (44.0%) in the ACP arm, 18 (64.3%) and 207 (56.7%) in the ABCP arm and 10 (41.7%) and 183 (49.5%) in the BCP arm had Grade 3-4 treatment-related adverse events, respectively. **Conclusions:** The ACP arm had the highest rate of new brain lesions, whereas the ABCP and BCP arms had similar, lower rates. Taken together with the trend toward delayed development of new brain lesions with ABCP, the data suggest that adding atezo to BCP may not reduce the rate of new brain lesion development but may delay the time to new lesion development. No new safety signals were observed in this exploratory analysis. Clinical trial information: NCT02366143. Research Sponsor: F. Hoffmann-La Roche, Ltd.

	ACP n = 402	ABCP n = 400	BCP n = 400
New Brain Lesions			
Yes, n (%)	48 (11.9)	28 (7.0)	24 (6.0)
No, n (%)	354 (88.1)	372 (93.0)	376 (94.0)
Time to New Brain Lesions			
Median (range), months	NE (0-46.9)	NE (0-45.9)	NE (0-42.3)
HR (95% CI)	1.55 (0.95, 2.55)	0.68 (0.39, 1.19)	NA
***P* value* (log-rank)**	0.08	0.17	NA

NE, not estimable.
**P* value is for descriptive purpose only.

9588 Poster Session (Board #354), Fri, 8:00 AM-11:00 AM

Plasma-derived cfDNA to reveal potential biomarkers of response prediction and monitoring in non-small cell lung cancer (NSCLC) patients on immunotherapy. *First Author: Francesco Vallania, Freenome, South San Francisco, CA*

Background: Immune checkpoint inhibitors have shown promising results in many advanced cancers, but the response rate remains low. Various molecular and cellular biomarkers, such as elevated tumor-infiltrating cytotoxic T cells and Natural Killer (NK) cells at baseline, are associated with response. Blood-based biomarkers to predict or monitor response remain challenging to develop. Here we investigate the potential of cell-free DNA (cfDNA) biomarkers to predict response to the PD-1 immune checkpoint inhibitor nivolumab in patients with refractory metastatic non-small cell lung cancer (NSCLC). **Methods:** Plasma from stage IV NSCLC patients enrolled in ALCINA (NCT02866149) was collected before (baseline, BL, n = 30) and at week 8 (W8, n = 17) of nivolumab therapy. Response was determined using RECIST 1.1 (responders n = 5; non-responders n = 25). Whole-genome sequencing was performed to characterize cfDNA fragments. Tumor fraction (TF) was assessed using ichorCNA. Cellular composition was estimated by deconvolution of cfDNA co-fragmentation patterns, and transcription factor activity was estimated by measuring binding site accessibility across the genome. **Results:** Although estimated TF at baseline did not predict response to nivolumab, NK cell levels estimated by cell-mixture deconvolution were significantly higher in responders at BL ($p < 0.05$). Furthermore, estimated monocyte levels at W8 strongly correlated with overall survival ($r = 0.75$, $p < 0.0005$, HR = 2.71) and were significantly higher in responders ($p < 0.05$). By evaluating changes in transcription factor binding activity, we identified factors with greater accessibility in non-responders at baseline (DEAF1, THAP11) and W8 (DUX4, PDX-1). **Conclusions:** Plasma cfDNA signatures may be useful for response prediction and monitoring in NSCLC patients on immunotherapy. Our results suggest that changes in the immune system, as reflected by cellular composition and transcriptional activity inferred from cfDNA, may provide biological insights beyond TF alone that may benefit biomarker discovery and drug target identification. Research Sponsor: None.

9589 Poster Session (Board #355), Fri, 8:00 AM-11:00 AM

Therapeutic impact of mutation subtypes and concomitant *STK11* mutations in *KRAS*–mutated non-small cell lung cancer (NSCLC): A result of nationwide genomic screening project (LC-SCRUM-Japan). *First Author: Yutaro Tamiya, National Cancer Center Hospital East, Kashiwa, Japan*

Background: *KRAS* mutations are one of the common oncogene drivers in non-small cell lung cancer (NSCLC), and the development of several targeted drugs for *KRAS*-mutated NSCLC is now ongoing. However, the clinical impact of *KRAS* mutation subtypes or concomitant other gene mutations in NSCLC patients (pts) remains unclear. **Methods:** In a nationwide genomic screening project (LC-SCRUM-Japan), we have prospectively analyzed lung cancer pts for genetic alterations and tumor mutation burden (TMB) by next-generation sequencing system, and for PD-L1 expression by immunohistochemistry (22C3 antibody). The therapeutic efficacy and survival of *KRAS*-mutated non-squamous (non-sq) NSCLC pts were evaluated using a clinico-genomic database of the LC-SCRUM-Japan. **Results:** A total of 5166 non-sq NSCLC pts enrolled from 2015 to 2019. *KRAS* mutations were detected in 794 pts (15%; G12C/G12D/G12V/G12A/G13X/others = 232/186/165/66/61/84). Among the 794 pts, TMB and PD-L1 expression were analyzed in 128 and 79, respectively, and 218 received PD-1/PD-L1 inhibitors (IO) after 1st-line chemotherapy. The median age was 66 years (range, 29-89). 142 pts (65%) were male and 172 (78%) were smokers. Concomitant *STK11* mutations were detected in 33 pts (15%) with no difference in the mutation frequency among *KRAS* mutation subtypes. *KRAS* G12C was significantly associated with high TMB (≥ 10 mut/Mb) ($p = 0.03$), and *KRAS* G12C or G12V with high PD-L1 expression (≥ 50%) ($p = 0.02$). In pts who received IO, median progression-free survival (mPFS) was significantly longer in pts with *KRAS* G12C or G12V than in those with other *KRAS* mutations (4.7 vs 2.0 months, hazard ratio (HR) 0.58 [95%CI 0.43-0.78], $p < 0.01$). Among pts with *KRAS* G12C or G12V, mPFS of IO was significantly shorter in pts with concomitant *STK11* mutations than in those without (1.8 vs. 5.7 months, HR 1.97 [95%CI 1.06-3.41], $p = 0.02$). These correlations were not observed in platinum-containing chemotherapy (Plt-CTx). There were also no significant differences in IO and Plt-CTx efficacies between with and without other concomitant mutations, such as *TP53*, *RB1*, *CDKN2A* and *PTEN* mutations. **Conclusions:** Non-sq NSCLC pts with *KRAS* G12C/V were more sensitive to IO therapies than those with other *KRAS* mutations, but *KRAS* G12C/V-positive pts with concomitant *STK11* mutations were less sensitive than those without. These results could be highly informative in the development of novel targeted therapies for *KRAS*-mutated NSCLC. Research Sponsor: Japan Agency for Medical Research and Development.

9590 Poster Session (Board #356), Fri, 8:00 AM-11:00 AM

Large scale clinico-genomic analyses among patients with BRAF-mutated non-small cell lung cancers (NSCLC) identified by nationwide genomic screening project (LC-SCRUM-Japan). *First Author: Tetsuya Sakai, National Cancer Center Hospital East, Kashiwa-Shi Chiba, Japan*

Background: *BRAF* mutations are functionally classified into three groups, comprisingV600-mutant kinase-activating monomers (class I), kinase-activating dimers (class II), kinase-inactivating heterodimers (class III). The difference of clinical outcomes and concomitant genetic alterations among the three classes in non-small cell lung cancers (NSCLC) are unclear. **Methods:** We have prospectively analyzed NSCLC patients (pts) for cancer-related genes by a next-generation sequencing system, Oncomine™ Comprehensive Assay, in a large-scale genome screening project in Japan (LC-SCRUM-Japan). The clinical characteristics and outcomes of pts with *BRAF*-mutated non-squamous (non-sq) NSCLC were comparatively evaluated among the three classes of *BRAF* mutations. **Results:** A total of 5166 non-sq NSCLC pts were enrolled into the LC-SCRUM-Japan from 2015 to 2019. *BRAF* mutations were detected in 176 pts (3%). Among the 176 pts, 153 (87%) were classified into the three classes according to the mutation variants, including 65 (42%) into class I, 52 (34%) into class II and 36 (24%) into class III. The remaining 23 were not classified into any of the three classes. Compared with class I, class II or class III was significantly associated with smoking ($P = 0.02$ and < 0.01, respectively). Concomitant *RAS* mutations were significantly more frequent in class II and class III than in class I ($P < 0.01$ and $= 0.04$, respectively). The frequency of concomitant *STK11* mutations was significantly higher in class III than in others ($P < 0.01$, respectively). There was no significant difference in the frequency of other oncogene and tumor suppressor gene mutations among the three classes. In the 1st-line platinum-containing chemotherapies for advanced or recurrent cases, median progression-free survival (mPFS) of class III pts was shorter than class I or class II pts (4.2, 11.5 and 4.8 months, I vs III; $P < 0.01$, II vs III; $P = 0.06$). In the treatment with 2nd-4th line PD-1/PD-L1 inhibitors, mPFS was not significantly different among the three classes. Overall survival of class III pts was significantly shorter than class I pts (11.9 vs 35.2 months, $P = 0.03$). **Conclusions:** Concomitant gene mutations and clinical features are largely different among the *BRAF* mutation classes. Especially in class III, concomitant *RAS* and *STK11* mutations are more frequent and clinical outcomes were significantly less favorable. These results suggest the need of novel therapeutic strategy based on the mutation class for *BRAF*-mutated lung cancers. Research Sponsor: None.

9591 Poster Session (Board #357), Fri, 8:00 AM-11:00 AM

Real-world (RW) outcomes for advanced non-small cell lung cancer (aNSCLC) patients (pts) with *EGFR* exon 19 deletions (x19del) stratified by deletion size. *First Author: Sai-Hong Ignatius Ou, Chao Family Comprehensive Cancer Center, University of California Irvine, Orange, CA*

Background: *EGFR* x19dels are well-established targetable drivers in NSCLC. Historically x19dels have been treated as a single group, but it's unclear whether responses vary for distinct subtypes. We compared demographic, clinical and genomic characteristics as well as outcomes to EGFR tyrosine kinase inhibitors (TKIs) for aNSCLC pts with x19dels of varying lengths using a RW Clinico-Genomic Database (CGDB). **Methods:** Eligible pts had a diagnosis of aNSCLC, received care within the Flatiron Health network between 1/2011-9/2019, and had comprehensive genomic profiling (CGP) by Foundation Medicine. Clinical characteristics, treatment history and RW progression were obtained via technology-enabled abstraction as previously described (Singal G, JAMA 2019). x19del length was evaluated for association with overall survival (OS) and RW progression-free survival (rwPFS) with Kaplan-Meier analysis and unadjusted/adjusted (practice type, gender, age at TKI start, EGFR TKI type, race) hazard ratios (HR/aHR) from Cox proportional hazards models adjusted for survival bias. **Results:** Among 6,577 aNSCLC pts, *EGFR* x19dels were detected in 336 cases (5%). E746_A750del was the most frequent (214; 64%) and generally 5 amino acid (aa) deletions (x19del-5) were the most common (241; 72%). Other deletions (x19del-other) of 6 (61; 18%), 3 (20; 6%), 4 (11; 3%) or 8 aa (3; 1%) were also observed. Among pts treated with 1st-line EGFR TKI monotherapy after CGP, the x19del-5 ($n = 70$) cohort was more frequently female compared to x19del-other ($n = 27$) (90% vs 59%, $p = 0.001$). No statistically significant differences in the frequency of co-occurring alterations were observed, specifically for genes associated with response to EGFR TKI response such as *CTNNB1* (14% vs 19%) and *PIK3CA* (10% vs 15%). 1st line EGFR TKIs used were similar for x19del-5 vs x19del-other (43% vs 41% osimertinib, 30% vs 37% erlotinib, 24% vs 22% afatinib, 3% vs 0% gefitinib). x19del-5 pts had similar median rwPFS (10.6 vs 10.6 months, HR: 0.73 [0.41-1.28], aHR:0.78 [0.38-1.59]) and median OS (29.2 vs 24.9 months, HR: 0.64 [0.32- 1.29], aHR: 0.75 [0.32-1.75]) compared to x19del-other. **Conclusions:** In a RW CGDB of 336 aNSCLC pts with *EGFR* x19dels**,** 5 aa x19dels were most common (71%) and 29% of cases had 3, 4, 6 or 8 aa x19dels . For pts included in the treatment cohort, no significant differences in rwPFS or OS were observed. These results suggest that x19del length does not significantly impact clinical outcomes to 1st-line EGFR TKIs. Research Sponsor: None.

9592 Poster Session (Board #358), Fri, 8:00 AM-11:00 AM

Genomic testing among patients (pts) with newly diagnosed advanced non-small cell lung cancer (aNSCLC) in the United States: A contemporary clinical practice patterns study. *First Author: Adam Gondos, F. Hoffmann-La Roche Ltd, Pharmaceutical Division, Personalized Healthcare Center of Excellence, Basel, Switzerland*

Background: We describe contemporary clinical patterns of guideline-mandated genomic testing in newly diagnosed US pts with aNSCLC. **Methods:** From the Flatiron Health electronic health record-derived de-identified database, we included pts with newly diagnosed advanced non-squamous cell carcinoma of the lung between 1.1.2018–6.30.2019 who had received first-line (1L) therapy. We defined inadequate testing as no successful test for at least one of four examined genes: *ALK*, *BRAF*, *EGFR*, and *ROS1*. We grouped pts according to testing received into users of next-generation sequencing (NGS) testing, including a subgroup using comprehensive genomic profiling (CGP, exemplified by Foundation Medicine, Inc.), users of non-NGS testing, and no testing. We describe the following aspects of genomic testing before the start of 1L therapy: occurrence of testing, patterns of use of testing technologies, occurrence of inadequate testing, test failures, percentage of pts with potentially missed targeted therapy with US Food and Drug Administration approval (no positive test and <4 successful tests), and recent trends in genomic testing. **Results:** Among 2971 included pts, 690 (23.2%) had no genomic testing before 1L treatment. Among pts who had a test (n=2281), 59.4% (n=1355) received NGS (CGP: 18.8%, n=429), while 40.6% (n=926) received non-NGS tests only. In the CGP user group, 79.7% of pts received no other type of test, compared with 29.8% of pts in the other NGS group. Inadequate testing was recorded in 13.4% of NGS-tested pts (CGP: 4.9%), compared with 52.5% of pts tested by non-NGS only. Test failures contributed to unsuccessful testing in 4.2% of pts tested by NGS (CGP: 1.2%) and in 6.8% of pts who received non-NGS tests. In the NGS group, 10.1% (CGP: 3.0%) of patients potentially missed a targeted therapy option, compared with 40.3% in the non-NGS group. *EGFR* and *ALK* testing were performed in $\geq$95% of pts, regardless of the testing group; however, only 83.6% and 55.7% of pts received tests for *ROS1* and *BRAF*, respectively, in the non-NGS group. In the latter group, for the first 6 months of 2019, 88.4% and 58.2% of pts were tested for *ROS1* and *BRAF* mutations, respectively. **Conclusions:** Not performing any, or performing only inadequate genomic testing in pts with newly diagnosed aNSCLC remains a concern in clinical practice. The use of NGS, particularly CGP, may help to avoid suboptimal testing, minimize test failures, and improve uptake of testing for newly introduced biomarkers, enabling individualized, targeted therapy. Research Sponsor: F. Hoffmann-La Roche Ltd, Basel, Switzerland.

9593 Poster Session (Board #359), Fri, 8:00 AM-11:00 AM

Updated overall survival (OS) and genomic analysis from a single-arm phase II study of dabrafenib (D) + trametinib (T) in patients (pts) with *BRAF* V600E mutant (Mut) metastatic non-small cell lung cancer (NSCLC). *First Author: David Planchard, Institut Gustave Roussy, Thoracic Team, Villejuif, France*

Background: The phase II multicenter, open label study, which evaluated efficacy and safety of D+T in pretreated (cohort B) and treatment (tx)-naive (cohort C) pts with *BRAF* V600E mut metastatic NSCLC. The results of the primary analysis have been reported. Here, we present an updated survival and genomic analysis data for cohorts B and C. **Methods:** Tx-naïve (n=36) and pretreated (n=57) pts received D 150 mg twice daily + T 2 mg daily. Primary objective: ORR, secondary objectives: PFS, DOR, OS, safety, tolerability and PK of D+T. Tumor samples were centrally tested using a NGS cancer targeted panel (Oncomine Dx Target test, ThermoFisher Scientific). KM curves and Cox regression models were used to evaluate potential associations between baseline genomic landscape and pt efficacy endpoints. **Results:** As of June 22, 2019, median (m) follow-up was 16.3 mo in tx-naïve pts and 16.6 mo in pretreated pts. mOS was 17.3 mo (95% CI: 12.3, 40.2; 3 yr OS: 40%) and 18.2 mo (95% CI: 14.3, 28.6; 3 yr OS: 33%) with 14/36 and 11/57 pts alive in tx naïve and pretreated pts respectively. Detailed efficacy results are presented in table. 57/62 tumor samples retrieved from 93 pts were centrally confirmed to have *BRAF V600E* mut; 5 non-confirmed BRAF tumors (3 pts had PR) were positive for *c-MET* T1010I, *KRAS* G12V, *ALK* fusion and 2 *JAK3* S493C with mPFS of 13.8 mo while OS was NE due to limited data points. Eleven pts (18%) had concomitant somatic mutations and/or genetic alterations in addition to *BRAF* V600E mut: 4 had alterations within PI3K pathway4 had concomitant mutations at *IDH1* R132X, and 3 pts had additional mutations at *BRAF* G466V, *KRAS* G13C and a *cMET* exon 14 skipping, respectively. Pts whose tumors had concomitant genetic alterations, particularly in PI3K pathway, showed a trend towards decreased PFS and OS. Safety profile was similar to previous reported results. **Conclusions:** This update of BRF113928 study reported improved and durable OS rates with combination D+T in *BRAF* V600E mut NSCLC pts. Co-occurring genetic alterations might influence clinical outcomes of such pts. Further validation is ongoing to corroborate current genomic findings. Clinical trial information: NCT01336634. Research Sponsor: Novartis Pharmaceuticals Corporation.

	Tx naive N=36	Pretreated N=57
ORR, n (%)[a]	23 (63.9)	39 (68.4)
95% CI	46.2, 79.2	54.8, 80.1
mDOR, mo[a]	10.2	9.8
95% CI	8.3, 15.2	6.9, 18.3
mPFS, mo[a]	10.8	10.2
95% CI	7.0-14.5	6.9-16.7
mOS, mo	17.3	18.2
95% CI	12.3, 40.2	14.3, 28.6
OS rates, % (95% CI)		
12 mo	74 55, 85	66 52, 77
24 mo	49 32, 65	41 28, 53
36 mo	40 24, 56	33 21, 46
48 mo	NA NA	26 15, 38

[a]Investigator assessment

9594 Poster Session (Board #360), Fri, 8:00 AM-11:00 AM

Patient-reported outcomes (PROs) in the randomized, phase III IMpower110 study of atezolizumab (atezo) vs chemotherapy in 1L metastatic NSCLC. *First Author: Filippo de Marinis, Istituto Europeo di Oncologia IRCCS, Milan, Italy*

Background: IMpower110 (NCT02409342) evaluated atezo (anti–PD-L1) monotherapy as 1L treatment in PD-L1–selected patients (pts) with metastatic NSCLC and met its primary endpoint with statistically significant and clinically meaningful OS benefit in TC3 or IC3 wild-type (WT; *EGFR/ALK*-negative) pts. PROs were prespecified endpoints to assess pt perspectives on overall clinical benefit. **Methods:** Pts were randomized 1:1 to receive atezo 1200 mg IV q3w (Arm A) or platinum-based chemo (Arm B; 4 or 6 21-day cycles). Arm B non-squamous pts received cisplatin (cis) 75 mg/m^2 or carboplatin (carbo) AUC 6 + pemetrexed 500 mg/m^2 IV q3w; Arm B squamous pts received cis 75 mg/m^2 + gemcitabine (gem) 1250 mg/m^2 or carbo AUC 5 + gem 1000 mg/m^2 IV q3w. PROs were assessed by the EORTC Quality of Life Questionnaire Core 30 (QLQ-C30) and lung cancer module QLQ-LC13. Time to confirmed deterioration (TTD) in QLQ-LC13 lung cancer symptoms (secondary endpoint) and change from baseline (BL) in global health status (GHS), functioning and lung cancer symptoms (exploratory endpoints) were analyzed in TC3 or IC3-WT pts. Clinically meaningful change was defined as a $\geq$10-point deterioration from BL. **Results:** Completion rates at BL (atezo, n = 107; chemo, n = 98) were high in both arms for the QLC-C30 (90% atezo, 86% chemo) and the QLC-LC13 (89% atezo, 85% chemo), and remained $>$ 80% at most visits. Mean BL scores for GHS, physical functioning, and role functioning were moderate, symptom burden was low, and all were similar in both arms. No differences in TTD were seen between arms for cough (HR, 0.98; 95% CI: 0.48, 2.03), chest pain (HR, 1.02; 95% CI: 0.47, 2.22), dyspnea (HR, 0.96, 95% CI: 0.57, 1.60), and 3-symptom composite score (HR, 0.92; 95% CI: 0.59, 1.44). Mean change in physical function from BL to wk 42 was modestly improved with atezo and greater than or similar to chemo. No clinically meaningful worsening in dyspnea, cough or chest pain was seen with atezo vs chemo. Mean change in cough and chest pain from BL numerically improved immediately after start of treatment and was maintained to wk 48 with atezo. Fatigue and nausea/vomiting scores numerically improved immediately with atezo and were maintained to wk 48. **Conclusions:** QLQ-C30 and QLQ-LC13 completion rates were high at BL and most study visits. TTD of lung cancer-related symptoms was similar in both arms, indicating pts' low BL symptom burden was maintained for a similar duration. Pts receiving atezo vs chemo sustained numerical improvements in physical function and no worsening in lung cancer-related symptoms. Clinical trial information: NCT02409342. Research Sponsor: F. Hoffmann-La Roche, Ltd.

9595 Poster Session (Board #361), Fri, 8:00 AM-11:00 AM

A phase II study of lorlatinib in patients (pts) with ALK-positive (ALK+) lung cancer with brain-only progression. *First Author: Ibiayi Dagogo-Jack, Massachusetts General Hospital, Boston, MA*

Background: Lorlatinib is a 3rd-generation ALK tyrosine kinase inhibitor (TKI) developed to penetrate the central nervous system (CNS) and overcome resistance to 2nd-generation (2nd-gen) ALK TKIs. In a phase II study, lorlatinib demonstrated significant intracranial (IC) activity after failure of 2nd-gen TKIs. As treatment discontinuation for extracranial (EC) progression can confound assessment of durability of IC response, we performed a phase II study (NCT02927340) to selectively evaluate lorlatinib activity in ALK+ pts with CNS-only disease. **Methods:** Between 11/2016 and 1/2019, 22 pts with IC progression on an ALK TKI with no other sites of measurable disease were enrolled at 2 institutions. Pts received lorlatinib at a starting dose of 100 mg QD. The primary endpoint was the IC disease control rate (DCR) at 12 weeks per modified RECIST v1.1. Secondary endpoints were IC objective response rate (ORR), duration of response (DOR), and progression-free survival (PFS). **Results:** Of the 22 pts enrolled, 21 (95%) had progressed on a 2nd-gen ALK TKI and 14 (64%) had previously received CNS radiation (median 21.1 months between radiation and lorlatinib). Median number of prior ALK TKIs was 2 (range 1-4). As of the data cutoff of 12/15/19, median follow-up was 14 months. At 12 weeks, the IC-DCR was 95%, including 8 pts with stable disease. Best IC ORR was 59% with 6 complete and 7 partial responses. Nine (41%) pts relapsed on study, including 3 IC-only, 5 EC-only, and 1 combined relapse. Four pts continued treatment beyond EC-only progression. Although median IC DOR and PFS were not estimable due to few progression events, the IC progression-free rate at 12 months was 81% (95% CI: 53%-94%). Twelve pts have discontinued study treatment due to progression (n = 6), edema (n = 1), pulmonary hypertension (n = 1), or transition to commercial lorlatinib (n = 4). **Conclusions:** Lorlatinib induces durable intracranial responses in pts with CNS-only progression on 2nd-gen ALK TKIs, suggesting that CNS-specific relapses are primarily driven by ALK-dependent mechanisms. Further studies are needed to characterize the molecular basis of sensitivity to lorlatinib in this unique subgroup of pts with ALK+ lung cancer. Clinical trial information: NCT02927340. Research Sponsor: Pfizer.

9596 Poster Session (Board #362), Fri, 8:00 AM-11:00 AM

Clinical characteristics and anti-PD-(L)1 treatment outcomes of KRAS-G12C mutant lung cancer compared to other molecular subtypes of KRAS-mutant lung cancer. *First Author: Kathryn Cecilia Arbour, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: *KRAS* mutations are identified in approximately 30% of NSCLC. There are no FDA approved targeted therapies for patients with KRAS-mutant non-small cell lung cancer (NSCLC) but novel direct inhibitors of KRAS G12C have shown some activity in early phase clinical trials. We hypothesized that patients with *KRAS*-G12C mutations may have distinct clinical characteristics and responses to systemic therapies compared to patients with non-G12C subtypes. **Methods:** We identified patients with KRAS-mutant lung cancers who underwent next-generation sequencing with MSK-IMPACT, between January 2014 and December 2018. Baseline characteristics were compared with the Chi-square and Fisher's exact test for categorical data and Wilcoxon rank-rum test for continuous data. Overall survival was calculated from time of diagnosis of metastatic/recurrent disease to date of death or last follow up, with left truncation to account for time of MSK-IMPACT. Overall survival was compared between groups using the Cox proportional-hazards model. Response evaluations where performed by independent thoracic radiologists according to RECIST 1. and compared between group with the Fisher's exact test. **Results:** We identified 1194 patients with KRAS-mutant NSCLC, 772 with recurrent or metastatic disease. Of patients with advanced disease, 46% (352/772) had mutations in *KRAS*-G12C and 54% harbored non-G12C mutations (15% G12D, 16% G12V, 8% G12A, 4% G13D). Co-mutation patterns were similar with respect to KEAP1 (p=0.9) and STK11 (p=1.0). Patients with non-G12C mutations had a higher proportion of never smokers (10% vs 1.4% p$<$0.001). The median OS from diagnosis was 13 months for G12C and non-G12C patients (p=0.99). 45% (347/772) received 1L or 2L line treatment with PD-(L)1 inhibitor. RECIST measurements were available for 290/347 cases (84%). ORR with anti-PD-(L)1 treatment was 24% vs 28% in G12C vs non-G12C patients (p=0.5). In patients with PD-L1 50% (n=103), ORR was 39% for G12C vs 58% non-G12C patients (p=0.06). **Conclusions:** KRAS G12C mutations are present in 12% of patients with NSCLC and represent a relevant subtype of NSCLC given KRAS G12C inhibitors now in clinical development. Baseline characteristics including co-mutation patterns are similar between patients with G12C and non-G12C, except for smoking history. The efficacy of KRAS G12C direct inhibitors will need to be compared to other available therapies for KRAS mutant NSCLC (chemotherapy and PD-(L)1 inhibitors) to identify most effective therapeutic strategy. Research Sponsor: None.

9597 Poster Session (Board #363), Fri, 8:00 AM-11:00 AM

A phase II study of osimertinib for patients with radiotherapy-naïve CNS metastasis of non-small cell lung cancer harboring EGFR mutations: The OCEAN study (LOGIK 1603/WJOG 9116L). *First Author: Kazushige Wakuda, Division of Thoracic Oncology, Shizuoka Cancer Center, Sunto-Gun, Shizuoka Prefecture, Japan*

Background: Approximately 15%–30% of patients treated with EGFR-TKIs experience central nervous system (CNS) progression. Although radiotherapy is a standard treatment for CNS metastasis, the efficacy of radiotherapy against CNS is poor. The aim of OCEAN study was to assess the efficacy of osimertinib for patients with radiotherapy-naïve CNS metastasis of NSCLC harboring EGFR mutations. **Methods:** OCEAN study was two-cohort phase II trial, 65 patients (T790M cohort; 40 patients and first-line cohort; 25 patients) with radiotherapy-naïve CNS metastasis of EGFR mutation-positive NSCLC was included. Patients were treated with osimertinib 80 mg once daily. The primary endpoint was the response rate of brain metastasis (BMRR) assessed by the PAREXEL criteria. We set a threshold value of 50% and an expected value of 70% based on the overall response rate (ORR) of AURA trial. Based on one-sided alpha = 0.05 and power = 0.8, the sample size of T790M cohort was calculated to be 40. Key secondary endpoints were progression-free survival (PFS), and ORR, BMRR assessed by the RECIST criteria. We are exploratorily assessing the blood concentration of osimertinib at day 22, which considered to represent steady state. In this report, we present the results of T790M cohort. **Results:** Between October 2016 to July 2019, 40 participants were recruited in the T790M cohort. The median age was 66.5 with 30.0% male. Eight patients had symptomatic CNS metastasis and most patient had multiple CNS metastasis (77.5%). BMRR assessed by PAREXEL criteria was 66.7% (95%CI: 54.3 – 79.1%) and BMRR assessed by RECIST was 70.0% (95%CI, 49.9 – 90.1%). Median PFS was 7.1 months (95%CI, 3.4 – 13.6 months) and ORR assessed by RECIST was 40.5% (95%CI, 24.7 – 57.9%). Treatment related pneumonitis was observed in 4 patients (10.0%). There was no grade 3 or higher toxicities that were found in more than 10%. **Conclusions:** This first study assessed the efficacy of osimertinib for patients with radiotherapy-naïve CNS metastasis of EGFR T790M mutation-positive NSCLC. The OCEAN study met primary endpoint. The results of this study suggested that patients with brain metastasis harboring EGFR T790M mutations had better to receive osimertinib prior to brain radiotherapy. Clinical trial information: 071180017. Research Sponsor: AstraZeneca.

9598 Poster Session (Board #364), Fri, 8:00 AM-11:00 AM

Blood serum amyloid A as potential biomarker of pembrolizumab efficacy for patients affected by advanced non-small cell lung cancer (NSCLC) over-expressing PD-L1: Early results of the FoRECATT Study. *First Author: Vincenzo Di Noia, Medical Oncology, Cliniche Humanitas Gavazzeni, Bergamo, Oncological Sciences, Catholic University of the Sacred Heart, Rome, Italy*

Background: Identifying the patients who may benefit the most from immune checkpoints inhibitors remains a great challenge for clinicians. The tumor-derived Serum Amyloid A (SAA) inhibits the immune-response in melanoma patients. Here we present the early results of FoRECATT study investigating on blood SAA as biomarker of response to upfront pembrolizumab in patients with advanced non-small-cell lung cancer (NSCLC). **Methods:** In this prospective study, patients with PD-L1 $\geq$ 50% receiving upfront pembrolizumab (P cohort) and with PD-L1 0-49% treated with chemotherapy (CT cohort), were evaluated for blood SAA and radiological response at baseline and every 9 weeks. Primary endpoint was response rate (RR) according to Response Evaluation Criteria in Solid Tumors 1.1; secondary endpoints were progression-free (PFS) and overall survival (OS). The most accurate SAA cut-off to predict response was established with ROC-analysis in the P cohort. **Results:** In the P Cohort (n = 42), the overall RR was 38%. After a median follow-up of 18.5 months (mo), baseline SAA $\leq$ the ROC-derived cut-off (29.9 mg/L; n = 14/42, 33%) was significantly associated with higher RR (53.6 *versus* 7.1%; OR 15, 95%CI 1.72-130.7, *P*= 0.009), longer PFS (17.4 *versus* 2.1 mo; *P*< 0.0001) and OS (not reached *versus* 7.2 mo; *P*< 0.0001) compared with SAA > 29.9 mg/L. In multivariate analysis, low SAA positively affects PFS (*P*= 0.001) and OS (*P*= 0.048) irrespective of ECOG PS, number of metastatic sites and pleural effusion. SAA monitoring (n = 40) was also significantly associated with survival endpoints: median PFS 17.4 *versus* 2.1 mo and median OS not reached *versus* 7.2 mo when SAA remained low (n = 14) and high (n = 12), respectively. In the CT Cohort (n = 30), RR was not significantly affected by SAA level, while low SAA at baseline (n = 17) was associated with better PFS (HR = 0.42, 95%CI 0.16-1.10, *P*= 0.02) and OS (HR = 0.16, 95% CI 0.04-0.55, *P*= 0.0004). **Conclusions:** Low SAA predicts a higher likelihood of response to upfront pembrolizumab only and good survival outcomes irrespective of treatment in advanced NSCLC patients. Therefore, a simple blood test might be useful to identify patients likely to derive better outcomes from immunotherapy. A further study (FoRECATT-2) is ongoing to confirm the results in a larger validation cohort and to assess the potential effect of SAA on immune response in vitro assays. Research Sponsor: None.

9599 Poster Session (Board #365), Fri, 8:00 AM-11:00 AM

Outcomes in patients with metastatic non-small cell lung cancer (mNSCLC) with brain metastases treated with pembrolizumab-based therapy. *First Author: Lova Sun, UPHS, Philadelphia, PA*

Background: Patients (pts) with mNSCLC with active brain metastases (BM) are often excluded from clinical trials; data on efficacy and safety of immunotherapy in this population are limited. We compared outcomes of pts with mNSCLC with and without BM who received pembrolizumab-based therapy. **Methods:** We conducted a retrospective single-center study of pts with mNSCLC treated with pembrolizumab (P) with or without chemotherapy. Progression-free survival (PFS) and overall survival (OS) were determined by Kaplan-Meier methodology and compared using multivariable Cox regression and log rank testing. **Results:** We identified 587 consecutive pts with mNSCLC who began P-based therapy between 8/2013 and 12/2018: 306 (52%) female, median age 67 years (range 32-98), 437 (74%) adenocarcinoma, and 508 (87%) former/current smokers. 388 (66%) patients received P in first line therapy, and 334 (57%) received single-agent P. 131 pts (22%) had detectable BM at baseline (start of P-based therapy). Pts with BM were younger (median 65 y vs 68 y, p < 0.01) and more likely to have adenocarcinoma (86% vs. 71%, p < 0.01) and baseline steroid use (22% vs 1%, p < 0.01). Presence of BM did not differ by race, sex, line of therapy, treatment regimen, or PD-L1 status. Of the 131 patients with detectable BM on pre-treatment brain MRI, 55 (42%) had stable BM as a result of prior local therapy, while 76 (58%) had active (new or growing) BM on pre-treatment imaging. Most patients with active BM underwent radiation therapy (RT) in either the 30 days before (n = 46) or 30 days after (n = 17) P start; of the remaining 13 treated with P-based therapy alone, intracranial responses included 2 CR, 2 PR, 3 SD, and 4 PD. As of 1/1/2020, with 15-month median follow up, there was no difference in mPFS (9.2 vs 7.3 months, p = 0.41) or mOS (18.3 vs 18.0 mo, p = 0.67) between pts with and without BM in our P-treated cohort. On multivariable analysis, female sex, ECOG 0-1, adenocarcinoma histology, and P as first line therapy were associated with improved PFS and OS. Presence of BM, baseline steroid use, and timing of local RT (before vs. after P) were not associated with inferior survival. **Conclusions:** In our single-center experience of pts with mNSCLC treated with P, pts with and without BM had similar PFS and OS. We observed several intracranial responses to P-based therapy alone, but most pts with active BM underwent local RT. mNSCLC pts with BM should be considered for P-based therapy; BM may be treated with RT immediately before or even after P with similar survival outcomes. Research Sponsor: None.

9600 Poster Session (Board #366), Fri, 8:00 AM-11:00 AM

Physiologic colonic uptake of ^{18}F-FDG on PET/CT predicts immunotherapy response and gut microbiome diversity in patients with advanced non-small cell lung cancer (NSCLC). *First Author: Lena Cvetkovic, Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM), Montréal, QC, Canada*

Background: Immune checkpoint inhibitors (ICI) represent the backbone treatment of advanced non-small cell lung cancer (aNSCLC) patients. Emerging evidence suggests increased gut microbiome (GM) diversity is associated with favorable response. Conversely, antibiotic-induced dysbiosis may be associated with deleterious outcomes in patients receiving ICI in multiple retrospective studies and one prospective study. ^{18}F-FDG physiologic colonic uptake on PET/CT increases following treatment with antibiotics and could be a surrogate marker for GM diversity and therefore clinical response. The aim of this study was to determine if ^{18}F-FDG physiologic colonic uptake prior to ICI initiation correlates with outcomes and GM metagenomics in patients with advanced NSCLC. **Methods:** 71 patients with aNSCLC who underwent PET/CT prior to ICI were identified. For each patient, the colon was manually contoured, SUVmax was measured in each segment of the colon by a nuclear medicine specialist and average SUVmax was calculated for the whole colon. Patients were stratified in two groups according to median colon SUVmax (low vs high uptake). ^{18}F-FDG physiologic colonic uptake was then compared to overall survival (OS), objective response (ORR), and progression-free survival (PFS). For patients with available stool samples (n = 10), GM composition was defined using metagenomics sequencing. **Results:** 71 patients (54% men, median age: 68 years) with aNSCLC were included in the study and ICI was the first line of therapy in 38% of those patients. The mean colon SUV for the low and high uptake groups were 1.41 (CI 95% 1.35-1.47) and 2.18 (CI 95% 1.90-2.46) respectively. The high uptake group had a higher proportion of non-responders (p = 0.033) and significant shorter PFS (4.1 months vs 11.3 months, p = 0.005). In the caecum, high uptake also correlated with numerically shorter OS (10.82 vs 27.56 months, p = 0.058) compared to low uptake group. Despite the low number of samples, metagenomics sequencing revealed that PLS-DA (Partial Least Squares Discriminant Analysis) for diversity was lower in the high SUV group (p = 0.008). **Conclusions:** Higher colon SUVmax on pre-ICI FDG PET/CT is associated with worse clinical outcomes and lower baseline GM diversity in patients with advanced NSCLC. Here, we propose that ^{18}F-FDG physiologic colonic uptake on PET/CT could serve as a surrogate marker of GM diversity and predicts clinical outcomes. Research Sponsor: None.

9601 Poster Session (Board #367), Fri, 8:00 AM-11:00 AM

ctDNA resistance landscape of lazertinib, a third-generation EGFR tyrosine kinase inhibitor (TKI). *First Author: Ji-Youn Han, Center for Lung Cancer, Research Institute and Hospital, National Cancer Center, Goyang, South Korea*

Background: While *EGFR* mutant (*EGFRm*) non-small cell lung cancer (NSCLC) patients usually experience improved clinical benefit with EGFR TKIs, most eventually progress. Understanding mechanisms of resistance (MoR) may allow for more personalized treatment. Lazertinib is an irreversible third generation EGFR TKI for which MoR are unknown. Obtaining sufficient tumor tissue for genotyping at progression is often difficult. Therefore, we utilized plasma ctDNA from patients treated with lazertinib to explore MoR. **Methods:** Plasma samples from 47 NSCLC patients in the phase 2 trial of lazertinib (NCT03046992) were collected at screening and progressive disease (PD) and underwent ctDNA NGS of 74 genes using Guarant360. All patients were positive for an *EGFR* Ex19del or L858R (*EGFRm*) and T790M by tissue testing at screening. Acquired, nonsynonymous, characterized mutations detected in a PD sample but not in the screening sample from the respective patient were considered putative MoR, excluding aneuploidy. Patients with detectable plasma *EGFRm* and/or T790M at screening were evaluable. **Results:** ctDNA was detected in 47 (100%) screening samples and 43/45 (96%) PD samples (two failed sequencing). An *EGFRm* was detected in 85% of patients at screening (n = 40), 38 of which had PD ctDNA results and were included in analysis. T790M was detected in 30 patients at screening and subsequently not detected at PD in 21 of these patients, 55% of all 38 included patients. Among the ten patients with T790M detected at PD, on-target MoR were detected in 7 (18% of all included patients) including *EGFR* C797S (n = 3, 8%), *EGFR* amplification (n = 3, 8%), and *EGFR* T854A (n = 1, 3%). All C797S were in cis with T790M. No on-target MoR were detected in patients without T790M detected at PD. Off-target MoR were seen in 34% of patients (13/38) including mutations in *PIK3CA* (13%; 2 E545K, 2 E542K, 1 E81K), *ERBB2* (5%; 1 D769H, 1 V777L), *KRAS* (3%; 1 G12C), and *BRAF* (3%; 1 G469A). Gene amplifications were detected in *CCND1* (n = 1, 3%), *CCNE1* (n = 2, 5%), *ERBB2* (n = 1, 3%), *FGFR1* (n = 1, 3%), *MET* (n = 4, 11%), and *PIK3CA* (n = 1, 3%), with some patients having multiple MoR. **Conclusions:** The spectrum of MoR identified in this cohort of patients treated with lazertinib is similar to that reported in other third generation EGFR TKIs, but with some differences in frequencies. The most common resistance mechanisms are T790M loss and *PIK3CA* alterations which may address the mechanism of action. Our findings suggest putative MoR of lazertinib and show that ctDNA NGS is an effective way to identify MoR in patients progressing on targeted therapy. Clinical trial information: NCT03046992. Research Sponsor: Yuhan Corporation, Other Government Agency.

9602 Poster Session (Board #368), Fri, 8:00 AM-11:00 AM

Efficacy and safety of alflutinib (AST2818) in patients with T790M mutation-positive NSCLC: A phase IIb multicenter single-arm study. *First Author: Yuankai Shi, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing Key Laboratory of Clinical Study on Anticancer Molecular Targeted Drugs, Beijing, China*

Background: Alflutinib (AST2818) is a third generation EGFR-TKI. This phase IIb, multicenter, single arm study (ALSC003, NCT03452592) aimed to assess the efficacyand safety of Alflutinib in patients with EGFR T790M mutated non-small cell lung cancer (NSCLC). **Methods:** Patients with locally advanced or metastatic EGFR T790M mutated NSCLC who progressed after first/second-generation EGFR-TKIs therapy or primary EGFR T790M mutation positive received 80 mg Alflutinib orally once daily. Tumor tissue samples underwent central laboratory testing for EGFR T790M mutation. The primary endpoint was objective response rate (ORR). Secondary endpoints included disease control rate (DCR), duration of response (DoR), progression-free survival (PFS), overall survival (OS) and safety. Efficacy was assessed by independent radiological review committee per RECIST 1.1. Safety was assessed by NCI CTCAE version 4.03. **Results:** From Jun 4, 2018 to Dec 8, 2018, 220 patients were enrolled with a median age of 61.0 (range 29 to 80) years. According to the AJCC version 8 staging system, 212 (96.4%) cases were in stage IV, and 8 (3.6%) cases in stage III. All patients had EGFR T790M mutation. By April 12, 2019, the ORR was 73.6% (95% CI 67.3–79.3). The DCR estimated at 6 and 12 weeks were 87.3% (95%CI 82.1-91.4) and 82.3% (95%CI 76.6-87.1), respectively. The median PFS was 7.6 months (95% CI 7.0–NA). Median OS and DoR have not been reached. 209 (95.0%) patients had at least one adverse events (AEs), which were mostly grade 1 or 2 and well tolerable. The most common AEs were increased aspartate aminotransferase (33 [15.0%]), upper respiratory tract infection (33 [15.0%]), and cough (33 [15.0%]). Grade 3 to 5 AEs occurred in 42 (19.1%) patients. The most common one was elevated γ-glutamyltransferase (n = 4). There were 3 deaths patients, 2 of which possibly not be related to the study drug, and 1 could not be determined. No interstitial pneumonia was reported. **Conclusions:** Alflutinib has promising efficacy and acceptable safety profile for the treatment of EGFR T790M mutated NSCLC patients. Clinical trial information: NCT 03452592. Research Sponsor: Shanghai Allist Pharmaceuticals co. ltd., China National Major Project for New Drug Innovation (2017ZX09304015, 2018ZX09301014009 and 2019ZX09201-002) and CAMS Innovation Fund for Medical Sciences (CIFMS) (2016-I2M-1-001).

9603 Poster Session (Board #369), Fri, 8:00 AM-11:00 AM

Longitudinal monitoring by next generation sequencing of plasma cell-free DNA in ALK-rearranged non-small cell lung cancer (NSCLC) patients treated with ALK tyrosine kinase inhibitors. *First Author: Minsuk Kwon, Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

Background: Patients with anaplastic lymphoma kinase-rearranged (ALK+) NSCLC inevitably acquire resistance to ALK inhibitors. We hypothesized that longitudinal monitoring of cell-free plasma DNA (cfDNA) next generation sequencing (NGS) could predict the response and resistance of TKI therapy in ALK+NSCLC **Methods:** Patients with ALK+ advanced NSCLC determined by standard tissue testing and planned for TKI therapy were prospectively recruited. Plasma was collected before therapy (n = 92), two months post-therapy (n = 58), and at progression (n = 35). Plasma DNA NGS analysis was done retrospectively by Guardant360. **Results:** From April 2015 to July 2019, 92 patients enrolled; 81 (88.0%) received *ALK* TKI as first-line (crizotinib, n = 59; alectinib, n = 22), 10 (10.9%) received TKI as second-line (alectinib, n = 6; crizotinib, n = 2; ceritinib, n = 1; brigatinib, n = 1), and 1 (1.1%) was treated in third-line (lorlatinib). At the cut-off date of January 28, 2020, 56 of 92 patients had disease progression. Circulating tumor DNA (ctDNA) was detected in 69 baseline samples (75%); among these were 43 *ALK* fusions (62.3%) and 1 *ALK* G1202R without fusion (1.4%). Fusions included *EML4-ALK* v1 (n = 19), *EML4-ALK* v3 (n = 14), *CLTC-ALK* (n = 1), *TPM3-ALK* (n = 1), *GCC2-ALK/CLIP4-ALK* (n = 1), and other *EML4-ALK* fusions (n = 7). Eight patients developed *ALK* resistance mutations after crizotinib therapy: L1196M (n = 5), G1269A (n = 1), G1202R (n = 1), and co-occurring F1174L, G1202R, and G1269A (n = 1). Two patients developed *ALK* resistance mutations after ceritinib: G1202R (n = 1), and co-occurring G1202R and T1151R (n = 1). The absence of detectable ctDNA at baseline was associated with longer progression-free survival (PFS; median 36.1 vs 11.6 months, HR 0.432, p = 0.004) and overall survival (OS; median not reached vs 27.9 months, HR 0.418, p = 0.034). Patients with clearance of ctDNA at two months (n = 29) had significantly longer PFS (median 25.4 vs 13.9 months, HR 0.343, p = 0.030) and OS (median not reached vs 25.7 months, HR 0.173, p = 0.035) than those without clearance (n = 22). Patients with co-occurring *TP53* alterations and *ALK* fusions at baseline (n = 9) showed shorter PFS (median 7.0 vs 12.5 months, HR 3.596, p = 0.0154) than those without *TP53* alterations (n = 35). **Conclusions:** NGS of cell-free plasma DNA is useful not only for the detection of *ALK* fusions and resistance mutations but also for assessing prognosis and monitoring the dynamic changes of genomic alterations in *ALK*+ NSCLC treated with ALK TKI. Research Sponsor: Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Korean government (MSIT) (No.NRF-2017M3A9G5060259)Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Kor.

9604 Poster Session (Board #370), Fri, 8:00 AM-11:00 AM

Nintedanib + docetaxel in lung adenocarcinoma patients (pts) following treatment with immune checkpoint inhibitors (ICIs): Updated efficacy and safety results of the ongoing non-interventional study (NIS) VARGADO (NCT02392455). *First Author: Christian Grohé, Department of Pneumology, ELK Berlin, Berlin, Germany*

Background: Nintedanib (Vargatef) is an oral triple angiokinase inhibitor targeting VEGF-, PDGF- and FGF receptor pathways. It is approved in the EU and other countries in combination with docetaxel for treatment of locally advanced, metastatic or locally recurrent NSCLC of adenocarcinoma histology after 1st line chemotherapy. ICI +/- chemotherapy has changed the standard of care for 1st line treatment of metastatic non-mutated NSCLC. However, currently, only limited clinical data are available to help guide treatment decisions after prior ICI therapy in subsequent lines. **Methods:** This updated analysis is part of the ongoing NIS VARGADO (cohort B), a prospective non-interventional study of nintedanib + docetaxel after 1st line chemotherapy for adenocarcinoma NSCLC. The analysis includes 57 pts who had previously received both chemotherapy and ICI treatment. **Results:** Median age was 61 years (range: 45 – 80), 32/57 pts (56.1%) were men, and 41/57 pts (71.9%) were ECOG PS 0/1. 12/57 pts (21.1%) had brain metastases, and 46/57 pts (80.7 %) were current or former smokers. 1st line chemotherapy treatments included pemetrexed (36/57 pts, 63.2%), cisplatin (29/57 pts, 50.9%), carboplatin (33/57 pts, 57.9%), bevacizumab (14/57 pts, 24.6%), vinorelbine (13/57 pts, 22.8%), paclitaxel (8/57 pts, 14.0%), and docetaxel (1/57 pts, 1.8%). 2nd line treatments included nivolumab (34/57 pts, 59.7%), pembrolizumab (14/57 pts, 24.6%), and atezolizumab (7/57 pts, 12.3%). Under nintedanib and docetaxel, ORR was 50% (20/40 pts); DCR was 85.0% (34/40 pts). Median PFS was 6.5 months (95%CI 4.8 – 8.7), median OS was 12.4 months (95%CI 11.4 – 14.1). Treatment emergent adverse events (TEAEs) grade ≥3, serious TEAEs, and TEAEs leading to discontinuation were observed in 30/57 pts (52.6%), 30/57 pts (52.6%), and 17/57 pts (29.8%), respectively. **Conclusions:** This updated analysis of the VARGADO study continues to show the clinical benefit and manageable safety profile of nintedanib plus docetaxel in patients who had previously received both chemotherapy and ICI treatment. These data add to the real-world evidence that can inform clinical decision-making after prior ICI therapy. Clinical trial information: NCT02392455. Research Sponsor: Boehringer Ingelheim Pharma GmbH & Co. KG.

9605 Poster Session (Board #371), Fri, 8:00 AM-11:00 AM

Establishment of the first international large-scale, genomic screening platform to identify patients with rare oncogene drivers in non-small cell lung cancer (NSCLC) in East Asia. *First Author: Shingo Matsumoto, National Cancer Center Hospital East, Kashiwa, Japan*

Background: A rapidly increasing number of oncogenic drivers have been identified in non-small cell lung cancer (NSCLC), and most of them occur in less than 5% of patients. Large-scale genomic screening to identify patients with rare driver alterations is thus necessary to enable precision medicine and to support the development of novel targeted therapies and companion diagnostics (CDx). **Methods:** A lung cancer genomic screening project (LC-SCRUM-Asia) capturing clinical outcome was established in 2013 with 206 institutions in Japan and 5 in Taiwan currently participating. A separate genomic screening project with similar structure was established in China (LC-IRICA-China) in collaboration with LC-SCRUM-Asia in 2019 (3 institutions enrolling, 17 about to open, 63 undergoing review). Samples are analyzed by a multi-gene PCR panel and targeted next-generation sequencing. The target is to enroll 70000 NSCLC patients (20000 from LC-SCRUM-Asia and 50000 from LC-IRICA-China) by 2022. **Results:** From March 2013, a total of 9383 lung cancer patients were enrolled in LC-SCRUM-Asia, and from October 2019, 1649 pts were included in LC-IRICA-China (January 2020). The rates of genomic alterations in LC-SCRUM-Asia: *EGFR* (17%) of which ex20ins (2%), *KRAS* (13%) of which G12C (4%), *ALK* fusions (2%), *ROS1* fusions (2%), *RET* fusions (2%), *HER2* ex20ins (3%), *MET* ex14skip (2%), *BRAF* V600E (1%), *NRG1* fusions (0.2%) and *NTRK3* fusions (0.03%). Corresponding rates in the initial 243 pts in LC-IRICA China: *EGFR* (45%) of which ex20ins (2%), *KRAS* (8%), *ALK* (5%), *ROS1* (2%), *RET* (1%), *HER2* (2%), *MET* ex14skip (1%), *BRAF*V600E (1%). Through the screening, 266 patients from Japan and Taiwan were enrolled into genotype-matched clinical trials of unapproved targeted drugs. In Japan, ROS1-, BRAF- and TRK-targeted therapies were successfully approved based on these clinical trials, and a NGS-based multigene CDx for EGFR/ALK/ROS1/BRAF targeted-therapies was approved based a concordance study using archival samples from the project. **Conclusions:** An East Asian international genomic screening platform has been established to enable precision medicine for patients, accelerate drug and diagnostic development in patients with very rare alterations and to help provide a deeper understanding of the underlying biology of NSCLC in East Asian patients. The screening network will be further expanded to other countries in East Asia in the near future. Research Sponsor: Japan Agency for Medical Research and Development (AMED), Pharmaceutical/Biotech Company.

9606 Poster Session (Board #372), Fri, 8:00 AM-11:00 AM

Outcomes in patients with advanced non-small cell lung cancer (aNSCLC) and high PD-L1 expression treated with immune checkpoint inhibitor monotherapy: An FDA-pooled analysis. *First Author: Sujay Yogesh Shah, Food & Drug Administration, Silver Spring, MD*

Background: Higher PD-L1 score ≥ 50% predicts for greater benefit to immune checkpoint inhibitor (ICI) therapy in first line (1L) treatment of aNSCLC. It has recently been reported that PD-L1 score ≥ 90% predicts for even greater benefit to 1L ICI monotherapy (Aguilar et al., 2019). We examined pooled clinical trial databases to examine the relationship between high PD-L1 expression across multiple ICI monotherapies in 1L and second line (2L) treatment of aNSCLC. **Methods:** Data was pooled from trials (five 1L and five 2L) of ICI for the treatment of patients with aNSCLC. We defined PD-L1 score as the proportion of tumor cell stained by the assay (total of four assays identified) and included patients in the analysis with PD-L1 score ≥ 50%. Tumor-infiltrating immune cell staining was not considered. Progression-free survival (PFS) and overall survival (OS) by line of therapy for patients with PD-L1 score ≥ 90% and patients with PD-L1 score 50-89% was analyzed. **Results:** A total of 1320 patients treated with ICI monotherapy were identified, 873 in 1L and 447 in 2L. Median follow-up was 9.6 months in 2L patients and 13.3 months in 1L patients. Patients receiving 2L ICI therapy with PD-L1 score ≥ 90% (N = 208) had longer PFS and OS compared to patients with PD-L1 score 50-89% (N = 239), with mPFS 7.1 vs. 4.2 months (HR = 0.66 [95% CI: 0.52-0.83]) and mOS NR vs. 15.8 months (HR = 0.66 [95% CI: 0.49-0.89]). 1L ICI therapy analysis revealed similar trends, as patients with PD-L1 score ≥ 90% (N = 405) had longer PFS and OS compared to patients with a PD-L1 score 50-89% (N = 468), with mPFS 8.3 vs. 5.4 months (HR = 0.78 [95% CI: 0.66-0.92]) and mOS 22.9 vs. 16.4 months (HR = 0.74 [95% CI: 0.61-0.90]). **Conclusions:** This analysis showed the potential of an enhanced clinical benefit in patients with aNSCLC and PD-L1 score ≥90% across ICI monotherapies in both the 1L and 2L treatment setting. These data will be further analyzed in real world populations. Research Sponsor: Food & Drug Administration.

9607 Poster Session (Board #373), Fri, 8:00 AM-11:00 AM

Phase II study of TAK228 in patients with advanced non-small cell lung cancer (NSCLC) harboring NFE2L2 and KEAP1 mutations. *First Author: Paul K. Paik, Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, NY*

Background: Despite past efforts, no targeted therapies exist for squamous cell lung cancer (LUSC) pts. We identified a heretofore untargeted oncogene (NFE2L2)/tumor suppressor (KEAP1) pair, each mutated in ~15% of LUSCs. NFE2L2 encodes NRF2, a transcription factor involved in the oxidative stress response and targeted for degradation by KEAP1. *NFE2L2* mutations (mut) occur only in an exon 2 hotspot (Neh2 domain), which is the binding site for KEAP1. Mutations in this region disrupt KEAP1 binding, leading to NRF2 nuclear translocation and increased mTOR signaling via RagD. We report translational studies and results from a phase 2 trial of the oral TORC1/2 inhibitor TAK228 in biomarker-selected pts. **Methods:** Cell line and xenograft experiments were performed using LK-2 LUSC (NFE2L2 E79K mut), A549 ADCL (KRAS G12S + KEAP1 loss), and SK-MES-1 LUSC cells (NFE2L2/KEAP1 WT) treated with TAK-228, everolimus, rapamycin, or deforolimus. Pts with stage IV LUSC harboring NFE2L2 or KEAP1 mut and ADCL harboring KRAS + KEAP1 co-mut were treated on an NCI CTEP phase 2 study of TAK228 3mg po qd (NCT02417701). Primary endpoint: ORR. Secondary endpoint: PFS. The study used a Simon 2-stage design for each cohort with H0 = 5% (N≥1/5 responses), HA = 40% (N≥2/10 responses). **Results:** TAK228 exhibited differential anti-tumor activity over TORC1 rapalogs in LK-2 and A549 cells. TAK228 alone was cytotoxic at sub-[μM] (IC50 68nM) in LK-2 cells; all other rapalogs had IC50s > 10μM. This was associated with marked decrease in TORC1/2 & MAPK signaling (decreased pS6, pAKT, pERK). Anti-tumor response was seen in LK-2 and A549 xenografts treated with TAK228. No anti-tumor/growth inhibitory responses were seen with any other rapalog. N = 21 evaluable pts have been treated (10 *NFE2L2*, 6 *KEAP1*, 5 *KRAS+NFE2L2/KEAP1*). Median age = 70; median prior lines tx = 2, smokers = 100%, median pack yrs = 39. Most common AEs included hyperglycemia (72%), fatigue (32%), diarrhea (32%), decreased appetite (32%). In *NFE2L2* mut LUSC pts, ORR = 20% (2/10 confirmed PR), DCR = 100% with median PFS = 8.9mos (95%CI 7-NR). In *KEAP1* mut LUSC pts, ORR = 17% (1/6 confirmed PR), DCR = 67% with PFS range = 1.8-8.6 mos. In *KRAS + NFE2L2/KEAP1* mut ADCL pts, ORR = 0% and DCR = 0%. **Conclusions:** TAK228 is tolerable with differential activity in *NFE2L2* (primary endpoint met) and *KEAP1* mutant LUSC. A randomized phase 2 trial of TAK228 + docetaxel vs. SoC chemotherapy in advanced LUSC pts with *NFE2L2/KEAP1* mut is in development (LungMAP S1900D) as is an NCI CTEP phase 1/1b trial of TAK228 + CB-839 in advanced NSCLC patients with *NFE2L2/KEAP1* mut (NCI #10327). Clinical trial information: NCT02417701. Research Sponsor: Druckenmiller Center for Lung Cancer Research Grant.

9609 Poster Session (Board #375), Fri, 8:00 AM-11:00 AM

Biomarker utilization in non-small cell lung cancer, are we treating after testing? *First Author: Elias Makhoul, Cedars-Sinai Medical Center, West Hollywood, CA*

Background: Targeted therapy in EGFR and ALK mutated non-small cell lung cancer (NSCLC) has been the standard of care for nearly a decade with subsequent FDA approvals for ROS1 and BRAF V600 mutated NSCLC occurring in 2016 and 2017. However, recent studies have shown suboptimal utilization of genomic profiling results in these patients. In 1 recent study of community oncologists, ~70% of EGFR/ALK+ patients received appropriate targeted therapy, while patients with other gene mutations (including BRAF and ROS1) only received targeted therapy ~30% of the time. Left unanswered was what patients were receiving instead and why. Additionally, it is unknown if this finding is generalizable to the academic setting. We aimed to investigate whether in our patient population, NSCLC patients with actionable mutations received associated FDA approved therapies and if not why. **Methods:** The pathology database was queried for all NSCLC with molecular testing (including qPCR, FISH and NGS) from 2009 to 2019. Patients with sensitizing EGFR, ALK, ROS1 or BRAF mutations that were detected after the first FDA approval for their respective targeted therapies were included for analysis with those lost to follow up subsequently excluded. Basic demographic and clinical variables were collected as well as treatment records. **Results:** 2160 NSCLC patients were evaluated (2160 EGFR, 1417 ALK, 810 ROS1, 589 BRAF). 468 patients were identified with targetable mutations (411 EGFR, 46 ALK, 5 ROS1, 6 BRAF). No patient had more than 1 targetable mutation. Of those patients, 248 were at an advanced stage and had clinical follow up (202 EGFR, 37 ALK, 4 ROS1, 5 BRAF). Of those patients 197/202 (97.5%), 33/37 (89.2%), 3/4 (75%) and 1/5 (20%) received EGFR, ALK, ROS1 or BRAF targeted therapy respectively. Across biomarkers 14/248 patients (5.6%) did not receive subsequent targeted therapy. 10 patients (5 EGFR, 3 ALK, 1 ROS1 and 1 BRAF) passed away before targeted therapy could be initiated. Physician choice and missed findings accounted for the remaining four cases. **Conclusions:** The vast majority of advanced NSCLC patients analyzed in this study received appropriate targeted therapy matched to genomic findings. The main reason (~4% of total cases) that patients did not receive therapy was due to rapidly progressive disease and death before it could be initiated. These findings are at odds with those published from the community setting. This may be due to multiple factors, including clinician education, ease of access to targeted therapies across patient populations and incomplete data in the previous study populations. Research Sponsor: None.

9610 Poster Session (Board #376), Fri, 8:00 AM-11:00 AM

Cabozantinib in combination with atezolizumab in non-small cell lung cancer (NSCLC) patients previously treated with an immune checkpoint inhibitor: Results from cohort 7 of the COSMIC-021 study. *First Author: Joel W. Neal, Stanford Cancer Institute, Stanford, CA*

Background: First-line immunotherapy with/without chemotherapy is standard of care for patients (pts) with advanced NSCLC; however, there is a need for effective treatment options after progression on a prior immune checkpoint inhibitor (ICI). Cabozantinib (C) may augment response to ICI by inhibiting kinases implicated in suppressing immune cell responses and has shown encouraging clinical activity in combination with ICI in other tumor types including RCC and HCC. COSMIC-021, a multicenter phase 1b study, is evaluating the combination of C with atezolizumab (A) in various solid tumors (NCT03170960). We report results from cohort 7 in NSCLC pts after prior ICI therapy. **Methods:** Eligible pts had ECOG performance status (PS) 0-1 and radiographic progression after one prior anti-PD-1/PD-L1 ICI given alone or in combination with chemotherapy for metastatic nonsquamous NSCLC. Up to 2 lines of prior systemic anticancer therapies were permitted. Pts received C 40 mg PO QD and A 1200 mg IV Q3W. CT/MRI scans were performed Q6W for the first year and Q12W thereafter. Primary endpoint is ORR per RECIST 1.1 by investigator. Other endpoints include safety, duration of response (DOR), progression-free survival, and overall survival. **Results:** Thirty pts with advanced NSCLC were enrolled. Median age was 67 yrs (range 41, 81), 43% were male, 57% had ECOG PS 1, and 23% had liver metastases. Median duration of prior ICI therapy was 4.8 months (mo; range 0.8, 29), and 15 (50%) pts were refractory to prior ICI (progressive disease as best response). As of December 20, 2019, the median follow-up was 8.9 mo (range 5, 20) with 9 (30%) pts continuing study treatment. The most common treatment related adverse events (TRAEs) of any grade were diarrhea (53%), fatigue (37%), nausea (23%), decreased appetite (20%), palmar-plantar erythrodysesthesia (20%) and vomiting (20%). Grade 3/4 TRAEs occurred in 14 (47%) pts, and 1 (3.3%) had grade 5 TRAEs of myocarditis and pneumonitis. Confirmed ORR per RECIST 1.1 was 23% (7 of 30 pts; all partial responses including 3 pts refractory to prior ICI). Time to response was 1.4 mo (range 1, 3), and median DOR was 5.6 mo (range 2.6, 6.9). DCR (CR+PR+SD) was 83%. **Conclusions:** The combination of C and A had an acceptable safety profile and showed encouraging clinical activity in pts with advanced NSCLC who had progressed after prior ICI therapy. The response rate was greater than previously observed with C monotherapy. Due to the promising data, enrollment in this cohort has been expanded and is ongoing. Clinical trial information: NCT03170960. Research Sponsor: Exelixis Inc.

9611 Poster Session (Board #377), Fri, 8:00 AM-11:00 AM

Resistance to lorlatinib in *ROS1* fusion-positive non-small cell lung cancer. *First Author: Jessica Jiyeong Lin, Massachusetts General Hospital, Boston, MA*

Background: Lorlatinib is a potent, brain-penetrant ROS1/ALK tyrosine kinase inhibitor (TKI), which has demonstrated efficacy in advanced *ROS1* fusion-positive (ROS1+) non-small cell lung cancer (NSCLC), including in patients (pts) previously treated with crizotinib. Despite initial benefit, however, most pts experience disease progression on lorlatinib. Mechanisms of resistance to lorlatinib in ROS1+ NSCLC are poorly understood. **Methods:** We analyzed repeat tumor biopsies derived from advanced ROS1+ lung cancer pts progressing on lorlatinib. Next-generation sequencing (NGS, n = 17) or whole exome sequencing (n = 1) was performed to detect mutations, indels, and copy number alterations. **Results:** Sixteen pts underwent a total of 18 repeat tumor biopsies after progression on lorlatinib. Fourteen had received prior crizotinib; two received prior crizotinib and entrectinib. Median duration of therapy on lorlatinib was 13.5 months (95% CI, 8.3-18.4). Among the 18 cases analyzed by sequencing, 7 (38.9%) harbored a *ROS1* resistance mutation, including G2032R (4/18, 22.2%), S1986F/L2000V (1/18, 5.6%), L2086F (1/18, 5.6%), and G2032R/S1986F/L2086F (1/18, 5.6%). Of note, ROS1 L2086F was a novel resistance mutation not previously reported in the literature, but analogous to ALK L1256F (a lorlatinib-resistant *ALK* mutation). Structural modeling studies showed that ROS1 L2086F causes steric interference with binding of lorlatinib, as well as crizotinib and entrectinib. In addition to ROS1 kinase domain mutations, NGS analyses also identified *MET* copy number gain in a lorlatinib-resistant case, validated by fluorescence in situ hybridization as high-level focal *MET* amplification (MET/CEP7 copy number ratio 6.3) without a concomitant *ROS1* resistance mutation. Duration of therapy on lorlatinib was significantly shorter in pts with a post-lorlatinib *ROS1* resistance mutation compared to those without (8.3 vs 18.1 months; p = 0.005). **Conclusions:** *ROS1* resistance mutations are observed in over one-third of cases progressing on lorlatinib, including the solvent front mutation G2032R and a novel L2086F mutation. These findings underscore the importance of developing next-generation ROS1 TKIs with activity against *ROS1* mutations, and the need to elucidate ROS1-independent resistance mechanisms. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

9613 Poster Session (Board #379), Fri, 8:00 AM-11:00 AM

Clinical and genomic analysis of non-small cell lung cancer (NSCLC) patients with MET exon14 skipping (METex14) mutations and responses to anti-MET therapy. *First Author: Andrew McKenzie, Sarah Cannon Research Institute, Nashville, TN*

Background: *MET* is a validated oncogene for molecular targeted therapy in non-small-cell lung cancer (NSCLC), and METex14 mutations result in *MET* overexpression. Studies with MET-targeting therapies have demonstrated high objective response rates and prolonged disease control. There are few clinical and genomic analyses of patients with METex14-positive NSCLC in the community setting. We herein characterize key clinical and genomic findings for patients harboring METex14 mutations. **Methods:** Sarah Cannon provides clinical research to partnering medical oncology practices who order broad-based NGS, from both tissue and blood, as a part of standard of care. Genospace, a clinico-genomic software tool, was used for identification of patients for clinical trials and analysis of clinical and genomic data. **Results:** Of 6521 lung cancer patients with NGS results, 66 (1.01%) harbored METex14 mutations (45.5% from blood and 54.5% from in tissue). The mean age at diagnosis was 75.7 and 21.2% developed brain metastases. Of the 66 patients with METex14 mutations, 69.5% are current/former smokers. Nineteen percent of former/current smokers and 7.6% of never smokers had PD-L1 scores of $>50\%$, respectively. The majority of METex14-positive patients either received standard of care (66.7%) or were unable to take (19.7%) 1st-line therapy. Patients who received chemotherapy (Chemo), immunotherapy (IO), and Chemo/IO in the first and second line settings responded to SOC treatment, and patients receiving anti-MET therapy benefited from therapy even after front-line SOC (table). Genomic analysis revealed the most common co-occurring mutations to be *EGFR, MET, NF1, KRAS,* and *BRCA2* (Freq = 8.7%, 8.7%, 8.7%, and 7.6%, respectively). **Conclusions:** Genospace enables real-time patient identification of METex14-positive NSCLC cases and analysis of these cases indicates that anti-MET therapy may be effective at any line of treatment. Genospace's clinico-genomic database was used to analyze treatment history, clinical correlates, and co-occurring mutations that may reveal novel treatment combination strategies or resistance mechanisms. Research Sponsor: Sarah Cannon.

	1st line		2nd Line		3rd Line		4th Line	
	# of patients	median TTF (days)	# of patients	median TTF (days)	# of patients	median TTF (days)	# of patients	median TTF (days)
Chemo	10	49	6	118.5	4	79	0	N/A
Chemo/IO	15	168	0	N/A	0	N/A	0	N/A
Chemo/radiation			8	44	1	50	1	876
IO	N/A							
EGFRi	1	227	3	70	1	78	0	N/A
METi	10	70	12	188	3	363	2	42.5
No tx	8	84	5	83	4	99.5	3	149
WEE1i	13	N/A	39	N/A	53	N/A	60	N/A
	1	47					1	36

9614 Poster Session (Board #380), Fri, 8:00 AM-11:00 AM

Effect of genomic and transcriptional alterations in first-line chemotherapy on subsequent immunotherapy in non-small cell lung cancer (NSCLC) patients. *First Author: Yayi He, Division of Medical Oncology, Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO*

Background: Recent studies have demonstrated that first-line immunotherapy has better therapeutic response than second-line immunotherapy in NSCLC patients. However, the mechanism behind this observation has not been elucidated. The aim of this study is to investigate the mechanism of unfavorable influence that the first-line chemotherapy exerts on subsequent immunotherapy. **Methods:** 29 NSCLC patients without tyrosine kinase inhibitor (TKI)-related driver gene (EGFR, ALK, ROS1, RET, BRAF, C-MET) mutations were enrolled in this study. Paired cancer tissues before and after chemotherapy were collected, and NGS-based WES and mRNA sequencing were performed. Sequencing data were analyzed with R packages and statistics analysis was performed with SPSS 20 software. $P \leq 0.05$ was regarded as statistically significant. **Results:** We found that the total number of SNV/INDEL mutations and the tumor mutational burden (TMB) decreased significantly following chemotherapy. The decrease of mutation burden correlated well with therapeutic response: patients with partial response (PR) exhibited significant decrease while patients with stable disease (SD) or progression of disease (PD) did not. Meanwhile, a sharp decrease in common mutations before and after chemotherapy was observed in PR and PD patients, but not SD patients, suggesting that mutational change reflected the therapeutic response. The change in copy number variations (CNVs) exhibited similar trends and correlation with therapeutic response. Subsequent analysis on mRNA levels revealed a sharp decrease in the expression levels of genes related to antigen processing and presentation as well as other factors relevant to immunotherapy response. Pathway enrichment analysis showed that the genes with decreased expression mainly represented immune-related signaling pathways or biological processes. **Conclusions:** Our study revealed a possible mechanism underlying unsatisfactory multiple-line immunotherapy following chemotherapy, and indicated that first-line chemotherapy may influence the tumor microenvironment to exert unfavorable influence on subsequent immunotherapy. Research Sponsor: Development and Reform ommission of Shenzhen Municipality (grant number XMHT20190104006), the Science and Technology Project of Shenzhen (grant number KQTD20161129103502213).

9615 Poster Session (Board #381), Fri, 8:00 AM-11:00 AM

Lorlatinib for advanced ALK and ROS1+ non-small cell lung cancer (NSCLC): Efficacy and treatment sequences in the IFCT-1803 LORLATU expanded access program (EAP) cohort. *First Author: Simon Baldacci, Thoracic Oncology Department, Lille University Hospital, Lille, France*

Background: Lorlatinib, a third-generation tyrosine kinase inhibitor targeting ALK and ROS1, has been made available in France starting October 2015 through an EAP for advanced, refractory, ALK+ NSCLC after the failure of chemotherapy and TKIs. Besides the landmark, multi-cohort phase II trial that assessed lorlatinib in ALK+ NSCLC, real-life evidence regarding the efficacy and safety, as well as treatment sequences including lorlatinib, is lacking. **Methods:** We report the cohort of consecutive patients with advanced, refractory, ALK or ROS1+ NSCLC enrolled in the French EAP of lorlatinib from October 2015 to October 2019. Data were collected from medical records by French Cooperative Thoracic Intergroup (IFCT) research study assistants on site. Primary endpoint was progression-free survival. **Results:** 200 patients were included: 143 (71.5%) ALK+, 57 (28.5%) ROS1+, 87 (44%) men, 127 (66%) never-smokers, and 167 (85%) stage IV disease. Mean age was 59 years. At the time of initiation of lorlatinib, 146 (74%) patients had Central Nervous System (CNS) disease (78 % for ALK+, 63% for ROS1+), 131 (76%) were PS 0/1. Lorlatinib was delivered as 2nd/3rd/4th/5th+ line in 3%/17%/27%/53%of ALK+ patients and in 30%/30%/16%/24%of ROS1+ patients, respectively. 150 (75%), 185 (93%), 138 (69%), and 80 (40%) patients had received prior chemotherapy, crizotinib, 2nd generation TKIs, and brain radiotherapy, respectively. Median PFS and OS from the initiation of lorlatinib were 11.8 (95% CI 7.3-14.6) months and NR (95% CI 18.6-NR) months, respectively for ALK+ patients and 7.6 (95% CI 6.2-10.2) months and 20.9 (95% CI 10.0-NR) months, respectively for ROS1+ patients. ORR and DCR were 46.2% (95% CI 37.6-54.7) and 86.2% (95% CI 80.2-92.1), respectively for ALK+ patients and 47.1% (95% CI 33.4-60.8) and 88.2% (95% CI 79.4-97.1), respectively for ROS1+ patients. CNS ORR was 41.7% (95% CI 33.3-50.1) and 37.7% (95% CI 24.7-50.8), respectively. With a median follow-up of 15.6 (95% CI 14.0-17.6) months, progression under lorlatinib treatment was observed in 71 (50%) ALK+ patients and 35 (61%) ROS1+ patients, and CNS progression in 24 (34%) and 8 (23%) patients, respectively. The safety profile of lorlatinib was consistent with published data. **Conclusions:** These real-life results confirmed lorlatinib as a major treatment option for patients with advanced refractory ALK or ROS1+ NSCLC. Research Sponsor: IFCT, Pharmaceutical/Biotech Company.

9616 Poster Session (Board #382), Fri, 8:00 AM-11:00 AM

Randomized phase I trial to evaluate *C*oncurrent *or S*equential *I*pilimumab, *N*ivolumab, and stereotactic body *R*adiotherapy in patients with stage IV non-small cell lung cancer (*COSINR Study*). *First Author: Jyoti D. Patel, Lurie Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL*

Background: Stereotactic body radiotherapy (SBRT) provides high rates of treated metastasis control, stimulates innate and adaptive immune pathways, and is safe in patients treated with anti-PD1 monotherapy following SBRT. We hypothesize that SBRT may improve outcomes for patients receiving immunotherapy through both direct cytoreduction and increased immunogenicity. Within this context, we conducted a phase 1 trial designed to evaluate the safety of combination immune checkpoint blockade with nivolumab and ipilimumab(N/Ip) plus sequential (Seq) or concurrent (Con) multisite SBRT (mSBRT) in patients with stage IV NSCLC. **Methods:** Treatment naïve patients (EGFR/ALK WT) with advanced NSCLC received SBRT to 1 to 4 metastases. Not all metastases were targeted, and metastases >65 mL were partially irradiated. Brain metastases were allowed on protocol, and those >3mm were treated prior to enrollment. SBRT dose varied by anatomic site and ranged from 45 to 50 Gy in 3 to 5 fractions with predefined dose de-escalation if excess dose-limiting toxicities were observed. Patients on Seq arm received N/Ip between 1-7 days after completion of SBRT. Patients in Con arm received N/Ip prior to completion of SBRT. N/Ip continued until progression, development of toxicity, or up to 2 years. Patients underwent pre- and post-treatment biopsy of one irradiated lesion. **Results:** A total of 35 patients (Seq/Con 19/16) were enrolled and evaluable for toxicity analysis (SBRT and at least 1 cycle N/Ip). Brain metastases were present in 27%. PD-L1 expression: 0% (16), 1-49% (10), >50% (9). Median number of metastases treated with SBRT was 3.2. 6 patients experienced DLT (4 pneumonitis), resulting in dose reduction in central lung Seq cohort of the organs at risk (OAR) by 20%. Median PFS by RECIST (total/Seq/Con) was 5.9 mo, 95% CI: 4.9-13.1/ 6.2 mo, 95% CI: 3.5-12.6/ 5.9 mo, 95% CI: 3.1-18.0. RECIST best response was 11% CR, 57% PR, 6% SD, and 26% PD. Treatment past first progression was allowed, and time to second line therapy (chemotherapy) by arm (Seq/Con) was NR/17.5 months. Median OS has not been reached with median follow up of 15mo. PDL1 status did not impact PFS ($p = 0.64$) nor OS ($p = 0.77$). **Conclusions:** Multisite SBRT and concurrent N/Ip was well tolerated. Responses appear durable as median OS was not reached. Multimodality therapy with mSBRT and dual checkpoint inhibitor therapy resulted in impressive tumor control and clinical benefit with promising efficacy. Clinical trial information: NCT03223155. Research Sponsor: BMS.

9618 Poster Session (Board #384), Fri, 8:00 AM-11:00 AM

FLT3 ligand (CDX-301) and stereotactic radiotherapy for advanced non-small cell lung cancer. *First Author: Nitin Ohri, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY*

Background: In a murine non-small cell lung cancer (NSCLC) model, we demonstrated synergy between localized radiotherapy and the dendritic cell growth factor fms-like tyrosine kinase 3 (FLT3) ligand. We now present results from a phase II study testing this combination in patients with advanced and treatment-refractory NSCLC. **Methods:** Advanced NSCLC patients with multi-focal active disease after at least one line of systemic therapy and ECOG performance status 0-2 received 5 daily subcutaneous injections of CDX-301 (75 μg/kg) concurrent with stereotactic body radiotherapy (SBRT, 30-54 Gy in 1-5 fractions based on target size and location) directed at a single site of disease. Additional "cycles" of SBRT and CDX-301 could be administered at least four months after the initial study treatment, at the discretion of the treating physicians. The primary endpoint was progression-free survival four months after treatment initiation (PFS4), with a hypothesis that the PFS4 rate would exceed 40%. Secondary endpoints included overall survival (OS) duration, responses on PET (PERCIST criteria) and CT (RECIST criteria), and dose-limiting toxicities (grade $\geq$3 adverse events within 30 days). Lesions targeted with SBRT were excluded from response assessments. The intended sample size was 29 subjects. Blood samples were obtained for flow cytometry and other analyses of immune activation. **Results:** Twenty-nine subjects received study therapy between October 2016 and January 2020. Subjects received a median of 3 lines (range: 1-5) of systemic therapy prior to study enrollment, including immune checkpoint inhibitors targeting the PD-1/PD-L1 axis in 26 subjects (90%). At the time of this analysis, the actuarial PFS4 rate is 60%, which exceeds our pre-specified efficacy objective. With a median follow-up duration for living patients of 12 months, the actuarial 12-month OS rate is 55%. Partial response of lesions not targeted with SBRT ("abscopal effect") was observed in 9 subjects (31%) using PET criteria and in 4 subjects (14%) using CT criteria. Seven subjects (24%) received a second course of SBRT and CDX-301 after initial study therapy. No dose-limiting toxicities have been observed. Only six subjects (21%) have received additional chemotherapy or immunotherapy after study treatment. **Conclusions:** The combination of CDX-301 and SBRT is well-tolerated and has activity as systemic therapy for advanced NSCLC. Additional studies to maximize the efficacy of this *in situ* vaccination approach with the addition of an agonist anti-CD40 antibody (CDX-1140) are planned. Clinical trial information: NCT02839265. Research Sponsor: U.S. National Institutes of Health.

9619 Poster Session (Board #385), Fri, 8:00 AM-11:00 AM

Dose escalation and expansion from the phase I study of DS-1062, a trophoblast cell-surface antigen 2 (TROP2) antibody drug conjugate (ADC), in patients (pts) with advanced non-small cell lung cancer (NSCLC). *First Author: Aaron Elliott Lisberg, Department of Medicine, Division of Hematology/Oncology, UCLA, Los Angeles, CA*

Background: TROP2 is an intracellular calcium signaling transducer overexpressed in NSCLC, portending poor survival. DS-1062 is a TROP2-targeting ADC with a novel topoisomerase 1 inhibitor (exatecan derivative, DXd) and promising preclinical antitumor activity. Updated results inclusive of 24 additional dose escalation pts and 32 dose expansion pts from an ongoing phase 1 study of DS-1062 in advanced/metastatic NSCLC are reported (NCT03401385/J101). **Methods:** Pts aged $\geq$18 (US) or $\geq$20 (Japan) with unresectable NSCLC refractory to/relapsed from standard treatment with measurable disease (RECIST v1.1) and available tumor for retrospective TROP2 evaluation were eligible. Primary objectives include maximum tolerated dose (MTD) identification, safety, and tolerability and secondary objectives include efficacy, pharmacokinetics, and incidence of anti-drug antibodies against DS-1062. Pts were eligible regardless of TROP2 level. **Results:** As of November 16, 2019, 95 pts were treated with $\geq$1 dose of DS-1062. 63 pts were treated during escalation at 0.27 (n = 4), 0.5 (n = 5), 1.0 (n = 7), 2.0 (n = 6), 4.0 (n = 6), 6.0 (n = 19), 8.0 (n = 8), and 10.0 (n = 8) mg/kg and 32 pts were treated in expansion at the MTD of DS-1062, 8 mg/kg. 59 pts (62%) discontinued (25 [42%] due to progressive disease per RECIST v1.1). Pts were exposed to a median of 3 treatment cycles (range, 1-19). In 88 response-evaluable pts, 22 had partial response (1 PR/6 pts at 2.0 mg/kg, 2 PR/6 pts at 4.0 mg/kg, 5 PR/18 pts at 6.0 mg/kg, 13 PR/34 pts at 8.0 mg/kg, and 1 PR/8 pts at 10.0 mg/kg; 14 PRs were confirmed and 8 PRs are awaiting confirmation). Treatment emergent adverse events (TEAEs) regardless of causality were reported in 91 of 95 pts (96%; 44 pts [46%] experienced $\geq$grade 3, 30 pts [32%] had serious events). Treatment-related TEAES were reported in 76 of 95 pts (80%; 17 pts [18%] experienced $\geq$grade 3, 8 pts [8%]) had serious events). Potential interstitial lung disease (ILD) occurred in 8 pts (8%; 2 at 6.0 mg/kg and 6 at 8.0 mg/kg); 6/8 with potential ILDs adjudicated as treatment-related (1 at 6.0 mg/kg [grade 2] and 5 at 8.0 mg/kg [1 grade 1, 2 grade 2, 1 grade 3, and 1 grade 5]). 14 escalation pts and 22 expansion pts remain on trial. Updated trial details/results will be presented. **Conclusions:** In this first-in-human study of DS-1062, treatment was well tolerated up to 8 mg/kg, and a dose effect on antitumor activity was observed over 2.0-10.0 mg/kg in heavily pretreated pts with prior progression on standard treatment. Clinical trial information: NCT03401385. Research Sponsor: Daiichi Sankyo.

9620 Poster Session (Board #386), Fri, 8:00 AM-11:00 AM

Genomic characterization and outcome evaluation of kinome fusions in a large non-small cell lung cancer population. *First Author: Fengying Wu, Shanghai Pulmonary Hospital, Shanghai, China*

Background: Lung cancer is the leading cause of cancer death worldwide. Kinase fusion represents an important type of somatic alterations which promote oncogenesis and serve as a diagnostic marker in lung cancer. This study aims to identify the landscape of kinase fusions in lung cancer and expand our understanding of druggable fusions, together providing valuable information for therapeutics decision making. **Methods:** We performed genomic profiling of tumor/plasma biopsies of a total of 18,839 Chinese lung cancer patients using next generation sequencing (NGS) by targeting 425 cancer-relevant genes. Patients' clinical characteristics and treatment history were retrospectively studied. **Results:** A total of 1,048 patients (5.56%, 1,048/18,839) were identified with kinase fusions, including 815 adenocarcinomas (ADCs) and 34 squamous cell carcinomas (SCCs). Briefly, a total of 198 unique gene fusion events have been observed, including 37 recurrent fusions and 114 novel fusions which have previously not been documented. ADC patients with kinase fusions were relatively younger than SCC patients (median: 53 vs 61 years old, $p< 0.01$). The most frequently observed fusion was *EML4-ALK* for both ADCs (50.0%) and SCCs (32.4%), followed by *FGFR3-TACC3* (29.4%) in SCCs and *KIF5B-RET* (11.8%), *CD74-ROS1* (9.2%), *CCDC6-RET* (3.9%) and *SLC34A2-ROS1* (2.3%) in ADCs, retrospectively. A total of 14 recurrent fusions including *FN1-ALK*, *MEMO1-ALK, CUX1-ALK*, *KIF13A-RET* and *PHF20-NTRK1* were also identified at low frequencies. Of note, *EML4-* or *STRN-ALK* fusion events mainly rearranged in the intron 19 of *ALK*, but the breakpoints of *VCL-ALK* were mostly located upstream of *ALK* exon 18. Meanwhile, *CD74-*, *SLC34A2-* and *TPM3- ROS1* rearrangement mainly occurred in the *ROS1* introns 31, 33 and 34. In addition, among patients with novel fusions, *RORB-ALK* and *AFF2-RET* may potentially function as oncogenic drivers in lung cancer and have demonstrated clinical benefit from crizotinib treatment. **Conclusions:** Our data have depicted a comprehensive overview of the landscape of kinase fusions in lung cancer, which helps recognize potentially druggable fusions and translate into therapeutic applications. Research Sponsor: None.

9621 Poster Session (Board #387), Fri, 8:00 AM-11:00 AM

Acquired resistance to PD-1 blockade in NSCLC. *First Author: Adam Jacob Schoenfeld, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Although durability is the trademark characteristic of response to PD-1 blockade, acquired resistance can occur. The frequency, patterns, and survival outcomes of patients with acquired resistance to PD-1 blockade are unknown. **Methods:** All patients with NSCLC treated with PD-1 blockade at MSKCC were examined. Acquired resistance was defined as initial CR/PR (by RECIST) followed by progression/death. Oligo vs systemic patterns of acquired resistance were defined as progression in ≤ 2 sites of disease or ≥ 3 sites of disease, respectively. **Results:** Of 1201 patients treated with PD-1 blockade, 243 (20%) achieved initial response and 189 (78%, 95% CI 72-83%) eventually developed acquired resistance (AR). Onset of AR was variable and decreased with longer duration of response (53% within 1 year, 37% 1-2 years, 10% $>$ 2 years). Patients with PD-L1 expression $<$ 50% and TMB $<$ 8mut/Mb were more likely to develop resistance compared those with PD-L1 expression $\geq$50% and TMB $\geq$8mut/Mb (OR 5.5, p = 0.02). Unlike organ sites of primary refractory disease, AR commonly occurred in lymph nodes (41%) and infrequently in the liver (6%). Patterns of AR were most commonly oligo rather than systemic (79/141 [56%], 39/141 [28%]); some patients died without radiographic progression (23/141 [16%]). Oligo-AR occurred later (median onset 13 vs 5.6 mo) and associated with improved post-progression survival (median OS 55.2 vs 9.2 mo, HR 6.0, p $<$ 0.001) compared to systemic-AR. Post-progression survival was highest in patients with AR compared to those with initial SD or PD to PD-1 blockade (median 18.9 vs 12.5 vs 4.4, p $<$ 0.001). Of 49 patients treated initially with locally-directed therapy for AR, 28 (57%) remain alive and systemic therapy-free. **Conclusions:** Acquired resistance to PD-1 blockade is common in NSCLC. Risk of acquired resistance is lower in biomarker-enriched patients and with increased duration of response. Patterns of acquired resistance is commonly oligo in nature, which is amenable to locally-directed therapy and can be associated with improved survival. Differences in organ-site distribution and post-progression survival suggest distinct biology associated with acquired resistance vs primary refractory disease. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

9622 Poster Session (Board #388), Fri, 8:00 AM-11:00 AM

Progression-free survival estimates in non-small cell lung cancer when RECIST is unavailable: Project GENIE's integration of genomic, therapeutic and phenomic data. *First Author: Jessica A. Lavery, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Molecular tumor profiling has become an integral component of oncology practice but linked genomic-phenomic data remain scarce. Recurrence, treatment response and progression are not structured consistently in medical records and this deficit has been a roadblock to discovery of biomarkers that are associated with favorable outcomes. **Methods:** The Genomics Evidence Neoplasia Information Exchange (GENIE) consortium is an AACR sponsored project to link and share genomic and phenomic data to promote discovery in precision medicine. 3 cancer centers that routinely perform somatic tumor profiling for advanced cancers agreed to curate anti-neoplastic treatment exposures and outcomes including recurrence, progression, response and survival using a standard method. 6 cancer types (lung, colorectal, breast, prostate, pancreas and bladder) were selected and a REDCAP database captures anti-neoplastic treatments, and specific elements from pathology, radiology and oncology reports. Curators abstract data using data fields that rely on the PRISSMM standard. "Real world" progression free survival (PFS) was identified based on curation of: 1) the text of radiologists' reports for CT, PET/CT, PET and MRI scans (PFS_I) and 2) medical oncologists' notes (PFS_M). PFS_I and PFS_M were estimated from the start of 1st line anti-neoplastic systemic therapy until progression or death for all patients with molecularly characterized non-small cell lung cancer (NSCLC). **Results:** Genomic sequencing was performed between 2015 and 2017 for 748 patients with NSCLC treated at three major cancer centers. Median age at diagnosis was 66 years (interquartile range 58, 73) and 43% were male. As shown in the table, when RECIST assessments are unavailable, estimates of PFS vary based on whether they are derived from radiologists' or oncologists' interpretations. **Conclusions:** Radiologists' reports and oncologists' reports provide different PFS estimates. Cohort studies should specify the method used to define "real world" endpoints. Project GENIE will have 1800 NSCLC patients with curated endpoints by the ASCO meeting. Research Sponsor: American Association for Cancer Research.

"Real World" PFS from 1st line treatment for NSCLC: estimates based on radiologists' reports (PFS_I) and oncologists' notes (PFS_M).

Regimen	N	PFS_I (months; 95% CI)	PFS_M (months; 95% CI)
Any therapy	468	7.6 (6.4, 9.2)	10.7 (9.9, 12.4)
Immunotherapy	45	3.7 (1.5, 6.0)	7.0 (4.4, 10.1)
Cytotoxic therapy	370	9.0 (7.4, 10.5)	11.5 (9.9, 14.0)
Targeted therapy	53	7.3 (4.9, 14.1)	11.1 (8.9, 24.4)

9623 Poster Session (Board #389), Fri, 8:00 AM-11:00 AM

SWOG S1400F (NCT03373760): A phase II study of durvalumab plus tremelimumab for previously treated patients with acquired resistance to PD-1 checkpoint inhibitor therapy and stage IV squamous cell lung cancer (Lung-MAP Sub-study). *First Author: Natasha B. Leighl, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: The Lung Cancer Master Protocol (Lung-MAP) is designed to evaluate novel targeted therapies in patients with advanced squamous lung carcinoma. In the S1400F sub-study (non-match), we tested whether combined CTLA-4 and PD-1 inhibition with durvalumab plus tremelimumab (D+T) could overcome primary or acquired resistance to anti-PD-(L)1 therapy. Response, progression-free (PFS) and overall survival, and safety in the acquired resistance cohort are reported herein. **Methods:** Patients with previously treated squamous lung carcinoma, performance status (PS) 0-1, and adequate organ function that developed disease progression after $\geq$24 weeks of anti-PD-(L)1 monotherapy were eligible. Prior severe immune-related toxicities, intervening systemic therapy and combination chemo-immunotherapy were not permitted. Patients received D1500 mg + T75 mg IV q28 days for 4 cycles then D maintenance until disease progression. The primary endpoint was best objective response (RECIST 1.1). Interim analysis for futility was planned after 20 patients evaluable for response were enrolled. If no responses were observed, the cohort would stop enrolment. **Results:** 30 eligible patients were accrued to the acquired resistance cohort. Median age was 68 years, 60% of patients were male, 33% PS 0 and had received a median of 2 prior lines of therapy (maximum 4). Best response to prior anti-PD-(L)1 therapy was CR/PR/SD in 3/7/20 patients, with a median duration of anti-PD-(L)1 therapy of 8.6 months (5.2-30.4). No objective responses were seen with D+T; 47% had SD as best response. Median PFS was 2.0 months (95% CI 1.6-2.9) and survival 7.5 months (95% CI 5.3-8.7). Among the 14 patients with SD as best response, the median PFS calculated from first disease assessment is 2.8 months (95% CI: 1.4-3.9). Grade$\geq$3 adverse events at least possibly related to protocol therapy were seen in 10/30 patients. These include 1 treatment-related death due to pneumonitis and 1 death not otherwise specified. Other adverse events include grade 3 confusion (1), dehydration (2), diarrhea (3), encephalopathy (1), weakness (1), hyperglycemia (1), hypoxia (1), lymphopenia (1), nausea, (1), neutropenia (1), thrombocytopenia (1), rash (1), vomiting (1), grade 4 dyspnea (1), leucopenia (1) and lymphopenia (1). **Conclusions:** D+T did not demonstrate activity in patients with acquired resistance to PD-1 checkpoint inhibitors and pretreated advanced squamous lung carcinoma. Clinical trial information: NCT03373760. Research Sponsor: U.S. National Institutes of Health, Lung-MAP trial supported in part by NIH/NCI grants CA180888, CA180819, CA180820, CA180821, CA180863, CA180868, and by AbbVie Inc., Amgen, AstraZeneca, Bristol-Myers Squibb Company, Genentech and Pfizer through the Foundation for the National Institutes of Health, in partnership with Friends of Cancer Research.

9624 Poster Session (Board #390), Fri, 8:00 AM-11:00 AM

BRIGHTSTAR: A pilot trial of local consolidative therapy (LCT) with brigatinib in tyrosine kinase inhibitor (TKI)-naïve ALK-rearranged advanced NSCLC. *First Author: Yasir Elamin, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Approximately, 95% of patients who have an initial response to ALK-TKIs exhibit an incomplete response resulting in residual disease that enables the emergence of acquired resistance. Eliminating residual disease using LCT may delay resistance emergence and improve clinical outcomes. **Methods:** This is a single center investigator-initiated trial that assesses the safety, feasibility and efficacy of brigatinib with LCT. Eligible patients have TKI-naïve ALK rearranged advanced NSCLC with any number of metastases. Patients treated with brigatinib for an induction period of 8 weeks followed by LCT with radiation and/or surgery. **Results:** Between 12/2018 and 01/2020, 17 out of 24 planned patients were enrolled. Median age 55 (range 33-73). At study entry, 15 patients had polymetastatic disease ($>$ 3 sites) while 2 had oligometastatic disease. As of February 1, 2020, 16 patients were evaluated for response and completed LCT while 1 patient remained on induction brigatinib. The disease control rate was 100% with an objective response rate of 94% (n = 15). Median follow up was 8 months (range 3-13) with no patients with disease progression to date. LCT used was radiation (n = 11), surgery (n = 3), surgery and radiation (n = 2). Among 5 patients who had surgery, 4 had lobectomy and mediastinal lymph node dissection (MLND), 1 had wedge resection with MLND, and 1 had adrenalectomy. Of these, 2 had complete pathological response and 1 had complete pathological response at the primary tumor. There were no grade $\geq$2 adverse events (AEs) related to LCT, including in 7 patients treated with concurrent brigatinib and radiation, and 6 patients treated with radiation while brigatinib was held. All patients continued brigatinib after LCT. Brigatinib-related severe AEs included grade 3: increased blood levels of creatine kinase, lipase, alanine aminotransferase, amylase (n = 1 each) and nausea (n = 1). One patient had grade 2 pneumonitis after 2 weeks of starting brigatinib, this resolved with steroids and brigatinib was resumed at a lower dose. **Conclusions:** Brigatinib with LCT is safe and feasible in patients with ALK-rearranged advanced NSCLC irrespective of number of metastatic sites. Brigatinib and LCT may be an effective therapeutic strategy in this subset of NSCLC patients. Clinical trial information: NCT03707938. Research Sponsor: Takeda.

TPS9625 **Poster Session (Board #391), Fri, 8:00 AM-11:00 AM**

Phase III trial comparing antibody-drug conjugate (ADC) SAR408701 with docetaxel in patients with metastatic non-squamous non-small cell lung cancer (NSQ NSCLC) failing chemotherapy and immunotherapy. *First Author: Melissa Lynne Johnson, Sarah Cannon Research Institute, Nashville, TN*

Background: Despite recent advances in the treatment of NSQ NSCLC, including the integration of immune checkpoint inhibitors (ICI) into first-line treatment of all patients, novel therapies are necessary at disease progression. Carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5), a cell-surface glycoprotein, is overexpressed in several tumor types, including NSQ NSCLC; ~20% of patients express high CEACAM5 levels. SAR408701 is an ADC combining a humanized antibody targeting CEACAM5 with the potent cytotoxic maytansinoid derivative DM4 and is expected to selectively deliver DM4 to CEACAM5-expressing cancer cells. In an interim analysis of a first-in-human study (NCT02187848) in patients with NSQ NSCLC and CEACAM5 expression in ≥50% of tumor cells, SAR408701 administered 100 mg/m^2 every 2 weeks showed an objective response rate (ORR) of 23% and a favorable safety profile (Gazzah A et al *J Clin Oncol*. 2019;37:15, 9072). **Methods:** In this randomized, open-label, phase 3 trial, patients receive either SAR408701 100 mg/m^2 IV every 2 weeks or the standard of care treatment docetaxel 75 mg/m^2 IV every 3 weeks. Randomization is stratified on ECOG performance status (PS), previous ICI treatment (sequential vs combination), and geographical region. Patients are ≥18 years with metastatic NSQ NSCLC after platinum-based chemotherapy and ICI treatment (anti-PD-1/PD-L1 monoclonal antibody), express CEACAM5 in ≥50% of tumor cells at ≥2+ intensity (central testing), and have ECOG PS 0–1. Exclusion criteria include untreated brain metastases, history of corneal disorders, and prior treatment with docetaxel, maytansinoid derivatives, or CEACAM5-targeting drugs. Tumor imaging occurs at baseline and every 8 weeks until disease progression. Primary endpoints are progression-free survival (PFS; RECIST v1.1 by independent blinded review committee) and overall survival (OS), both analyzed by Kaplan-Meier method, stratified log-rank test, and stratified Cox proportional hazard model. Study success is defined either on PFS or OS, with a strong type-I error control for multiple hypotheses. Secondary endpoints are ORR and duration of response (RECIST v1.1), health related quality of life (EORTC QLQ-C30 and EORTC QLQ-LC13), and safety (adverse events graded by NCI CTCAE v5). Approximately 554 randomized patients (277 per arm) is adequate to reach both PFS and OS events. The study opened in Nov 2019, and as of Feb 7, 2020, 20 sites in 8 countries are activated. Clinical trial information: NCT04154956. Research Sponsor: Sanofi.

TPS9626 **Poster Session (Board #392), Fri, 8:00 AM-11:00 AM**

Randomized phase II study of canakinumab (CAN) or pembrolizumab (PEM) as monotherapy or in combination as neoadjuvant therapy in patients (Pts) with surgically resected (Stage IB-IIIA) non-small cell lung cancer (NSCLC): CANOPY-N. *First Author: Tony S. K. Mok, The Chinese University of Hong Kong, Hong Kong, China*

Background: Complete surgical resection is the standard treatment (tx) for pts with stage I-IIIA NSCLC. 5-year survival rates range from 19-50%, with most pts dying from distant recurrence. Neoadjuvant or adjuvant chemotherapy improves overall survival (OS) by only 5% in pts with NSCLC, and new tx options are needed. Preliminary data with PD-1 or PD-L1 inhibitors as neoadjuvant therapy has shown major pathologic responses (MPR) or pathologic complete responses (pCR) in pts with early stage NSCLC. CANTOS study demonstrated reduced incidence of NSCLC and decreased lung cancer-related mortality with CAN (IL-1β inhibitor) versus placebo, in a dose-dependent manner for pts with atherosclerosis. In pre-clinical NSCLC humanized models, tx with CAN±anti PD-1 inhibitor could lead to anti-tumor activity. Combination of CAN and PEM is expected to enhance the efficacy of PD-1 inhibition by inhibiting dysregulated inflammation in tumor microenvironment. Based on available evidence, CANOPY-N study was designed to evaluate effect of CAN and PEM as monotherapy or in combination as neoadjuvant tx for pts with resectable NSCLC. **Methods:** CANOPY-N (NCT03968419) is a phase II, randomized, open-label study evaluating effect of CAN or PEM monotherapy or in combination as neoadjuvant tx in resectable NSCLC pts. Histologically confirmed stage IB-IIIA, tx-naive, ECOG PS 0-1 NSCLC pts eligible for surgery and with a planned surgical resection in approximately 4-6 weeks (after 1st dose of study tx), are eligible to participate. An archival (if obtained up to 6 months before 1st day of tx) or new biopsy is required. Approximately 110 pts will be randomized in 2:2:1 ratio (stratified by histology [squamous/non-squamous]) to one of the tx arms to receive a total of 2 doses (200 mg Q3w) of CAN alone (n = 44) or in combination with PEM (n = 44) or PEM (n = 22) with safety follow-up up to 130 days from last study drug dose. Primary endpoint is to determine MPR rate (≤10% of residual viable tumor cells at time of surgery), secondary endpoints include determination of ORR, MPR rate based on local review, surgical feasibility rates, anti-drug antibodies incidence and PK parameters. Clinical trial information: NCT03968419. Research Sponsor: Novartis Pharmaceuticals Corporation.

TPS9627 **Poster Session (Board #393), Fri, 8:00 AM-11:00 AM**

A phase II randomized study of telaglenastat, a glutaminase (GLS) inhibitor, versus placebo, in combination with pembrolizumab (Pembro) and chemotherapy as first-line treatment for KEAP1/NRF2-mutated non-squamous metastatic non-small cell lung cancer (mNSCLC). *First Author: Ferdinandos Skoulidis, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Mutational activation of the KEAP1/NRF2 pathway occurs in >20% of NSCLC patients (pts). KEAP1/NRF2 activation protects tumor cells from diverse forms of oxidative stress and promotes tumor growth and survival. In pts w/ advanced NSCLC, mutation of the KEAP1/NRF2 pathway is associated w/ dramatically reduced survival and poor outcomes following standard-of-care therapy. These tumors have increased dependence on GLS-mediated conversion of glutamine to glutamate due to upregulation of NRF2 target genes involved in glutamine metabolism. Telaglenastat (CB-839), an investigational, first-in-class, potent, oral GLS inhibitor, has demonstrated preclinical activity in KEAP1/NRF2-mutated NSCLC cell lines and xenograft models. This study will evaluate the safety and efficacy of telaglenastat + standard-of-care pembro and chemotherapy as 1L therapy for KEAP1/NRF2-mutated non-squamous mNSCLC (NCT04265534). **Methods:** This phase II, randomized, multicenter, double-blind study will enroll ~120 pts with histologically or cytologically documented stage IV non-squamous NSCLC w/ KEAP1 or NRF2 mutation, no prior systemic therapy for mNSCLC, measurable disease (RECIST v1.1), ECOG PS 0-1, and no EGFR, ALK, ROS, or other actionable mutation w/ available approved therapy in 1L setting. KEAP1 or NRF2 mutations will be determined by next generation sequencing (NGS), and study-provided liquid biopsy NGS will be available. Pts will be randomized 1:1 to receive telaglenastat (800 mg BID PO) or placebo, in combination with pembro, carboplatin, and pemetrexed at standard doses on day 1 of each 21-day cycle. Pts will be stratified by STK11/LKB1 mutational status and M stage of cancer (M1a-b vs M1c). The study will include an initial safety run-in period (n=12; 1 cycle). Co-primary endpoints are safety and investigator-assessed progression-free survival (RECIST v1.1). Secondary endpoints include overall response rate, duration of response, overall survival, and efficacy analysis in the subgroup of pts w/ biochemical confirmation of KEAP1/NRF2 pathway activation. Findings of this novel NGS biomarker-selected study will inform the efficacy and safety profile of telaglenastat + standard-of-care chemoimmunotherapy for 1L treatment of KEAP1/NRF2-mutated, non-squamous mNSCLC. Clinical trial information: NCT04265534. Research Sponsor: Calithera Biosciences, Inc.

TPS9628 **Poster Session (Board #394), Fri, 8:00 AM-11:00 AM**

A phase I/II study of REGN5093, a MET x MET bispecific antibody, in patients with MET-altered advanced non-small cell lung cancer (NSCLC). *First Author: Tracey Rowlands, Regeneron Pharmaceuticals, Inc., Tarrytown, NY*

Background: Mesenchymal-epithelial transition (MET) factor is a transmembrane tyrosine kinase receptor activated by hepatocyte growth factor (HGF). Aberrant activation of MET via gene amplification or gene mutations, as well as MET protein overexpression, has been reported in NSCLC and other cancer types and can promote tumorigenesis. REGN5093 is a human bispecific antibody that binds to two distinct epitopes of MET, blocking HGF binding and inducing internalization and degradation of MET. REGN5093 prevents MET-mediated signaling and inhibits growth of MET-driven tumor cells without inducing MET-driven biological responses (DaSilva et al, *CCR*, 2019; PMID: 31848185). **Methods:** This Phase I/II, first-in-human, multicenter study is investigating the safety, tolerability, pharmacokinetics (PK), and efficacy of REGN5093 in patients with MET-altered advanced NSCLC who have received all available approved therapies (NCT04077099). Key eligibility criteria include age ≥18 years, Eastern Cooperative Oncology Group performance status of ≤1, and documented presence of either *MET* exon 14 gene mutation and/or *MET* gene amplification and/or elevated MET protein expression. Patients are required to provide a biopsy during screening for assessment of MET biomarkers. Key exclusion criteria include prior MET-targeted biologic therapy (expansion cohorts only). Prior therapy with tyrosine kinase inhibitors are not exclusionary in any part of the study. For each patient, the study comprises a screening period of up to 28 days, followed by 3-week cycles of REGN5093 monotherapy. Study treatment will continue until confirmed disease progression or other protocol-defined reason for discontinuation. The study has two parts: dose escalation and dose expansion. Dose escalation will proceed via 4+3 design until a maximum-tolerated dose is reached or a recommended Phase II dose selected. The primary objective of the dose escalation part is to assess safety (incidence and severity of adverse events and Grade ≥3 laboratory abnormalities), tolerability (incidence of dose-limiting toxicities), and PK of REGN5093. During the expansion phase, patients will be allocated to cohorts according to the type(s) of documented biomarkers of MET-altered disease. Anti-tumor activity based on objective response rate per Response Evaluation Criteria in Solid Tumors version 1.1, determined by CT or MRI, will be the primary endpoint in the expansion cohorts. The study is currently open for enrollment. Clinical trial information: NCT04077099. Research Sponsor: Regeneron Pharmaceutical, Inc.

TPS9629 **Poster Session (Board #395), Fri, 8:00 AM-11:00 AM**

Phase II randomized trial of carboplatin + pemetrexed + bevacizumab, +/- atezolizumab in stage IV non-squamous non-small lung cancer (NSCLC) patients who harbor a sensitizing EGFR mutation or have never smoked. *First Author: Joseph Nicholas Bodor, Fox Chase Cancer Center, Philadelphia, PA*

Background: Stage IV NSCLC patients who are never-smokers or with EGFR-mutated tumors generally do not benefit from single-agent immunotherapy. Retrospective subgroup analyses from recent phase III trials suggest that immunotherapy-chemotherapy +/- VEGF inhibition may overcome resistance to PD-L1 inhibitors in these patients, however prospective research on this is needed. This trial will examine a patient population with stage IV non-squamous disease who either have tumors that possess an EGFR exon 19 or 21 mutation or who are never-smoker wild-types, to determine whether the PD-L1 inhibitor atezolizumab in combination with pemetrexed, carboplatin, and bevacizumab can improve outcomes. **Methods:** This is a randomized, phase II, multi-center, open-label trial to assess pemetrexed/carboplatin and bevacizumab +/- atezolizumab in 117 subjects with stage IV non-squamous NSCLC. Randomization will be 2:1 favoring the + atezolizumab arm. Patients are stratified by EGFR mutation status (i.e. EGFR exon 19 or 21 vs. never-smoker wild-type). Never-smoker wild-type is defined as smoking $<$ 100 cigarettes in a lifetime and without any EGFR mutation or ALK or ROS1 rearrangement. Patients with EGFR exon 19 or 21 mutated tumors must have progression of disease or intolerance of treatment with one or more prior TKIs. Primary endpoint is progression-free survival (PFS). Secondary endpoints include overall survival (OS), overall response rate, duration of response, and time to response. Primary objective is to compare PFS between arms. Secondary objectives include a safety analysis in all treated subjects, and comparisons of PFS and OS between arms for the patient subset with EGFR-mutated tumors. Correlative studies include interrogating flow cytometry-based peripheral blood biomarkers, examining the role of desmoplasia in local tumor immunosuppression, and assessing the contribution of estrogen metabolites to tumorigenesis. This study opened in August 2019 with 2 patients enrolled at the time of submission. Twenty U.S. sites through the NCCN are participating. This study was approved and funded by the National Comprehensive Cancer Network (NCCN) Oncology Research Program from general research support provided by Genentech, Inc. Clinical trial information: NCT03786692. Research Sponsor: F. Hoffmann-La Roche Ltd./Genentech.

TPS9630 **Poster Session (Board #396), Fri, 8:00 AM-11:00 AM**

Phase IIa study of marrow infiltrating lymphocytes (MILs), an adoptive T cell therapy, alone or in combination with nivolumab in non-small cell lung cancer (NSCLC). *First Author: Martin Edelman, Fox Chase Cancer Center, Philadelphia, PA*

Background: Primary or secondary resistance to anti-PD-1 may be due to loss of T cell function. Persistent antigen stimulation can lead to impaired CD8+ T cell function, which often results in acquired resistance to PD-1 inhibition. It is unclear whether reinvigoration of tumor infiltrating cells or recruitment of novel T cells impart the activity of anti-PD-1 therapy. The bone marrow is a reservoir for antigen experienced memory T cells. We have previously shown that MILs can be generated for patients with hematologic malignancies and solid tumors including patients with NSCLC. MILs are the product of the activation and expansion of bone marrow T cells with a polyantigenic memory phenotype that recognize tumor antigens, are cytotoxic to autologous tumor and are able to persist over a long period of time. In a pre-clinical study of NSCLC, MILs were able to be expanded in all patients tested. Furthermore, all of the NSCLC products tested showed specificity to shared NSCLC antigens. The combination of adoptive cell therapy (ACT) with checkpoint inhibitors (CPIs) has distinctive positive effects on CD8 and CD4 T cell subsets, with the possibility for complete tumor control. We hypothesize that patients with NSCLC who have relapsed on anti-PD-1 treatment could benefit from an infusion of non-exhausted, central memory-enhanced, antigen specific T cells i.e. MILs which can delay the induction of tumor-associated anergy and augment the overall effectiveness of immunotherapy. **Methods:** Patients with advanced NSCLC who have progressed following prior anti-PD-1 therapy, with sufficient bone marrow reserve and an ECOG 0-1 are eligible. In eligible patients, bone marrow (200 mL) will be harvested and processed. Patients will undergo lymphodepletion (fludarabine 300 mg/m^2/day and cyclophosphamide 30 mg/m^2/day on days -5,-4,-3) followed by infusion of MILs on day 0. In Part 1, up to 6 patients will be administered MILs alone on day 0. In Part 2, approximately 20 subjects will be administered MILs on day 0 followed by NIVO 480 mg Q4W starting on day 1. The objectives of the study are to assess safety of MILs alone and in combination with NIVO, as well as efficacy. The first patient was treated in December 2019. Clinical trial information: NCT04069936. Research Sponsor: None.

TPS9631 **Poster Session (Board #397), Fri, 8:00 AM-11:00 AM**

A phase II trial of durvalumab (MEDI4736) and tremelimumab with chemotherapy in metastatic EGFR mutant non-squamous non-small cell lung cancer (NSCLC) following progression on EGFR tyrosine kinase inhibitors (TKIs) (ILLUMINATE). *First Author: Chee Khoon Lee, St George Hospital, Kogarah, Australia*

Background: Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) have proven remarkably effective in the treatment of advanced EGFR mutant non-small cell lung cancer (NSCLC). However, drug resistance is inevitable and outcomes with subsequent platinum-pemetrexed chemotherapy are poor. The role of immune-checkpoint inhibitor monotherapy in EGFR mutant NSCLC remains uncertain with trials demonstrating inferior survival outcomes compared to chemotherapy. However, a recent randomised study with combination checkpoint inhibitor-chemotherapy demonstrated improved survival over chemotherapy alone in this patient population. This study aims to evaluate the efficacy and tolerability of combination dual immune-checkpoint blockade, durvalumab and tremelimumab, with platinum-pemetrexed chemotherapy in metastatic EGFR mutant NSCLC following progression on EGFR-TKIs. **Methods:** This international phase II cohort study will recruit 100 participants from Australia and Taiwan with advanced EGFR mutant NSCLC following disease progression with EGFR-TKIs [Cohort 1 (n=50): T790M mutation negative on tissue and plasma; Cohort 2 (n=50): T790M mutation positive on tissue and/or plasma, and progression on3rd generation TKIs]. Participants will receive 4 cycles of induction durvalumab 1500mg and tremelimumab 75mg with platinum-pemetrexed chemotherapy every 3 weeks, followed by maintenance durvalumab 1500mg and pemetrexed 500mg/m2 every 4 weeks until disease progression. Response will be assessed at 6 and 12 weeks, then 8-weekly during the first year, and 12-weekly thereafter. Major endpoints include objective tumour response rate (OTRR; RECIST1.1; primary), disease control rate, OTRR (iRECIST), progression-free survival, overall survival, and adverse events. Correlative studies include biomarker assessment as potential predictive/prognostic factors. ILLUMINATE is a collaboration between the Australasian Lung Cancer Trials Group, National Health Research Institutes (Taiwan) and the NHMRC Clinical Trials Centre, University of Sydney. As of 6/2/2020, 11 of planned 100 participants have been recruited. Clinical trial information: NCT03994393. Research Sponsor: AstraZeneca.

TPS9632 **Poster Session (Board #398), Fri, 8:00 AM-11:00 AM**

Randomized phase III study of first-line pembrolizumab plus pemetrexed/platinum followed by pembrolizumab and maintenance olaparib versus pemetrexed in patients with metastatic nonsquamous non-small cell lung cancer (NSCLC): KEYLYNK-006. *First Author: Jhanelle Elaine Gray, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: First-line treatment with pembrolizumab + pemetrexed/platinum improved clinical outcomes in patients with advanced non-squamous NSCLC in KEYNOTE-021 and KEYNOTE-189. Poly(ADP-ribose) polymerase inhibitors (PARPi), including olaparib, have been shown to upregulate PD-L1 expression in preclinical studies, and preliminary evidence suggests potential therapeutic benefit and acceptable safety with PARPi plus anti–PD-(L)1 therapy. KEYLYNK-006 (NCT03976323) evaluates first-line pembrolizumab + pemetrexed/platinum followed by pembrolizumab + olaparib vs pembrolizumab + pemetrexed in patients with metastatic nonsquamous NSCLC. **Methods:** This phase III, randomized, open-label trial enrolls patients aged $\geq$18 years with histologically/cytologically confirmed treatment-naive, metastatic, nonsquamous NSCLC. Patients (target n = 792) receive induction pembrolizumab 200 mg + pemetrexed 500 mg/m^2 + carboplatin AUC 5 mg/mL/min or cisplatin 75 mg/m^2 Q3W for 4 cycles. Patients with PR/CR or SD are randomized (target n = 618) 1:1 to pembrolizumab 200 mg Q3W (31 cycles) + maintenance olaparib 300 mg twice daily or pembrolizumab + pemetrexed 500 mg/m^2 Q3W stratified by ECOG PS (0 vs 1), PD-L1 tumor proportion score ($<$50% vs $\geq$50%), and response (CR/PR vs SD). Tumor imaging per RECIST version 1.1 ($\leq$5 per organ; maximum 10 total lesions) by central review (BICR) is performed at baseline and Q6W until 60 weeks after randomization, then Q9W until disease progression, start of new cancer therapy, study withdrawal, or death. Primary endpoints are PFS (RECIST 1.1 by BICR) and OS estimated by the Kaplan-Meier method, stratified log-rank test, and Cox proportional hazard model with Efron's method of tie handling. Secondary endpoints are safety and quality of life; ORR and duration of response are exploratory endpoints. AEs are monitored throughout the study until 30 days after the last dose of treatment (90 days for serious AEs) and graded using NCI CTCAE, version 4.0. The study began enrolling in June 2019. Clinical trial information: NCT03976323. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

TPS9633 Poster Session (Board #399), Fri, 8:00 AM-11:00 AM

AcceleRET Lung: A phase III study of first-line pralsetinib in patients (pts) with RET-fusion+ advanced/metastatic non-small cell lung cancer (NSCLC). *First Author: Benjamin Besse, Gustave Roussy Université Paris Sud, Villejuif, France*

Background: RET gene fusions have been identified as oncogenic drivers in multiple tumor types, including 1-2% of NSCLC, but no selective RET inhibitors are approved for use. The investigational RET inhibitor, pralsetinib, potently and selectively targets oncogenic RET alterations, including those that confer resistance to multikinase inhibitors. In the registration-enabling phase 1/2 study (ARROW; NCT03037385), pts with RET-fusion+ NSCLC treated with 400 mg once daily (QD) of pralsetinib (N = 80) after platinum-based chemotherapy achieved an overall response rate (ORR) of 61% (95% CI 50, 72; 2 responses pending confirmation) per independent central review. In addition, a promising ORR of 73% (all centrally confirmed responses) was attained in the treatment naïve cohort (N = 26). Most treatment-related adverse events were grade 1-2 across the entire safety population treated at 400 mg QD (N = 354). AcceleRET Lung, an international, open-label, randomized, phase 3 study, will evaluate the efficacy and safety of pralsetinib versus standard of care (SOC) for first-line treatment of advanced/metastatic RET fusion+ NSCLC (NCT04222972). **Methods:** Approximately 250 pts with metastatic RET-fusion+ NSCLC will be randomized 1:1 to oral pralsetinib (400 mg QD) or SOC (non-squamous histology: platinum/pemetrexed ± pembrolizumab followed by maintenance pemetrexed ± pembrolizumab; squamous histology: platinum/gemcitabine). Stratification factors include intended use of pembrolizumab, history of brain metastases, and ECOG PS. Key eligibility criteria include no prior systemic treatment for metastatic disease; RET-fusion+ tumor by local or central assessment; no additional actionable oncogenic drivers; no prior selective RET inhibitor; measurable disease per RECIST v1.1. Pts randomized to SOC will be permitted to cross-over to receive pralsetinib upon disease progression. The primary endpoint is progression-free survival (blinded independent central review; RECIST v1.1). Secondary endpoints include ORR, overall survival, duration of response, disease control rate, clinical benefit rate, time to intracranial progression, intracranial ORR, safety/tolerability and quality of life evaluations. Recruitment has begun with sites (active or planned) in North America, Europe and Asia. Clinical trial information: NCT04222972. Research Sponsor: Blueprint Medicines.

TPS9635 Poster Session (Board #401), Fri, 8:00 AM-11:00 AM

Phase III trial of sitravatinib plus nivolumab vs. docetaxel for treatment of NSCLC after platinum-based chemotherapy and immunotherapy (SAPPHIRE). *First Author: Ivor John Percent, Florida Cancer Specialists South/Sarah Cannon Research Institute, Port Charlotte, FL*

Background: Sitravatinib is an oral spectrum-selective tyrosine kinase inhibitor that targets the TAM (TYRO3/AXL/MERTK) and split (VEGFR2/KIT) family receptor tyrosine kinases (RTKs), as well as MET. Inhibition of TAM RTKs may promote the depletion of myeloid-derived suppressor cells (MDSCs) in the tumor microenvironment (TME) and repolarize tumor associated macrophages towards the pro-inflammatory M1 phenotype. Inhibition of the split RTKs may reduce immunosuppressive regulatory T cells in addition to MDSCs within the TME. Given these pleiotropic immune-stimulating effects, sitravatinib may reverse resistance to checkpoint inhibitor therapy (CIT) and augment the antitumor immune response of nivolumab in patients (pts) with non-small cell lung cancer (NSCLC). An ongoing Phase 2 study (MRTX-500) demonstrates clinical activity of this combination in pts with metastatic non-squamous NSCLC after progression on or after CIT. **Methods:** Global, randomized, open-label, Phase 3 study of sitravatinib in combination with nivolumab vs docetaxel in pts with advanced non-squamous NSCLC who have progressed on or after CIT. Pts must have also received platinum-based chemotherapy either in combination with CIT or prior to CIT. Pts are randomized (1:1) to receive oral sitravatinib 120 mg once daily in continuous 28-day cycles combined with nivolumab IV 240 mg every 2 weeks or 480 mg every 4 weeks vs treatment with docetaxel 75 mg/m^2 IV every 3 weeks. Patients are stratified based on number of prior treatment regimens in the advanced setting, ECOG performance status, and presence of brain metastases. Key eligibility criteria include duration of treatment of CIT of at least 4 months, discontinuation of prior treatment with CIT $<$ 90 days prior to the date of randomization, and absence of symptomatic or uncontrolled brain metastases. The primary endpoint is overall survival (OS). Key secondary endpoints include safety and tolerability, ORR, PFS, PROs, and PK. OS will be analyzed using Kaplan-Meier methods and the stratified log-rank test to estimate and compare the median OS between the two treatment arms with 95% CI. An IDMC will review safety at regular intervals and efficacy at a planned interim analysis based on OS. Enrollment is ongoing. Clinical trial information: NCT03906071. Research Sponsor: Mirati Therapeutics, Inc.

TPS9636 Poster Session (Board #402), Fri, 8:00 AM-11:00 AM

A phase III, open-label, randomized study of atezolizumab in combination with carboplatin + paclitaxel + bevacizumab compared with pemetrexed + cisplatin or carboplatin with stage IV non-squamous non-small cell lung cancer (NSCLC) with activating EGFR mutation or ALK translocation (ATLAS Trial). *First Author: Sehhoon Park, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

Background: In patients with activating EGFR mutations and ALK fusion, target specific tyrosine kinase inhibitor (TKI) showed significant survival improvement compared to the cytotoxic chemotherapy. However, the questions remain which combination strategy will be the best option for the patients who have failed from TKI. Especially, the role of an immune checkpoint inhibitor (ICI) in this population is still unclear. This study is designed and conducted based on the recent subgroup analyses from the IMpower 150 study which showed the positive clinical outcomes of atezolizumab combined with VEGF inhibitor and conventional cytotoxic chemotherapy in EGFR mutation and ALK translocation. **Methods:** This study is the phase III, open-label, multicenter study of atezolizumab in combination with bevacizumab + carboplatin + paclitaxel (ABCP, Arm A) compared with pemetrexed + cisplatin or carboplatin (Arm B). The study population will be randomized to either Arm A (n = 152) or Arm B (n = 72) based on two stratification factors, EGFR vs. ALK and presence of brain metastases. In Arm A, patients will be treated with 4 or 6 cycles of ABCP followed by maintenance atezolizumab and bevacizumab every three weeks. In Arm B, pemetrexed maintenance therapy will be applied every three weeks after 4 or 6 cycles of pemetrexed + cisplatin or carboplatin. As key inclusion criteria, the patients must be diagnosed with stage IV non-squamous non-small cell lung cancer with either activating EGFR mutation or ALK translocation. All the patients need to be cytotoxic chemotherapy naïve and must have experienced disease progression to treatment with at least one EGFR or ALK TKI. If the patients have T790M mutation after 1st or 2nd generation EGFR TKI, second line 3rd generation EGFR TKI treatment is mandatory. The number of T790M positive patients is restricted to under 30% of the entire study population. The primary endpoint is progression-free survival and the major secondary endpoints are overall survival, objective response rate and duration of response. A total of 228 subjects will be enrolled to detect a hazard ratio of 0.67. The first subject received treatment in Aug. 2019 and 19 patients receive the treatment. This study is opened in 3 sites and expected to be opened at 18 sites in South Korea. The time point for the primary analyses is Q3. 2022. Clinical trial information: NCT03991403. Research Sponsor: Roche/Genentech.

TPS9637 Poster Session (Board #403), Fri, 8:00 AM-11:00 AM

TRIDENT-1: A global, multicenter, open-label Phase II study investigating the activity of repotrectinib in advanced solid tumors harboring *ROS1* or *NTRK1-3* rearrangements. *First Author: Robert Charles Doebele, University of Colorado, Aurora, CO*

Background: Repotrectinib is a next-generation ROS1/TRK inhibitor with $>$ 90-fold greater potency than crizotinib against ROS1 and $>$ 100-fold greater potency than larotrectinib against TRK. Preclinical studies demonstrated inhibitory activity of repotrectinib against ROS1 resistance mutations, including the solvent-front mutation (SFM) G2032R. In the phase 1 portion of the study, repotrectinib was found to be well tolerated with encouraging antitumor activity including a 91% confirmed overall response (cORR) in TKI-naïve *ROS1+* NSCLC pts. In *ROS1+* NSCLC pts who received 1 prior chemo and 1 prior TKI, the cORR was 57% at the clinical dose of 160 mg QD or above. Intra-cranial (IC) activity was observed in *ROS1+* NSCLC pts with measurable CNS disease (100% IC-ORR in TKI-naïve and 75% IC-ORR in patients with 1 prior TKI). Encouraging antitumor activity was observed in pts with NTRK+ solid tumors. **Methods:** A global phase 2 study was initiated and is actively enrolling. The primary endpoint for the Phase 2 study is cORR assessed by BICR (Blinded Independent Central Review) using RECIST v1.1, in each expansion cohort in pts with advanced solid tumors that harbor a ROS1 or NTRK1/2/3 gene fusion. Secondary endpoints include duration of response (DOR), progression-free survival (PFS), overall survival (OS), IC-ORR, IC-PFS, and quality of life assessments. All pts need to have RECIST 1.1 measurable disease confirmed by BICR and ECOG performance score $\leq$1. Repotrectinib is administered at 160 mg QD for 14 days and, if tolerated, the dose can be increased to 160 mg BID. Approximately 320 pts ($\geq$12 years old) will be enrolled into 6 defined expansion cohorts, depending on the status of previous treatment with TKIs and cancer types (see table below). Clinical trial information: NCT03093116. Research Sponsor: Turning Point Therapeutics Inc.

Cohort #	Tumor Type	Prior Treatment	Sample Size (pts)
1	*ROS1*+NSCLC	*ROS1* TKI-naive	55
2		1 Prior *ROS1* TKI AND 1 Platinum-based Chemo	100
3		2 Prior *ROS1* TKIs AND 1 Platinum-based Chemo	40
4		1 Prior *ROS1* TKI and NO Prior Chemo OR Immunotherapy	Up to 30
5	*NTRK*+solid tumors	*TRK* TKI-naïve	55
6		*TRK* TKI-pretreated (up to 2 prior TKIs)	40

TPS9638 Poster Session (Board #404), Fri, 8:00 AM-11:00 AM

A phase II study of atezolizumab and cobimetinib in PD-1/PD-L1 inhibitor resistant or refractory non-small cell lung cancer: ETCTN #10166. *First Author: Stephen V. Liu, Georgetown University, Washington, DC*

Background: Use of checkpoint inhibitors, alone or with chemotherapy, has emerged as the preferred standard treatment for patients with advanced, driver-negative non-small cell lung cancer (NSCLC). While outcomes are superior to chemotherapy alone, only a subset of patients achieve durable response and long term survival. One potential mechanism of primary resistance to checkpoint inhibitors is the lack of tumor-infiltrating lymphocytes. Inhibition of mitogen-activated protein kinase (MAPK) kinase (MEK) increases the number of CD8+ T-cell within a tumor and has shown synergy with anti-programmed death-ligand 1 (PD-L1) antibodies. The combination of the MEK inhibitor cobimetinib and the PD-L1 antibody atezolizumab has led to limited responses in colorectal cancer, a tumor typically non-responsive to checkpoint inhibition. This phase II trial explores the combination of cobimetinib and atezolizumab in patients with PD(L)1-refractory NSCLC. **Methods:** This phase II study is being conducted through the Experimental Therapeutics Clinical Trials Network (ETCTN #10166). Eligible patients have advanced NSCLC with primary resistance to anti-PD(L)1 therapy (defined as progression noted within 6 months of initiating therapy) and tumor amenable to serial core biopsy. Patients will receive atezolizumab 840mg intravenously every 2 weeks and cobimetinib 60mg orally for 21 days in 28-day cycles. Two cohorts will enroll in parallel, defined by presence or absence of a KRAS mutation. Each cohort will employ a Simon two-stage design to test a null rate of 5% vs. 25% (power = 0.90, □ = 0.10). If > 1 of 9 patients in stage 1 achieve a partial response, an additional 15 patients are enrolled and if > 3 patients achieve a durable response, the combination will be worthy of further investigation. The primary endpoint is durable (> 6 months) response rate. Secondary endpoints are overall response rate, progression free survival, overall survival, duration of response and adverse events. Biopsies performed at baseline and after 3 weeks of therapy will assess the change in the density of tumoral CD8+ T-cells. Whole exome sequencing and immune cell profiling will also be performed on serial samples. Enrollment was initially limited to KRAS-mutant NSCLC. Prespecified activity goal for the first stage of accrual has been met; second stage accrual began in September 2019. Enrollment to the KRAS wild-type cohort will commence. Clinical trial information: NCT03600701. Research Sponsor: U.S. National Institutes of Health.

10000 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Pembrolizumab versus placebo after complete resection of high-risk stage III melanoma: New recurrence-free survival results from the EORTC 1325-MG/Keynote 054 double-blinded phase III trial at three-year median follow-up. *First Author: Alexander M. Eggermont, Princess Máxima Center, Utrecht, Netherlands*

Background: We conducted the phase 3 double-blind EORTC 1325/KEYNOTE-054 trial to evaluate pembrolizumab vs placebo in patients (pts) with resected high-risk stage III melanoma. Based on 351 recurrence-free survival (RFS) events and at a median follow-up of 1.25 years (yrs), pembrolizumab improved RFS (hazard ratio (HR) 0.57, P<0.0001) as compared to placebo (Eggermont, NEJM 2018). This led to the approval of pembrolizumab adjuvant treatment by EMA and FDA. **Methods:** Eligible pts included those ≥18 yrs of age with complete resection of cutaneous melanoma metastatic to lymph node(s), classified as AJCC-7 stage IIIA (at least one lymph node metastasis >1 mm), IIIB or IIIC (without in-transit metastasis). A total of 1019 pts were randomized (stratification by stage and region) to pembrolizumab at a flat dose of 200 mg (N=514) or placebo (N=505) every 3 weeks for a total of 18 doses (~1 year) or until disease recurrence or unacceptable toxicity. The 2 co-primary endpoints were RFS in the intention-to-treat overall population and in pts with PD-L1-positive tumors. Here, we report an updated RFS analysis based on a longer follow-up. **Results:** Overall, 15%/46%/39% of pts had stage IIIA/IIIB/IIIC. At 3.05-yr median follow-up, pembrolizumab (190 RFS events) compared with placebo (283 RFS events) prolonged RFS, in the overall population and in the PD-L1 positive tumor subgroup (see Table). RFS was consistently prolonged across subgroups, in particular according to AJCC-7 staging, BRAF-V600 E/K mutation status. **Conclusions:** Pembrolizumab, administered at 200 mg every 3 weeks for up to 1 year as adjuvant therapy, provided, at a 3-yr median follow-up, a sustained improvement in RFS, which was clinically meaningful, in resected high-risk stage III melanoma. This improvement was consistent across subgroups. In the overall population, the 3-yr cumulative incidence of distant metastasis being the first recurrence was 22.3% (pembrolizumab group) vs 37.3% (placebo group) (HR 0.55, 95% CI 0.44-0.69). Clinical trial information: NCT02362594. Research Sponsor: Merck.

		3-yr RFS rate		Stratified by stage at randomization	
	N pts	Pembrolizumab	Placebo	HR	CI (HR)*
Overall population	1019	64%	44%	0.56	0.47-0.68
PD-L1 positive	853	65%	46%	0.57	0.43-0.74
PD-L1 negative	116	57%	33%	0.45	0.23-0.90
Stage IIIA	152	81%	66%	0.50	0.22-1.16
Stage IIIB	472	66%	47%	0.56	0.39-0.81
Stage IIIC	395	54%	32%	0.57	0.40-0.81
BRAF-mutated	440	62%	37%	0.51	0.36-0.73
BRAF-WT	448	62%	47%	0.66	0.46-0.95

10001 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Long-term benefit of adjuvant dabrafenib + trametinib (D+T) in patients (pts) with resected stage III *BRAF* V600–mutant melanoma: Five-year analysis of COMBI-AD. *First Author: Axel Hauschild, University Hospital Schleswig-Holstein, Kiel, Germany*

Background: Previous results of the COMBI-AD trial (NCT01682083) showed a significant relapse-free survival (RFS) benefit with 12 mo of adjuvant D+T vs placebo (PBO) in pts with high-risk resected stage III *BRAF* V600E/K–mutant melanoma. In the primary analysis, 3-year RFS rates with D+T vs PBO were 58% vs 39% (hazard ratio [HR], 0.47 [95% CI, 0.39-0.58]; $P < .001$). An interim analysis of overall survival (OS) yielded 3-year OS rates of 86% with D+T vs 77% with PBO (HR, 0.57 [95% CI, 0.42-0.79]). Here we report data from 5-year analyses including long-term RFS and an updated cure rate model. **Methods:** COMBI-AD is a randomized, Phase III trial evaluating 12 mo of adjuvant D 150 mg twice daily + T 2 mg once daily vs 2 matched PBOs in pts with resected stage III *BRAF* V600E/K–mutant melanoma. Pts were stratified by *BRAF* status and disease stage (per AJCC 7 criteria). The primary endpoint is RFS; secondary endpoints include OS and distant metastasis–free survival (DMFS). A Weibull mixture cure rate model was applied to estimate the fraction of pts who will remain relapse free in the long term. As all patients had completed treatment by the time of the primary analysis, updated safety analyses were not performed. **Results:** This analysis represents a median follow-up of 60 mo for the D+T arm and 59 mo for the PBO arm. As of the data cutoff (Nov 8, 2019), 190 of 438 pts in the D+T arm and 262 of 432 pts in the PBO arm had an RFS event. Median RFS was not reached (NR; 95% CI, 47.9 mo-NR) with D+T vs 16.6 mo (95% CI, 12.7-22.1 mo) with PBO (HR, 0.51 [95% CI, 0.42-0.61]). The 4- and 5-year RFS rates were 55% (95% CI, 50%-60%) and 52% (95% CI, 48%-58%) with D+T vs 38% (95% CI, 34%-43%) and 36% (95% CI, 32%-41%) with PBO. These findings match those estimated by the cure rate model. The RFS benefit with D+T was evident across all AJCC 7 substages (HR [95% CI]: IIIA, 0.61 [0.35-1.07]; IIIB, 0.50 [0.37-0.67]; IIIC, 0.48 [0.36-0.64]). Median DMFS was NR in either arm but favored D+T (HR, 0.55 [95% CI, 0.44-0.70]). OS was not updated at this data cutoff as the prespecified number of events for the final OS analysis had not yet occurred. **Conclusions:** This 5-year analysis confirms the long-term benefit of adjuvant D+T in pts with resected stage III *BRAF* V600E/K–mutant melanoma. Clinical trial information: NCT01682083. Research Sponsor: Novartis Pharmaceuticals Corporation.

10002 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

First safety and efficacy results of PRADO: A phase II study of personalized response-driven surgery and adjuvant therapy after neoadjuvant ipilimumab (IPI) and nivolumab (NIVO) in resectable stage III melanoma. *First Author: Christian U. Blank, Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: OpACIN-neo tested 3 dosing schemes of neoadjuvant (neoadj) IPI+NIVO and identified 2 cycles of IPI 1mg/kg + NIVO 3mg/kg (I1N3) as the most favorable with a pathologic (path) response rate (pRR) of 77% and 20% grade 3-4 irAEs. After 17.6 months median FU, 1/64 (2%) patients (pts) with path response vs 13/21 (62%) of the non-responders (> 50% viable tumor cells; pNR) had relapsed. We hypothesized that therapeutic lymph node dissection (TLND) could be omitted in pts achieving a complete or near-complete path response (≤10% viable tumor cells; major path response, MPR) in the index node (largest LN metastasis: ILN), whereas additional adjuvant (adj) therapy might improve the outcome of pNR pts. **Methods:** PRADO is an extension cohort of the multi-center phase 2 OpACIN-neo study that aims to confirm the pRR and safety of neoadj I1N3 and to test response-driven subsequent therapy. Pts with RECIST 1.1 measurable clinical stage III melanoma were included to receive 2 cycles of neoadj I1N3 after marker placement in the ILN. ILN resection was planned at wk 6. Pts that achieved MPR in the ILN did not undergo TLND; pts with pPR (> 10 – ≤50% viable tumor cells) underwent TLND; and pts with pNR underwent TLND and received adj NIVO or targeted therapy (TT) for 52 wks +/- radiotherapy (RT). Primary endpoints were pRR in the ILN and 24-month RFS. Estimated toxicity rates at wk 12 were calculated using a Kaplan Meier based method. **Results:** Between Nov 16, 2018 and Jan 3, 2020, 99 of 114 screened pts were eligible and enrolled. So far, 86 pts had ≥12 wks FU. 70/99 pts achieved a path response in the ILN (pRR 71%, 95% CI 61% - 79%); 60 (61%) had MPR. TLND was omitted in 58 (97%) of the MPR pts. There were 28 non-responders; 7 developed distant metastasis before ILN resection. To date, 8 of the 21 pNR pts had adj NIVO, 7 had adj TT and 7 had adj RT. The estimated grade 3-4 irAE rate at wk 12 was 24%. Due to toxicity, 10 pts (10%) received only 1 cycle I1N3 and in 3 pts ILN resection was not performed: 2 of these pts underwent TLND at wk 9 and one pt was not evaluated for path response. At data cutoff, the surgery-related grade 1,2 and 3 AE rates were 29%, 10% and 0% in pts who underwent ILN resection only vs 21%, 30% and 9% in pts who underwent subsequent TLND (p = 0.004). At ASCO 2020 all pts will have reached ≥12 wks FU. **Conclusions:** Neoadj I1N3 treatment induced a high pRR with tolerable toxicity. TLND was omitted in a major subset of pts, reducing surgical morbidity. Longer FU is needed to report safety and RFS when TLND is omitted in MPR pts. Clinical trial information: NCT02977052. Research Sponsor: BMS.

10003 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A phase II study to evaluate the need for > two doses of nivolumab + ipilimumab combination (combo) immunotherapy. *First Author: Michael A. Postow, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Standard of care nivolumab (nivo) + ipilimumab (ipi) combo immunotherapy is given for 4 doses in patients (pts) with unresectable stage III/IV melanoma. Whether 4 doses are needed is questionable as retrospective data suggest pts treated with <4 doses of combo due to toxicity can have durable benefit. No prospective trials have evaluated the efficacy of intentionally giving <4 doses of combo in unresectable stage III/IV melanoma. **Methods:** In this phase 2, multicenter clinical trial (n=60), pts with unresectable stage III/IV melanoma received 2 doses of nivo (1mg/kg) + ipi (3mg/kg) followed by a CT scan at week 6. Pts with complete (CR) or partial responses (PR) by RECIST 1.1 or stable disease without an increase in total measurable tumor burden had protocol defined early favorable anti-tumor effect (FATE) and ceased combo, transitioning to maintenance nivo. Pts without FATE at week 6 received the standard third and fourth doses of combo followed by maintenance nivo. The primary endpoint was response rate by RECIST 1.1 at week 12. Secondary endpoints included additional efficacy assessments and safety. **Results:** 41 pts (68%) had FATE at week 6. The best overall response rates (CR + PR) by RECIST at week 12 or any time afterwards were 48% (95% CI: 35.2-61.6%) and 53% (95% CI: 40.0-66.3%), respectively. 18%, 58%, 12%, 10% had 1, 2, 3, 4 doses of combo, respectively. With a median follow-up of 11 months, any grade treatment-related toxicity occurred in 100% (57% grade 3-4) of pts. Three pts died due to treatment-related toxicity (2 myocarditis, 1 possible adrenal insufficiency). Among the 19 pts without FATE at week 6 and not selected to de-escalate combo after dose 2, no pts ultimately responded with ongoing combo dosing. **Conclusions:** The first 2 doses of nivo + ipi appear to drive combo's response efficacy and toxicity. Early radiographic imaging at week 6 may be able to identify pts who do not respond to combo dosing beyond dose 2. Randomized studies are planned to evaluate 1 dose of combo to see if efficacy is maintained with reduced toxicity. Clinical trial information: NCT03122522. Research Sponsor: Bristol Myers-Squibb.

10004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Significant antitumor activity for low-dose ipilimumab (IPI) with pembrolizumab (PEMBRO) immediately following progression on PD1 Ab in melanoma (MEL) in a phase II trial. *First Author: Daniel Olson, University of Chicago Comprehensive Cancer Center, Chicago, IL*

Background: Combination PD1 + CTLA4 antibodies (Abs) shows greater response rate (RR) versus PD1 Ab alone in MEL, but RR after initial PD1 Ab progression awaits robust investigation. CTLA4 Ab alone after PD1 Ab progression has a historical RR of 13%. We report final results of the first prospective clinical trial evaluating IPI 1mg/kg + PEMBRO immediately following progression on PD1 Ab (NCT02743819). **Methods:** Patients (pts) with advanced MEL, no prior CTLA4 Ab for metastatic disease, and who had progressed on PD1 Ab as immediately prior therapy (or non-CTLA4 Ab combination) were eligible. Pts received PEMBRO 200 mg + IPI 1 mg/kg Q3W for 4 doses, then PEMBRO alone for up to two years. The primary endpoint was RR by irRECIST. After 35 pts, the study met its primary endpoint with 10/22 evaluable pts achieving a response. The trial was expanded to enroll a total of 70 pts in open-label accrual to further describe the RR for this regimen in an exploratory fashion. The data analysis cutoff was January 30, 2020. **Results:** 67/70 accrued patients were evaluable for treatment response. Prior treatments included 60 on PD1 Ab alone and 10 on PD1 Ab-based combinations. Of these, 10 pts had progressed in the adjuvant setting. Median length of treatment on prior PD1 Ab was 4.8 months. Response assessments included 4 CR, 17 PR and 16 SD for a RR of 31% (21/67) in evaluable pts, and 30% (21/70) in all enrolled pts. 4 pts with a PR and 6 with SD had unconfirmed responses making the irRECIST response rate 25% (17/67) and 24% (17/70) among evaluable and enrolled pts, respectively. Median progression free survival (PFS) was 4.7 mo (95% CI: 2.8-8.3) and PFS at six months was 45% (95% CI: 33%-57%). 15/70 (21%) pts experienced ≥ grade 3-4 drug-related AEs, the most common being diarrhea, rash and transaminase elevation. PD-L1 positive vs negative status from historical tumor specimens did not associate with RR. **Conclusions:** This is the largest prospective study of IPI 1mg/kg + PEMBRO, demonstrating significant antitumor activity and tolerability in MEL post-PD1 Ab. Clinical trial information: NCT02743819. Research Sponsor: Merck via Investigator Sponsored Trial.

10005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Ipilimumab (IPI) alone or in combination with anti-PD-1 (IPI+PD1) in patients (pts) with metastatic melanoma (MM) resistant to PD1 monotherapy. *First Author: Ines Pires Da Silva, Melanoma Institute Australia, Sydney, Australia*

Background: PD1 induces long-term responses in approximately 30% of MM pts, however 2/3 are resistant (innate or acquired) and will require further treatment. A subset of these pts will benefit from IPI or IPI+PD1, but these pts are yet to be identified. We sought to determine; i) response rate (RR) and survival to IPI+/-PD1 after PD1 progression, and ii) clinical predictors of response and survival to IPI+/-PD1. **Methods:** MM pts resistant to PD1 and then treated with IPI+/-PD1 were studied. Demographics, disease characteristics and baseline blood parameters were examined. Univariate, multivariate and backward elimination technique analyses were performed to create predictive models of response and overall survival (OS). **Results:** Of 330 MM pts resistant to PD1 (median time to prog 2.9 months [0.5 – 42.3], 12% adjuvant, 88% metastatic; 70% innate, 30% acquired), 161 (49%) had subsequent IPI and 169 (51%) had IPI+PD1. Characteristics at start of IPI+/-PD1 were similar in IPI vs IPI+PD1 groups (stage M1D 27% vs 34%; elevated LDH 38% vs 40%), except IPI group had more ECOG ≥1 (60% vs 34%) and less BRAF mutation (mut) (21% vs 37%). Median follow-up from start of IPI+/-PD1 was 22.3 months (19.8 - 25.8); RR was 22%, higher in IPI+PD1 (31%) vs IPI (12%) ($p < 0.01$). PFS and OS at 1 year were 20% and 48%, respectively; better with IPI+PD1 (27%/57%) vs IPI (13%/38%) ($p < 0.01$). PD1 setting (adjuvant/metastatic) and response did not impact response to IPI+/-PD1. Most pts progressing on adjuvant PD1 had IPI+PD1 (88%) and RR was 33%. Neither the interval between PD1 and IPI+/-PD1 nor use of other drugs affected response to IPI+/-PD1. RR was similar in BRAF WT (23%) vs BRAF mut (RR 21%) pts. In BRAF WT pts, RR was higher with IPI+PD1 vs IPI (38% vs 9%, $p < 0.01$), while RR was similar with IPI (24%) or IPI+PD1 (19%) in BRAF mut pts. One third of BRAF mut pts had BRAF inhibitors (BRAFi) prior to IPI+/-PD1 and lower RR (13%) vs those without BRAFi (RR = 25%, $p > 0.05$). High grade (≥G3) toxicity (tox) was similar with IPI+PD1 (30%) or IPI (34%, $p = 0.48$), and was not associated with response. Stage III/M1A/M1B, normal LDH and treatment with IPI+PD1 were the best predictors of response (AUC = 0.69). These factors, in addition to sex (male), ECOG PS = 0, BRAF mut, progressed/recurred > 3 months on PD1, and absence of bone mets were the best predictors of longer OS (AUC = 0.74). **Conclusions:** In pts resistant to PD1, IPI+PD1 has higher RR, longer survival, yet similar high grade tox than IPI alone. Predictive models of response & survival will help select pts for IPI+/-PD1 after progressing on PD1. Research Sponsor: None.

10006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Long-term follow up of lifileucel (LN-144) cryopreserved autologous tumor infiltrating lymphocyte therapy in patients with advanced melanoma progressed on multiple prior therapies. *First Author: Amod Sarnaik, Moffitt Cancer Center, Tampa, FL*

Background: Treatment options are limited for patients with advanced melanoma who have progressed on checkpoint inhibitors and targeted therapies. Adoptive cell therapy using tumor-infiltrating lymphocytes (TIL) leverages and enhances the body's natural defense against cancer and has shown durable responses in heavily pretreated melanoma patients. **Methods:** C-144-01 is a global Phase 2 open-label, multicenter study of efficacy & safety of lifileucel in patients with unresectable metastatic melanoma who have progressed on checkpoint inhibitors and BRAF/MEK inhibitors, if $BRAF^{V600}$ mutant. We report on Cohort 2 (N = 66) patients who have received TIL. Tumors were resected at local institutions, processed in central GMP facilities for TIL production, manufactured, cryopreserved & shipped back to sites in a 22-day process. Therapy consisted of one week of lymphodepletion, a single lifileucel infusion, and up to 6 IL-2 doses. ORR was based on RECIST v1.1 by investigator assessment. Data cutoff was Feb 2, 2020. **Results:** Baseline characteristics: 3.3 mean prior therapies (anti-PD1 100%; anti-CTLA-4 80%; BRAF/MEK inhibitor 23%), high baseline tumor burden (106 mm mean target lesion sum of diameters), 44% liver/brain lesions, 40.9% LDH > ULN. ORR by investigator was 36.4% (2 CR, 22 PR) and DCR was 80.3%. Mean time to response was 1.9 months (range: 1.3-5.6). After a median study follow-up of 17.0 months, median DOR (mDOR) was still not reached. Six responders have progressed, 2 have died and 2 started other anti-cancer therapy without progression. The adverse event profile was consistent with the underlying advanced disease and the lymphodepletion and IL-2 regimens. Additional follow-up data will be available for presentation. **Conclusions:** Lifileucel treatment results in a 36.4% ORR and mDOR was not reached at 17.0 months of median study follow up in a heavily pretreated metastatic melanoma patients with high baseline disease burden who progressed on multiple prior therapies, including anti-PD1 and BRAF/MEK inhibitors, if $BRAF^{V600}$ mutant. Clinical trial information: NCT02360579. Research Sponsor: Iovance Biotherapeutics, Inc.

10007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Overall survival and biomarker analysis of a phase Ib combination study of toripalimab, a humanized IgG4 mAb against programmed death-1 (PD-1) with axitinib in patients with metastatic mucosal melanoma. *First Author: Xinan Sheng, Peking University Cancer Hospital and Institute, Beijing, China*

Background: Metastatic mucosal melanoma responds poorly to PD-1 blockade therapy in comparison with cutaneous melanoma. Vascular endothelial growth factor (VEGF) is indicated to play an important immunosuppressive role in mucosal melanoma. Combination of VEGF inhibition with PD-1 blockade might provide therapeutic opportunities. Toripalimab was approved as a second-line treatment for metastasis melanoma in Dec 2018. This study is to evaluate the safety and clinical efficacy of toripalimab combined with axitinib for the treatment of metastatic mucosal melanoma. (Clinical trial ID: NCT03086174). **Methods:** Patients with metastatic melanoma receive 1 or 3 mg/kg toripalimab Q2W in combination with 5 mg axitinib BID until disease progression, unacceptable toxicity, or voluntary withdrawal. Clinical response is assessed every 8 weeks according to RECISTv1.1. Tumor PD-L1 expression, tumor mutational burden (TMB), and gene expression profile (GEP) will be evaluated for correlation with clinical response. **Results:** From April 2017 to April 2018, 33 patients were enrolled in the study. No DLT or treatment related death was observed. 97% patients experienced treatment related AE (TRAE) and 39.4% patients experienced Grade 3-4 TRAEs. Most common TRAEs include diarrhea, proteinuria, hand and foot syndrome and hypothyroidism. Only one patient discontinued treatment due to TRAE. Among 29 treatment naïve mucosal melanoma patients, 14 PR and 11 SD were observed for an ORR of 48.3% and a DCR of 86.2%. The median DOR was 13.7 months. The median PFS was 7.5 months and the median OS was 20.7 months. PD-L1 expression or TMB had no significant differences in responders versus non-responders. In contrast, GEP scores of eight selected immune-related and four angiogenesis-related genes showed strong correlation with clinical response, whereas previous published immune related signature or angiogenesis signature alone had no correlation. **Conclusions:** Toripalimab combined with axitinib is a promising treatment option for metastatic mucosal melanoma. GEP scores of selected immune-related and angiogenesis-related genes might predict the response to the combination. A randomized 3-arm Phase 2 trial has been initiated to compare toripalimab plus axitinib with toripalimab or axitinib alone. Clinical trial information: NCT03086174. Research Sponsor: Shanghai Junshi Bioscience Co., LTD.

10008 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Single-center phase I/Ib study of concurrent intrathecal (IT) and intravenous (IV) nivolumab (N) for metastatic melanoma (MM) patients (pts) with leptomeningeal disease (LMD). *First Author: Isabella Claudia Glitza, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: MM pts with LMD have a dismal prognosis, with a median overall survival (OS) < 3 months and no approved therapies. IT administration of interleukin-2 (IL2) achieves survival in ~15% of MM LMD pts, but at cost of severe toxicities. Given the favorable clinical activity and safety of systemic anti-PD1, we hypothesized that IT N administration is safe and can achieve clinical benefit in pts with LMD. **Methods:** The primary objectives of this first-in-human study (NCT03025256) were to determine the safety and the maximum tolerated dose (MTD) of IT N given with IV N in MM pts with LMD. Eligible pts had MM, ECOG PS < / = 2, and evidence of LMD by MRI and/or CSF cytology. Dexamethasone < / = 4mg/daily was allowed. For cycle 1, IT N is administered via intraventricular reservoir on day (D) 1; Blood and CSF is collected at multiple time points for translational research. For subsequent cycles (every 14 days), pts receive IT N on D1, followed by IV N 240 mg on D2. IT N doses evaluated were 5, 10, and 20 mg. Bayesian mTPI methodology was used to define the MTD. The study was recently amended to allow for concurrent BRAF/MEK inhibitor(i) treatment. **Results:** To date, 15 pts have been treated: two at 5, three at 10, and 10 at 20 mg IT N. Median age at LMD diagnosis was 41.8 (30.9-73.2) years; 6 pts are male. All pts had radiographic evidence of LMD and neurological symptoms; 8 pts had positive CSF cytology. 12 pts received prior therapies for their MM: anti-PD1 (n = 11), BRAFi/MEKi (n = 9), chemo (n = 2), IT IL2 (n = 4) other (n = 2). 11 pts had prior XRT, including whole brain RT (n = 7). 1 pt was treatment-naïve. The median numbers of IT N doses was 4 (1-42). No grade (Gr) 4-5 AEs were attributed to IT N or IV N; only 4 events (Gr 1, n = 2; Gr2, n = 2) were possibly related to the IT N. With a median follow-up of 18.7 weeks (1-83.3 wks), the median OS is 46.1 weeks (0.1-83.3). Clinical response data, translational research endpoints, including changes in CSF cytokines and cfDNA, will be reported. **Conclusions:** The trial demonstrates the feasibility of prospective clinical trials in MM patients with LMD. The combination of IT/ IV N was safe and well-tolerated, with no unexpected systemic or neurological toxicity. Final presentation will include results of LMD composite response assessment, comparative analysis of longitudinal CSF/blood samples to assess immunologic effects. Finally, the interim OS of the patients is encouraging, and supports further evaluation of IT administration of immunotherapy agents for pts with MM and LMD. Clinical trial information: NCT03025256. Research Sponsor: Bristol- Myers Squibb.

10009 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Integrative tumor and immune cell multi-omic analyses to predict melanoma response to immune checkpoint blockade. *First Author: Valsamo Anagnostou, Bloomberg~Kimmel Institute for Cancer Immunotherapy, Baltimore, MD*

Background: The complex crosstalk between tumor and immune cells during immune checkpoint blockade mandates the development of integrated models to interpret the antitumor immune response and predict clinical outcome. **Methods:** We performed comprehensive genomic, transcriptomic and T cell repertoire analyses on tumor biopsies from 64 patients with advanced melanoma receiving nivolumab +/- ipilimumab on CheckMate-038 (NCT01621490). Tumor biopsies were obtained at baseline and 2-4 weeks on therapy. Machine learning and Cox proportional hazards regression analyses were employed to integrate multi-omics features in predictive models of response, defined by RECISTv1.1 as complete and partial response, and survival (PFS and OS). **Results:** Responding patients had a higher tumor mutation burden (TMB) than non-responders. Expressed TMB more accurately predicted overall survival than genomic TMB (log rank p = 0.028 vs 0.078). High tumor aneuploidy was associated with worse prognosis especially for the patients in the nivolumab + ipilimumab group (log rank p = 0.01). TCR sequencing of paired tumors before and on-treatment revealed that responders had a significantly higher number of unique TCR clones at baseline and more clonotypic shifts on-treatment (p = 0.0018). Gene rearrangement analyses using transcriptome data identified a higher number of rearrangements involving immunoglobulin (Ig) genes in baseline tumors from responders. Deconvolution of transcriptomic data confirmed an enrichment in tumor associated B cells in baseline tumors of responders, suggesting that pre-existing B cell infiltration is a predictor of clinical outcome. Random forests were utilized to integrate Ig rearrangements, expressed TMB and tumor aneuploidy, into a predictive model of response that was superior to TMB (AUC = 0.89 and 0.65 respectively). Multivariate Cox proportional hazards analysis incorporating the same features was utilized to generate a risk score for each patient; those with high risk scores had a significantly shorter PFS compared to low risk patients (median PFS 1.45 months vs 29.01 months, log rank p = 3.4e-06, HR = 9.18, 95% CI: 3.14-26.85). **Conclusions:** Our findings highlight the multi-faceted interactions between the tumor and the immune system and the importance of pre-existing T and B cell immunity in driving clinical response and PFS after immune checkpoint blockade, laying the groundwork for integration of genomic and immune features into predictive models that may ultimately optimize therapeutic decisions. Research Sponsor: Bristol Myers Squibb.

10010 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Using machine learning to predict immunotherapy response in advanced melanoma. *First Author: Paul Johannet, NYU School of Medicine, New York, NY*

Background: Several predictors of response to checkpoint inhibitors show potential, but use pathological assays and/or molecular characterization, which limits their clinical utility outside of the academic setting. We aimed to develop a streamlined approach by leveraging information immediately available through standard care. Here, we present a computational method that integrates deep learning on histology specimens with clinicodemographic variables to predict treatment outcomes in advanced melanoma. **Methods:** We used hematoxylin and eosin (H&E) sections from 72 patients (*n*= 153 slides) from New York University (NYU) to build a Segmentation Classifier that distinguishes tumor, lymphocyte, and connective tissue. Using pre-treatment H&E slides from 121 NYU patients (*n* =302 slides), we trained a Response Classifier to predict response by selectively analyzing tumor regions. We then developed a logistic regression classifier that combines neural network output with clinicodemographic variables. The classifiers were tested on an independent cohort of 32 patients from Vanderbilt University (*n* =42 slides). Area under the curve (AUC) was calculated as a measure of prediction accuracy. **Results:** The Segmentation Classifier distinguished tumor, lymphocyte, and connective tissue with AUCs 0.886-0.984. For the Response Classifier, optimal learning conditions were identified through training on NYU patients and testing on Vanderbilt patients (AUCs 0.685 and 0.728, respectively). The fully trained Response Classifier performed with AUC 0.711 on Vanderbilt patients. The logistic regression model performed with enhanced prediction accuracy with AUC 0.803 on NYU patients and AUC 0.793 on Vanderbilt patients. **Conclusions:** Histology slides and patients' clinicodemographic characteristics are readily available through routine standard of care and have the potential to predict immunotherapy response. Our approach is time-efficient, reproducible, and requires minimal resource allocation, thus overcoming multiple common barriers to generalizability for contemporary biomarkers. Research Sponsor: SPORE P50 CA016087, MRA Established Investigator Award.

10011 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Autoantibodies as predictors for survival and immune-related adverse events in checkpoint inhibition therapy of metastasized melanoma. *First Author: Jessica Cecile Hassel, Department of Dermatology and National Center for Tumor Diseases (NCT), Heidelberg University Hospital, Heidelberg, Germany*

Background: Increasing evidence suggests that the B cell response in cancer patients is an important component of anti-tumour immunity. Autoantibodies targeting tumour and self-antigens may serve as biomarkers of anti-tumour and auto-immunity. As they can be measured in patient' sera, they have great potential as clinical routine biomarkers. The objective of this study was to explore if autoantibodies are associated with survival and immune related adverse events (irAE) in patients with metastatic melanoma under checkpoint inhitibor (CPI) therapy. **Methods:** Pre-treatment serum samples from 333 metastatic melanoma patients receiving CPI therapy at 5 European centers were retrospectively used to identify autoantibody signatures for survival and irAE. We designed a cancer immunotherapy antigen array comprising 832 autoimmune and tumour antigens as well as immune and cancer pathway proteins. Statistical tests were separately performed for patients treated with anti-CTLA4 (alone or in combination) and with anti-PD1 antibody monotherapy. Cox-regression analysis and univariate statistical tests were applied for biomarker discovery. Progression free and overall survival was measured from treatment initiation to tumor progression or death date. irAE were recorded including onset date and grade (CTC-AE). **Results:** For each therapy group we identified a set of autoantibody reactivities in untreated melanoma patients that were associated with the development of irAEs and/or survival. The identified autoantibodies target a diverse set of antigens comprising neoantigens (p53), cancer testis antigens (MAGEB4), paraneoplastic antigens (gephyrin), autoantigens (ribosomal proteins, Nor-90) and FGFR1. Autoantigens that correlated with irAE and survival were e.g. anti-MAGEB4 and anti-FGFR1. Elevated anti-MAGEB4 pre-treatment levels were associated with longer overall survival (p = 0.002, HR = 0.77) and the development of irAEs (p = 0.002, HR = 1.27) in ipilimumab +/- nivolumab treated patients. Higher pre-treatment anti-FGFR1 antibodies were associated with shorter survival (p = 0.008, HR = 1.27) and a lower a lower frequency of irAEs (p = 0.04, HR = 0.69) in these patients. **Conclusions:** We identified autoantibody targets suggesting a diverse B cell response to antigens expressed in tumours and those associated with autoimmunity. Depending on the specific antigen, the immune response towards those antigens may be associated with anti-tumour or pro-tumour responses. Research Sponsor: Oncimmune Germany GmbH.

10012 Poster Discussion Session; Displayed in Poster Session (Board #361), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Update on overall survival in COLUMBUS: A randomized phase III trial of encorafenib (ENCO) plus binimetinib (BINI) versus vemurafenib (VEM) or ENCO in patients with *BRAF* V600-mutant melanoma. *First Author: Helen Gogas, First Department of Medicine, National and Kapodistrian University of Athens School of Medicine, Athens, Greece*

Background: Treatment of patients with *BRAF* V600–mutant melanoma includes BRAF/MEK-inhibitor combinations based on demonstrated benefits on progression-free survival (PFS) and overall survival (OS). To better understand the proportion of patients who derive long-lived benefit and their characteristics, we performed an updated analysis of OS and other endpoints from the COLUMBUS trial. **Methods:** In Part 1 of COLUMBUS, 577 patients with advanced/metastatic *BRAF* V600–mutant melanoma, untreated or progressed after first-line immunotherapy, were randomized 1:1:1 to ENCO 450 mg QD + BINI 45 mg BID (COMBO450) vs VEM 960 mg BID (VEM) or ENCO 300 mg QD (ENCO300). An updated analysis including PFS, OS, objective response rate (ORR), and safety was conducted after an additional 24 months' follow-up from the initial analysis. The study is ongoing. **Results:** At data cutoff (November 2019, as-is data), events had occurred in 65%, 59%, and 75% of patients in the COMBO450, ENCO300, and VEM treatment arms, respectively. Across arms, median follow-up for OS was 60.6 months (mo), with median OS of 33.6 mo (95% CI, 24.4–39.2) for COMBO450, 23.5 mo (95% CI, 19.6–33.6) for ENCO300, and 16.9 mo (95% CI, 14.0–24.5) for VEM. Compared to VEM, COMBO450 decreased the risk of death by 38% (HR, 0.62 [95% CI, 0.49–0.79]). Updated median PFS was COMBO450, 14.9 mo (95% CI, 11.0–20.2), ENCO300, 9.6 mo (95% CI, 7.4–14.8), and VEM, 7.3 mo (95% CI, 5.6–7.9). PFS was longer for COMBO450 vs VEM (HR, 0.52 [95% CI, 0.40–0.67]). A landmark analysis showed a higher rate of OS for COMBO450 at each year analyzed, with OS rates at 4 years of 39%, 37%, and 26% COMBO450, ENCO300, and VEM, respectively. Updated safety analysis confirmed the beneficial long-term tolerability of COMBO450. **Conclusions:** In the COLUMBUS trial, results for updated PFS and OS with COMBO450 continue to demonstrate long-term benefits in patients with *BRAF* V600–mutated melanoma. Clinical trial information: NCT01909453. Research Sponsor: Pfizer Inc.

10013 Poster Discussion Session; Displayed in Poster Session (Board #362), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Long-term survival from pembrolizumab (pembro) completion and pembro retreatment: Phase III KEYNOTE-006 in advanced melanoma. *First Author: Georgina V. Long, Melanoma Institute Australia, The University of Sydney, Royal North Shore Hospital, Mater Hospital, Sydney, Australia*

Background: 5-year follow-up of the phase 3 KEYNOTE-006 study (NCT01866319) showed pembro improved OS vs ipilimumab (ipi) in patients (pts) with advanced melanoma. 3-y OS rate from pembro completion for pts who completed 2 y of pembro was 93.8%. Results with 8 mo of additional follow-up are presented to inform clinical care. **Methods:** Eligible pts with ipi-naive advanced melanoma, ≤1 prior therapy for *BRAF*-mutant disease, and ECOG PS 0 or 1 were randomized to pembro 10 mg/kg Q2W or Q3W for ≤2 y or ipi 3 mg/kg Q3W for 4 doses. Pts discontinuing pembro with CR, PR, or SD after ≥94 weeks were considered pts with 2-y pembro. Pts who stopped pembro with SD, PR or CR could receive ≤12 mo of additional pembro (2nd course) upon disease progression if still eligible. ORR was assessed per immune-related response criteria by investigator review. OS was estimated using the Kaplan-Meier method. Pembro arm data were pooled. Post hoc ITT efficacy analyses are shown. **Results:** Median follow-up from randomization to data cutoff (Jul 31, 2019) was 66.7 mo in the pembro and 66.9 mo in the ipi arms. OS outcomes are shown in Table. For the 103 pts with 2-y pembro (30 CR, 63 PR, 10 SD), median follow-up from completion was 42.9 mo (95% CI, 39.9-46.3).Median DOR was not reached. 36-mo OS from pembro completion was 100% (95% CI, 100.0-100.0) for pts with CR, 94.8% (95% CI, 84.7-98.3) for pts with PR, and 66.7% (95% CI, 28.2-87.8) for pts with SD. 15 pts received 2nd-course pembro; BOR in 1st course was 6 CR, 6 PR, and 3 SD. Median time from end of 1st course to start of 2nd course was 24.5 mo (range, 4.9-41.4). Median follow-up in pts who received 2nd-course pembro was 25.3 mo (range, 3.5-39.4). Median duration of 2nd-course pembro was 8.3 mo (range, 1.4-12.6). BOR on 2nd course was 3 CR, 5 PR (ongoing responses, 7 pts), 3 SD (ongoing, 2 pts), and 2 PD (1 death); 2 pts pending. **Conclusions:** Pembro improves the long-term survival vs ipi in pts with advanced melanoma, with all pts who completed therapy in CR still alive at 5 years. Retreatment with pembro at progression in pts who stopped at SD or better can provide additional clinical benefit in a majority of pts. Clinical trial information: NCT01866319. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	Deaths (additional since last data cutoff Dec 3, 2019), n	Median OS (95% CI), mo	HR	5-Y OS rate (95% CI), %
Pembro (N = 556)	328 (4)	32.7 (24.5-41.6)	0.74	39.7 (35.5-43.8)
Ipi (N = 278)	173 (1)	15.9 (13.3-22.0)	–	31.0 (25.3-36.9)
1L pembro (n = 368)	203 (1)	38.7 (27.3-50.8)	0.72	43.3 (38.0-48.4)
1L ipi (n = 181)	111 (1)	17.1 (13.8-26.2)	–	33.0 (25.8-40.3)
2L pembro (n = 97)	125 (3)	23.5 (16.8-34.2)	0.78	32.3 (25.5-39.3)
2L ipi (n = 187)	62 (0)	13.6 (10.7-22.0)	–	27.3 (18.3-37.0)

10014 Poster Discussion Session; Displayed in Poster Session (Board #363), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The nature and management of acquired resistance to PD1-based therapy in melanoma. *First Author: Adriana Hepner, Melanoma Institute Australia, Sydney, Australia*

Background: Anti-PD1 therapy (PD1), either alone or in combination with anti-CTLA4, has high initial response rates, but 20% of patients (pts) with complete response (CR) and 60% with partial response (PR) experience disease progression by 5 years. The nature and best management of this acquired resistance (AR) remains unknown. **Methods:** Consecutive pts from 16 centers who achieved CR or PR to PD1-based therapy and who later progressed were examined. Demographics, disease characteristics, nature of progression and subsequent treatments were examined. **Results:** 300 pts were identified, median age was 64y, 133 (44%) BRAF mutant and 55 (18%) had target therapy (TT) prior to PD1-based therapy. 173 (58%) received PD1 alone, 114 (38%) PD1+CTLA4 and 13 (4%) PD1 + an investigational drug. 89 (30%) pts had CR, 210 (70%) pts had PR. Median time to AR was 12.6 mo (95% CI, 11.3, 14.2) and 142 (47%) progressed while still on drug. Most pts (N = 194, 65%) progressed in a single organ site, and in a solitary lesion (N = 154, 51%). 38 (25%) progressed in the brain only. AR was in new lesion in 136 (45%), existing lesions in 106 (35%), and both new and existing lesions in 58 (19%). For those with solitary lesion progression, 51 (33%) had local (L) treatment alone, 54 (35%) had local and systemic (L+ST), 46 (30%) had systemic therapy alone (ST) and 3 (2%) had no further treatment (BSC). If progression was non-solitary, 89 (61%) had ST, 33 (23%) L+ST, 17 (12%) L alone and 7 (5%) BSC. For those who received ST after AR, first ST (ST1) was PD1 alone in 130 (51%) [53, 41% continuation, 77, 59% reinduction], PD1+CTLA4 in 31 (12%), CTLA4 alone in 15 (6%), targeted therapy in 49 (19%) and investigational drugs in 29 (11%). Median follow-up from AR was 20 mo (95% CI 18-22). The ORR to ST1 was 46% for PD1 alone (56% continuation, 42% reinduction), 56% for PD1+ CTLA4, 0% for CTLA4 alone, 20% for investigational drugs and 67% for TT. Median OS from AR was 38 mo (95% CI, 34.6-NR). 2y-OS was 69% in those with solitary progression compared to 55% for the pts that had a non-solitary progression ($p < 0.001$). There was no difference in OS by ST1 class. Detailed analyses including nature and management of AR while on PD1 or after discontinuation will be presented, as will site-specific AR outcomes. **Conclusions:** Acquired resistance to PD1-based therapy in melanoma is usually oligometastatic, occurring approximately one year after PD1 start. Most pts with isolated progression have local therapy, and the most frequent subsequent systemic therapy is PD1-alone. Patients with AR can have meaningful survival, with median OS over 3 years from AR. Research Sponsor: None.

10015 Poster Discussion Session; Displayed in Poster Session (Board #364), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Twenty-four months RFS and updated toxicity data from OpACIN-neo: A study to identify the optimal dosing schedule of neoadjuvant ipilimumab (IPI) and nivolumab (NIVO) in stage III melanoma. *First Author: Elisa A. Rozeman, Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: Early results of the OpACIN-neo study testing 3 different dosing schedules of neoadjuvant IPI + NIVO demonstrated that 2 cycles IPI 1mg/kg + NIVO 3mg/kg (IPI1NIVO3, arm B) was the most favorable schedule with 20% grade 3-4 immunotherapy-related adverse events (irAEs) and a pathologic response rate (pRR) of 77%. After a median follow-up (FU) of 8.3 months, none of the 64 patients (pts) with a pathologic (path) response (< 50% viable tumor cells) versus 9/21 (43%) without a path response had relapsed. Here, we present the updated 2-year RFS, EFS and long-term toxicity data. **Methods:** In the phase 2 multi-center OpACIN-neo trial, 86 stage III melanoma pts with resectable and RECIST 1.1 measurable lymph node metastasis were randomized between 3 different dosing schedules of neoadjuvant IPI + NIVO: arm A: 2x IPI3+NIVO1 Q3W (n = 30), arm B: 2x IPI1+NIVO3 Q3W (n = 30), and arm C: 2x IPI3 Q3W followed by 2x NIVO3 Q2W (n = 26). Lymph node dissection was scheduled at week 6. Primary endpoints were toxicity, radiologic RR and pRR; RFS and EFS were secondary endpoints. **Results:** After a median FU of 24.6 months, the median RFS and EFS was not reached in any of the 3 arms. In total, 2 pts progressed before surgery, 12 pts relapsed (11 pts without path response and 1 pt with pCR) and 5 pts died (4 due to melanoma and one pt due to toxicity). Estimated 24-months RFS was 84% (95% CI 76-92%) for the total population, 97% (95% CI 93-100%) for pts with a path response and 36% (95% CI 17-74%) for pts without a path response. Estimated 24-months EFS for the total population was 82% (95% CI 74-91%). RFS and EFS did not differ between the arms. Of the 81 pts alive, 55 (68%) have ongoing irAEs; only 2 (3%) pts have ≥ grade 3 irAEs. Most frequent ongoing irAEs were vitiligo (35%), fatigue (14%), sicca syndrome (11%), rash (10%), arthralgia (7%) and endocrine toxicities (20%). 17 pts need hormone replacement therapy: 11 (14%) thyroid hormone and 7 (9%) hydrocortisone. No difference between treatment arms was observed. Ongoing surgery-related AEs were observed in 31 (38%) pts of which lymphedema was seen most frequently (17 pts; 21%). **Conclusions:** Extended follow-up data shows that 2 cycles of neoadjuvant IPI + NIVO without adjuvant therapy induces durable RFS. While almost no ongoing high-grade irAEs were observed, the majority of pts have low-grade ongoing toxicities. These outcomes strongly support the need to test 2 cycles of neoadjuvant IPI1+NIVO3 versus adjuvant anti-PD-1 in a randomized phase 3 trial. Clinical trial information: NCT02977052. Research Sponsor: BMS.

10016 Poster Discussion Session; Displayed in Poster Session (Board #365), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Melanoma recurrence after adjuvant targeted therapy: A multicenter analysis. *First Author: Prachi Bhave, Alfred Health, Melbourne, VIC, Australia*

Background: Adjuvant targeted therapy (TT) improves relapse free survival (RFS) in patients (pts) with BRAF mutant stage 3 melanoma. The outcomes and optimal management of pts who relapse after adjuvant TT is unknown. **Methods:** Pts from 21 centres with recurrent melanoma after adjuvant TT were included. Disease characteristics, adjuvant therapy, recurrence, treatment at relapse and outcomes were examined. **Results:** 87 pts developed recurrent melanoma; 21 (24%) during and 66 (76%) after cessation of adjuvant TT. Median time to 1st recurrence was 16.3 months with median follow up after 1st recurrence of 31 months. 30 (34%) pts recurred locoregionally, 51 (59%) pts developed distant recurrence and 6 (7%) pts had both. Of those who recurred locoregionally, 23/30 (77%) pts underwent surgery to no evidence of disease, only 3 (13%) of which received adjuvant anti-PD1 therapy, and 15/30 (50%) subsequently developed distant disease. 29 (33.3%) pts have died. 75 (86%) pts received systemic therapy at either 1st or subsequent recurrence. 40 (46%) pts received 1st line anti-PD1 based therapy (single agent anti-PD1, anti-PD1 with ipilimumab or anti-PD1 with investigational agent), 12 (14%) pts received ipilimumab monotherapy, 18 (21%) pts received retreatment with combination BRAF/MEK inhibitors and 5 (6%) pts received other agents (chemotherapy, TVEC). 57 (66%) pts had disease that was assessable for response rate (RR). RR after relapse was 69.7% (23/33) to 1st line anti-PD-1 based therapy, 46% (6/13) to TT and 9% (1/11) to ipilimumab monotherapy (Table). Median overall survival (OS) from date of 1st recurrence for all pts was not reached. OS varied by drug class received as 1st line systemic therapy after relapse. 3 year OS was 79% for anti-PD-1 based therapy, 55% for TT and 25% for ipilimumab. **Conclusions:** This study demonstrates that pts who relapse after adjuvant TT may respond to subsequent immunotherapy at similar rates to the treatment naïve setting. Research Sponsor: None.

Response rate to first-line systemic therapy after recurrence.

	Anti-PD-1 +/- trial drug (N=19)	Ipilimumab + Nivolumab (N=14)	Targeted therapy (N=13)	Ipilimumab alone (N=11)
Complete Response	4	5	2	1
Partial Response	9	5	4	0
Stable Disease	0	0	2	1
Progressive Disease	6	4	5	9
Response Rate	**68%**	**71%**	**46%**	**9%**

10017 Poster Discussion Session; Displayed in Poster Session (Board #366), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Final analysis of relapse-free survival in a multicenter, double-blind, placebo-controlled trial of seviprotimut-L polyvalent melanoma vaccine after resection of high-risk melanoma. *First Author: Craig L. Slingluff, University of Virginia School of Medicine, Charlottesville, VA*

Background: Seviprotimut-L is a vaccine prepared from antigens of 3 human melanoma cell lines, administered with alum. Prior formulations induced T cell and antibody responses and improved survival in a small phase II clinical trial. Part B1 of MAVIS (Melanoma Antigen Vaccine Immunotherapy Study, a three part, Phase III clinical program), was a multicenter, double-blind, placebo-controlled trial to assess efficacy of seviprotimut-L, with the primary endpoint of relapse-free survival (RFS). The goal of Part B1 was to guide design of the pivotal Part B2. **Methods:** Patients with AJCC v7 stage IIB-III cutaneous melanoma, after surgical resection, age 18-75, ECOG PS 0-1, were randomized 2:1 to seviprotimut-L 40 mcg or placebo, injected subcutaneously every 2 weeks x 5, then monthly x 4, then every 3 months x 9. Patients were stratified by stage (IIB/C, IIIA, IIIB/C). Target enrollment was 325. The study was powered for assessment of RFS, with target hazard ratio (HR) of 0.625, one-sided alpha of 0.10, and power 80%. Final data are presented. **Results:** 347 patients were randomized. Arms were well-balanced. Treatment-related adverse events (AEs) led to discontinuation in 0.4% and 0%, respectively, for vaccine and placebo arms. There were no treatment-related SAEs. By intent-to-treat (ITT) analysis, RFS was not significantly longer for seviprotimut-L in the full study population but trended toward benefit (HR 0.88). Subgroup analysis based on planned stratification revealed the hazard ratio (HR) for the Stage IIB/IIC subset (randomization stratum, n=111) to be 0.65 (95% CI [0.37, 1.17]), favoring seviprotimut-L. Age can decrease immune competence: RFS was longer with vaccine for patients age <60 overall (N = 191, HR = 0.64 [0.38, 1.08]) and among Stage IIB/C patients (N = 52, HR = 0.32 [0.12, 0.86]). The effect modification interaction p value for age for stage IIB/IIC patients was 0.056. In a multivariable RFS model, for IIB/IIC patients <60 with ulceration (n=38), HR = 0.209 [0.07,0.61]. For overall survival, for patients < 60, HR = 0.41 [0.33,1.14] (n=191, 19 deaths) and for those ≥60, HR = 0.92 [0.39,2.12] (n = 156, 24 deaths). **Conclusions:** Seviprotimut-L is very well-tolerated. Subgroup efficacy analyses identified populations who may benefit from Seviprotimut-L: those with Stage IIB/IIC melanoma and those under age 60. These data support design of the definitive part B2 of the MAVIS phase III trial to test seviprotimut-L for stage IIB/C patients, with stratification by age and ulceration. Clinical trial information: NCT01546571. Research Sponsor: Polynoma.

10018 Poster Discussion Session; Displayed in Poster Session (Board #367), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II study of cemiplimab in patients (pts) with advanced cutaneous squamous cell carcinoma (CSCC): Longer follow-up. *First Author: Danny Rischin, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia*

Background: Cemiplimab monotherapy achieves clinically meaningful activity in pts with advanced CSCC (metastatic [mCSCC] or locally advanced [laCSCC] not amenable to curative surgery or curative radiation) and has a safety profile consistent with other anti–PD-1 agents. Based on initial data (median follow-up of 9.4 months in the pivotal study, NCT02760498), cemiplimab (cemiplimab-rwlc in the US) was approved for the treatment of pts with advanced CSCC. Historical data shows median overall survival (OS) of approximately 15 months with conventional chemotherapy or EGFR inhibitors (ASCO 2019, e21033). We present ~1-year additional follow-up from the largest prospective data set in advanced CSCC. **Methods:** Pts received cemiplimab 3 mg/kg Q2W (Group [Gp] 1; mCSCC; Gp 2, laCSCC) or cemiplimab 350 mg Q3W (Gp 3, mCSCC). The primary endpoint was objective response rate (ORR; complete response + partial response) per independent central review (ICR). Data presented here are per investigator review (INV); ICR data will be available at the meeting. **Results:** 193 pts were enrolled (Gp 1, n = 59; Gp 2, n = 78; Gp 3, n = 56). 128 pts had received no prior anti-cancer systemic therapy, 65 pts were previously treated. As of Oct 11, 2019 (data cut-off), median duration of follow-up was 15.7 months (range: 0.6–36.1) among all pts; 18.5 months (range: 1.1–36.1) for Gp 1, 15.5 months (range: 0.8–35.0) for Gp 2, and 17.3 months (range: 0.6–26.3) for Gp 3. ORR per INV was 54.4% (95% CI: 47.1–61.6) for all pts; 50.8% (95% CI: 37.5–64.1) for Gp 1, 56.4% (95% CI: 44.7–67.6) for Gp 2, and 55.4% (95% CI: 41.5–68.7) for Gp 3. ORR per INV was 57.8% (95% CI: 48.8–66.5) among treatment-naïve pts and 47.7% (95% CI: 35.1–60.5) among previously treated pts. Median duration of response (DOR) has not been reached (observed DOR range: 1.8–34.2 months). In responding pts, estimated proportion of pts with ongoing response at 24 months was 76.0% (95% CI: 64.1–84.4). Median OS has not been reached. Estimated OS at 24 months was 73.3% (95% CI: 66.1–79.2). The most common treatment-emergent adverse events (TEAEs) by any grade were fatigue (34.7%), diarrhea (27.5%), and nausea (23.8%). The most common grade ≥3 TEAEs were hypertension (4.7%) and anemia and cellulitis (each 4.1%). **Conclusions:** For pts with advanced CSCC, cemiplimab achieves ORRs, DOR and survival superior to what has been reported with other agents. Clinical trial information: NCT02760498. Research Sponsor: Regeneron Pharmaceuticals, Inc. and Sanofi.

10019 Poster Discussion Session; Displayed in Poster Session (Board #368), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

CheckMate 067: Long-term outcomes in patients with mucosal melanoma. *First Author: Alexander Noor Shoushtari, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Mucosal melanoma is a rare but aggressive malignancy with a poor prognosis. Here we report 5-y outcomes in a subgroup of patients with mucosal melanoma treated in CheckMate 067 with nivolumab plus ipilimumab (NIVO+IPI), NIVO alone, or IPI alone. **Methods:** Patients with previously untreated stage III or IV melanoma were randomized 1:1:1 to receive NIVO 1 mg/kg + IPI 3 mg/kg for 4 doses Q3W followed by NIVO 3 mg/kg Q2W, NIVO 3 mg/kg Q2W + placebo, or IPI 3 mg/kg Q3W for 4 doses + placebo until progression or unacceptable toxicity. Mucosal histology was not a stratification factor, and patients with mucosal melanoma were identified by local investigators in the study. Descriptive subgroup analyses were performed to evaluate efficacy (objective response rate [ORR], progression-free survival [PFS], overall survival [OS]), and safety. **Results:** A total of 79 patients with mucosal melanoma were treated. With a minimum follow-up of 60 mo, NIVO+IPI treatment was associated with the highest 5-y ORR (43% [vs 30% with NIVO and 7% with IPI]), PFS (29% [vs 14% and 0%, respectively]), and OS (36% [vs 17% and 7%, respectively]; Table), consistent with trends in the intent-to-treat (ITT) population; however, efficacy outcomes were generally less favorable overall relative to the ITT population. Complete response rates were higher with NIVO+IPI (14%) relative to monotherapy (NIVO, 4%; IPI, 0%) in patients with mucosal melanoma. Safety outcomes, including the grade 3/4 treatment-related adverse event rates of 54%, 26%, and 25%, respectively, were similar to the ITT population. **Conclusions:** This 5-y analysis showed that patients with mucosal melanoma in CheckMate 067 had similar safety outcomes but poorer long-term efficacy vs the ITT population. Patients with mucosal melanoma treated with NIVO+IPI appeared to have more favorable survival outcomes than those treated with NIVO or IPI alone. Novel therapies are needed to further improve long-term benefit in patients with mucosal melanoma. Clinical trial information: NCT01844505. Research Sponsor: Bristol-Myers Squibb, Grant (P30CA008748, to Dr. Wolchok) from the National Cancer Institute, and a grant (to Dr. Larkin) from the National Institute for Health Research Royal Marsden–Institute of Cancer Research Biomedical Research Centre.

	Mucosal			ITT[a]		
NIVO+IPI (n = 28)	NIVO (n = 23)	IPI (n = 28)	NIVO+IPI (n = 314)	NIVO (n = 316)	IPI (n = 315)	
ORR, % (95% CI)	43 (24–63)	30 (13–53)	7 (1–24)	58 (53–64)	45 (39–50)	19 (15–24)
PFS						
Median, mo (95% CI)	5.8 (2.7–19.3)	3.0 (2.5–13.9)	2.6 (2.6–2.8)	11.5 (8.7–19.3)	6.9 (5.1–10.2)	2.9 (2.8–3.2)
5-y rate, % (95% CI)	29 (13–48)	14 (4–32)	0	36 (31–42)	29 (24–35)	8 (5–12)
OS						
Median, mo (95% CI)	22.7 (5.6–NR)	20.2 (5.6–33.6)	12.1 (6.4–20.2)	NR (38.2–NR)	36.9 (28.2–58.7)	19.9 (16.8–24.6)
5-y rate, % (95% CI)	36 (19–53)	17 (5–35)	7 (1–20)	52 (46–57)	44 (39–50)	26 (22–31)

NR, not yet reached. [a]Larkin J, et al. *N Engl J Med* 2019;381:1535–1546.

10020 Poster Discussion Session; Displayed in Poster Session (Board #369), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Heterogeneous response and irAE patterns in advanced melanoma patients treated with anti-PD-1 monotherapy from different ethnic groups: Subtype distribution discrepancy and beyond. *First Author: Xue Bai, Department of Renal Cancer & Melanoma, Peking University Cancer Hospital and Institute, Beijing, China*

Background: Programmed cell death receptor-1 (PD-1) monotherapy is the standard first line therapy for advanced cutaneous melanoma, with efficacy, toxicity, and their correlations well established. Yet these remain poorly characterized for non-Caucasians and for certain rarer melanoma subtypes. **Methods:** Clinical data from melanoma patients treated with anti-PD-1 monotherapy between 2009 and 2018 was collected retrospectively from three independent institutions from the US and China. Tumor response, survival outcome, and organ/system-specific immune-related adverse effects (irAEs) were directly compared between different subgroups. **Results:** Among 626 patients, 411 were Caucasian, 214 non-Caucasian; 369 had cutaneous melanoma, and 257 other subtypes. Both ethnicity and melanoma subtype were independently associated with benefit and irAEs. In multivariate analyses, Caucasians had significantly higher objective response rate (ORR) (OR 2.0, 95% CI 1.1-3.5), but this did not translate into a survival advantage (PFS, HR 0.8, 95% CI 0.6-1.1; OS, HR 1.0, 95% CI 0.7-1.4); melanoma of unknown primary shared similar response and survival profile with cutaneous, while acral (ORR, OR 0.4, 95% CI 0.2-0.9; PFS, HR 1.6, 95% CI 1.1-2.2; OS, HR 1.3, 95% CI 0.8-1.9), mucosal (ORR, OR 0.4, 95% CI 0.2-0.9; PFS, HR 1.4, 95% CI 1.0-2.0; OS, HR 1.7, 95% CI 1.1-2.6) and ocular (ORR, OR 0.1, 95% CI 0-0.6; PFS, HR 2.3, 95% CI 1.4-3.6; OS, HR 2.2, 95% CI 1.3-3.6) melanomas had inferior outcomes. Non-Caucasian cutaneous patients had a significantly worse ORR than Caucasians with cutaneous melanoma ($P < .01$). Distinct irAE patterns were observed, exemplified by lower incidence of most irAEs (although more frequent pneumonitis) in Caucasians, and higher and lower liver irAE incidence in ocular and mucosal melanomas, respectively. Endocrine, musculoskeletal and skin irAEs were associated with improved PFS and OS across ethnicities and nearly all melanoma subtypes, whereas heterogeneity existed for other irAE types. **Conclusions:** Ethnicity and melanoma subtype are associated with distinct response patterns, survival outcomes, and irAE profiles in the setting of anti-PD-1 monotherapy. More research is needed to elucidate the molecular and immunologic determinants of these variable outcomes. Research Sponsor: None.

10021 Poster Discussion Session; Displayed in Poster Session (Board #370), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The IMPemBra trial, a phase II study comparing pembrolizumab with intermittent/short-term dual MAPK pathway inhibition plus pembrolizumab in melanoma patients harboring the BRAFV600 mutation. *First Author: Elisa A. Rozeman, Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: Continuous combination of MAPK inhibition (MAPKi) and anti-PD-(L)1 has been investigated by several trials to improve outcome of BRAFV600 mutated melanoma patients. A major obstacle for continuous combination is the high frequency (~60%) of grade 3-4 treatment-related adverse events (TRAE) for which many patients need to discontinue (~40%). In a preclinical model we showed that short-time MAPKi induces T cell infiltration and is synergistic with anti-PD-1. In patients T cell infiltration increased after short-term MAPKi, while after > 2 weeks this was often diminished. The aim of this phase 2b study was to identify the optimal duration of MAPKi with dabrafenib (BRAFi) + trametinib (MEKi) in combination with pembrolizumab (anti-PD-1) in terms of safety, feasibility and immune-activating capacity. **Methods:** Treatment-naïve BRAFV600E/K mutant advanced melanoma patients started pembrolizumab (PEM) 200mg Q3W and were randomized in week 6 to continue PEM only (cohort 1) or to receive in addition intermittent dabrafenib (D) 150 mg BID + trametinib (T) 2mg QD for 2 x 1 week (cohort 2), 2 x 2 weeks (cohort 3), or continuous for 6 weeks (cohort 4). All cohorts continued PEM for up to 2 years. Primary endpoints were safety and treatment-adherence. Secondary endpoints were objective response rate (ORR, RECIST 1.1) at week 6, 12, 18 compared to baseline and PFS. **Results:** Between June 2016 and August 2018, 32 patients have been included; 56% were male, 50% had M1c disease and the majority had a BRAFV600E mutation (81%) and a baseline LDH level > ULN (87%). Grade 3-4 TRAE were observed in 12%, 12%, 50%, and 62% of patients in cohort 1, 2, 3, and 4, respectively. All planned D+T was given in 88%, 63%, and 38% of patients in cohort 2, 3, and 4. Most patients needed to interrupt or discontinue D+T due to fever or elevated liver enzymes. ORR at week 6, week 12, and week 18 were 38%, 62%, and 62% in cohort 1, 25%, 62%, and 75% in cohort 2, 25%, 50%, and 75% in cohort 3 and 0%, 62%, and 50% in cohort 4. After a median follow-up of 17.4 months, the median PFS of patients treated with PEM monotherapy was 10.6 months compared to 27.0 months for patients treated with PEM and short-term/intermittent D+T ($p = 0.13$). **Conclusions:** Combination of PEM plus intermittent D+T seems more feasible and tolerable than continuous triple therapy. Intermittent short-time combination therapy might be equally effective, enables therapy with MAPKi as a second line, and therefore warrants further investigation in a larger patient cohort. Clinical trial information: NCT02625337. Research Sponsor: MSD.

10022 Poster Discussion Session; Displayed in Poster Session (Board #371), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase II, multicenter study of encorafenib/binimetinib followed by a rational triple-combination after progression in patients with advanced BRAF V600-mutated melanoma (LOGIC2). *First Author: Reinhard Dummer, Skin Cancer Center in the Department of Dermatology at University Hospital Zürich, Zürich, Switzerland*

Background: LOGIC2 evaluates the benefit of a 3rd agent added to encorafenib (enco)/binimetinib (bini), selected at progression based on the genetic tumor evolution. **Methods:** In part I/run-In, pts were treated with enco/bini until disease progression (as defined per RECIST v1.1). Foundation One NGS was applied on a baseline sample and on a PD sample. Based on the genetic evolution between the biopsy at inclusion (bxI) and at progression (bxPD) and clinical considerations, pts entered part II and received one of four 3rd agent additions to enco/bini combinations: A. LEE011 (CDK4/6 inhibitor), B. BKM120 (PI3K inhibitor), C. INC280 (c-Met inhibitor), or D. BGJ398 (FGFR inhibitor). An adaptive Bayesian logistic regression model (BLRM) guided by the escalation with overdose control (EWOC) principle was used to make dose escalation decisions. Assessments include objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and safety. Data cutoff for this analysis was May 12, 2019. Data is as is. Part 1 of study is ongoing. Part 2 of study is closed to enrollment. **Results:** 58 pts enrolled into part II (group A=38; B=6; C=13; D=1). 29 pts were assigned to treatment based on bxPD results (Table). In groups A, B, and C, the confirmed ORR was 5.3%, 0%, and 0%, and the DCR was 26.3%, 16.7%, and 15.4%, with median PFS of 2.1, 1.6, and 2.2 months, respectively. Safety was consistent with known profiles of the individual agents. **Conclusions:** Triple therapy is feasible when a 3rd agent is added to enco/bini at progression based on genetic alterations, although activity observed was low. Further exploration to identify patterns of resistance susceptible to the addition of a 3rd agent is needed. Gene alterations for enrollment into part 2. Clinical trial information: NCT02159066. Research Sponsor: Pfizer Inc.

3rd agent	Gene symbol	Mutations (amino acid change, (n))	Amplification[$] n	Loss of copy[¥] n	Total Alterations (n=29)
A. LEE011	KRAS	A146V (n=1)			1
	NRAS	Q61R (n=2), Q61K (n=4)*			6
	HRAS	G13R (n=1)			1
	CDKN2A	splice site 151-1G>A (n=2), V126D (n=1), D146fs*12+ (n=1), E61* (n=1), Y44fs*1 (n=1)	7		13
	BRAF	2			2
	CDK4	R24H (n=1)			1
	MAP2K1	F53I (n=1)			1
B. BKM120	PTEN		1		1
	PIK3CA	M1043V(n=1)		1	
C. INC280	MET		2		2

*1 patient has both Q61K and Q61R [$]Amplication = copy number ratio >1, [¥]Loss of copy= copy number ratio < 1.

10023 Poster Discussion Session; Displayed in Poster Session (Board #372), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Time to central nervous system (CNS) metastases (mets) with atezolizumab (A) or placebo (P) combined with cobimetinib (C) + vemurafenib (V) in the phase III IMspire150 study. *First Author: Paolo Antonio Ascierto, Fondazione IRCCS-Istituto Nazionale dei Tumori, Naples, Italy*

Background: The phase 3 IMspire150 study (NCT02908672) demonstrated improved progression-free survival with first-line combination treatment with A+C+V vs P+C+V in patients (pts) with previously untreated *BRAF*^{V600} mutation–positive advanced melanoma. Here we report incidence and time to development of CNS mets with A+C+V vs P+C+V in the IMspire150 study. **Methods:** Eligible pts were randomized 1:1 to receive A+C+V or P+C+V. A or P were given on day 1 and 15 of each 28-day cycle after an initial cycle of C+V. Incidence and time to development of CNS mets were evaluated in pts with no history of CNS mets at baseline confirmed by magnetic resonance imaging/computed tomography (MRI/CT). On study MRI/CT assessments were performed as clinically indicated. Time-to-event outcomes were estimated using the Kaplan-Meier method and competing risks analysis. Sensitivity analyses were conducted using landmark analysis at time of initiation of A or P. **Results:** 514 pts were randomized to receive A+C+V (n = 256) or P+C+V (n = 258); 244 and 247 pts, respectively, had no history of CNS mets at baseline. After a median follow-up of 18.9 months, CNS mets had developed in 52/244 pts (21%) in the A+C+V arm and 62/247 pts (25%) in the P+C+V arm. In both arms, pts with CNS mets were more likely to have other known unfavorable prognostic factors: elevated LDH, presence of liver mets, and/or higher tumor burden. Cumulative incidence of CNS mets as first site of progressive disease with A+C+V vs P+C+V was 8% vs 9%, 16% vs 19%, 20% vs 24%, and 23% vs 26% at 6, 12, 18, and 24 months, respectively (hazard ratio [HR] 0.87; 95% CI 0.60-1.26). Estimated CNS mets-free survival rates for A+C+V vs P+C+V were 91% vs 90%, 81% vs 75%, 74% vs 66%, and 69% vs 62% at 6, 12, 18, and 24 months, respectively, with a trend for improved CNS mets-free survival with A+C+V (HR 0.79; 95% CI 0.55-1.14). Results of landmark analyses for CNS mets-free survival and cumulative incidence of CNS mets were similar to those in the overall analysis. **Conclusions:** The addition of anti–programmed death-ligand 1 to C+V is associated with numerically lower rates of interval development of CNS mets, consistent with the overall benefit observed for A+C+V in the study. This finding requires further follow-up to fully assess the magnitude of benefit of A+C+V on CNS mets-free survival. Clinical trial information: NCT02908672. Research Sponsor: F. Hoffmann-La Roche Ltd.

10024 Poster Session (Board #373), Fri, 8:00 AM-11:00 AM

The impact of BRAF mutation status on clinical outcomes with single-agent PD-1 inhibitor versus combination ipilimumab/nivolumab. *First Author: Vincent The-Luc Ma, University of Michigan, Ann Arbor, MI*

Background: Nearly half of all metastatic melanoma patients possess the BRAF V600 mutation. Several therapies are approved for BRAF mutant metastatic melanoma, but it is unclear if there is a differential outcome to various immunotherapy regimens. Our aim was to better assess if BRAF mutation status has any impact on survival to combination ipilimumab/nivolumab (I/N) versus single-agent PD-1 inhibitor (PD-1i). **Methods:** We performed a single center, retrospective analysis on a cohort of patients diagnosed with metastatic or unresectable melanoma from 2012 to 2019 at the University of Michigan who were treated with standard I/N or PD-1i (nivolumab or pembrolizumab). A univariate analysis of progression free survival (PFS) and overall survival (OS) was stratified by treatment type and BRAF mutation status. A multivariate Cox regression of survival was used to compare the effects of the treatment groups adjusted by BRAF status, age, gender, pre-treatment LDH level, prior treatment status, and brain metastases status. **Results:** 323 patients were identified. 132 had BRAF V600 mutation and 191 had BRAF wildtype (WT) status. 138 patients received I/N and 185 patients received PD-1i. In our univariate analysis, there was no difference in PFS [HR: 0.72, 95% CI, 0.46 – 1.13] or OS [HR: 0.78, 0.44 – 1.38] with I/N versus PD-1i in the BRAF mutant cohort, but there was improved PFS [HR: 0.55, 0.35 – 0.88) and OS [HR: 0.52, 0.28 – 0.95] with I/N compared to PD-1i in the BRAF WT group. In the multivariate analysis, the BRAF WT group continued to show PFS benefit with I/N compared to PD-1i [HR: 0.57, 95% CI, 0.35 – 0.95], but the OS benefit no longer achieved statistical significance [HR: 0.54, 0.28 – 1.03]. **Conclusions:** Our study results were discordant with the observation in the landmark CheckMate 067 trial, which noted improved PFS and OS with I/N compared to nivolumab alone in the BRAF mutant group and no difference in the BRAF WT group. In our real-world retrospective analysis, I/N over PD-1i should be considered as initial immunotherapy for metastatic melanoma patients regardless of BRAF mutation status, but even more favorably in BRAF WT. Research Sponsor: None.

10025 Poster Session (Board #374), Fri, 8:00 AM-11:00 AM

Initial report of treatment of uveal melanoma with hepatic metastases with yttrium90 internal radiation followed by ipilimumab and nivolumab. *First Author: David R. Minor, California Pacific Medical Center Research Institute, San Francisco, CA*

Background: Hepatic metastases from uveal melanoma have no established therapy, with a median survival of only 6-12 months. To date therapy with checkpoint inhibitors has yielded minimal results. To take advantage of possible synergy between radiation and immunotherapy we treated patients with yttrium90 internal radiation followed by immunotherapy. **Methods:** Patients received yttrium90 (Sir-Spheres) via hepatic artery infusion in two treatments, one to each lobe 3-4 weeks apart, followed in 3-6 weeks by ipilimumab and nivolumab for 4 doses, then nivolumab maintenance. **Results:** We are presenting interim results because of the excessive toxicity seen when these FDA-approved modalities were used in sequence with the FDA-approved dosages. Initially dosing of yttrium90 (Y90) followed the package insert "BSA method" but after 8 patients we had 5 cases of grade 3-4 hepatic toxicity; in 4 cases the toxicity was observed after just the Y90. One case of cirrhosis occurred in a patient whose liver received 40-45Gy; her cirrhosis was felt most likely due to the Y90. Y90 dosing was then reduced to limit dosage to normal liver to 35Gy, and none of the next 5 patients have had more than grade 2 hepatic toxicity. Dosage to the normal liver is approximated by the MIRD formula: Actual delivered liver dose [Gy] = 50 * Administered activity [GBq] * (1 – Lung shunt fraction) / kg of treated liver. If calculated dose was $>$ 35GY, dosage in GBq is reduced proportionally. Toxicity in the first 5 patients to receive immunotherapy included one grade 4, two grade 3 and two grade 2 hepatic toxicities, and only 3 of the 5 patients received more than one dose of ipilimumab. We then reduced dosing of ipilimumab from 3mg/kg x 4 to 1mg/kg x 4 because of this excessive autoimmune toxicity. Of 13 patients, 10 received both Y90 and immunotherapy, and 3 had responses (1 CR, 2 PR) with 3 patients stable $>$ 5months. Median progression-free survival for all patients is 27 weeks and median overall survival is greater than 48 weeks. Treatment with Y90 produced an over 50% fall in peripheral blood lymphocytes which was reversed in most patients by the immunotherapy. **Conclusions:** With dose modifications this therapy appears feasible and objective tumor responses were seen. Sequential therapy with Y90 and immunotherapy appears tolerable if radiation to normal liver is limited to 35Gy and ipilimumab dose is 1mg/kg. Clinical trial information: NCT02913417. Research Sponsor: California Pacific Medical Foundation.

10026 Poster Session (Board #375), Fri, 8:00 AM-11:00 AM

Combination anti-PD-1 and ipilimumab (ipi) therapy in patients with advanced melanoma and pre-existing autoimmune disorders (AD). *First Author: Lauren Julia Brown, Crown Princess Mary Cancer Care Centre, Westmead, NSW, Australia*

Background: Clinical trials of immunotherapy exclude patients (pts) with pre-existing AD. While retrospective data exist regarding the efficacy and safety of single agent ipi and anti-PD1 antibodies (PD1) in pts with AD, no data are available regarding the safety and efficacy of combination therapy in pts with AD, which has a higher toxicity risk. **Methods:** Pts with melanoma and pre-existing AD treated with combination ipi/PD1 were retrospectively identified from 10 international centres. Data regarding AD, treatment, toxicity and outcomes were examined. **Results:** Fifty-five pts were included, 46 were treated with ipi/nivolumab and 9 with ipi/pembrolizumab. 40 had an ipi dose of 3mg/kg while 15 had a lower dose regimen. 9 pts received prior PD1 therapy; 3 suffered moderate immune-related adverse events (irAE) with no flares of AD on single agent PD1. Pre-existing AD included inflammatory bowel disease (IBD), thyroiditis, rheumatoid arthritis (RA), multiple sclerosis and psoriasis. 10 pts had active symptoms of AD and 13 were immunosuppressed at commencement of ipi/PD1. Eighteen pts (33%) experienced a flare of their AD including 4/7 with RA, 3/6 with psoriasis, 5/9 with IBD, 3/18 with thyroiditis, 1/1 with Sjogren's syndrome, 1/1 with polymyalgia, 1/1 with Behcet's syndrome. Median time to flare was 19 days (range 4 – 167). 13 pts were managed with steroids, 5 required additional immunosuppressants. 7 pts were hospitalised for management of flare (5 with IBD, 2 with RA). 2 pts required intensive care and vasopressors for severe IBD flare, quiescent prior to ipi/PD1. One for diarrhoea and shock and one for duodenal perforation. 8 pts ceased treatment due to flare (3 with IBD, 2 with RA, 1 with Behcet's, 1 with Sjogren's). Thirty-seven pts (67%), experienced an irAE unrelated to their AD, 38% G3 or G4. The most frequent irAEs were colitis (n = 16), hepatitis (n = 12), endocrinopathies (n = 12), with 13 pts experiencing an irAE in $\geq$ 2 organs. 9 pts experienced both AD flare and an irAE. 20 pts (36%) ceased immunotherapy due to irAEs. ORR was 55% (54% in PD1 naive pts), at a median follow up of 14 months, 77% of responses ongoing. ORR in pts who had a flare of their AD was 44% and in pts on immunosuppression was 46%. Median PFS was shorter in pts who had a flare of AD compared with those who did not (2.6 vs 9 months; P-value 0.047). **Conclusions:** Combination ipi/PD1 shows efficacy comparable to clinical trial populations in pts with pre-existing AD and advanced melanoma. Whilst there was a substantial risk of flare of AD, no increased frequency of irAE's was observed. Research Sponsor: None.

10028 Poster Session (Board #377), Fri, 8:00 AM-11:00 AM

The anti–PD-1 antibody spartalizumab in combination with dabrafenib and trametinib in advanced *BRAF* V600–mutant melanoma: Efficacy and safety findings from parts 1 and 2 of the Phase III COMBI-i trial. *First Author: Georgina V. Long, Melanoma Institute Australia, The University of Sydney, and Royal North Shore and Mater Hospitals, Sydney, NSW, Australia*

Background: Treatment (tx) with checkpoint inhibitors or targeted therapy improves outcomes in patients (pts) with *BRAF* V600–mutant advanced melanoma; however, many pts subsequently progress and die. Preliminary evidence suggests that targeted therapy may enhance the impact of checkpoint inhibitors and improve efficacy compared with either treatment alone. **Methods:** COMBI-i is investigating first-line spartalizumab 400 mg every 4 wk + dabrafenib 150 mg twice daily + trametinib 2 mg once daily in pts with unresectable or metastatic *BRAF* V600–mutant melanoma (NCT02967692). We report efficacy and safety data from parts 1 (run-in cohort) and 2 (biomarker cohort), with a median follow-up of 24.3 mo. Response was assessed per RECIST v1.1. The randomized part 3 is ongoing. **Results:** 36 pts were enrolled (part 1: n = 9; part 2: n = 27); 20 (56%) had stage IV M1c disease and 15 (42%) had elevated lactate dehydrogenase (LDH) levels ($\geq$ upper limit of normal). At the data cutoff (August 19, 2019), tx was ongoing in 10 pts (28%). The confirmed investigator-assessed objective response rate (ORR) was 78% (n = 28), with 16 complete responses (CRs; 44%) and 12 partial responses (33%). Median duration of response (DOR; 10/28 responders with events) was not reached (NR); 24-mo DOR rate was 53.4% (95% CI, 29%-73%). Median progression-free survival (PFS) was 22.7 mo; 24-mo PFS rate was 41.4% (95% CI, 23%-59%). At the cutoff, median overall survival (OS) was NR, with a 24-mo OS rate of 74.1% (95% CI, 56%-86%). In pts with elevated LDH, ORR was 67%, with 4 CRs (27%); median PFS was 10.7 mo (95% CI, 4.6-19.1 mo), and median OS was NR. The estimated 24-mo PFS and OS rates in these pts were 26.7% and 52.5%, respectively. All pts had $\geq$ 1 tx-related adverse event (TRAEs); 26 (72%) had grade $\geq$ 3 TRAEs. The most common grade $\geq$ 3 TRAEs were pyrexia (17%), increased lipase (11%), neutropenia (11%), increased blood creatine phosphokinase (8%), and increased γ-glutamyltransferase (8%). AEs leading to discontinuation of all 3 study drugs occurred in 6 pts (17%). All-causality grade $\geq$ 3 AEs requiring immunosuppressive medication occurred in 19 pts (53%). One pt died of cardiac arrest that was not considered tx related. **Conclusions:** The combination of spartalizumab + dabrafenib + trametinib resulted in high ORR and CR rates, with a high frequency of durable responses, including in patients with poor prognostic factors. Clinical trial information: NCT02967692. Research Sponsor: Novartis Pharmaceuticals Corporation.

10029 Poster Session (Board #378), Fri, 8:00 AM-11:00 AM

Association between complete response and survival in advanced melanoma treated with talimogene laherparepvec (T-VEC) plus ipilimumab (ipi). *First Author: Jason Alan Chesney, James Graham Brown Cancer Center, University of Louisville, Louisville, KY*

Background: This is the first randomized trial testing the addition of an oncolytic virus to an immune checkpoint inhibitor for advanced melanoma. At the 3-year (yr) follow-up, the combination (combo) of T-VEC and ipi demonstrated durable and statistically superior objective response rate (ORR) over ipi alone (36.7% vs. 16.0%; odds ratio, 3.0; 95% CI, 1.6–6.0; $P = 0.002$). Complete response (CR) rate was 21.4% with the combo and 6.0% with ipi. Median overall survival (OS) was not reached in either arm. In this post hoc analysis, we utilized the 3-yr landmark data to explore the relationship between CR and OS in the combo arm. **Methods:** Pts with unresectable, stage IIIB-IV melanoma were randomized 1:1 to receive combo or ipi alone. T-VEC was administered intratumorally on day 1 of week (wk) 1 at 10^6 plaque-forming units (PFU)/mL followed by subsequent doses at 10^8 PFU/mL on day 1 of wk 4, and every 2 wks thereafter. Ipi (3 mg/kg) was given every 3 wks starting on day 1 of wk 6 for up to 4 doses. Response was assessed by investigators per immune-related response criteria every 12 wks until disease progression. The primary endpoint was ORR; key secondary endpoints were OS, progression-free survival, and safety. **Results:** 198 pts were randomized (98 to combo; 100 to ipi). As of February 25, 2019, the median follow-up time was 40.0 mos (range: 0.2–63.7) for the combo arm. Among 98 pts who received combo, 21 (21.4%) had a best overall response of CR including 8 who converted from an initial partial response (PR), 15 (15.3%) had PR, 19 (19.4%) had stable disease, 30 (30.6%) had progressive disease, and 13 (13.2%) were unevaluable. Of 21 pts achieving CR, 17 (81%) had ECOG status of 0, 16 (76.2%) had stage IIIB-IVM1a disease, and 16 (76.2%) had no visceral metastases. Median duration of CR was not reached (range: 5.4[+]–58.2[+] mos); 19 of 21 CRs lasted more than 6 months. The baseline tumor burden was lower in pts with CR than in those with non-CR. Median OS was not reached in pts with CR (range: 25.1[+]–63.7[+] mos) and was 47.6 mos (range: 0.2[+]– 63.7[+] mos) in pts with non-CR (Log-rank $P = 0.0005$). The Kaplan–Meier estimated 3-year OS rate was 100.0% for patients with CR and 52.3% for those with non-CR. **Conclusions:** CR rate was higher with T-VEC plus ipi than with ipi alone in pts with advanced melanoma (21.4% vs. 6.0%). In the combo arm, CR was associated with prolonged OS, and pts with CR tended to have better ECOG performance status, earlier-stage disease, and lower baseline tumor burden, as compared with those with non-CR. Clinical trial information: NCT01740297. Research Sponsor: Amgen Inc.

10030 Poster Session (Board #379), Fri, 8:00 AM-11:00 AM

Surrogate endpoints for overall survival in anti-programmed death-1 and anti-programmed death ligand 1 trials of advanced melanoma. *First Author: Run-Cong Nie, Sun Yat-Sen University Cancer Center, Guangzhou, China*

Background: The mechanisms of action of anti-PD-1/PD-L1 agents are markedly distinct from those of cytotoxic agents, thus a critical issue that is under investigation is what is the optimal endpoint and how should tumor response be evaluated in anti-PD-1/PD-L1 trials for metastatic melanoma. Here, we assessed surrogacy of objective response rate (ORR), disease control rate (DCR) and progression-free survival (PFS) for overall survival (OS) in anti-PD-1/PD-L1 trials of metastatic melanoma through a meta-analysis of randomized controlled trials (RCTs). **Methods:** PubMed and EMBASE were searched for phase 2/3 RCTs till June 2019 investigating anti-PD-1/PD-L1 agents. Treatment effect (hazard ratio or odds ratio) on potential surrogates (ORR/DCR/PFS) and OS were collected. At trial level, we assessed the correlation between treatment effect on potential surrogates and OS, weighted by sample size, fixed and random effect models, and calculated the surrogate threshold effect (STE). Sensitivity analyses and leave-one-out cross-validation approach were performed to evaluate the robustness of our findings. **Results:** We included 8 RCTs (4,110 patients; 11 comparisons). We did not identify strong correlations between ORR (coefficient of determination [R^2]: 0.09 to 0.25), DCR (0.41 to 0.57) and OS. However, we noted a strong correlation between PFS and OS, with R^2 of 0.82 in sample size, 0.75 in fixed effect, and 0.72 in random effect model weighting, the robustness of which was further verified by leave-one-out cross-validation approach. Sensitivity analyses with restriction to trials with less than 50% crossover (R^2: 0.94-0.94), phase 3 trials (R^2: 0.94-0.95), large trials (R^2: 0.78-0.86) and first-line trials (R^2: 0.83-0.91) strengthened the correlation. The STE for PFS was 0.78. **Conclusions:** PFS may be the appropriate surrogate for OS in anti-PD-1/PD-L1 trials of metastatic melanoma. A future anti-PD-1/PD-L1 trial would need less than 0.78 for PFS of the upper limit of confidence interval to predict an OS benefit. Research Sponsor: None.

10031 Poster Session (Board #380), Fri, 8:00 AM-11:00 AM

Does body mass index really predict the response to systemic therapies in metastatic melanoma: A multicenter study from the MelBase French National Cohort? *First Author: Yoann Di Filippo, Dermatology Department, Nice Hospital,, Nice, France*

Background: Obesity is an established risk factor for several cancers and higher body mass index (BMI) is associated with poor prognosis. These data are still debated in melanoma. Furthermore, recently the concept of "obesity paradox" has emerged. In a large cohort published by *McQuade JL et al*, higher BMI was associated with better survival in patients with metastatic melanoma (MM) especially for those treated with targeted therapy (TT) and immune checkpoint inhibitors (ICI). We studied the association between BMI and progression-free survival (PFS) and overall survival (OS) in patients with MM treated with systemic therapies. **Methods:** This study was conducted from the prospective MelBase cohort (NCT02828202). Patients with MM treated with first-line ICI, TT, or CT were included. BMI was categorized by WHO criteria. Underweight patients were excluded. The co-primary outcomes were the associations between BMI and PFS or OS, stratified by treatment, sex and age. Multivariate analyses were performed. **Results:** A total of 1214 patients were analyzed. The majority of them were treated with ICI, followed by TT. Obese patients represented 22% of cohort (Table). Median follow-up was 13.5 months. The patients who were overweight or obese did not have different PFS ($p = 0.88$) or OS ($p = 0.25$) than patients with normal BMI. Stratifying this cohort by treatment received, age, sex and others parameters (such as LDH, number of metastatic site) did not revealed any difference. Multivariate analysis did not change the results. **Conclusions:** BMI was not associated with clinical outcomes in our cohort, especially in ICI and TT groups. Thus, we did not confirm the results presented by *McQuade JI et al.* with a cohort quite similar in term of size. Because BMI is too simplistic and then an imperfect measure of body composition, the published data are not reproducible. We caution the oncologists, about BMI as valuable predictive marker of survival for melanoma patients. Research Sponsor: None.

Characteristics at baseline	Whole population	18.5 < BMI < 24.9 Normal	25 < BMI < 29.9 Overweight	30 < BMI Obese
Number of patients	1214	516	429	269
Age, years (mean)	63.8	62.4	65.4	63.8
Sex	738	281	299	158
Men	476	235	130	111
Women				
AJCC 7th edition	479	184	168	127
III/M1a/M1b	735	334	260	141
M1c				
Brain metastases	228	112	75	41
Yes				
ECOG PS	772	329	283	160
0	338	142	113	83
≥1				
Mutations Status	469	211	156	102
BRAFV600	219	86	86	47
NRAS				
LDH	603	249	214	140
Normal	351	145	122	84
High				
First line treatment	761	308	278	175
Immune checkpoint inhibitors	389	173	135	81
Target therapy	64	35	13	16
Chemotherapy				

10032 Poster Session (Board #381), Fri, 8:00 AM-11:00 AM

Surgery for unresectable stage IIIC and IV melanoma in the era of new systemic therapy. *First Author: Stephanie Blankenstein, Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands*

Background: Over the past decade opportunities for surgical treatment in metastatic melanoma patients have re-emerged due to the development of novel systemic therapies. However, selecting patients who will benefit from surgery after systemic therapy is still difficult. The aim of this study is to present data on outcomes of surgery in patients with unresectable stage III and IV melanoma, who have previously been treated with immune checkpoint inhibitors (ICI) or targeted therapy, to provide insight in which patients may benefit from surgery. **Methods:** Data was extracted from the prospectively collected, nationwide, Dutch Melanoma Treatment Registry (DMTR) onunresectable stage IIIC or advanced/metastatic stage IV melanomapatients who obtained disease control with systemic therapy and underwent subsequent surgery. Disease control was defined as a complete response (CR), partial response (PR) or stable disease (SD). After disease control was achieved with systemic therapy, progressive disease (PD) was allowed as a most recent status of disease prior to surgery, to avoid excluding patients with oligoprogression. Major exclusion criteria were non-cutaneous melanoma and brain metastases. **Results:** Of 3959 patients in the DMTR database, 154 patients met our inclusion criteria. Of these patients, 79 (51%) were treated with ICI, 61 (40%) with targeted therapy and 9.1% with study or other treatments before surgery. The best response to systemic therapy was a CR in 5.2%, PR in 46.1% and SD in 44.2% of patients. At a median follow-up of 10.0 months (IQR 4-22) after surgery, the median overall survival (OS) had not been reached in our cohort and median progression free survival (PFS) was 9.0 months (95% CI 6.3-11.7). A multivariate cox regression analysis showed that when surgery led to CR or PR, the PFS and OS were better than if surgery led to SD or PD ($p < 001$). Also, ICI seemed to be more favorable than targeted therapy in both PFS (median of 15 versus 7 months) and OS (median not reached versus 32 months) ($p = 0.026$ and $p = 0.003$). **Conclusions:** We conclude that selected unresectable stage IIIC or stage IV melanoma patients might benefit from surgery after achieving disease control with systemic therapy. Expected residual tumor after surgery could be an important selection criterion. Especially patients undergoing surgery after initial tumor response on ICI have a chance of long-term survival. Research Sponsor: None.

10033 Poster Session (Board #382), Fri, 8:00 AM-11:00 AM

Health-related quality of life (HRQL) in patients with advanced cutaneous squamous cell carcinoma (CSCC) treated with cemiplimab: Post hoc exploratory analyses of a phase II clinical trial. *First Author: Michael Robert Migden, Departments of Dermatology and Head and Neck Surgery, University of Texas, MD Anderson Cancer Center, Houston, TX*

Background: Cemiplimab-rwlc (cemiplimab), a PD-1 Inhibitor, showed a robust clinical response in patients (pts) with metastatic (mCSCC) or locally advanced (laCSCC) CSCC not eligible for curative surgery/radiation. This post hoc exploratory analysis examined data from the EORTC cancer specific 30-item HRQL questionnaire (QLQ-C30) for pts participating in a cemiplimab phase 2 clinical trial (clinicaltrials.gov NCT02760498). **Methods:** Adults (N = 193) with invasive CSCC, ≥1 lesion and ECOG performance status ≤1 received IV cemiplimab 3mg/kg q2w (mCSCC n = 59; laCSCC n = 78) or 350mg q3w (mCSCC n = 56). At baseline (BL) and day 1 of each treatment cycle, pts were administered the QLQ-C30. Mixed effects repeated measures (MMRM) models were used to estimate mean change from BL to cycle 5 (C5) for domains/items of the QLQ-C30. For pts with data from BL to C5, the proportion who reported clinically meaningful improvement or worsening (≥10 points) or maintenance (those who did not have ≥10 point change) on each domain was determined for combined and individual treatment groups. **Results:** BL scores indicated moderate to high levels of functioning and low symptom burden. From BL to C5, a clinically meaningful improvement in pain score was observed (least squares [LS] mean [standard error] change -12.1 [2.1]; $P < .0001$); other domains/items remained stable or showed a trend towards improvement (LS mean changes < 10 points). By C5, the majority of pts experienced clinically meaningful improvement or remained stable across key domains (Table). Similar findings were observed on individual symptoms (85%-94% for dyspnea, nausea/vomiting, diarrhea, constipation, appetite loss) and in each treatment group. **Conclusions:** Cemiplimab-treated patients achieved a clinically meaningful reduction in pain and most pts either improved or maintained their HRQL, function with low symptom burden. Clinical trial information: NCT02760498. Research Sponsor: Regeneron Pharmaceuticals, Inc. and Sanofi.

Difference from baseline at C5 on key QLQ-C30 domains (all combined groups).

	No. (%) of pts		
Domain	Clinically meaningful improvement	Stable	Clinically meaningful worsening
Global Health Status/QoL (n = 98)	41 (42)	42 (43)	15 (15)
Physical function (n = 99)	21 (21)	63 (64)	15 (15)
Role function (n = 99)	29 (29)	47 (47)	23 (23)
Emotional function (n = 98)	30 (31)	56 (57)	12 (12)
Social function (n = 98)	35 (36)	44 (45)	19 (19)
Fatigue (n = 99)	43 (43)	31 (31)	25 (25)
Pain (n = 99)	43 (43)	42 (42)	14 (14)
Insomnia (n = 98)	30 (31)	56 (57)	12 (12)

10034 Poster Session (Board #383), Fri, 8:00 AM-11:00 AM

Effect of first-line spartalizumab + dabrafenib + trametinib on immunosuppressive features detected in peripheral blood and clinical outcome in patients (pts) with advanced BRAF V600–mutant melanoma. *First Author: Reinhard Dummer, University Hospital Zürich Skin Cancer Center, Zürich, Switzerland*

Background: Spartalizumab + dabrafenib + trametinib has previously shown a high response rate of 78% (28 of 36 pts), with a complete response (CR) rate of 42%. A correlative analysis of gene expression signatures (GES)/pathways using whole-transcriptome RNA-seq data from tissue showed that pts with a CR had significantly lower expression levels of immunosuppressive factors in the tumor microenvironment (TME) at baseline (BL). Here we analyze BL peripheral blood markers in the same cohort of pts to assess whether liquid markers can also predict response and clinical outcome to spartalizumab + dabrafenib + trametinib. **Methods:** The Phase III COMBI-i study (NCT02967692) is evaluating spartalizumab + dabrafenib + trametinib in pts with previously untreated *BRAF* V600–mutant unresectable or metastatic melanoma. In parts 1 (safety run-in; n = 9) and 2 (biomarker cohort; n = 27), blood and tissue samples were collected at BL, on treatment after 2-3 wk and 8-12 wk, and at disease progression. Lactate dehydrogenase (LDH) and other blood-based markers (including cytokine profiling [n = 45] and blood RNA-seq [114 signatures]) were assessed in all 36 pts. Pts were divided into 2 groups of 24 and 12 pts based on progression-free survival (PFS) of > 1 or < 1 y. **Results:** In addition to LDH, previously described blood markers such as neutrophil to lymphocyte ratio (NLR) and plasma IL-8 were identified among other neutrophil and immunosuppressive features as top candidates associated with PFS > 1 y. Low plasma IL-8 levels were also associated with CR, and multivariate models suggested that IL-8 may add independent predictive value to LDH and NLR for PFS > 1 y and CR. Pts with high IL-8 levels in the circulation were characterized by high neutrophil chemokine signaling ($\rho = 0.553$) and high neutrophil markers ($\rho = 0.466$) in the tumor as measured by RNA-seq GES levels. We observed a decrease in plasma IL-8 levels from BL upon treatment with spartalizumab + dabrafenib + trametinib. **Conclusions:** Our peripheral blood marker analysis confirmed recent findings from tissue samples that intratumoral immunosuppressive features may preclude a CR and are associated with poor outcomes. High BL plasma IL-8 levels may be associated with an immunosuppressive TME. Further validation is warranted; the randomized placebo-controlled part 3 of COMBI-i is ongoing. Clinical trial information: NCT02967692. Research Sponsor: Novartis Pharmaceuticals Corporation.

10035 Poster Session (Board #384), Fri, 8:00 AM-11:00 AM

Phase I trial of autologous cMET-directed CAR-t cells administered intravenously in patients with melanoma & breast carcinoma. *First Author: Payal D Shah, Abramson Cancer Center at the University of Pennsylvania, Philadelphia, PA*

Background: Advanced relapsed/refractory melanoma and metastatic triple-negative breast cancer are lethal diseases for which effective therapies are limited. We conducted a pilot phase I clinical trial (NCT03060356) to establish the safety and feasibility of intravenous autologous chimeric antigen receptor (CAR) T cell immunotherapy targeting cMET, a cell-surface antigen that is highly expressed in these cancers. **Methods:** Subjects had metastatic or unresectable melanoma (Mel) or triple-negative breast cancer (BC) with ≥30% expression of cMET on archival tissue or screening biopsy. Eligible subjects had measurable disease and progression on at least 1 prior therapy. Patients (pts) received up to 6 doses ($1x10^8$ total T-cells per dose) of RNA electroporated anti-cMET CAR T cells over a 2-week period without antecedent lymphodepleting chemotherapy. Subjects underwent pre- and post-infusion biopsies. The primary objective was to determine feasibility and safety of treatment. **Results:** 77 subjects (39 mel, 38 BC) were prescreened for tumor cMET expression and 37 (17 mel, 20 BC) met the eligibility threshold. Seven pts (4 BC, 3 Mel) received cMET-directed CAR T infusions on study. Mean age was 50 years (35-64); median (M) ECOG 0 (0-1); M prior lines of chemotherapy/immunotherapy were 4/0 for BC pts and 1/3 for Mel pts. 6 of 7 pts received all planned CAR T cell infusions, and 1 received 5 infusions. 5 pts experienced grade (G) 1 or G 2 toxicity that was possibly or definitely related to study. Toxicities occurring in ≥1 pt included: anemia (n = 3), fatigue (n = 2), and malaise (n = 2). No G ≥3 toxicities or cytokine release syndrome were observed. No pts discontinued therapy due to toxicity. Best response was stable disease in 4 pts (2 BC, 2 Mel) and PD in 3 pts (2 BC, 1 Mel). Messenger RNA signals corresponding to CAR T cells were detected by RT-PCR in the peripheral blood of all pts during the infusion period and in 2 pts after the infusion period. 6 pts underwent baseline biopsy and 4 pts underwent post-infusion biopsy. Immunohistochemical stains of CD3, CD4, CD8, CD163, L26, PD1, PDL1, Foxp3, Ki67, Granzyme B and Phospho-S6 were performed on pre- and post-treatment tissue biopsies and are being evaluated. **Conclusions:** Intravenous administration of RNA-electroporated cMET-directed CAR T cells was safe and feasible. Future directions include examination of this target using a lentiviral construct in combination with lymphodepleting chemotherapy. Clinical trial information: NCT03060356. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

10036 Poster Session (Board #385), Fri, 8:00 AM-11:00 AM

A phase II study of ERK inhibition by ulixertinib (BVD-523) in metastatic uveal melanoma. *First Author: Elizabeth Iannotti Buchbinder, Beth Israel Deaconess Medical Center, Boston, MA*

Background: Uveal melanoma is a rare and aggressive subset of melanoma that is minimally responsive to traditional therapies. Greater than 80% of uveal melanomas have a mutation in GNAQ or GNA11 which lead to downstream signaling through the MAPK pathway. This has led to efforts to treat uveal melanoma with MEK inhibition with mixed results. Ulixertinib (BVD-523) is a potent and reversible small molecule ATP-competitive inhibitor of both ERK1 and ERK2 protein kinases which has undergone phase I testing. **Methods:** We performed a phase II study to determine the efficacy and safety of BVD-523 in patients with metastatic uveal melanoma. This was conducted as a Simon two-stage design with a total sample size of 25 patients (pts) and an initial evaluation of efficacy after 13 pts. Two responses were required to continue to the second stage. **Results:** From April 2018 to April 2019 thirteen pts were enrolled. Pts were predominantly female (69%) with a median age of 64 yrs. (34 -76). Sites of metastasis included liver (84.6%) and lung (30.8%). Grade 3 and 4 toxicities associated with therapy were consistent with BVD-523 and other ERK inhibitors and included LFT elevation, hyponatremia, pruritis, amylase elevation, anemia and rash. The best response, per RECIST 1.1, was stable disease (SD) in 4 pts, and disease progression (PD) in 7 patients. Two patients were unevaluable for response due to withdrawing themselves from the study. Median time to progression was 2.0 months (90% CI: 1.8 – 3.6 mos.). There were eight deaths due to disease progression with a median survival time of 6.9 months (90%CI: 3.2 to 8.3 mos.). Analysis of correlative data from pre- and on-treatment biopsies exploring the change in expression of key signaling proteins relating to treatment is underway. **Conclusions:** ERK inhibition with ulixertinib (BVD-523) did not demonstrate activity in patients with metastatic uveal melanoma. The toxicities observed on study were consistent with what would be expected with MAPK pathway inhibition. Clinical trial information: NCT03417739. Research Sponsor: BioMed Valley Discoveries, Inc.

10037 Poster Session (Board #386), Fri, 8:00 AM-11:00 AM

A proteomic biomarker discovery platform for predicting clinical benefit of immunotherapy in advanced melanoma. *First Author: Yuval Shaked, Technion, Haifa, Israel*

Background: Immune checkpoint inhibitor-based immunotherapies that target CTLA-4 and the PD-1/PD-L1 axis have revolutionized the treatment of advanced melanoma due to their remarkable clinical benefit. However, only a limited number of patients respond to treatment. Therefore, biomarkers to identify appropriate candidates who will benefit from such therapy are needed. Our previous studies have identified therapy-induced, host-mediated mechanisms that drive resistance to a variety of cancer treatment modalities. Here, we explored whether assessing the systemic host-mediated response to immunotherapy can serve as a basis for predicting clinical outcome in melanoma patients. **Methods:** The cohort consisted of 34 advanced melanoma patients receiving anti-PD-1 monotherapy or anti-PD-1 and anti-CTLA-4 combination therapy. Clinical benefit was assessed. Plasma samples were obtained from patients at baseline and 2-4 weeks after a single treatment. Proteomic profiling of plasma samples was performed using ELISA-based protein arrays. A generalized linear model (GLM) was applied to a subset of the cohort (n = 13) to identify a proteomic signature that can predict clinical response to treatment. The predictive signature was then tested on the entire cohort (n = 33), excluding one patient with stable disease. **Results:** We identified a 10-protein signature that accurately distinguishes between responders and non-responders with an area under the curve (AUC) of 0.84 (confidence interval: 0.69-0.99, p-value 5.56E-04), and sensitivity and specificity of 0.94 and 0.79, respectively. These results are currently being validated in a larger cohort in an ongoing prospective study (PROPHETIC trial, NCT04056247). To explore the biological basis of resistance to immunotherapy, we performed a pathway enrichment analysis. Multiple mechanisms of resistance were identified in the non-responder group, including signaling pathways associated with immunosuppression and inflammation. Comparison between the two treatment modalities revealed pathways unique to each treatment, implying important differences between the two regimens. **Conclusions:** Our study provides insights into mechanisms of resistance to immunotherapy and paves the way towards the discovery of novel predictive biomarkers for patient stratification in melanoma. Research Sponsor: OncoHost.

10038 Poster Session (Board #387), Fri, 8:00 AM-11:00 AM

Spatial proximity of CD8 T cells to tumor cells as an independent biomarker for response to anti-PD-1 therapy. *First Author: Maarten Slagter, Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: Only a subset of advanced melanoma patients respond to anti-PD-1 (aPD1) monotherapy. Upfront identification of (non-)responsiveness would help guide first-line treatment decisions, prevent overtreatment and unnecessary risk for toxicities. T cell density and expression of T cell related genes have been associated with response to aPD1, but are imperfect predictors. We investigated whether spatial proximity of CD8 T cells to tumor cells improves upon the predictive value of T cell density alone. **Methods:** Pretreatment tumor specimens from melanoma patients treated with aPD1 in the Netherlands Cancer Institute were stained for DAPI, SOX10/Melan-A, CD4, CD8, FOXP3 and PD-1 by multiplex immunofluorescence. Sections were imaged on Vectra and analyzed using HALO to optimize marker thresholds and demarcate tumor and stroma. T cell proximity to tumor cells was evaluated as difference in area under the curve between i) a spatial G-function quantifying T cell density around tumor cells in tumor areas and ii) analogous null distributions obtained by random permutation of cell labels. This assessment of co-clustering is independent of cell density and heterogeneity therein and does not reflect repulsion of T cells to stromal/marginal areas. Clinical characteristics, RECIST response and survival were collected from patient records. Associations between T cell density, T cell proximity to Sox10/Melan-A^{+} tumor cells, other clinical biomarkers (LDH, M stage and WHO performance status) and response were examined in a Bayesian hierarchical logistic regression. **Results:** Tumor specimens of 98 patients were included, of whom 45 were treated with aPD1 as first-line therapy and 33 had an objective response. CD8 T cell proximity to tumor cells was associated with response in an independent, comparatively strong, and tissue dependent manner (cutaneous tissue: 2.78 [2.45, 3.17], visceral: 2.30 [1.95, 2.72], lymphoid: 2.12 [1.88, 2.40], format: maximal posteriori odds ratio [89% equal-tailed credibility interval]), in a multivariate model correcting for CD8 T cell density (1.74 [1.62, 1.88]), LDH (1.93 [1.72, 2.16]), M stage (0.92 [0.87, 0.98]) and WHO performance status (0.79 [0.72, 0.88]). Our model achieved an area under the ROC curve of 77.7%, whereas an analogous model omitting the proximity variable achieved 73.1%. **Conclusions:** Our analyses show that spatial proximity of CD8 T cells to tumor cells functions as an independent biomarker for response to aPD1 and suggests that preexisting CD8 T cell tumor reactivity is reflected by this spatial proximity. Research Sponsor: None.

10039 Poster Session (Board #388), Fri, 8:00 AM-11:00 AM

Association of prior immune checkpoint blockade (ICB) with longer progression-free survival (PFS) in patients treated with intermittent versus continuous dabrafenib and trametinib: A post-hoc analysis of S1320. *First Author: Alain Patrick Algazi, Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA*

Background: S1320 is a phase 2 randomized clinical trial presented at the 2020 AACR Annual Meeting in April demonstrating that continuous dosing of dabrafenib and trametinib yields longer PFS than intermittent dosing of these agents in patients with BRAF$^{V600E/K}$ melanoma. Here we look at the association between prior exposure to ICB and PFS in patients randomized to either intermittent or continuous dosing on S1320. **Methods:** Patients without disease progression after 8 weeks of dabrafenib and trametinib were randomized 1:1 to proceed with intermittent therapy (3-week-off, 5-week-on) or to stay on the continuous daily dosing schedule. The design called for 206 randomized patients with the primary outcome of PFS. Response assessments were made using RECIST v1.1 at 8-week intervals. A post-hoc analysis assessed differences in PFS in the pool of all randomized patients based on prior exposure to anti-PD1 antibodies, a randomization stratification factor. Kaplan-Meier estimates and multivariable Cox regression models (controlling for pre-randomization age, Zubrod performance status, LDH, unknown primary, M-Stage) were used to evaluate the association between this stratification factor and PFS. **Results:** Of 242 patients treated on study, 105 were randomized to continuous dosing, 101 to intermittent dosing, and 36 were not randomized due to disease progression at 8 weeks or other factors. 37% of the 242 enrolled and 37% of the 206 randomized patients had previously been treated with ICB. Among all randomized patients, there were no differences in baseline characteristics comparing patients with and without prior immune checkpoint inhibitor exposure: age median 62 vs 59, LDH elevation 37% vs 39%,, stage IVB/C 73% vs 64%, Zubrod performance status 0, 57% vs 58%. PFS was longer in patients with prior ICB exposure (hazard ratio = 0.60, 95% confidence interval 0.41,-0.98, median = 6 vs 9 months from randomization, 8 vs 11 months from starting treatment). There was no difference in the association between prior ICB exposure and PFS between arms (interaction p-value = 0.62). **Conclusions:** In patients without early progression on dabrafenib and trametinib, PFS was longer with prior to exposure to ICB . Although the groups had similar baseline characteristics and rates of randomization, these results could still be influenced by non-controlled factors influencing clinicians' decisions to start a patient on immune versus targeted therapy. Clinical trial information: NCT02196181. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

10040 Poster Session (Board #389), Fri, 8:00 AM-11:00 AM

A phase II study of vorolanib (CM082) in combination with toripalimab (JS001) in patients with advanced mucosal melanoma. *First Author: Lu Si, Department of Renal Cancer & Melanoma, Peking University Cancer Hospital and Institute, Beijing, China*

Background: Vorolanib (CM082) is a multi-target tyrosine kinase inhibitor including VEGF, PDGF, c-kit, and Flt-3. Toripalimab (JS001) is a humanized IgG4 mAb against programmed death-1 (PD-1) with clinical activity in metastasis melanoma but not in its mucosal subtype. In this phase II study (NCT03602547), we investigated the safety and efficacy of CM082 in combination with JS001 in patients (pts) with advanced mucosal melanoma. **Methods:** The study enrolled pts from 18 to 75 years-old with histologically confirmed metastatic mucosal melanoma, ECOG PS 0-1, no prior systemic anti-cancer treatment. Eligible pts were treated with CM082 tablet (150 or 200 mg once daily) combined with JS001 (240mg every 2 weeks, IV, Q2W) until confirmed disease progression or unacceptable toxicity. Clinical response was evaluated every 8 week. The primary endpoint was overall response rate (ORR) using RECIST v1.1. Secondary endpoints included progression-free survival (PFS), overall survival (OS), disease control rate (DCR), duration of remission (DOR), and time to first remission (TTR) according to RECIST v1.1 and iRECIST. The safety was also assessed. **Results:** Between July 2018 and April 12, 2019, 40 pts (19 pts in 150mg group; 21 pts in 200mg group) were enrolled and 38 pts were evaluable for tumor response (150mg n = 18, 200mg n = 20), with 4 (22.2%) confirmed partial response (PR), 6 (33.3%) stable disease (SD) and 8 (44.4%) progression disease (PD) in the 150mg CM082 group; 3 (15%) PRs (including 2 unconfirmed), 10 (50%) SD, and 7 (35%) PD were reported in the 200mg CM082 group. Tumors shrank in 10 pts (56%) in the 150mg group and 10 pts (50%) in the 200mg group. At data cut-off (November 28, 2019), 29 pts had PFS events (150mg n = 12; 200mg n = 17). The median PFS was 5.7 (95% CI 2.0, NE) months and 5.6 (1.9, 7.7) months in the two groups, respectively. The most common treatment-related adverse events (AEs) were grade 1 or 2, including leukopenia, elevated LDH, increased ALT, neutropenia, increased AST, and elevated GGT. Common grade 3 or higher adverse events ($>$ 10%) were increased ALT (12 pts, 30%), increased AST (11 pts, 27.5%), neutropenia (6 pts, 15%) and elevated GGT (6 pts, 15%). Eight pts had 9 serious AEs (SAEs). The study is still ongoing and more data will be presented in the future. **Conclusions:** PFS benefit was observed in both 150mg and 200mg subgroups. This study demonstrated potentially improved efficacy with predictable toxicities of CM082 in combination with JS001 therapy, which may be an effective treatment option for pts with advanced mucosal melanoma. Clinical trial information: NCT03602547. Research Sponsor: Betta Pharmaceuticals Co.,Ltd.

10041 Poster Session (Board #390), Fri, 8:00 AM-11:00 AM

FDG-PET metabolic tumor volume in advanced melanoma treated with ipilimumab and nivolumab (ipi/nivo). *First Author: Amir Iravani, Peter MacCallum Cancer Centre, Melbourne, Australia*

Background: Predictors of outcomes of immune checkpoint inhibitors (ICI) are desirable. We aim to investigate the prognostic value of ^{18}F-fluorodeoxyglucose-PET/CT (FDG-PET) parameters at baseline and response monitoring of patients (pts) with advanced melanoma receiving ipi/nivo. **Methods:** From 2016-2019, melanoma pts who received ipi/nivo and had PET Response Criteria In Solid Tumors (PERCIST) measurable lesions on baseline FDG-PET were included. Baseline whole-body metabolic tumor volume (wbMTV), tumor stage, mutational status, ECOG performance score, lactate dehydrogenase (LDH) and treatment-line were correlated with overall survival (OS) in univariate and multivariate Cox-regression analysis. Response were assessed for a subset of pts with post-treatment FDG-PET based on PERCIST. **Results:** Of 162 pts receiving ipi/nivo, 122 pts (median age: 61; male: 73%; ECOG 0: 78%; raised LDH: 52%; M1c: 39%, M1d: 45% and BRAF$^{V600E/K}$mutation: 45%) met eligibility criteria. Forty percent received ipi/nivo as first-line treatment, 48% as second-line (25% post BRAF inhibitor(i)/MEKi and 23% post single-agent ICI) and 12% as third-line. At median follow-up of 21 months (mths), median OS was 20 mths (95% CI 11-not reached [NR]). Pts with above the median wbMTV had shorter OS than those with below the median wbMTV (NR vs 10 mths, 95% CI 8-NR; HR 2.0, 95% CI 1.2-3.4, p = 0.009). In multivariate analysis, wbMTV, ECOG and treatment-line were independently associated with OS. In 106 pts with post-treatment FDG-PET, 24 mths OS rate was higher for those with objective response (OR): 91% (95% CI 82-100%) vs stable disease:55% (27-100%) vs progressive disease:17% (8-35%) as best response, p < 0.001. OR was higher in first-line compared to second or third-line treatment, 75% vs 29-33% vs 23%, respectively, p = 0.0012. **Conclusions:** Increased baseline FDG-PET wbMTV is an independent prognostic biomarker in pts with advanced melanoma receiving ipi/nivo. FDG-PET response accurately predicts outcome. Research Sponsor: Peter MacCallum Cancer Centre Foundation.

		Univariable		Multivariable	
Variable		**HR (95% CI)**	**P**	**HR (95% CI)**	**P**
wbMTV	Higher median vs lower median	2.0 (1.2, 3.4)	0.009	2.0 (1.1, 3.6)	0.015
LDH	> 1xUNL vs NL	1.3 (0.7-2.5)	0.4		
	> 2xUNL vs NL	1.7 (0.7-4.0)			
ECOG	1/2 vs 0	3.4 (2-5.9)	< 0.0001	3.2 (1.7-6.3)	0.0005
Stage	M1d vs IIIC/M1a/M1b/M1c	1.8 (1.1-3.1)	0.02	1.37 (0.7-2.6)	0.3
Mutation	NRAS vs BRAF	0.5 (0.3-1.0)	0.07	4.3 (1.1-17.2)	0.1
	WT vs BRAF	0.6 (0.3-1.1)		4.0 (1.0-15.3)	
Treatment-line	2nd post BRAFi/MEKi vs 1st	4.4 (2.1-8.9)	0.0006	13.8 (3.3-58)	0.0008
	2nd post ICI vs 1st	2.8 (1.3-5.9)		4.1 (1.8-9.6)	
	3rd vs 1st	3.5 (1.5-8.1)		9.9 (2.2-44.3)	

10042 Poster Session (Board #391), Fri, 8:00 AM-11:00 AM

Real-world outcomes of advanced melanoma patients not represented in phase III trials. *First Author: Rawa Ismail, Dutch Institute for Clinical Auditing, Leiden, Netherlands*

Background: A large proportion of patients with advanced melanoma is not represented in phase III clinical trials, due to ineligibility. Real-world efficacy evidence of immune- and targeted therapies in these patients is lacking. We aimed to provide insight in survival outcomes of systemically treated patients who were not represented in the phase III trials in order to support clinical decision-making. **Methods:** Systemically treated ineligible patients with advanced melanoma diagnosed between 2014-2017 were analyzed. Prognostic importance of factors associated with overall survival (OS) was assessed by Kaplan Meier method, Cox regression models, predicted OS probabilities of prognostic subgroups and a conditional inference survival (decision) tree. **Results:** Of 2,536 systemically treated patients with advanced melanoma, 1,004 (40%) patients were ineligible for phase IIII trials. Ineligible patients had a poorer median OS (mOS) compared to eligible patients (8.8 vs 23 months). Eligibility criteria most strongly correlated with survival in ineligible systemically treated patients with ECOG Performance Score (PS) ≥2 vs PS 0-1 (HR 1.95 (95%CI: 1.52-2.5)), symptomatic brain metastases (BM) vs absent BM (HR 1.71 (95%CI: 1.34-2.18)) and LDH > 500 U/l vs normal (HR 1.89 (95%CI: 1.49-2.41)). All other factors for ineligibility were not associated with OS. By combining ECOG PS, BM and LDH, 18 subgroups were created. The 3-year survival probability of patients with ECOG PS ≤1, asymptomatic BM and normal LDH was 35.1%. Patients with ECOG PS of ≥2 with or without symptomatic BM had a mOS of 6.5 and 11.3 months and a 3-year survival probability of 9.3% and 23.6% respectively. In the decision tree, the covariate with the strongest predictive distinctive character for survival was LDH, followed by ECOG PS. Prognosis of LDH of > 500 U/L is infaust, although still long-term survival is possible (3-year survival probability of 15.3%). The decision tree showed the prognosis of patients with symptomatic BM can be good if ECOG PS is 0 and patients are aged ≤55 years (mOS of 22.3 months). **Conclusions:** Patients with advanced melanoma not represented in phase III trials treated with systemic therapy can achieve long term survival. LDH was the strongest predictive factor associated with survival, followed by ECOG PS and symptomatic BM. Other factors for ineligibility were not associated with OS. These results, together with the decision tree, can be used to provide insight in outcomes to facilitate the shared decision-making process when comparative studies are not available. Research Sponsor: None.

10043 Poster Session (Board #392), Fri, 8:00 AM-11:00 AM

Estimating treatment-free survival (TFS) over extended follow-up in patients (pts) with advanced melanoma (MEL) treated with immune-checkpoint inhibitors (ICIs): Five-year follow-up of CheckMate 067. *First Author: Meredith M. Regan, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA*

Background: We previously defined a novel outcome, TFS, to characterize the time between ICI therapy cessation and subsequent therapy initiation/death. TFS is part of an integrated analysis to comprehensively describe how pts spend overall survival (OS) time, on and off treatment, with/without treatment-related toxicity. We reported survival states, including TFS, in ICI-treated pts with MEL in the phase 3 CheckMate 067 trial (NCT01844505) over the 36-mo period since randomization (Regan. *J Clin Oncol.* 2019); 60-mo results are presented here. **Methods:** Data were analyzed for 937 pts with MEL who started treatment with nivolumab (NIVO) plus ipilimumab (IPI), NIVO, or IPI in CheckMate 067. TFS was defined as the area between the Kaplan–Meier (KM) curves for 2 conventional time-to-event endpoints defined from randomization: time to protocol therapy cessation and time to subsequent therapy/death. TFS was also divided into TFS with/without grade ≥3 treatment-related adverse events (TRAEs), and OS was estimated. The area under each KM curve was estimated by the 60-mo restricted mean (r-mean) time to event and expressed as a percentage of the 60-mo period. Bootstrapped 95% CIs were calculated for differences. **Results:** Over the 60-mo period, pts spent an average of 33%, 17%, and 20% of time free of treatment after receiving NIVO+IPI, NIVO, and IPI, respectively (r-mean TFS, 19.7, 9.9, and 11.9 mo; Table). NIVO+IPI-treated pts had r-mean TFS that was 9.8 mo longer than NIVO-treated pts (95% CI, 6.7–12.8) and 7.8 mo longer than IPI-treated pts (95% CI, 4.6–11.0). Mean TFS with grade ≥3 TRAEs remained a small proportion of the 60-mo period at 3%, 2%, and < 1% with NIVO+IPI, NIVO, and IPI, respectively. **Conclusions:** With extended follow-up, average TFS with/without toxicity represented greater percentages of the 60-mo vs 36-mo period for NIVO+IPI and NIVO, but not for IPI. Pts treated with NIVO+IPI continued to have TFS twice as long as those treated with NIVO alone, due to earlier therapy cessation for toxicity without disease progression and subsequent resolution of many of those toxicities. The majority of TFS time was spent without grade ≥3 TRAEs across all arms. Research Sponsor: Bristol-Myers Squibb.

Estimated r-mean TFS time and survival states over 60-mo follow-up.

	r-mean time (mo)		
Survival state	**NIVO+IPI**	**NIVO**	**IPI**
Time on protocol therapy	12.3	16.9	2.6
TFS	19.7	9.9	11.9
TFS without grade ≥3 TRAEs	18.1	9.0	11.7
TFS with grade ≥3 TRAEs	1.6	0.9	0.2
Survival after subsequent therapy initiation	6.6	9.3	13.9
OS	38.6	36.1	28.4

10044 Poster Session (Board #393), Fri, 8:00 AM-11:00 AM

CA209-9JC: A phase II study of first-line nivolumab (NIVO) in patients (pts) with locally advanced or metastatic cutaneous squamous cell carcinoma. *First Author: Rodrigo Ramella Munhoz, Hospital Sírio Libanês, São Paulo, Brazil*

Background: Cutaneous squamous cell carcinoma (cSCC) is among the most frequent malignancies worldwide, and an increasing incidence has been documented over the past decades. For those not amenable to treatment with curative intent, immune checkpoint blockade (ICP) with anti-PD-1 monoclonal antibodies emerged as a novel therapeutic option, supported by evidences of high mutational burden and expression of PD-L1. In this single-arm study, we sought in investigate the activity of NIVO in pts with advanced cSCC (AcSCC). **Methods:** We conducted a Simon two-stage, open-label, phase II study to evaluate the safety/efficacy of NIVO for up to 24 systemic-treatment-naïve pts with metastatic and/or locally advanced cSCC. NIVO at 3mg/kg was administered intravenously every 2 weeks (w) until disease progression, unacceptable toxicity or 12 months of treatment. The primary endpoint was the best objective response rate (bORR) at 24w as per RECIST criteria. Tumor measurements were performed every 12w. Secondary endpoints included safety/tolerability, progression-free survival (PFS) and overall survival (OS). **Results:** Between October 2018 and October 2019, 24 pts with AcSCC were enrolled, with a median age of 74 years (range 48-93) and a male/female ratio of 1.4:1. Most frequent primary sites were head/neck (42%), trunk (29%) and extremities (25%); identified risk factors included chronic sun exposure or burn scars in 66 % and 12.5 %, respectively. Upon enrolment, the proportions of patients with locally advanced, locoregional (regional lymph node involvement) and metastatic disease were 16.6%, 66.6% and 16.6%, respectively. At data cut off (median number of doses of NIVO: 15), 15 pts (62.5%) remain on treatment and 6 pts have progressed and/or died. Three pts completed 12 months of treatment and entered surveillance. Among 22 pts evaluable for response (n = 2 have not reached 12w of treatment), the bORR was 54.5% (12/22), and disease control (stable disease or objective response) was achieved in 77% (17/22). Median duration of response, PFS and OS have not been reached. Grade ≥3 treatment-related adverse events occurred in 21% of the pts, and 1 patient discontinued NIVO due to toxicities. **Conclusions:** NIVO resulted in robust antitumor activity and good tolerability in systemic treatment-naïve pts with AcSCC. There were no new safety signals, despite the inclusion of individuals at advanced ages. These data provide further evidence to support the use of ICP as the standard treatment option for pts with AcSCC. Clinical trial information: NCT03834233. Research Sponsor: BMS.

10045 Poster Session (Board #394), Fri, 8:00 AM-11:00 AM

Response to immune checkpoint inhibitor (ICI) rechallenge after high-grade immune related adverse events (irAE) in patients (pts) with metastatic melanoma (MM). *First Author: Payal Shah, New York University Langone Medical Center, New York, NY*

Background: ICIs have transformed MM mortality. Pts receiving ICIs may experience high-grade irAEs that limit continuation of treatment per current guidelines. We aimed to evaluate the safety and response rate of ICI rechallenge. **Methods:** 551 MM pts treated with ICI were retrospectively reviewed from Jan 2014 to Jan 2020 after IRB approval. The incidence of a recurrent irAE in pts with ICI rechallenge within the same drug class after an initial high-grade (Grade III/IV) irAE was evaluated. Age, gender, irAEs, and outcomes were descriptively analyzed within the rechallenged cohort. **Results:** 32.7% of pts (180/551) experienced a high-grade irAE. 60.0% of these (108/180) pts were on combination therapy with at least one ICI. 50.6% (91/180) of pts were rechallenged with ICI within the same drug class. The rechallenged cohort had a median age of 63.8 [range: 28-86] years and 48.4% was female. The cohort's initial irAE occurred at a median of 7.6 weeks from treatment onset with Grade 3/4 severity of 60.0% /40.0% (91). Toxicities included colitis 27.5% (25/91), hepatitis 23.1% (21/91), skin toxicity 22.0% (20/91), adrenal insufficiency 5.5% (5/91) hypophysitis 5.5% (5/91), neurological abnormality 4.4% (4/91), pancreatitis 3.3% (3/91), hematological abnormality 3.3% (3/91), arthralgia 3.3% (3/91), myalgia 3.3% (3/91), pneumonitis 2.2% (2/91), insulin dependent diabetes 1.1% (1/91), fatigue 1.1% (1/91), vasculitis 1.1% (1/91), and hyponatremia 1.1% (1/91). ICI rechallenge occurred at a median of 9.7 weeks from the first Grade 3/4 irAE. 51.8% (29/56) pts initially treated with combo were rechallenged with combo, while 48.2% (27/56) were rechallenged with single agent ICI. Of pts initially treated with single ICI, 60% (21/35) were rechallenged with single agent ICI and 40% (14/35) with combo. With a median follow-up of 21.1 months after rechallenge, irAEs occurred in 75.8% (69/91), with 44.9% of irAEs (31/69) presenting as a different type from the initial event and 31.9% (22/69) as high-grade events. There were no rechallenge irAE-related deaths. Within the rechallenge cohort, 39.6% (36/91) of pts had disease progression. Clinical benefit was achieved in 60.4% (55/91) of pts: 40.7% (37/91) complete response, 11.0% (10/91) partial response and 8.8% (8/91) stable disease. **Conclusions:** ICI rechallenge can be safely administered in pts with MM after recovery from an initial high-grade irAE. Rechallenge irAE's did not always reflect initial irAE's. Close monitoring for any type or grade of IRAE is recommended. Research Sponsor: None.

10046 Poster Session (Board #395), Fri, 8:00 AM-11:00 AM

Discordant response comparing 18F-FDG PET/CT with response assessment by RECIST in patients with advanced melanoma treated with immune checkpoint blockade. *First Author: Milton Jos De Barros E Silva, A.C. Camargo Cancer Center, São Paulo, Brazil*

Background: Immune checkpoint blockade (ICB) has changed the natural history advanced melanoma (AM). Based on phase III trial, which used RECIST criteria, the complete response (CR) rate with anti-PD1 therapy is around 20%. In daily practice, PET/CT is a useful tool to evaluate response to treatment in melanoma patients. Little is known about the number of patients who achieve metabolic CR by PET/CT but with anatomic residual disease and their prognosis. **Methods:** We conducted a retrospective analysis of patients with AM treated with ICB who achieved metabolic CR by PET/CT but with residual disease on tomography and compared to patients with RECIST CR in a high-volume cancer center. Progression-free (PFS) and overall survival (OS) were obtained by Kaplan Meier method and log-rank test. **Results:** One hundred seventy pts with AM treated with anti-PD1 (79%) or anti-PD1 + anti- CTLA4 (21%) betweenSeptember 2013 and December 2019 were analyzed. At a median follow-up of 23.6 months, seventy-five (44%) pts achieved CR. RECIST criteria: 22 pts (29.3%) and metabolic CR: 53 pts (70.7%). All patients with metabolic CR had RECIST partial response. The median total time on treatment was 14.8m (95%CI:0.9-42.3). The median time to reach CR was 5.4m (95%CI: 3-39). The median time of treatment after CR was 6.8m (95%CI: 0-21.4). The rate of CR patients off treatment at the moment of this analysis was 69%. The median follow-up after discontinuing treatment was 5.2m. There was no difference in PFS (36 month-rate: 84.4% vs 74%, p:0.64) and OS (36 month-rate: 100% vs 86.3%, p:0.14) between pts with CR based on RECIST or PET-CT, respectively. Median time for PFS and OS have not been reached until the date cut-off. Nine pts have relapsed (12%). Seven of them had residual disease on tomography but with no metabolic active lesion(s) at the time of the end of treatment. **Conclusions:** Twice more patients achieve complete response considering only metabolic parameters on PET/CT compared to RECIST criteria and they seem to have comparable prognosis. Research Sponsor: None.

10047 Poster Session (Board #396), Fri, 8:00 AM-11:00 AM

A first-in-human phase I/II study of HL-085, a MEK Inhibitor, in Chinese patients with NRASm advanced melanoma. *First Author: Xuan Wang, Peking University Cancer Hospital and Institute, Beijing, China*

Background: MEK inhibitors have confirmed effects on malignant tumors, especially for those induced by RAS/RAF dysfunction. There is no effective drug in clinic for NRASm advanced melanoma. HL-085 is a selective MEK inhibitor, showing good safety and efficacy in preclinical studies. This study is a phase I/II study to evaluate the safety, tolerability, pharmacokinetic and preliminary anti-cancer activity of HL-085 in patients(pts) with NRASm advanced Melanoma. **Methods:** The phase I/II study is conducted using a "3+3" regimen for dose escalation. The pts are treated with HL-085 at a starting dose of 0.5mg BID to 18mg BID. Adverse events (AEs) are reported per NCI CTCAE version 5.0. Preliminary anti-cancer activity is evaluated by ORR, DCR, PFS and DoR. **Results:** Total 33 pts were enrolled in the study. The histologic types were acral (51.4%), mucosal (27.2%) and other (21.2%). The NRAS mutation types were Q61 (72.7%), G12 (18.2%) with half for G12D, and G13 (9.1%). Most AEs were G1 or G2, and the most common drug-related AEs were rash, increased creatine phosphokinase, peripheral edema, increased alanine aminotransferase and aspartate aminotransferase. No dose-limited toxicity was observed. PK analysis was shown linear PK profile with no obvious accumulation. Among 12 evaluable pts over 9 mg, 4 pts were at the stage of M1c with 1 liver metastasis. Average targeted tumor size was 74.6mm with the largest 184 mm. 10 pts achieved tumor shrinkage [60% with Q61, 20% with G12D, 10% each with G12S and G13R]. 4 pts (2 acral, 1 mucosal and 1 other, each pt has mutaiton type of Q61R,Q61L, Q61K and G12S respectively) had confirmed partial response(PR) [median treatment duration 26.6 weeks (wks) with longest 47.6 wks]). 6 pts achieved stable disease (SD) (median treatment duration 15.72 wks with longest 24 wks), and 66.7% were over 14 wks . The median PFS was 17.4 wks, and confirmed best ORR was 33.3% with DCR 83.3% . **Conclusions:** Our data demonstrated that HL-085 is well tolerated, with manageable side-effects and promising anti-cancer activity in pts with NRASm advanced melanoma. Clinical trial information: NCT 03973151. Research Sponsor: Shanghai KeChow Pharma.

10048 Poster Session (Board #397), Fri, 8:00 AM-11:00 AM

Clinical outcomes with early-elective discontinuation of PD-1 inhibitors (PDi) at one year in patients (pts) with metastatic melanoma (MM). *First Author: Rebecca Pokorny, Department of Pharmacy, Huntsman Cancer Institute at the University of Utah, Salt Lake City, UT*

Background: Randomized trials of PDi in MM permitted treatment for 2 years (pembrolizumab) or more (nivolumab). However, the optimal treatment duration is unknown, and shorter courses may be effective. We reviewed clinical outcomes of pts who electively discontinued PDi at 1 year at our institution. **Methods:** We performed a real-world, observational cohort study of pts with MM treated with single-agent PDi from 1/1/2015 to 12/31/2018 at Huntsman Cancer Institute. This was a continuous series of pts who made the joint decision with their provider to electively discontinue PDi at 1 year ($>$ 6 mos and $<$ 18 mos) in the setting of ongoing treatment response or disease stability. Exclusion criteria: PDi with other systemic therapy, discontinuation due to disease progression or immune-related adverse event, and PDi in neoadjuvant, adjuvant, or clinical trial settings. Local therapies, as in real-world, were allowed. Best objective response (BOR) per RECIST 1.1 at PDi discontinuation, progression-free survival (PFS) and retreatment characteristics were analyzed. **Results:** Of 485 pts who received PDi, 52 met inclusion criteria. Median age was 60.5 years and 26.9% were female. Median duration of PDi from first to last dose was 11.1 mos (95% CI 10.5 - 11.4). BOR was complete response in 13 (25%), partial response in 28 (53.8%), and stable disease in 11 (21.2%) pts. After median follow-up of 20.5 mos (range 3 - 49.2) from treatment discontinuation, 39 (75%) pts remained without disease progression (median PFS not reached). Only 13 (25%) pts progressed. Median time to progression after treatment discontinuation was 3.9 mos (range 0.7-30.9). Of the 13 pts, 7 immediately underwent successful localized treatment to the solitary site of progression (3 SRS/SBRT, 4 resection; followed by PDi in 2), 5 were retreated with PDi and 1 received BRAF/MEK followed by PDi. Retreatment with PDi controlled disease in all 5 pts. All pts except 1 were alive at data cut-off. **Conclusions:** In the largest continuous series of pts with MM who electively discontinued PDi after 1 year of treatment, the majority remained without progression on follow-up. Risk of disease progression even in pts with residual disease on imaging was low, and retreatment was effective. Strengths of our study include real-world cohort and treatment pattern analysis. Limitations include single-institution, retrospective design. After prospective validation, elective PDi discontinuation at 1 year may reduce financial and PDi-related toxicity without sacrificing outcomes. Research Sponsor: None.

10049 Poster Session (Board #398), Fri, 8:00 AM-11:00 AM

Activity and safety of third-line BRAF-targeted therapy (TT) following first-line TT and second-line immunotherapy (IT) in advanced melanoma. *First Author: Victoria Atkinson, University of Queensland, Brisbane, Australia*

Background: Patients with advanced melanoma who progress on 1st line TT and 2nd line IT have limited treatment options. We explored the safety and efficacy of re-treatment with 3rd line TT. **Methods:** was pooled from 6 centers in Australia from 2009-2018. Eligible patients with BRAF V600 mutant melanoma had 1st line therapy with a BRAF/MEK inhibitor, 2nd line IO and were re-challenged with a BRAF/MEK inhibitor. **Results:** 90 patients were included; median age 61 years, 78% BRAF V600E, 89% ECOG 0-1 at baseline. 1st line TT was combination BRAF/MEK inhibitors in 80%, predominately dabrafenib/trametinib. Response to 1st line therapy was CR 20%, PR 41%, SD 17% and PD 13% and median duration of therapy was 7.2 months (0-33 months). 70% stopped for progressive disease, 9% toxicity and 16% had a planned switch to immunotherapy. For 2nd line IT, 49% had PD-1 alone, 33% had PD-1+CTLA-4, 14% had CTLA-4 alone. Only median duration on IT was 67 days (0-23 months), 81% ceased for PD, 14% for toxicity. Of patients who had a planned switch to IO before 1st line TT progression, one patient responded to second line IO with SD as BORR, there were no other responses to 2nd line IO in the planned switch group. At 3rd line TT re-challenge, 54% were AJCC stage IVd, 34% IVc, 51% had elevated LDH, 59% ECOG 0-1. 47% were re-challenged with dabrafenib/trametinib, 33% vemurafenib/cobimetinib, 11% encorafenib/binimetinib. BORR was 28%, with median duration on 3rd line TT 81 days. The OS was 1.7 years, with 34% alive at time of analysis. **Conclusions:** Despite progression on 1st line TT and 2nd line IT, patients may experience meaningful response and on re-challenge TT. Research Sponsor: None.

10050 Poster Session (Board #399), Fri, 8:00 AM-11:00 AM

Circulating tumor DNA (ctDNA) using Guardant360 to predict response in BRAF V600 WT metastatic melanoma (MM) patients (pts) receiving immune checkpoint inhibitors (ICI). *First Author: Jenny HJ Lee, Westmead Hospital Cancer Care, Sydney, Australia*

Background: ctDNA detected by ddPCR predicts ICI response in MM, although its utility is limited to pts with known recurring mutations eg. *BRAF*, *NRAS*, *KIT*. We sought to overcome this limitation by using a next generation sequencing approach in *BRAF V600* wild type (WT) MM pts. **Methods:** Plasma was collected at baseline and Week (wk) 6 in 35 *BRAF V600* WT MM pts treated with ICI. Cell free (cf)DNA was analyzed using Guardant360 and only somatic non-synonymous and promoter variants were considered. Pts who failed cfDNA extraction at baseline were excluded (n = 3). Favorable ctDNA was defined as undetectable ctDNA at wk 6 and unfavorable ctDNA defined as detectable ctDNA at wk6. Response was according to RECIST at first restaging. **Results:** Of the evaluable 32 pts (64 plasma samples), median baseline cfDNA quantity was 33ng (range 4-657ng) and ctDNA was detected in 29/32 pts (91%). All 3 pts with undetectable baseline ctDNA had less than 10ng cfDNA compared to only 1/29 pts with detectable baseline ctDNA. Number of mutations identified in the 29 ctDNA-positive pts was 4 per pt (range 1-22). Response assessment was performed on 30 evaluable pts. Candidate driver mutation(s) in *BRAF*, *NF1*, or *N/K/HRAS* were identified in 26/30 pts. These mutations were often detected with other established mutations involved in tumorigenesis (eg. *TERT* promoter), or passenger mutations (eg. clonal hematopoiesis). Analysis of driver mutations revealed a sensitivity and specificity in predicting treatment failure of 92% and 93%, respectively (table). When all mutations identified were evaluated for treatment response, 9/18 responding pts retained some ctDNA at wk 6, although this never included *TERT* variants. The resulting sensitivity and specificity in predicting treatment failure changed to 100% and 50%, respectively, when all cfDNA variants were included. **Conclusions:** The extensive coverage of Guardant360 improves ctDNA detection in *BRAF V600* WT MM pts, allowing non-invasive, rapid, and longitudinal assessment of response in a broader population. The expanded coverage also identifies passenger variants of potential non-MM origin, eg. clonal hematopoiesis, and with significant overlap with ctDNA, it is not possible to distinguish between the two in the circulation. We therefore recommend identification and monitoring of known cancer driver mutations only. Research Sponsor: National Health and Medical Research Council.

	Driver mutation (n = 26)		***TERT* promoter (n = 20)**		**All mutations (n = 30)**	
	Favorable	Unfavorable	Favorable	Unfavorable	Favorable	Unfavorable
PR/CR	13	1	10	0	9	9
SD/PD	1	11	1	9	1	11

10052 Poster Session (Board #401), Fri, 8:00 AM-11:00 AM

Preclinical and clinical studies of a class I/IV HDAC inhibitor, mocetinostat, in melanoma. *First Author: Jeffrey S. Weber, Laura and Isaac Perlmutter Cancer Center, NYU Langone Medical Center, New York, NY*

Background: Mocetinostat is a class I/IV HDAC inhibitor with HDAC1/2/3/11 activity. Preclinical murine data suggest that HDAC inhibition has immune activity and may augment the clinical benefit of checkpoint inhibition. Several trials are assessing the effects of adding HDAC inhibition to PD-1 blockade. **Methods:** Patients with therapy-naive metastatic melanoma were treated in a pilot phase Ib trial with nivolumab at 3 mg/kg/ipilimumab at 1 mg/kg every three weeks four times and a starting dose of mocetinostat at 70 mg orally three times a week in a 12-week induction cycle followed by 12-week maintenance cycles of nivolumab 240 mg every 2 weeks and mocetinostat at the same dose and schedule as induction. Endpoints were toxicity, definition of a recommended phase 2 dose and preliminary assessment of response as well as correlative marker determination. Peripheral blood mononuclear blood cells from patients were tested *in vitro* at varying concentrations of mocetinostat, and its impact on T, regulatory T and myeloid-derived suppressor cell phenotypes were assessed by flow cytometry, as well as cytokine production by Luminex. **Results:** In the mocetinostat, nivolumab and ipilimumab phase I trial, 10 patients were treated, including 5 males and 5 females with a median age of 59. There were 2 complete and 5 partial responses confirmed; 6 of 7 are maintained at a median of 16 months of follow up. Three patients had progressive disease. Seven patients had grade 3-4 immune related adverse events; in 3 they were multiple. No patients died. *In vitro*, mocetinostat at doses from 125 to 500 nM increased relative percentage of CD4/CD8 central memory T cells, and decreased IL-6 levels while increasing interferon-gamma production ($p = 0.005$). Percentages of regulatory T and monocytic myeloid-derived suppressor cells were decreased by mocetinostat ($p = 0.005$), which also down-modulated regulatory T cell function by reducing FOXP3, HELIOS and GARP ($p = 0.001$). **Conclusions:** *In vitro*, mocetinostat promoted accumulation of central memory CD8 and CD4 T cells from melanoma patients, and decreased percentages and suppressive activity of T regulatory cells and myeloid-derived suppressor cells. In a pilot clinical trial, mocetinostat combined with nivolumab and ipilimumab in treatment-naïve metastatic melanoma patients exhibited a response rate of 70% with long duration of response but all ten patients treated had at least one grade 3 or 4 immune-related toxicity. De-escalation of the mocetinostat dose to 50 mg three times a week was felt to be indicated due to the toxicity of the triple regimen. Clinical trial information: NCT03565406. Research Sponsor: Mirati Pharmaceuticals.

10053 Poster Session (Board #402), Fri, 8:00 AM-11:00 AM

Risk of disease progression (PD) following discontinuation of BRAF±MEK targeted therapies for reasons other than PD in patients (pts) with metastatic or unresectable melanoma. *First Author: Francesca Corti, Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: In pts with metastatic melanoma bearing BRAF V600E/K mutations BRAF V600±MEK inhibitors are administered until PD/unacceptable toxicity. In patients achieving durable responses, outcomes following discontinuation for reasons other than PD are largely unknown. **Methods:** We identified all patients who interrupted BRAF±MEK inhibitors for reasons other than PD after complete (CR) or partial response (PR) from a clinical dataset of patients with *BRAF* mutated metastatic/unresectable melanoma treated with targeted therapy at a single Institution. **Results:** We included 24 pts. Fifteen (62.5%) and 9 (37.5%) pts were treated respectively with BRAF inhibitor monotherapy and BRAF+MEK inhibitor combination. All pts had normal baseline LDH and ECOG PS0, 2 (8%) pts had brain metastases and 15 (62.5%) had multi-organ metastatic involvement. Dose reduction was required for 12 (50%) pts. Median treatment duration was 59 (12-88) months. Causes of discontinuation were unacceptable toxicity (19 pts-79%) and consent withdrawal (5 pts-21%). At the time of discontinuation, 17 (71%) and 7 (29%) pts had achieved respectively CR and PR. At a median follow up of 31 (8-59) months after treatment discontinuation, 9 (37.5%) pts had experienced PD. Median time to PD after treatment discontinuation was 9 (3-16) months. At time of PD, 2 (22%) pts displayed involvement of new organ sites. Risk of PD following discontinuation was respectively 31% and 45% at 12 and 24 months. Neither baseline characteristics nor treatment duration and time to best response influenced risk of PD; we found a non-significant trend towards higher risk of relapse for patients interrupting treatment with residual disease compared to those who interrupted treatment after achieving CR [HR 3.3; 95%CI (0.8–14.1); log-rank $p = 0.081$]. After PD, 6 pts received BRAF+MEK inhibitors with a response rate of 100% and 3/6 pts achieving CR. **Conclusions:** In a subset of patients with favorable prognostic characteristics and retained sensitivity to BRAF±MEK inhibitors, treatment discontinuation was associated with relevant risk of relapse with about one third of pts experiencing PD within one year. Biomarker studies are needed to identify pts who might safely discontinue therapy due to sustained toxicity, especially after achieving CR. Research Sponsor: None.

10054 Poster Session (Board #403), Fri, 8:00 AM-11:00 AM

Landmark analysis of immunotherapy duration and disease free survival in advanced melanoma patients with a complete response. *First Author: Grayce N. Selig, Department of Medicine, University of Pennsylvania, Philadelphia, PA*

Background: Checkpoint blockade improves survival in patients with melanoma, with durable complete responses (CR) after stopping therapy. Based on data from KEYNOTE-001, immunotherapy is often continued for 24 months in patients with confirmed CR. Outcomes with treatment of less than 24 months hav not been adequately evaluated and reported. If equally efficacious, shorter courses would potentially reduce health care costs and toxicity. **Methods:** 45 patients with locally advanced stage III and IV melanoma who received immunotherapy (pembrolizumab, nivolumab or ipilimumab/nivolumab) as 1st line or subsequent therapy, achieved a CR, and stopped therapy were identified under an IRB approved protocol at Penn. Disease Free Survival (DFS) was defined as time from declaration of CR until recurrence or date of analysis (1/15/20). Landmark DFS from time of CR was analyzed based on duration of therapy (less than or greater than 7 months, based on early trial requirements to treat patients with confirmed CR for at least 6 months). Rationale for stopping (toxicity or CR) was also analyzed. **Results:** Of 45 patients with CR, 27 (60%) were treated less then 7 months (median 4.8, range 1 day to 6.7 months) and 18 (40%) were treated for greater than 7 months (median 12.4, range 7.5 to 24.2 months). Patients who were treated for less than 7 months had a median DFS from time of CR of 30.4 months (95% CI 23.7 to 37.2, range 2.9 to 65.7 months). Patients treated for greater than 7 months had a median DFS of 28.0 months (95% CI 18.9 to 37, range 8.5 to 73.7 months). Patients who stopped due to toxicity (N = 17, 40%) had a median treatment duration of 3.7 months. Their median DFS from time of CR was 30.4 months (95% CI 20.7 to 40.1, range of 2.9 to 65.7 months). Patients who stopped due to CR (N = 28, 60%) had a median treatment duration of 8.5 months. Their median DFS was 27.6 months (95% CI 21.2 to 34 range 7.2 to 73.7 months). Two of 27 (7.4%) patients treated for less then 7 months and 3 out of 18 (16%) patients treated greater than 7 months recurred after stopping. One out of 17 (5.8%) recurred after stopping for toxicity vs. 4/28 (14.3%) who stopped after CR. **Conclusions:** Patients who stop therapy at less than 7 months have CRs that are equally durable as those treated longer than 7 months, without reduction in landmark DFS. Patients who stopped therapy due to toxicity and then achieved a CR had no difference in DFS compared to patients treated until CR. There was no significant difference in recurrence after achieving a complete response in patients treated for a longer vs shorter treatment course. Research Sponsor: None.

10057 Poster Session (Board #406), Fri, 8:00 AM-11:00 AM

Long-term immune-related adverse events under PD-1 inhibitors: a multicenter prospective cohort study (MELBASE). *First Author: Charlee Nardin, Dermatology, CHU de Besançon, Besançon, France*

Background: PD-1 inhibitors (anti-PD1) are frequently associated with immune-related adverse events (IRAE). Since melanoma patients included in clinical trials were frequently treated during two years, data on IRAE occurring after 2 years of treatment are lacking. This study aimed to describe IRAE in melanoma patients treated with anti-PD1 for longer than 2 years in a real-life setting. **Methods:** Patients were screened from MelBase, a French multicentric biobank dedicated to the prospective follow-up of unresectable stage III or IV melanoma. All patients who received anti-PD1 for at least 2 years between January 2013 and November 2019 were included. Among them, patients who experienced IRAE and long-term IRAE defined as IRAE occurring after 2 years of anti-PD1 were identified. **Results:** Among 1849 patients with advanced melanoma included in Melbase, 119 patients received anti-PD1 monotherapy during at least 2 years, from January 2013 to November 2019, with a median follow-up of 41.7 months (25.2-57.5). Patients characteristics at treatment initiation were: male gender (61%), mean age of 63 years old, past history of autoimmune disease (11%), BRAF WT (72%), AJCC stage IV (84%), brain metastases (22%), ECOG 0-1 (88%) and normal LDH (56%). Patients were treated with Nivolumab (n = 53) or Pembrolizumab (n = 66). IRAE occurred in 99 patients (83%) with a median time of 13.3 months (0-53.9), including severe IRAE (grade 3 or 4) in 30 patients (30%). Long-term IRAE, mostly grades 1-2, occurred in 52 patients (43%). Long-term IRAE led to 5 hospitalizations (4%) of which 4 were grades 3-4. Among patients with long-term IRAE, 45 patients (87%) previously experienced IRAE within the first 2 years of anti-PD1 and 29 patients (56%) experienced multiple IRAE. **Conclusions:** Our data demonstrate that long-term IRAE are frequent especially in patients who already experienced IRAE within the first two years of treatment. These data should be taken into account to establish formal recommendations on the duration of anti-PD1 therapy. Research Sponsor: BMS, MSD, Novartis, Roche.

10059 Poster Session (Board #408), Fri, 8:00 AM-11:00 AM

Clinical outcomes in patients with $BRAF^{V600}$ mutant melanoma and undetectable circulating tumor DNA treated with dabrafenib and trametinib. *First Author: Alain Patrick Algazi, Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA*

Background: Circulating tumor DNA (ctDNA) analysis has been promoted as a less-invasive surrogate assay for tumor-tissue based tumor oncogene analysis. Here, we associate detection of BRAF mutant ctDNA with PFS and OS in patients with tissue-confirmed $BRAF^{V600}$ mutant melanoma enrolled in S1320, a randomized phase 2 clinical trial of continuous versus intermittent dosing of dabrafenib and trametinib. **Methods:** Patients with $BRAF^{V600}$ melanoma received continuous therapy with dabrafenib and trametinib for 8 weeks after which patients were randomized 1:1 to proceed with intermittent treatment on a 3-week-off, 5-week-on schedule or to continue with continuous therapy. Pre-treatment blood samples were interrogated using the Guardant 360 ctDNA assay for all exons of 30 known oncogenes including BRAF and for all exons with known oncogenic mutations in the COSMIC database in 40 additional oncogenes. Clinical responses were assessed at 8-week intervals by RECIST v1.1 and PFS and OS estimates were compared using log-rank test in patients with detectable versus undetectable $BRAF^{V600}$ mutant ctDNA,. **Results:** Somatic $BRAF^{V600E}$ or $BRAF^{V600K}$ ctDNA was detected in 34 of 50 patients with baseline (before lead-in cycle 1) blood samples available for analysis including 16 of 23 (70%) patients randomized to continuous dosing, 15 of 21 (71%) randomized to intermittent dosing, and 3 of 6 (50%) who were not randomized due to disease progression at 8 weeks or other factors. Four additional patients had other detectable somatic mutations but no detectable $BRAF^{V600}$ ctDNA at baseline, and 12 patients had no detectable somatic ctDNA mutations at baseline. Detection of $BRAF^{V600}$ ctDNA was associated with baseline disease stage (p = 0.008). There was no difference in the overall response rate based on baseline ctDNA detection. Detection of ctDNA at baseline was associated with worse PFS (median $BRAF^{V600}$ ctDNA positive = 5.8; 95% CI: 4.2-9.6 months, $BRAF^{V600}$ ctDNA negative = 21.4 mos; 95% CI 10.4-NA; measured from registration to lead-in cycle 1, p = 0.001) and OS ($BRAF^{V600}$ ctDNA positive = 17.8 mos; 95% CI 9.76-NA, $BRAF^{V600}$ ctDNA negative = not reached; 95% CI NA-NA, p = 0.0021). **Conclusions:** The absence of detectable $BRAF^{V600}$ ctDNA at baseline is associated with improved PFS and OS in patients receiving treatment with dabrafenib and trametinib. Clinical trial information: NCT02196181. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

10060 Poster Session (Board #409), Fri, 8:00 AM-11:00 AM

Association of pathogenic germline variant KDR Q472H with angiogenesis and resistance to treatment in melanoma. *First Author: Margaret Chou, The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York, NY*

Background: Preclinical data suggest that melanoma angiogenesis promotes resistance to MAPK-pathway (MAPKi) and immune checkpoint inhibitors (ICIs). However, phase II clinical trials of anti-angiogenic therapy in melanoma were disappointing. We previously identified a pathogenic germline variant Q472H in the kinase insert domain receptor [KDR Q472H; vascular endothelial growth factor receptor-2 (VEGFR-2)] in 35% of primary melanoma patients. We hypothesize that KDR Q472H promotes resistance to MAPKi or ICIs, and that combined MAPKi or ICI and VEGF pathway inhibition may improve outcomes in patients harboring the variant. **Methods:** Metastatic melanoma (MM) patient clinical data and biospecimens enrolled in the NYU Langone Medical Center Melanoma program were studied. KDR status was determined by TaqMan assays. Tumor microvessel density (MVD) was assessed by CD34 immunohistochemistry. The impact of KDR Q472H on the tumor microenvironment was determined by RNA-seq and Nanostring. Synergy between BRAF (dabrafenib) and VEGFR-2 (lenvatinib) inhibitors in KDR-genotyped MM cell lines was assessed using cell proliferation assays and the Chou-Talalay method. Synergy between ICIs and anti-VEGFR-2 was evaluated *in vivo* using a B16 melanoma model. **Results:** We studied 221 MM patients (38% KDR Q472H variants). KDR Q472H variant was significantly associated with higher tumor MVD (P = 0.002). Among the MAPKi-treated patients, KDR Q472H homozygotes had shorter median progression-free survival (PFS, 3.3 vs 9.7 months, P = 0.009) than KDR wild type (WT). In patients treated with anti-PD-1-based therapies, response rates were lower in KDR Q472H variant patients compared to WT (P = 0.012), with shorter median PFS (8.4 months vs not reached, P = 0.0443). Transcriptomic analyses identified an immunosuppressive phenotype in KDR Q472H tumors, with reduced expression of genes associated with chemotaxis, inflammation, T cell activity, and antigen presentation. Consistent with this finding, VEGFR-2 blockade in a KDR Q472H B16 mouse melanoma model augmented the anti-melanoma immune response. KDR Q472H cell lines displayed synergistic cytotoxicity with dabrafenib and lenvatinib, compared to KDR WT cells. **Conclusions:** Our data demonstrate that melanoma patients with pathogenic germline variant KDR Q472H may be more resistant to both ICIs and MAPKi. Anti-angiogenic therapy should be reconsidered within this specific subset of patients in prospective clinical trials. Research Sponsor: P50 CA225450 NYU Melanoma SPORE, P30 CA016087 Cancer Center Support Grant.

10061 Poster Session (Board #410), Fri, 8:00 AM-11:00 AM

Integrated biomarker study of neoadjuvant pepinemab and nivolumab in patients with resectable metastatic melanoma. *First Author: Michael C. Lowe, Department of Surgery, Emory University, Atlanta, GA*

Background: SEMA4D has broad immunomodulatory effects in the tumor microenvironment (TME); blocking SEMA4D in combination with checkpoint inhibitors (CI) promotes immune infiltration, reduces recruitment of myeloid cells, enhances T cell activity, and promotes tumor regression. We hypothesized that adding pepinemab (VX15/2503), which targets SEMA4D, to CI would increase immunomodulatory effects and augment response in melanoma (NCT03769155). **Methods:** Patients with resectable stage IIIB/C/D melanoma were enrolled to control (no neoadjuvant therapy) or treatment cohorts (n = 8 in four cohorts of pepinemab plus nivolumab, ipilimumab, nivolumab/ipilimumab or alone). Here we report results from patients receiving two doses of nivolumab (360mg) and pepinemab (15mg/kg) every three weeks followed by surgery. Primary endpoint was T cell infiltration into the TME; secondary endpoints include pathologic response rates, peripheral immune profile, and safety. **Results:** Ten patients are reported: two were controls, eight received neoadjuvant therapy. Two patients had pathologic complete response, one had a near-complete pathologic response ($<$ 1% viable tumor), one had a partial response (41% viable tumor) and four had stable disease (73-90% viable tumor). All neoadjuvant patients underwent surgery without delay; one patient experienced grade 3 post-operative cellulitis. There were two treatment-related grade 3 adverse events (weakness and arthralgia). Pharmacodynamic studies confirmed saturation of PD-1 and SEMA4D in peripheral and tumor-infiltrating T cells. T/B cell ($CD8^+/CD20^+$) ratios, a surrogate for T cell infiltration, were higher in post-treatment tumors compared to pre-treatment and were higher in the tumor bed compared to normal adjacent tissue. Flow cytometric evaluation identified an increase in $CD26^{hi}$ $CD4^+$ and $CD8^+$ tumor-infiltrating effectors in treated patients compared to controls and an increase in peripheral frequencies of the PD-1-responsive effector HLA-$DR^+CD38^+Ki67^+$ $CD4^+$ and $CD8^+$ T cells following treatment. Treatment increased infiltration of myeloid populations into the TME, increased expression of PD-L1 on TME myeloid populations, and increased expression of the SEMA4D receptor Plexin-B2 on the surface of TME $CD45^-$ and M2 macrophages and MDSC. **Conclusions:** Neoadjuvant nivolumab and pepinemab results in increased T cell infiltration with excellent major response rate (38%) and expected safety profile. We continue to enroll patients using other rational combinations of pepinemab and CI. Clinical trial information: NCT03769155. Research Sponsor: Vaccinex, Inc.

10062 Poster Session (Board #411), Fri, 8:00 AM-11:00 AM

The use of plasma proteomic markers to understand the biology of immunotherapy response. *First Author: Arnav Mehta, Dana–Farber Cancer Institute, Boston, MA*

Background: Despite recent successes with immune checkpoint blockade (ICB) in melanoma, the prognosis for most patients remains dire. Whereas small fraction of patients are able to achieve disease control, most do not respond or are limited by immune-related toxicities. Robust non-invasive predictors of ICB response have the potential to guide clinical decision and alter management of patients, however, no such predictors currently exist. **Methods:** We applied a highly-multiplex Proximity Extension Assay to simultaneously detect $>$ 1000 proteins in the plasma of anti-PD-1 treated melanoma patients. Our cohort comprised 116 patients, 66 responders (R) and 50 non-responders (NR). Additional 65 patients comprised a validation cohort with 30 R and 35 NR, and included 50 patients who developed treatment-related toxicities. Plasma samples were collected at baseline, 6-weeks and 6-months after starting the treatment. A subset of patients had single-cell RNA-seq performed on tumor tissue. Group differences and treatment effects were evaluated by linear model with maximum likelihood estimation for model parameters and Benjamini and Hochberg multiple hypothesis correction. **Results:** At baseline, 6 significantly differentially expressed (DE) proteins were identified between R and NR. Elevated expression of ST2 and IL-6, two key immunoregulatory proteins were found in NR. At 6-weeks, more dynamic changes occurred and 79 significantly DE proteins were identified between R and NR, including proteins implicated in primary or acquired resistance as IL-8, MIA, TNFR1 and potential novel targets as MCP-4/CCL13, ICOSLG and VEGF. Proteomic changes identified at baseline and 6-weeks were more profound at 6-months, and moreover 238 proteins were confirmed significant between R and NR. Importantly, we were able to leverage these differences to build classifiers of R and NR subsets. We compared mRNA expression of DE proteins within the tumor microenvironment by leveraging scRNAseq data from a subset of these patients. Enriched expression of these genes was uncovered in certain myeloid and exhausted T cell subsets, thus shedding insight into the potential role of these cell subsets in ICB response. **Conclusions:** Plasma proteomic profiling of anti-PD1 treated patients identified important tumor and immune changes associated with response. Non-invasive means discovery of circulatory protein biomarkers may predict sensitivity to immunotherapy and uncover biological insights underlying primary resistance. Research Sponsor: Olink proteomics.

10063 Poster Session (Board #412), Fri, 8:00 AM-11:00 AM

Survival analysis between narrower surgical margins and guideline-recommended margins for excision of cutaneous squamous cell carcinoma: A multicenter, retrospective study of 1,204 Japanese cases. *First Author: Natsuki Baba, Saitama Medical University International Medical Center, Saitama, Japan*

Background: Controversy exists regarding the optimal surgical margin for cutaneous squamous cell carcinoma (cSCC). Current NCCN Guidelines recommend excision with a 4–6-mm clinical margin for low-risk cSCC and wider ($>$ 6-mm) clinical margin for high-risk cSCC tumors. However, adherence to this guideline is often difficult, as high-risk cSCCs frequently occur on the faces of elderly patients. Thus, we aim to investigate the correlation between different surgical margins and prognosis in patients with cSCC. **Methods:** Patients with cSCC who had undergone surgical excision of the primary site between 2011 and 2019 at 11 Japanese institutions were included in this study. Patients were divided into two groups: the standard margin group (SMG) with excisions adhering to the guideline-recommended margins, and narrower margin group (NMG) with excisions with narrower margins than are guideline-recommended. Local recurrence-free survival (LRFS), relapse-free survival (RFS), and overall survival (OS) were estimated using Kaplan–Meier analysis and compared between the two groups. **Results:** A total of 1204 patients with cSCC (SMG, 637; NMG, 567) were included in this study. RFS was significantly lower in SMG than in NMG (5-year RFS 72% vs 79%; P = 0.03); however, no statistically significant differences were observed between the two groups in LRFS (5-year LRFS 80% vs 82%; P = 0.41) or OS (5-year OS 84% vs 83%; P = 0.90). Due to striking statistical significance in several characteristics of patients between the two groups, subgroup analyses, focusing on the cohort of head and neck cSCCs, were also performed. The patient characteristics were similar between SMG and NMG in both the T1-sized tumor ($<$ 2 cm, SMG, 182; NMG, 250) and T2-sized tumor (2 cm $\leq$ tumor $<$ 4 cm, SMG, 130; NMG, 136) cohorts, based on AJCC-TNM staging (8th edition). There were also no significant differences between the SMG and NMG in LRFS (5-year LRFS, T1: 80% vs 86%; P = 0.59; T2: 85% vs 84%; P = 0.84), RFS (5-year RFS, T1: 80% vs 81%; P = 0.84; T2: 77% vs 76%; P = 0.99), or OS (5-year OS, T1: 82% vs 87%; P = 0.42; T2: 88% vs 85%; P = 0.68). Furthermore, when the NMG was divided into the two margin groups (margins reduced by $<$ 3 mm or $\geq$3 mm from the standard margin), no significant difference was observed in LRFS, RFS, and OS. **Conclusions:** This study did not reveal a significant impact of the size of clinical excision margins on survival in patients with cSCCs. Strikingly, the narrower margins may be more appropriate for $<$ 4 cm-sized head and neck cSCCs. Research Sponsor: National Cancer Center Research and Development Fund.

10064 Poster Session (Board #413), Fri, 8:00 AM-11:00 AM

Health-related quality of life in stage III melanoma patients treated with neoadjuvant ipilimumab and nivolumab followed by index lymph node excision only, compared to therapeutic lymph node dissection: First results of the PRADO trial. *First Author: Noëlle Milena Jane Van den Heuvel, Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: Neoadjuvant ipilimumab and nivolumab induces high pathologic response rates of 74-78% (OpACIN and OpACIN-neo trial), thus the role of Therapeutic Lymph Node Dissections (TLND) in patients with major pathologic responses (MPR: pathological (near) complete response) is now unclear. In the PRADO trial, TLND was omitted in patients with MPR in their index lymph node ((ILN), the largest LN marked prior to neoadjuvant therapy). We sought to determine if less extensive surgery is associated with better Health Related Quality of Life (HRQoL). These are the first results of the comparison of HRQoL between patients undergoing a TLND or less extensive ILN excision. **Methods:** HRQoL was assessed with the European Organisation for Research and Treatment of Cancer QoL questionnaire-C30 (QLQ-C30). A generalized estimation equation was used to assess the difference in HRQoL outcomes between patients who underwent TLND (pathological non- and partial-responders, pNR/pPR) versus those who did not (pathological (near)complete responders, pNCR/pCR). Differences were adjusted for age, gender and follow-up (FU, in weeks), but not for pathological responses (pNR, pPR, pNCR & pCR). Differences in QLQ-C30 scores were classified as clinically important according to published guidelines. **Results:** A total of 49 patients from the PRADO study had reached at least 24 weeks FU, and were included in the first explorative analysis. The median age of this study population was 58 years (range, 22-84). Questionnaire completion rates were high: 94% at baseline, 100%, 90%, 88% at week 6, 12 and 24, respectively. Sixteen (33%) patients underwent TLND versus 33 (67%) who had ILN excision only. Over a FU period of 24 weeks, patients who underwent TLND scored significantly lower on global (68 vs 78, adjusted difference (diff) = -9.53, p = .005), physical (84 vs 94 diff = -11.1, p = $<$ .001), emotional (69 vs 83, diff = -11.7, p = .001), role (70 vs 85, diff = -13, p = .004), and social functioning (81 vs 91, diff = -8.9, p = .016) and had a higher symptom burden of fatigue (35 vs 23, diff = 11.1, p = .004), insomnia (38 vs 18, diff = 16.6, p = .002) and financial impact (12 vs 4, diff = 7.9, p = .027) than patients undergoing ILN excision only. These differences were indicated as clinically relevant. **Conclusions:** First results from PRADO suggest that reducing the extent of surgery following neoadjuvant immunotherapy might result in better HRQoL of high-risk stage III melanoma patients. Clinical trial information: NCT02977052. Research Sponsor: Bristol Myers Squibb.

10065 Poster Session (Board #414), Fri, 8:00 AM-11:00 AM

Cemiplimab as first intervention for patients with locally advanced cutaneous squamous cell carcinoma. *First Author: Jennifer Lynn Atlas, Levine Cancer Institute-Atrium Health, Charlotte, NC*

Cemiplimab as First Intervention for Patients with Locally Advanced Cutaneous Squamous Cell Carcinoma (cSCC) **Background:** Cutaneous squamous cell carcinoma is the second most common non-melanoma skin cancer. Early stage disease is managed with local intervention in the form of surgery or radiation and translates into cure for greater than 95% of the patients. Patients with high risk disease who have large primary lesions, neural, or nodal involvement are usually not amenable to cure with local intervention and may experience significant morbidity, disfigurement, or functional deficits. These patients had no effective systemic treatment options until recent approval of cemiplimab. We report the outcomes for upfront treatment with cemiplimab in locally advanced cSCC. **Methods:** This is a single institution retrospective study of patients with locally advanced cSCC defined as those requiring more than simple excision and/or complex repair or regional disease with nodal involvement who received at least two doses of cemiplimab between January 1, 2018 through January 17, 2020. Patients with radiologically measurable disease had response evaluated per RECIST criteria. Patients who had no measurable disease had their clinical response (complete resolution or healing of primary lesion) assessed per treating physician and need or lack of local intervention documented. Adverse events were assessed and graded per CTCAE criteria. The primary end point was to ascertain the need for local intervention. **Results:** Thirty six patients were eligible. Twenty-two (61%) patients treated with upfront cemiplimab were able to avoid local intervention with surgery and/or radiation; four patients progressed or died on treatment. Three (8%) patients received local intervention. Eleven (31%) patients are still receiving cemiplimab and local intervention decision is pending. The overall response rate was 69% and the clinical benefit rate was 92%. The median treatment duration was six months and the median number of doses received was six. Adverse events occurred in 31% of patients; the most common adverse event was dermatitis. **Conclusions:** Upfront treatment with cemiplimab in patients with locally advanced cSCC obviated need for disfiguring/complex surgery or radiation in majority of patients. Cemiplimab was tolerated well; no new safety signals were observed. Neo-adjuvant phase II study is in development. Research Sponsor: None.

10066 Poster Session (Board #415), Fri, 8:00 AM-11:00 AM

Using digital-image analysis of tumor-infiltrating lymphocytes to predict survival outcomes in primary melanoma. *First Author: Margaret Chou, The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York, NY*

Background: Inclusion of tumor-infiltrating lymphocytes (TIL) into AJCC staging criteria has been proposed due to evidence suggesting its prognostic significance. However, subjective inter-observer discordance prevents adoption of semi-quantitative TIL grading (e.g. absent, non-brisk, brisk) into clinical practice. We hypothesize that digital-image analysis (DIA) of TIL can provide a standardized, quantitative scoring system that more accurately predicts survival compared to currently used semi-quantitative grading methods. **Methods:** Clinical data and tumor specimens were analyzed from prospectively enrolled primary melanoma patients in the New York University Interdisciplinary Melanoma Cooperative Group with median follow-up of 5 years. H&E-stained slides were digitized using an Aperio ScanScope at 20X magnification. QuPath software was used for automated TIL quantification. Cox regression analysis was used to assess the improved prognostic value of TIL on recurrence-free (RFS) and overall survival (OS). Patients were separated into high- and low-TIL groups using a score threshold determined by the Youden Index. **Results:** 453 patients (18% stage I, 42% stage II, 40% stage III) were scored using automated TIL assessment and scores were significantly correlated with better RFS and OS per 10% increase in TIL (stage adjusted hazard ratio [aHR] = 0.92 [0.84-1.00] for RFS and aHR = 0.90 [0.83-0.99] for OS). A model combining TIL score with stage increased prognostic ability for both RFS (0.68 to 0.70, P = 0.02) and OS (0.62 to 0.64, P = 0.01), as assessed by concordance indices (C-index). Kaplan-Meier curves of high- ($>$ 16.6%) versus low-TIL ($\leq$16.6%) patients showed clear separation in RFS and OS (median RFS = 155 vs 48 months, P $<$ 0.001; median OS = 155 vs 89 months, P = 0.002). For comparison, a subset of the cohort (n = 250) was semi-quantitatively graded (absent, non-brisk, brisk) by an attending melanoma pathologist; however, this did not significantly differentiate RFS between groups (P $>$ 0.05). **Conclusions:** A standardized, quantitative TIL scoring system significantly improved prediction of RFS and OS in primary melanoma patients compared with semi-quantitative TIL grading. Incorporation of quantitative TIL scoring into prognostic algorithms, such as AJCC criteria, should be considered. Research Sponsor: P50 CA225450 NYU Melanoma SPORE, Other Foundation, P30 CA016087 Cancer Center Support Grant.

10067 Poster Session (Board #416), Fri, 8:00 AM-11:00 AM

Radiomic signatures to predict response to targeted therapy and immune checkpoint blockade in melanoma patients (pts) on neoadjuvant therapy. *First Author: Rivka R. Colen, UPMC Hillman Cancer Center, Pittsburgh, PA*

Background: Metastatic melanoma pt outcomes have been revolutionized by targeted therapy (TT) and immune checkpoint blockade (ICB), which are now being evaluated in the neoadjuvant (neoadj) setting. While tumor-based biomarkers may help predict response, predictors of response obtained by less invasive strategies could greatly benefit pt care and allow real-time treatment response monitoring. Radiomic signatures derived from computerized tomography (CT) images have recently been shown to predict response to ICB in stage IV pts. However, the association of radiomic features with pathological response following neoadj therapy has not been assessed. We sought to determine if radiomic assessment predicts pCR in pts receiving neoadj TT and ICB. **Methods:** We collected data for a cohort of melanoma pts with locoregional metastases who were treated with neoadj TT (n = 33) or ICB (n = 30). Pts received systemic therapy for 8-10 weeks prior to planned surgical resection. Responses were evaluated radiographically (RECIST 1.1) and via pathological assessment (evaluating for pathologic complete response; (pCR) versus $<$ pCR). Thirty two pts (19 ICB; 13 TT) were included in the radiomics analysis based on the availability of appropriate CT imaging. A total of 310 unique radiomic features (10 histogram-based and 300 second-order texture features) were calculated from each extracted volume of interest (VOI). Feature extraction was performed on baseline and initial on-treatment pre-operative CT scans. Features associated with pCR were assessed using a feature selection approach based on Least Absolute Shrinkage and Selection Operator (LASSO). Selected features were used to build a classification model for prediction of pCR to ICB or TT. Leave-One-Out Cross-Validation was performed to evaluate the robustness of the estimates. **Results:** Out of 310 radiomic features, three features measured at baseline were able to predict a pCR to neoadj ICB or TT with sensitivity, specificity and accuracy of 100%, though these signatures were non-overlapping. In the on-treatment pre-operative scans, 3 distinct features (also non-overlapping and distinct from the predictive pre-treatment signatures) also predicted pCR to ICB and TT with 100% sensitivity, specificity and accuracy. **Conclusions:** Radiomic signatures in baseline and on-treatment CT scans accurately predict pCR in melanoma pts with locoregional metastases treated with neoadj TT or ICB. These provocative findings warrant further investigation in larger, independent cohorts. Research Sponsor: None.

10068 Poster Session (Board #417), Fri, 8:00 AM-11:00 AM

Using a clinicopathologic and gene expression model to identify melanoma patients at high risk for disease relapse. *First Author: Alexander M. Eggermont, Princess Máxima Center, Utrecht, Netherlands*

Background: The identification of early stage melanoma patients at high risk for relapse is still difficult. Roughly 50% of melanoma deaths occur in patients who were initially diagnosed with nonmetastatic melanoma. Therefore, a strong clinical need has emerged for diagnostic tools that can identify melanoma patients at high risk for relapse. Here, we assessed the performance of a recently developed model (Bellomo et al., JCO Precis Oncol. 2020: in press), combining clinicopathologic and gene expression variables (CP-GEP), in identifying melanoma patients that have a high risk for disease relapse. **Methods:** We assessed the prognostic performance of the CP-GEP model in a cohort of 837 consecutive melanoma patients from Mayo Clinic who had a sentinel lymph node biopsy (SLNb) performed within 90 days of their diagnosis. The CP-GEP model combines Breslow thickness and patient age, with the expression of 8 genes in the primary tumor, to stratify patients according to their risk of relapse: CP-GEP High Risk or CP-GEP Low Risk. The main clinical endpoint of this study was five-year relapse free survival (RFS). **Results:** Patients were stratified based on SLNb status and CP-GEP classification. 76% of the patients were SLNb negative and had an RFS of 79% versus 52% for SLNb positive patients; HR, 3.21; P $<$ 0.0001. 60% of the patients were identified as CP-GEP High Risk and had an RFS of 62% versus 87% for CP-GEP Low Risk patients; HR, 4.12; P $<$ 0.0001. Within the SLNb negative group (637 patients of which 65% stage I), 51% of patients were classified as CP-GEP High Risk. Here, RFS was 70% for CP-GEP High Risk patients versus 89% for CP-GEP Low Risk patients; HR, 3.61; P $<$ 0.0001. The prognosis of these CP-GEP High Risk patients is similar to stage IIC/IIIA patients with reported RFS ranging from 63% to 77%. This confirms the heterogeneity in prognosis among patients with stage I/II melanoma disease. **Conclusions:** The CP-GEP model can be successfully used to stratify patients based on their risk for relapse. In particular, it can be used to identify SLNb negative patients with a high risk for disease relapse who may benefit from therapeutic interventions. Independent validation studies are ongoing to validate the CP-GEP model in various patient populations. Research Sponsor: Mayo Clinic, U.S. National Institutes of Health.

	Stratification	Number of patients	RFS	DMFS	MSS
837 cohort	None	837	73%	80%	91%
	SLNb negative	637	79%	86%	93%
	SLNb positive	200	52%	64%	85%
	CP-GEP Low Risk	337	87%	92%	96%
	CP-GEP High Risk	500	62%	72%	88%
637 SLNb negative	CP-GEP Low Risk	310	89%	94%	97%
	CP-GEP High Risk	327	70%	78%	89%

10069 Poster Session (Board #418), Fri, 8:00 AM-11:00 AM

Vismodegib (V) for organ preservation for locally advanced (LA) orbital/periocular basal cell carcinoma (BCC). *First Author: Francis P. Worden, University of Michigan, Ann Arbor, MI*

Background: LA BCC of the eye/lacrimal drainage system most often requires disfiguring radical surgery, possibly including exenteration. As an alternative to radical surgery, we evaluated ophthalmologic outcomes following treatment with V using a novel Visual Assessment Weighted Score (VAWS) in patients (pts) with locally advanced periocular BCC. **Methods:** In this open label, non-randomized trial, pts with globe- and lacrimal-threatening orbital/periocular BCC were scored with VAWS prior to treatment with 150 mg of V daily. Pts were evaluated by ophthalmic exam (OE) every 3 mo & with MRI/CT at 5-9 mo. Pts with progressive disease (PD) were offered salvage surgery. Tumor response was assessed by RECIST v1.1. Responders (CR, PR, SD) continued V if tolerating therapy. Pts with intolerable side effects stopped V & were offered surgery of their residual tumor. Post-surgical specimens were assessed for histologic presence of BCC by a dermatopathologist. The primary endpoint, maintenance of visual function, was evaluated by VAWS at final post treatment assessment (FPTA), 1 yr after the start of V or 2 mo post-surgery. A VAWS of 21/50 was considered successful, representing preservation of a functional eye. **Results:** 50 pts were planned for enrollment, but the study was stopped early for benefit. From 06/25/2015 to 05/16/2019, 35 pts signed consent; 1 was a screen failure; 34 (97%) received V & 35 were evaluable for analysis by ITT; 1 died from aspiration pneumonia. The median time on study was 261 days. Average treatment with V was 223 days. 32 (91%) underwent OE & 27 (77%) had an MRI/CT. 27 (77%) underwent surgery & 33 (94%) attained organ preservation. Overall response rate (ORR) on OE was 84% (0%-PD,6%-SD,29%-PR,54%-CR, 11% not assessed(NA)). ORR by MRI/CT was 72% (0%-PD,6%-SD, 26%-PR,46%-CR,22% NA). 31 (89%) were scored with VAWS at 3 mo & 30 (86%) at FPTA. The mean VAWS at baseline was 44/50, 46/50 at 3 mo, & 47/50 at FPTA. Of the 35 pts scored at baseline by VAWS, 1 (3%) had a major decline during follow up, 5 (14%) a minor decline, 27 (77%) stable/improved, & 2 (6%) NA. No pts experienced grade 3-5 events. Of the 27 post-surgical pathologic specimens evaluated for histological response, 67% had NED, 22% had clear margins, & 11% had BCC to the margin. Two pts have recurred & underwent Mohs surgery. **Conclusions:** Treatment with V led to organ preservation for pts with LA periocular BCC, with preservation of visual function. Vismodegib is practice changing as neoadjuvant therapy for LA BCC of the eye/lacrimal drainage system in which surgery would result in unacceptable morbidity. Clinical trial information: NCT02436408. Research Sponsor: Genetech, institutional funding from the University of Michigan.

10070 Poster Session (Board #419), Fri, 8:00 AM-11:00 AM

Checkpoint inhibitor treatment in patients with isolated in-transit melanoma metastases. *First Author: Lucy Storey, Christie NHS Foundation Trust, Manchester, United Kingdom*

Background: In the context of multiple in-transit melanoma metastases without nodal involvement, a variety of treatment modalities have historically been employed including surgery, laser, isolated limb perfusion/infusion, intralesional interleukin-2, T-VEC and electrochemotherapy. Unfortunately, most patients treated with these modalities experience subsequent disease progression. While checkpoint inhibitors (CPI) are a standard of care for bulky unresectable stage III and for stage IV melanoma, patients with isolated in-transit metastases were rarely included in registration studies. There are anecdotal reports of lower response rates in these patients despite them having disease characteristics that would usually be associated with a good response. **Methods:** We report data from 11 retrospective patient cohorts treated at cancer centres across Europe who received CPI between 2016 and April 2019. All patients had multiple in-transit metastases without clinical or radiological evidence of nodal or distant disease. Disease response was assessed using CT, PET-CT or MRI depending on clinical indication. All patients had at least one prior resection of loco-regional relapsed disease and were deemed not curable by further surgery. **Results:** Sixty three patients meeting criteria were identified, 40 females and 23 males. Median age was 72 years and 54 (86%) patients had a normal lactate dehydrogenase (LDH). 19 (30%) patients had a BRAF mutation. At treatment initiation, the majority 55 (87.3%) received single agent PD-1 inhibitor, 7 (11.1%) combination ipilimumab + nivolumab and 1 (1.6%) received single agent anti-CTLA 4. The overall response rate was 62% for the full population. The response rate with anti-PD1 monotherapy was 59%. With a median FU of 23 months, the median PFS was 26 months, median OS not reached. OS estimates with 95% CI: 12 month - 93% (87-100%), 24 month - 88% (80-98%), 36 month - 80% (67-95%). **Conclusions:** The results show a high response rate to CPI in patients with in-transit metastases and support early treatment with CPI following identification of in-transit metastases not curable with surgery whilst disease characteristics remain favourable. Research Sponsor: None.

10072 Poster Session (Board #421), Fri, 8:00 AM-11:00 AM

KRT-232, a first-in-class, murine double minute 2 inhibitor (MDM2i), for TP53 wild-type ($p53^{WT}$) Merkel cell carcinoma (MCC) after anti–PD-1/L1 immunotherapy. *First Author: Michael K.K. Wong, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: MCC is an aggressive neuroendocrine skin cancer with very poor prognosis. Immune checkpoint inhibition was recently shown to benefit some patients (pts). There are few effective treatments (tx) and no standard of care for those who relapse on or are refractory to anti-PD-1/L1 agents (R/R). In $p53^{WT}$ MCC, oncoproteins from the Merkel cell polyomavirus can inhibit p53 tumor suppressor functions via L-MYC/EP400-dependent activation of MDM2. KRT-232, a potent, selective, orally available MDM2i, is being evaluated in pts with $p53^{WT}$MCC who are R/R to anti-PD-1/L1 tx. **Methods:** In stage 1 of this open-label, multicenter, phase 2 study (NCT03787602) pts initially received KRT-232 240mg QD days 1-7 of a 21 day (d) cycle (cy). This cohort was closed due to Grade (Gr) 3/4 cytopenias and pts were moved to 240mg QD days 1-5 of a 28d cy to allow for hematologic recovery. Two new arms were opened: 240mg and 180mg QD days 1-5 of a 28d cy. The primary endpoint is objective response rate (ORR) by RECIST 1.1. Secondary endpoints include duration of response, progression-free survival, overall survival, and safety and tolerability of KRT-232. **Results:** At the time of this analysis, 11 pts were treated with KRT-232: 6 on the 240mg 7/21d, 3 on the 240mg 5/28d and 2 on the 180mg 5/28d schedules. Median age was 66; 46% of pts had ECOG 1 (range 0-1), the median prior lines of systemic therapy was 3 (range 1-4) and 82% had prior radiation tx. Treatment-emergent adverse events (AEs), regardless of grade or causality, were reported in all pts: 55% had Gr 3-4 AEs and 36% had serious AEs (SAEs). The most common AEs included neutropenia (55%), anemia, leukopenia and thrombocytopenia (each 45%), diarrhea, nausea and fatigue (each 36%), and lymphopenia, hypomagnesaemia, lipase increase and sinus tachycardia (each 27%). SAEs were mainly due to cytopenias. One Gr 5 AE of respiratory failure/ascites was attributed to progression. Median time on study was 11.3 wks (range 1.3-20.9). Two of 11 pts on active tx have not yet reached the first response assessment (wk 6). Of the 9 pts who have reached wk 6, 2 PRs and 1 SD (converted to PR at wk 12) were reported. At the second response assessment (wk 12), 2 PRs were reported; one of the PRs at wk 6 has not yet reached wk 12. The ORR was 33% (3/9 pts). **Conclusions:** KRT-232 demonstrates promising monotherapy activity in MCC $p53^{WT}$ pts who failed anti-PD-1/L1 tx. This is the first clinical proof-of-concept for inhibiting the MDM2 pathway in MCC. Safety and efficacy continue to inform KRT-232 dose and schedule optimization. Clinical trial information: NCT03787602. Research Sponsor: Kartos Therapeutics, Redwood City, CA, USA.

10073 Poster Session (Board #422), Fri, 8:00 AM-11:00 AM

Patient-reported outcomes (PROs) from the phase III IMspire150 trial of atezolizumab (A) + cobimetinib (C) + vemurafenib (V) in patients (pts) with *BRAF*$^{V600+}$melanoma. *First Author: Karl D. Lewis, University of Colorado Comprehensive Cancer Center, Aurora, CO*

Background: In IMspire150, A+C+V significantly improved investigator-assessed progression-free survival vs placebo (Pbo)+C+V in previously untreated pts with unresectable stage IIIc/IV *BRAF*$^{V600+}$melanoma. PRO data from this trial are now reported. **Methods:** 514pts were randomized 1:1 to 28-day cycles of A+C+V or Pbo+C+V. Pts received C+V in cycle 1; A or Pbo was added on days 1 and 15 from cycle 2 onward. Pts completed the EORTC QLQ-C30 questionnaire on day 1 of cycle 1 (baseline), days 1 and 15 of cycle 2 and cycle 3, day 1 from cycle 4 onward, within 28-d of treatment discontinuation, and ≤6 months post-treatment. Prespecified secondary PRO endpoints were time to confirmed deterioration (TTCD; defined as time from randomization to first ≥10-point decrease from baseline held for 2 consecutive assessments, or 1 assessment followed by death on treatment) in quality of life (QoL) and physical functioning (PF). Prespecified exploratory endpoints were TTCD in role functioning (RF); mean change from baseline and percentage of pts with a clinically meaningful change (≥10 points from baseline) in QoL, PF, and RF. **Results:** Questionnaire completion rates were > 80% for most of the treatment period. At baseline, mean QoL, PF, and RF scores were moderate to high (Table). At week 6 (cycle 2), following initiation of A, QoL, PF, and RF scores declined, but returned to near-baseline levels at week 10 (cycle 3) and were largely maintained until week 36 (cycle 10), when < 50% of pts contributed data. In this time, ≥56% pts in both arms did not experience a clinically meaningful deterioration in QoL, PF, and RF. TTCD on QoL (hazard ratio [HR] 1.23; 95% CI 0.90-1.67), PF (HR 1.27; 95% CI 0.93-1.74), and RF (HR 1.15; 95% CI 0.86-1.55) favored Pbo, but only one-third of pts overall experienced a confirmed deterioration. **Conclusions:** PRO data showed that A+C+V did not worsen QoL, PF, and RF in pts with advanced *BRAF*$^{V600+}$melanoma, thus supporting its use as a treatment option. Clinical trial information: NCT02908672. Research Sponsor: F. Hoffmann-La Roche Ltd.

	Mean (SD) score, baseline	Mean (SD) change from baseline, week 6	Mean (SD) change from baseline, week 10
A+C+V (QoL)	70.6 (21.4)	-9.10 (22.9)	-2.07 (20.4)
Pbo+C+V (QoL)	70.8 (23.0)	4.11 (21.6)	1.43 (19.6)
A+C+V (PF)	84.0 (20.8)	-6.55 (19.4)	0.26 (16.7)
Pbo+C+V (PF)	85.3 (19.0)	1.96 (17.3)	-0.12 (15.4)
A+C+V (RF)	79.8 (28.4)	-12.0 (30.9)	-3.63 (25.1)
Pbo+C+V (RF)	80.1 (28.0)	0.11 (31.0)	-0.94 (26.5)

10074 Poster Session (Board #423), Fri, 8:00 AM-11:00 AM

Efficacy of imiquimod in the management of lentigo maligna. *First Author: Brigitte Dréno, Department of Dermatology-Oncology, Nantes University, CHU Nantes, CIC1413, CRCINA, Nantes, France*

Background: Lentigo maligna (LM), a melanocytic proliferation occurring on photoexposed skin, might progress to LM melanoma. Surgery is recommended as first-line treatment. However, the main challenge is the size of the excision inducing often-aesthetic injuries on the face and thus often refused by patients. The excision margins of 5 to 10 mm remain without international consensus. Several studies have shown that imiquimod induced LM regression, acting *by enhancing IFN-*γ production and effector function of T cells. The main goal of this study is to investigate the effect of imiquimod versus placebo in neoadjuvant setting to decrease the excision size as from the first surgical procedure. **Methods:** We performed a prospective, randomized, open, multicenter, phase III clinical study (NCT01720407). The health authority and ethics committee approvals were obtained and all subjects signed an informed consent. The primary endpoint was to demonstrate that in neoadjuvant situation, imiquimod could reduce the surgical excision size of LM with a healthy tissue margin of 5 mm. The main inclusion criteria were: Patients $>$ 18 years fit for surgery. LM of the head histologically confirmed and not previously treated. Surface lesion $\geq$ to 1cm^2 and $\leq$ to 20cm^2. The two treatment arms were imiquimod or placebo followed by LM excision. Imiquimod or placebo were applied once daily, 5 days/week for 4 weeks followed by 5 mm margin surgery performed four weeks after the last treatment application. For sample size, 268 patients were expected to demonstrate a difference of 15% between the two arms in a bilateral situation with an alpha risk of 5% and a beta risk of 20%. **Results:** The trial involved 273 patients, 238 (105 men (44%) and 133 women (56%), mean age of 71 $\pm$ 10.2 years, were analyzed in modified ITT. Statistical analysis was performed on 122 patients in the imiquimod arm and 116 patients in the placebo arm. For the primary endpoint, the first extralesionnal excision has been achieved for 112 (91.8%) patients in the imiquimod arm and for 98 (84.5%) placebo patients group. There was no significant difference (p value = 0.1067) between the two arms. However, regarding the surface of LM, imiquimod allowed a highly significant reduction (4.2 cm^2 $\pm$ 4.6 to 2.3 cm^2 $\pm$ 3.3) compared to LM treated by placebo (4.0 cm^2 $\pm$ 3.5 to 4.0 cm^2 $\pm$3.3; p $<$ 0.0001). **Conclusions:** This randomized prospective study shows that imiquimod reduces the LM area (-50%) after one month of treatment. Reducing the surface of LM with imiquimod is not associated with a higher risk of intralesional excision (marge 5mm), with a significant esthetic result (less excised surface). Clinical trial information: NCT01720407. Research Sponsor: French Hospital Clinical Research Program in Cancer.

10075 Poster Session (Board #424), Fri, 8:00 AM-11:00 AM

Adjuvant crizotinib in high-risk uveal melanoma following definitive therapy. *First Author: Shaheer Khan, Columbia University Irving Medical Center, New York, NY*

Background: Uveal melanomas (UM) measuring at least 12mm in base diameter with a class 2 signature as defined by gene expression profiling (DecisionDx-UM) are characterized by high metastatic risk, with a median time to recurrence of 32 months. No therapy has been shown to reduce this risk. The growth factor receptor Met is highly expressed in UM. We have previously shown that crizotinib, an inhibitor of Met, is an effective adjuvant therapy in preclinical models *(Surriga et al, Mol Cancer Ther 2013).* We therefore conducted a phase II study of adjuvant crizotinib in high-risk UM. **Methods:** Eligibility included: primary lesion $\geq$12mm in base diameter; class 2 by DecisionDx-UM testing; definitive therapy within 120 days before starting crizotinib; and, no evidence of metastatic disease. Patients (pts) received 12 four-week cycles of crizotinib (250 mg twice daily). Surveillance imaging (chest CT and MRI abdomen/pelvis) were performed q3 months. The primary endpoint was distant relapse-free survival (RFS). Secondary endpoints were overall survival (OS) and toxicity. We hypothesized that the addition of crizotinib would increase the 32 month RFS from 50% to 75% (α = 0.05; β = 0.11). **Results:** As of 1/31/2020, 34 pts had enrolled and received at least one dose of study drug with median age of 60 (range, 26-86); 41% female; and median ECOG PS 0 (range, 0-1). 2 pts could not be evaluated for the primary endpoint due to early withdrawal and loss to follow-up. The median time from primary treatment to crizotinib initiation was 60 days (range, 0-106). All pts experienced a treatment-related adverse event (AE) of any grade. 11/34 (32%) experienced a grade 3 or 4 AE, the most common being transaminase elevation (n = 8/11). 9 pts (28%) did not complete the full 48-week treatment course due to disease recurrence (n = 5) or toxicity (n = 4). An additional 5 pts required dose reduction due to hepatic toxicity or diarrhea. 15/32 evaluable pts developed distant disease relapse, with 14 developing relapse within 32 months. With a median duration of follow up of 28.7 months, the median RFS was 30.6 months (95% CI: 27.8-58.5%). The median OS was not reached. **Conclusions:** The use of adjuvant crizotinib in patients with high-risk UM did not reduce rates of relapse in this multicenter, single arm trial. 9/32 (28%) pts required dose modification or discontinuation due to AE which may have limited efficacy. Further investigations of adjuvant treatment options are warranted. Clinical trial information: NCT02223819. Research Sponsor: Pfizer Inc., Columbia University

10076 Poster Session (Board #425), Fri, 8:00 AM-11:00 AM

Effect of automated TIL quantification in early-stage melanoma on accuracy of standard T staging using AJCC guidelines. *First Author: Michael Moore, Columbia University Medical Center, New York, NY*

Background: Patients diagnosed with early stage melanoma are at risk of recurrence and death. Adjuvant therapy decreases risk but incurs toxicity and expense. While tumor-infiltrating lymphocytes (TILs) improve prognosis, studies have shown conflicting results due, at least in part, to inter-observer variability. Thus, TILs are not included in standard American Joint Committee on Cancer (AJCC) staging. Here, we quantitatively analyze TILs in hematoxylin and eosin (H&E) melanoma images using two machine learning algorithms. **Methods:** H&E images were evaluated by two methods for patients with resectable stage I-III melanoma from Columbia (N = 81) and validated using samples from Geisinger and Moffitt (N = 128). For both methods, H&E images were manually annotated using open source software, QuPath, to specify tumor regions. For Method A, images were divided into patches and, for each patch, a probability was generated to detect lymphocytes. Patches above a set threshold were considered to be "TIL positive". Ratio of TIL positive patches to total patches was assessed for every image. For Method B, a classifier was manually trained in QuPath and then applied on each image to determine the ratio of the areas of all immune cells to all tumor cells as previously published. Cutoff values to define high and low risk groups were established based on a test set and then validated in an independent cohort. **Results:** Both methods distinguished patients with visceral recurrence from those without for the Columbia training set (Method A p = .0015, Method B p = .043). Using Method A, Kaplan-Meier curve at the selected cutoff also correlated significantly with disease specific survival (DSS) for Columbia (p = .022) and was validated in the Geisinger/Moffitt (p = .046) cohort. Cox analysis using Method A showed that TIL status predicted DSS in the validation set (p = .047) and added significantly to depth and ulceration (HR = 3.43, CI: 1.047-11.257, p = .042). **Conclusions:** Both open source machine learning algorithms find significantly higher TILs in patients who do not develop metastasis. Notably, Method A may add to standard predictors, such as depth and ulceration. These results demonstrate the promise of computational algorithms to enhance visual grading, and suggest that digital TIL evaluation may add to current AJCC staging. Research Sponsor: U.S. National Institutes of Health, Other Foundation, Melanoma Research Alliance.

Multivariable Cox table for validation cohort using Method A.

	Hazard Ratio	95% CI	*P*
TIL Score	3.43	1.047 to 11.257	0.042
Depth	1.09	1.010 to 1.183	0.028
Ulceration	2.66	1.420 to 4.973	0.002

10077 Poster Session (Board #426), Fri, 8:00 AM-11:00 AM

Incidence and trends of skin cancer in the United States, 1999-2016. *First Author: Hoa Van Le, BMS, Princeton, NJ*

Background: Cutaneous skin cancer is among the most common malignancies in US. While Surveillance, Epidemiology and End Results (SEER) data are vital to estimate its incidence, delays and under-reporting remained major limitations. Surveillance is hindered due to exclusion from states' reportable diseases and possible outpatient diagnoses' omission from registries. Thus, exact incidence has not been known. This study determined skin cancer incidence and trends from 1999 to 2016 in a nationally representative sample. **Methods:** New melanoma, non-melanoma and other skin cancer cases among adults aged $\geq$20 years were identified in the National Health and Nutrition Examination Survey (NHANES), 1999-2016. Crude and age-adjusted incidences and 95% CIs were estimated by survey year cohorts (1999-2008 and 2009-2016) based on the 2000 US standard population. Sex and age-stratified longitudinal trends were examined in age and sex-adjusted regression models. Statistical analyses accounted for complex survey design with examination sample weight and adjusted for nonresponse. Sensitivity analyses included unadjusted, sex- and age- adjusted modeling. Statistical significance was determined by 2-sided *p*-value of .05. **Results:** Among 47,172 adults and 21,192 non-Hispanic whites from 1999-2016, the overall age-standardized incidences of skin cancer per 100000 persons were 390.9 (95% CI: 312-469.7) and 519 (95% CI: 413.8-624.3), respectively. The median age at first diagnosis was 72.2 (mean = 69.8, IQR = 57.5-79.5 years). The incidence was higher in men than women (474.7 vs 313.8 per 100000 persons, $p<$ .001) and increased with older age ($p<$ .001). Between 1999-2008 and 2009-2016, the incidence was significantly higher in those older than 70, 75 and 80 ($p \leq$.01). Rising incidence was also observed in overall population, women, and by approximately 90% among those older than 70. Sensitivity analyses showed similar trends. **Conclusions:** Our incidence rates for skin cancer were high, particularly in the elderly. From 1999 to 2016, the incidence increased in women and those 70 and older, a concerning observation given the aging population. As understanding susceptible groups has public health implications, our study provided an updated depiction of skin cancer incidence and trends in US. Research Sponsor: None.

Trends in incidence of skin cancer per 100000 persons among US adults 20 Years and older by sex and age group, 1999-2016.

	1999-2008	2009-2016	p for trend
Overall	299.4	491.1	0.02
Men	382.9	574.7	0.12
Women	222.9	414.0	0.03
≥ 70 y	1278.1	2424.9	$<$ 0.01
≥ 75 y	1481.2	3592.6	$<$ 0.01
≥ 80 y	2200.3	5403.2	$<$ 0.01

10078 Poster Session (Board #427), Fri, 8:00 AM-11:00 AM

Exploring the clinical efficacy of the total body skin exam. *First Author: Tanner Harding, University of Central Florida College of Medicine, Orlando, FL*

Background: The clinical efficacy of the total body skin exam has long been the subject of debate. A 2016 report by the United States Preventative Services Task Force (USPSTF) found the current body of evidence was "insufficient to assess the balance of benefits and harms of visual skin examination by a clinician to screen for skin cancer in [asymptomatic] adults.'' However, the USPSTF based its recommendations on studies evaluating mainly the ability of primary care physicians to diagnose melanoma through total body skin exams (TBSE). This study seeks to address this insufficiency in the current literature by exploring the clinical efficacy of the dermatology provider performed TBSEs as a screening tool with respect to the detection of malignant melanoma (MM), squamous cell carcinoma (SCC), and basal cell carcinoma (BCC). **Methods:** A search was performed within the electronic medical record of a large multi-state dermatology group practice for all instances of new and established patient office visits occurring from 1 January 2018 to 31 December 2019. Per practice policy, it is denoted whether each office visit includes a TBSE or partial skin exam (PSE). The number of MM, SCC, and BCC diagnoses made within the context of each class of skin exam was analyzed. **Results:** Of the 930,706 office visits analyzed, 438,027 TBSEs and 492,679 PSEs were performed. For each of the three types of skin cancer surveyed, the number of cancers diagnosed in the context of a TBSE was significantly greater than the number diagnosed in the context of a PSE. One MM was diagnosed per 161.0 TBSEs and 371.3 PSEs (X^2 ($df = 1$, $N = 930706$) = 662, $p < 0.001$). One SCC was diagnosed per 56.7 TBSEs and 108.4 PSEs (X^2 ($df = 1$, $N = 930706$) = 1258.5, $p < 0.001$). One BCC was diagnosed per 10.2 TBSEs and 17.8 PSEs (X^2 ($df = 1$, $N = 930706$) = 5884, $p < 0.001$). **Conclusions:** Skin cancer is detected at significantly higher rates in TBSEs than PSEs. The finding that one MM is detected in 161 TBSEs may be compared to one cervical cancer is detected in 3,776 Pap smears. Thus, a TBSE is 23.5 times more likely to identify a MM than a Pap smear is to identify a cervical cancer. This trend holds even when adjusted for prevalence. Further analysis will allow for the comparison of exam types with respect to patient age, staging, lesion size, and Breslow depth at time of cancer diagnosis. This continued analysis will allow for a more detailed risk benefit-analysis and insight into the clinical efficacy of the TBSE. Research Sponsor: None.

TPS10079 Poster Session (Board #428), Fri, 8:00 AM-11:00 AM

Design and rationale of MASTERKEY-115 phase II trial of talimogene laherparepvec (T-VEC) with pembrolizumab (pembro) in patients with advanced melanoma who progressed on prior anti-programmed cell death-1 (anti-PD-1) therapy. *First Author: Jason Alan Chesney, James Graham Brown Cancer Center, University of Louisville, Louisville, KY*

Background: Treatment options are limited for patients with advanced metastatic or unresectable melanoma, especially after anti-PD-1 failure. T-VEC is an intralesional oncolytic viral immunotherapy designed to selectively replicate in tumor cells and induce local and systemic antitumor response. Pembro promotes T cell activity by blocking PD-1 receptors. Combining T-VEC and pembro may produce robust antitumor activity by increasing T cell activation and blocking T cell inhibition, with a tolerable safety profile. The MASTERKEY-115 trial will evaluate safety and efficacy of T-VEC combined with pembro in patients with advanced melanoma who experienced progressive disease (PD) on prior anti-PD-1 therapy. **Methods:** NCT04068181 is a phase 2, open-label, single-arm, multicenter trial of T-VEC with pembro in patients with advanced melanoma and PD on prior anti-PD-1. The study is expected to enroll approximately 100 patients and comprises 4 cohorts. Cohorts 1 and 2 will receive anti-PD-1 in a locally recurrent or metastatic setting and experienced PD within 12 weeks of the last anti-PD-1 dose (Cohort 1: PD or stable disease prior to confirmed PD; Cohort 2: complete or partial response prior to confirmed PD). Cohorts 3 and 4 will receive adjuvant anti-PD-1 and were disease-free for $<$ 6 months (Cohort 3) or $\geq$ 6 months (Cohort 4) prior to confirmed PD. Enrollment criteria include adults with histologically confirmed unresectable or metastatic stage IIIB–IVM1d melanoma, measurable and injectable disease, ECOG PS 0-1, and prior anti-PD-1 ($\geq$ 2-3 consecutive cycles within 8 weeks, immediate prior treatment before enrollment). The primary endpoint is objective response rate per modified RECIST. Key secondary endpoints assess efficacy (objective response rate, best overall response, complete response rate, response duration, durable response rate, disease control rate, progression-free survival, overall survival), safety (incidence of treatment-emergent and treatment-related adverse events, abnormal laboratory tests), and time to subsequent anticancer therapy. The study began enrolling patients in January 2020 and enrollment is ongoing. Clinical trial information: NCT04068181. Research Sponsor: Amgen, Inc.

TPS10080 Poster Session (Board #429), Fri, 8:00 AM-11:00 AM

A phase I study of CX-4945 administered orally twice daily to patients with advanced basal cell carcinoma. *First Author: Zeynep Eroglu, Department of Cutaneous Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Smoothened inhibitors (SMOi) targeting the Hedgehog (Hh) pathway have been approved for the treatment of patients with locally advanced Basal Cell Carcinoma (laBCC) or metastatic BCC (mBCC). Unfortunately, resistance against SMO inhibitors (SMOi) can develop. Targeting the signaling cascade downstream of SMO, in this case via a novel small molecule inhibitor, could obviate this issue. Casein Kinase 2 (CK2) affects the terminal component of the Hh signaling pathway by promoting Gli2 stability and Gli2's interaction with target genes. Given the interplay between CK2 and GLI-2 and the importance of Hh signaling activation, CX-4945, a potent CK2 inhibitor, may provide benefits for the BCC patients with resistance or intolerance to SMOi. **Methods:** A phase I trial (NCT03897036) to explore various treatment durations of CX-4945 was designed for patients with laBCC or mBCC; with endpoints include safety (CTCAE v5) and objective response rate by RECIST 1.0 for mBCC and composite response for laBCC. Major eligibility criteria include progression or intolerability to SMO inhibitors; laBCC patients must not be surgical candidates and must have received prior radiation unless contraindicated, and basosquamous histology is excluded. The first phase of the trial uses a 3+3 design to test the tolerance of a CX-4945 dose of 1000 mg bid for a duration of 28 days continuously. If 2 out of 3, or 2 out of 6 patients experience a DLT, the regimen of 1000 mg bid for 21 days followed by 7 days off (already tested in prior CX-4945 Phase I trials in other tumor types) will be selected as the recommend phase 2 dose (RP2D). Upon determining the RP2D, a dose-expansion phase will further evaluateCX-4945 in two cohorts (laBCC & mBCC), with 10 patients enrolled in each. Currently, we are enrolling patients and collecting sufficient data for the determination of RP2D in this patient population; thus, further assessments are required to determine the safety, tolerability, and efficacy of CX-4945 in advanced BCC. Clinical trial information: NCT03897036. Research Sponsor: Senhwa Biosciences.

TPS10081 Poster Session (Board #430), Fri, 8:00 AM-11:00 AM

A phase II study evaluating atezolizumab (A), cobimetinib (C), and vemurafenib (V) in patients (pts) with BRAF-mutant melanoma and central nervous system (CNS) metastases (mets). *First Author: Paola Queirolo, Division of Medical Oncology for Melanoma, Sarcoma, and Rare Tumors, IEO, European Institute of Oncology IRCCS, Milan, Italy*

Background: CNS mets, a common complication of melanoma, are associated with poor survival prognosis (median of 4-5 months). The rationale for combining PD-L1 pathway blockade using atezolizumab (A) with the small molecule *BRAF* pathway–targeted inhibitors cobimetinib (C) and vemurafenib (V) for the treatment of $BRAF^{V600}$ mutation–positive melanoma is based on preclinical and translational evidence supporting the synergistic antitumoral effects of these approaches. Recently, the phase 3 IMspire150 study (NCT02908672) demonstrated improved progression-free survival outcomes with A + C + V vs C + V. **Methods:** This phase 2 study (NCT03625141) is currently evaluating A + C + V in pts with $BRAF^{V600}$ mutation–positive advanced melanoma and CNS mets. The study originally included a parallel cohort evaluating A + C in pts with $BRAF^{V600}$wild-type advanced melanoma and CNS mets. This cohort was closed at an enrollment of 15 pts after the primary analysis of the phase 3 IMspire170 study (NCT03273153), which showed no added benefit with A + C vs pembrolizumab in pts with $BRAF^{V600}$ wild-type disease. Eligible pts are aged $\geq$18 years with histologically confirmed melanoma and magnetic resonance imaging–confirmed brain mets $\geq$5 mm in at least 1 dimension. In addition, pts should not have received prior systemic treatment for metastatic disease; they were required to have ECOG performance status $\leq$2 and adequate hematologic and end organ function. Prior stereotactic or surgical therapy of $\leq$10 brain mets is allowed. The primary endpoint is intracranial objective response rate (ORR) with A + C + V in $BRAF^{V600}$mutation–positive melanoma as assessed by an independent review committee. Key secondary endpoints include investigator-assessed intracranial ORR, extracranial ORR, overall ORR, safety, and quality of life. Exploratory biomarker analyses are planned. The sample size for the cohort will be approximately 60 pts. No formal statistical hypothesis is being tested in this study. The primary study analysis and the analyses of all efficacy endpoints and safety summaries will be based on data collected $\leq$6 months after the last pt is enrolled. Clinical trial information: NCT03625141. Research Sponsor: F. Hoffmann-La Roche Ltd.

TPS10082 Poster Session (Board #431), Fri, 8:00 AM-11:00 AM

A phase II trial of nivolumab in combination with talazoparib in unresectable or metastatic melanoma patients with mutations in BRCA or BRCAness. *First Author: Tamara A. Sussman, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH*

Background: Melanoma has a response rate of 10-15% with anti-PD-1 re-challenge in the refractory setting. Newer targeted therapies in melanoma are needed, especially once patients progress on immune checkpoint inhibitor (ICI) therapy. Analysis of TCGA and the Cleveland Clinic's Gross Family Melanoma Registry reveals that a significant proportion (~40%) of melanoma patients possess somatic (31.6%) or germline (TCGA: 4.2%; Registry: 8.3%) mutations in homologous recombination repair genes, which may serve as a therapeutic target. PARP inhibitors, specifically talazoparib, have demonstrated synthetic lethality, potent PARP trapping activity, and increased immunogenicity of tumor cells by promoting T cell and NK cell infiltration *in vitro* and *in vivo*. Moreover, augmentation of the STING pathway via PARP inhibition modulates the tumor microenvironment, impacting PD-L1 expression and type I interferon production. Therefore, the use of talazoparib in combination with the ICI, nivolumab, may have a synergistic immunomodulatory and antitumor effect. **Methods:** This phase II, single arm, open label trial aims to enroll 37 primary or recurrent unresectable or metastatic melanoma patients harboring a somatic or germline mutation or deletion in *BRCA* or *BRCA*ness (genes including *ARID1A/B/2, ATM, ATR, BAP1, BARD1, BLM, BRCA1/2, BRIP1, CDK4/12, CHEK1/2, DSS1, EMSY, ERCC3, FANCA/D2, HDAC2, IDH1, LIG3/4, MDC1, MLH1/3, MRE11, NBN, PALB2, PRKDC, RAD50/51/54, XRCC6*) who have progressed on prior ICI therapy. Patients will be treated with nivolumab 480mg IV every 4 weeks and talazoparib 1mg PO daily. The primary objective is to determine clinical efficacy of the combination therapy, as measured by the objective response rate. The trial is designed to test the null hypothesis that ORR $\leq$ 10% and is powered to detect an effect size of ORR $\geq$ 30%. Secondary objectives include PFS, OS, immune-related objective response rate (irORR), irPFS, and treatment-related adverse events. Associations with clinical response will be assessed with correlative studies of PD-L1 expression, ctDNA, tumor mutational burden, copy number variation, and the phenotypic and functional characterization of circulating and tumor infiltrating immune cells. The study is currently open and enrolling patients. Clinical trial information: NCT04187833. Research Sponsor: Pfizer, Internal funding.

TPS10084 Poster Session (Board #433), Fri, 8:00 AM-11:00 AM

A phase III, randomized, double-blind study of adjuvant cemiplimab versus placebo post-surgery and radiation therapy (RT) in patients (pts) with high-risk cutaneous squamous cell carcinoma (CSCC). *First Author: Danny Rischin, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia*

Background: CSCC is the second most common skin cancer. While the surgical cure rate for CSCC is $>$ 95%, a proportion of pts are considered to have high risk for recurrence as assessed by immune status, primary disease stage, extent of nodal involvement, presence of extracapsular extension, and prior treatment. Post-operative RT is recommended for pts with high-risk features, but relapse with locoregional recurrence or distant metastases may still occur. This study evaluates the efficacy of cemiplimab, a human anti–PD-1 monoclonal antibody, as an adjuvant therapy for pts with CSCC with high-risk features, after surgery and RT. **Methods:** This randomized, placebo-controlled, double-blind, multicenter, Phase 3 study will evaluate cemiplimab as an adjuvant treatment for pts with high-risk CSCC, based on surgical and clinicopathologic findings, who have completed surgery and post-operative RT (NCT03969004). Immunocompromised pts were excluded. The trial will enrol 412 pts from about 100 sites in North America, Europe, and Asia-Pacific regions. Pts with at least one of the following high-risk features are eligible: a) nodal disease with extracapsular extension b) in-transit metastases c) T4 lesion d) perineural invasion, and e) recurrent CSCC with at least one other risk factor. In Part 1 (blinded), pts will be randomized 1:1 to receive cemiplimab 350 mg or placebo intravenously every 3 weeks (Q3W) for up to 48 weeks. In optional Part 2 (unblinded), pts in the placebo arm who experience disease recurrence or pts in the cemiplimab arm who experience disease recurrence $\geq$3 months after completion of 48-week treatment in Part 1 will be eligible to receive open-label cemiplimab 350 mg Q3W for up to 96 weeks. Key objectives are to compare disease-free survival (primary) as well as overall survival, freedom from locoregional relapse, and distant relapse (secondary) of adjuvant cemiplimab vs placebo in pts with high-risk CSCC. This study is currently open for enrollment. Clinical trial information: NCT03969004. Research Sponsor: Regeneron Pharmaceutical, Inc. and Sanofi.

TPS10085 Poster Session (Board #434), Fri, 8:00 AM-11:00 AM

A phase II study of anti-PD1 monoclonal antibody (Nivolumab) administered in combination with anti-LAG3 monoclonal antibody (Relatlimab) in patients with metastatic melanoma naive to prior immunotherapy in the metastatic setting. *First Author: Anjali Rohatgi, UPMC Hillman Cancer Center, Pittsburgh, PA*

Background: Novel checkpoint inhibitors are a promising treatment for advanced melanoma, as only a fraction of patients have durable responses to current FDA-approved immunotherapy. Lymphocyte activation gene 3 (LAG3) is an inhibitory checkpoint receptor on CD4+ and CD8+ T cells, where engagement results in suppression of T cell activation and proliferation. LAG3 and PD1 are co-expressed on T cells during T cell receptor signaling and are down-regulated after antigen clearance. Persistent stimulation leads to prolonged LAG3 and PD1 expression and to T cell exhaustion, a possible mechanism of resistance to immunotherapy. Both LAG3 and PD1 are expressed on tumor-infiltrating T cells in melanoma. Murine tumors treated with both anti-LAG3 and anti-PD1 have demonstrated increased tumor regression than tumors in mice treated with either single agent. Further, a phase I trial has demonstrated safety of combined anti-LAG3 monoclonal antibody, relatlimab and anti-PD1 monoclonal antibody, nivolumab. **Methods:** This phase II, single-center clinical trial is designed to enroll treatment naive patients with unresectable or metastatic melanoma to ultimately receive combined relatlimab and nivolumab after a lead-in arm where patients are randomized to receive relatlimab, nivolumab, or the combination for the first 4 week cycle. For the lead-in phase, patients will have baseline and post-treatment blood and tumor sampling. Disease assessment by imaging will occur after the lead-in phase at 4 weeks. After completion of the lead-in phase, all patients proceed to combination therapy with disease assessment at 12-week intervals. The primary endpoint for the lead-in phase is to evaluate changes in immune cell populations in peripheral blood and tumor with the single agents and combination treatment. The primary endpoint for the combination phase is best overall anti-tumor response. Secondary clinical endpoints include progression-free survival, overall survival, duration of response and toxicity. Exploratory endpoints are to determine the mechanistic effects of anti-LAG3 and anti-PD1 on the blood and tumor microenvironment, cytokine signatures, and correlation of these with clinical response. The study is currently accruing with enrollment of 9 out of 42 patients. Clinical trial information: NCT03743766. Research Sponsor: Bristol-Meyers-Squib.

TPS10086 Poster Session (Board #435), Fri, 8:00 AM-11:00 AM

A phase Ib study of endogenous SLC45A2-specific cytotoxic T cells for the treatment of patients with metastatic uveal melanoma. *First Author: Suzanne Phillips, MD Anderson Cancer Center, Houston, TX*

Background: Overall survival (OS) for patients (pts) with advanced uveal melanoma (UM) is poor with a median survival of approximately 12 months. Roughly half of all pts with UM will develop distant metastatic disease despite effective treatment of the primary site. Metastatic UM has a 90% prevalence of liver involvement. Currently, there are no specific FDA-approved treatments for metastatic UM and consensus guidelines recommend participation in a clinical trial. Modern treatments such as checkpoint inhibitors and targeted therapy have less impressive outcomes in UM. Our group has identified peptide epitopes of SLC45A2, a melanosomal transport protein, that is highly expressed in UM and present at very low levels in normal melanocytes. We demonstrated that cytotoxic T cells against SLC45A2 were able to kill HLA-matched UM cell lines. Through the use of enabling technologies, SLC45A2-specific cytotoxic T cells can be isolated and expanded ex-vivo from peripheral blood for use in endogenous T cell (ETC) therapy (a form of adoptive cellular therapy). These activated ETCs can then be infused to traffic to tumor sites. CTLA4 is a T-cell surface protein that binds to B7 with a higher affinity than the costimulatory receptor CD28, providing an inhibitory signal to T-cells. Anti-CTLA4 blockade can divert this inhibition and release the brake on antigen-specific T-cell activation of ETC. We hypothesize that antigen-specific ETCs infused via hepatic artery will be safe and tolerable for UM pts with liver metastasis. **Methods:** We are conducting a first-in-human clinical trial (NCT03068624) of ETC therapy targeting SLC45A2 in combination with anti-CTLA4 in pts with metastatic UM. Pts who express HLA-A*02:01 or A*24:02 undergo apheresis to collect T cells. Their cells then undergo ex vivo cloning and interleukin-21 primed expansion. Hepatic arterial infusion of ETCs will ensure direct localization to the target organ of interest. Conditioning with low-dose cyclophosphamide (300 mg/m2) occurs on Day -2. Hepatic arterial infusion of ETCs on Day 0 is followed by low dose subcutaneous interleukin-2 (IL-2) twice daily for 14 days. The initial dose escalation phase is a 3+3 design with a starting dose level of 3.3×10^9 cells/m^2 of ETCs alone. Once the maximum tolerated dose of ETCs is established, the dose expansion phase will include ETCs in combination with anti-CTLA4 (Ipilimumab). The primary objective is to evaluate the safety of this first in human T cell regimen. Secondary objectives are to evaluate the in vivo persistence and anti-tumor efficacy. Clinical trial information: NCT03068624. Research Sponsor: U.S. National Institutes of Health, Other Government Agency, NCI MD Anderson SPORE in Melanoma.

TPS10087 Poster Session (Board #436), Fri, 8:00 AM-11:00 AM

Personalized combination of neoadjuvant domatinostat, nivolumab and ipilimumab in macroscopic stage III melanoma patients stratified according to the interferon-gamma signature: The DONIMI study. *First Author: Irene L.M. Reijers, Netherlands Cancer Institute, Amsterdam, Netherlands*

Background: Previous OpACIN and OpACIN-neo studies, investigating neoadjuvant ipilimumab (IPI) plus nivolumab (NIVO), demonstrated high pathologic response rates (74-78%) and favorable long-term outcomes in patients (pts) achieving pathologic response; at 36 and 18 months follow-up, respectively, only 1/71 (1.4%) pts with response has relapsed. In contrast, pts without pathologic response (pNR) have a poor prognosis; 15/23 (65.2%) have relapsed so far. This emphasizes the need for baseline biomarkers predictive of non-response and new neoadjuvant treatment combinations for these pts. In our previous studies, baseline interferon-gamma (IFN-γ) signature low pts were less likely to respond to neoadjuvant IPI plus NIVO. The DONIMI study tests the combination of NIVO +/- IPI with domatinostat (DOM), a class 1 histone deacetylase inhibitor, according to the IFN-γ signature in the tumor. Based on the signature previously described by Ayers et al. we have developed a neoadjuvant IFN-γ signature algorithm that will be used for the first time to classify pts in this prospective trial. **Methods:** The aim of this two-center investigator-initiated phase 1b study is to assess the safety and feasibility of neoadjuvant NIVO +/- DOM +/- IPI in 45 stage III melanoma pts with RECIST 1.1 measurable de-novo or recurrent disease. IFN-γ signature high pts (n = 20) will be randomized (stratified by center) to Arm A (2 cycles NIVO 240mg q3wk) or Arm B (2 cycles NIVO 240mg q3wk + DOM 200mg twice daily (BID), d1-14, q3wk). IFN-γ signature low pts (n = 25) will be randomized to Arm C (2 cycles NIVO 240mg q3wk + DOM 200mg BID, d1-14, q3wk) or Arm D (2 cycles NIVO 240mg q3wk + IPI 80mg q3wk + DOM 200mg once daily (OD), d1-14, q3wk). Based on safety data of the first 5 pts in arm D, the remaining pts will be treated with either a higher dosing scheme (200mg BID, d1-14, q3wks), a lower dosing scheme (100mg OD, d1-14, q3wks) or the same dosing scheme (200mg OD, d1-14, q3wks). The primary endpoint is safety and feasibility. A treatment arm will be declared as not feasible if 2/5 or 3/10 pts cannot adhere to the preplanned time of surgery (week 6 +/- 1week) due to treatment-related adverse events. Biopsies (week 0, 3), blood samples (week 0, 3, 6, 12) and feces (week 0, 3, 6) will be collected for translational research. The first patient was enrolled on January 23th, 2020. Clinical trial information: NCT04133948. Research Sponsor: 4SC.

TPS10088 Poster Session (Board #437), Fri, 8:00 AM-11:00 AM

A phase II study of neoadjuvant pembrolizumab and lenvatinib for resectable stage III melanoma: The neopele study. *First Author: Maria Gonzalez, Melanoma Institute Australia, North Sydney, Australia*

Background: Recent clinical trials of neoadjuvant (neo-adj) ipilimumab combined with nivolumab (OpACIN & OpACIN-neo) in resectable stage III melanoma show that a pathological response (< 50% viable tumour at the tumour bed as determined by histopathological analysis) is associated with a prolonged relapse-free survival compared to no pathological response. Furthermore, recurrences seldom occur in those who have a pathological response following neo-adj immunotherapy with only 1/71 pts (1.4%) having recurred. In contrast, 15/23 (65.2%) pts with no pathological response have relapsed to date. The NeoPeLe trial will test the hypothesis that the synergistic combination of PD-1 blockade (pembrolizumab) with anti-angiogenic/multiple RTK inhibitor (lenvatinib) will result in a high rate of pathological response in the resected surgical specimen with a low rate of toxicity. Tissue and blood biomarkers are drawn at several timepoints and correlated to clinical and pathological endpoints to explore mechanisms of response and resistance. We will compare pathological response rate, and other clinical outcomes in this study, with previously published neo-adj clinical trials to select the best schedules for larger-scale clinical testing. Across neo-adj studies, we will also analyse the tissue collected to explore determinants of the optimal therapy for individual pts, whilst minimising toxicity. **Methods:** Eligible pts with stage IIIB/C/D, resectable and measurable (RECIST 1.1) nodal metastatic melanoma will be enrolled to this phase II single-centre trial (n = 20). All pts undergo complete nodal resection (RES) at wk 6 following neo-adj therapy with pembrolizumab (200mg, IV, 3 wkly) and lenvatinib (20mg, oral, daily). Adjuvant therapy with pembrolizumab is given for 46 wks after RES. After 52 wks of the study treatment, pts will be followed for relapse and survival for 5 years. CT and FDG PET/CT are used to measure response and exclude progression in the neo-adj phase, and to monitor for recurrence during adj and post treatment phases. Blood and tumour samples are collected at baseline, day 8, RES and at relapse if feasible. Faecal samples are collected at baseline and before RES. The primary endpoint is the complete pathological response rate at RES following 6 wks of neo-adj therapy. Secondary endpoints include RECIST response, metabolic response, OS, RFS, safety/tolerability, surgical outcomes, quality of life, and biomarker analyses. Clinical trial information: NCTNCT04207086. Research Sponsor: Melanoma Institute Australia and Merck.

TPS10089 Poster Session (Board #438), Fri, 8:00 AM-11:00 AM

Phase II single-arm multi-center study of adjuvant ipilimumab in combination with nivolumab in subjects with high-risk ocular melanoma. *First Author: Suthee Rapisuwon, Georgetown University, Lombardi Comprehensive Cancer Center, Washington, DC*

Background: Treatment of primary ocular melanoma is often very effective, with local recurrence rates of < 5%. However, distant recurrence is as high as 50% depending on features of the primary tumor. These data emphasize the need for effective adjuvant therapy for patients with locally treated ocular melanoma. Several adjuvant treatments have been developed for patients with high-risk cutaneous melanoma, including ipilimumab and nivolumab monotherapies and an ongoing trial is exploring the nivolumab/ipilimumab combination (CA209-915), but patients with high-risk ocular melanomas have been excluded from these trials. As yet there is no approved adjuvant treatment for high-risk ocular melanoma patients. **Methods:** We are conducting a Phase II single-arm multi-center study of adjuvant ipilimumab in combination with nivolumab in subjects with high-risk ocular melanoma. This study aims to generate efficacy and safety data for adjuvant this regimen in patients with locally treated high-risk ocular melanoma with 3-year risk of relapse > 50%. The primary endpoint is 3-year relapse-free survival rate. Secondary endpoints are median relapse-free survival, median overall survival, 3-year overall survival rate and safety. All patients will receive nivolumab 240mg IV every 2 weeks plus ipilimumab 1mg/kg IV every 6 weeks. Subjects may receive up to 25 doses of nivolumab and 8 doses of ipilimumab. The accrual goal is 50 patients across all participating institutions. Subjects treated in this study will be matched with controls selected from a contemporaneously collected OM registry, "contemporaneous control" in order to better assess efficacy. Control subjects will be from institutions not participating in this trial, will otherwise meet the trial eligibility criteria and will be further matched with trial participants for various demographic and risk factors to the extent possible. The study is enrolling in 6 comprehensive cancer centers in the US. Clinical trial information: NCT3528408. Research Sponsor: Bristol-Myers Squibb.

TPS10090 Poster Session (Board #439), Fri, 8:00 AM-11:00 AM

S1801: A randomized phase II trial of adjuvant versus neoadjuvant pembrolizumab (PEM) for melanoma. *First Author: Sapna Pradyuman Patel, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Although long term outcomes for most patients with early-stage melanoma is excellent following surgery, patients who have high-risk features such as lymph node involvement have poorer outcomes. Adjuvant therapy (AT) is currently considered for patients with stage III melanoma and selected patients with resected stage IV melanoma. Currently, AT for melanoma is anti-PD-1 or targeted therapy in the presence of a BRAF mutation. At this time we are not able to predict which patients will derive benefit from AT and experience cure. While curative surgery is the goal of early treatment of primary melanoma, some cases with bulky nodal involvement are at high risk of local or distant recurrence despite upfront surgery. Neoadjuvant treatment (NAT) offers the benefit of an early on-treatment pathological sample that can be profiled for biomarkers and correlated with survival. Treating with anti-PD1 while tumor transiently remains in the body may generate a stronger immune response from tumor-infiltrating lymphocytes against *in vivo* tumor antigens compared to the traditional adjuvant setting where antigen is presented by microscopic residual tumor burden. Pilot studies using NAT with have been initiated in melanoma. Multidisciplinary coordination in these cases is paramount. In these studies, an improvement in relapse-free survival and overall survival has been observed; additionally, pathologic response rates to NAT have been estimated in small studies. **Methods:** S1801 is a randomized phase II study of AT versus NAT with PEM (NCT03698019). Patients with measurable, clinically detectable and resectable cutaneous, acral, and mucosal melanomas without brain metastasis are eligible. Patients are randomized 1:1 to the AT or the NAT. Patients getting AT receive surgery first followed by 18 doses of PEM 200 mg IV every 3 weeks. Patients getting NAT receive 3 doses of pre-operative PEM followed by surgery and then 15 doses of adjuvant PEM. Radiation may be given on either arm after surgery, at the investigator's discretion. Primary endpoint is event-free survival measured from the date of randomization to the date of first documented progression that renders the patient unable to receive planned protocol surgery, failure to begin AT within 84 days of surgery, relapse after surgery, or death due to any cause. Safety monitoring is conducted with disease progression and toxicity thresholds. The key Translational Medicine objective of this trial is to determine the pathologic response rate to NAT with 3 doses of PEM. Enrollment is at 94 of a planned 500 patients. Clinical trial information: NCT03698019. Research Sponsor: U.S. National Institutes of Health.

10500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Randomized phase II trial of MIBG versus MIBG/vincristine/irinotecan versus MIBG/vorinostat for relapsed/refractory neuroblastoma: A report from the New Approaches to Neuroblastoma Therapy Consortium. *First Author: Steven G. DuBois, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, MA*

Background: ^{131}I-metaiodobenzylguanidine (MIBG) remains one of the most active agents for neuroblastoma. It is not clear if putative radiation sensitizers improve upon this activity. The primary aim of this trial was to identify the MIBG treatment regimen with highest response rate among: MIBG monotherapy (Arm A); MIBG/Vincristine/Irinotecan (Arm B); MIBG/Vorinostat (Arm C). The secondary aim was to compare toxicity across arms. **Methods:** We conducted a multicenter, randomized phase II trial. Patients 1-30 years with relapsed/refractory high-risk neuroblastoma were eligible with at least one MIBG-avid site and adequate autologous stem cells (ASCs). All patients received MIBG 18 mCi/kg on Day 1 and ASC on day 15. Patients on Arm A received only MIBG; patients on Arm B also received vincristine (2 mg/m^2) IV on Day 0 and irinotecan (50 mg/m^2) IV daily on Days 0-4; patients on Arm C also received vorinostat (180 mg/m^2) orally once daily on days -1 to 12. The primary endpoint was response after one course according to NANT response criteria. The trial was designed as a pick-the-winner study with a maximum of 105 eligible and evaluable patients to ensure an 80% chance that the arm with highest response rate is selected, if that response rate is at least 15% higher than the other arms. **Results:** 114 patients enrolled. Three patients were ineligible and 6 eligible patients never received MIBG, leaving 105 eligible and evaluable patients (36 Arm A; 35 Arm B; and 34 Arm C; 55 boys; median age 6.5 years). 9 patients had received prior MIBG monotherapy, 65 prior irinotecan, and 7 prior vorinostat. After one course, the response rates (Partial Response or better) on Arms A, B, and C were 17% (95% CI 7-33%), 14% (5-31%), and 32% (18-51%). An additional 4, 4, and 7 patients met NANT Minor Response criteria [partial response in one disease category (e.g., bone marrow) and stable disease in other categories] on Arms A, B, and C, respectively. On Arms A, B, and C, rates of any grade 3+ non-hematologic toxicity were 19%, 49% and 32%; rates of grade 3+ diarrhea were 0%, 11%, 0%; and rates of grade 3+ febrile neutropenia were 6%, 11%, and 0%. **Conclusions:** The combination of vorinostat/MIBG had the highest response rate, with manageable toxicity. Vincristine and irinotecan do not improve the response rate to MIBG and are associated with increased toxicity. These data provide response rates for MIBG monotherapy in a contemporary patient population assessed with current response criteria. Clinical trial information: NCT02035137. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

10501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Randomized comparisons of bevacizumab (B) and irinotecan (I), added to temozolomide (T), in children with relapsed or refractory high-risk neuroblastoma (RR-HRNB): First survival results of the ITCC-SIOPEN BEACON-Neuroblastoma phase II trial. *First Author: Keith Wheatley, University of Birmingham, Birmingham, United Kingdom*

Background: BEACON is a randomized phase 2 trial assessing whether inhibiting angiogenesis with bevacizumab adds to the activity of chemotherapy and evaluating chemotherapy regimens for children with RR-HRNB. **Methods:** Patients with RR-HRNB were eligible. There were randomizations (rand), in a 3x2 factorial design, to: T, IT or topotecan (To)-T, +/- B. Toxicity and response were reported in 2019 (ASCO, ESMO). Survival outcomes – progression-free (PFS) and overall (OS) – for the I and B rands are reported here (To rand is still open). The B rand used a relaxed alpha (1-sided p=0.2) for PFS as its phase 2 success criterion; the I rand was Bayesian. Cox model hazard ratios (HR) <1.0 indicate benefit for I or B. Heterogeneity tests (HT) assessed interactions between B and I. Analysis was intention-to-treat. **Results:** From 2013-19, 160 patients were randomized to B v. no B, including 121 to I v. no I, with: median age 5.8 years; 113 and 47 measurable and evaluable disease; 67 and 93 refractory and relapsed disease; 35 had MYCN amplification. Median follow-up was 15.4 months. PFS and OS are shown in the table. In the main comparisons (I v. no I, B v. no B), I improved PFS and OS (98% probability that true HR<1.0 for both) and B just met its success criterion (PFS: 1p=0.20; OS: 1p=0.19). However, there was some, but not conclusive, evidence of a positive interaction between B and I for both PFS (HT: p=0.06) and OS (HT: p=0.12). If real, this would suggest that adding either I (IT) or B (BT) to T does not improve outcome, but adding both (BIT) does. Twice as many patients had serious adverse events with BIT (57%) than with T (26%) or IT (27%), with BT at 40%. **Conclusions:** The BEACON results show that single agent T is suboptimal. Statistical uncertainty about an interaction between I and B means two further interpretations are possible: 1) IT and possibly BT are better than T; 2) IT and BT are not better than T, but I and B together (BIT) are better. Hence, a definitive conclusion on the best combination(s) to take forward is not currently possible and further randomized evaluation is needed. Clinical trial information: ISRCTN40708286. Research Sponsor: Cancer Research UK.

PFS and OS by treatment arm.

		2-yr survival (%)			
Randomization	**Arm**	**PFS**	**HR (95% CI)**	**OS**	**HR (95% CI)**
B (n=160)	No B (T/IT)	30	0.85	37	0.84
	B (BT/BIT)	35	(0.59-1.23)	51	(0.56-1.24)
I (n=121)	No I (T/BT)	27	0.66	34	0.63
	I (IT/BIT)	39	(0.43-1.00)	56	(0.41-0.99)
I stratified by B	T (n=31)	30	1.02	35	0.92
	IT (n=30)	24	(0.57-1.84)	38	(0.49-1.73)
BT (n=30)	24	0.45	34	0.46	
BIT (n=30)	52	(0.25-0.82)	73	(0.24-0.86)	

10502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Segmental chromosome aberrations and clinical response impact outcome of inss stage III patients ≥18 months with unfavorable histology and without MYCN amplification: A Children's Oncology Group (COG) report. *First Author: Navin R. Pinto, Seattle Children's Hospital, Seattle, WA*

Background: Patients with INSS stage III neuroblastoma represent a heterogeneous population with respect to disease presentation and prognosis and controversy exists regarding the most effective treatment algorithms. Patients ≥18 months of age with INSS Stage 3 tumors that are unfavorable histology (UH) and *MYCN*-non-amplified (*MYCN*-NA) represent a small cohort of patients with an outcome intermediate of those with favorable histology tumors and *MYCN* amplified tumors. The presence of Segmental Chromosome Aberrations (SCA) may predict outcome; however, their impact specifically in this cohort of patients has not been reported. **Methods:** Eligible patients enrolled on therapeutic protocols A3973 (n=34), ANBL0532 (n=27), and biology protocol ANBL00B1 (n=101 with 29 treated on A3973/ANBL0532) with stage III disease, *MYCN*–NA, UH and age ≥18 months at diagnosis were analyzed. Copy number alterations and loss of heterozygosity (LOH) for relevant loci were scored for gains/losses by two independent reviewers. **Results:** The 5-year EFS/OS for children ≥18 months with stage III, *MYCN*–NA, UH disease treated on A3973 and ANBL0532 was 73.0±8.1%/ 87.9±5.9% and 61.4±10.2%/ 73.0±9.2%, respectively, with no statistical differences in EFS or OS between the two cohorts (p=0.1286 and p=0.2180, respectively). In the combined cohort of patients enrolled on A3973 and ANBL0532, statistically significant differences were found (p(s) <0.0001) in patients with CR/VGPR (n=39) and PR (n=13) having better outcomes than <PR (n=5) (5-year EFS: 74.0±7.6% vs. 75.0±12.5% vs. 0%; 5-year OS: 84.4±6.2% vs. 100% vs. 20.0±17.9%). Subjects with chromosome 11q loss/LOH had an inferior outcome in comparison to those without 11q loss/LOH (10-year EFS: 44.4+/-24.1% vs. 78.1+/-9.4%, p=0.01; 10-year OS: 62.4+/-15.9% vs. 85.9+/-7.8%, p=0.02)). Patients with 1p loss/LOH and 2p gain also showed trend towards worse event-free survival (p=0.086 and p=0.088, not statistically significant) but not in overall survival. **Conclusions:** High-risk therapy that included single myeloablative therapy led to an 81.6±5.3%5-year OS in patients ≥18 months with UH and *MYCN*–NA stage III neuroblastoma. Response to therapy is a powerful predictor of survival and the presence of chromosome 11q loss/LOH is also associated with inferior outcomes. These patients should continue to be treated on high-risk clinical trials. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

LBA10503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

The pediatric precision oncology study INFORM: Clinical outcome and benefit for molecular subgroups. *First Author: Cornelis Martinus van Tilburg, Hopp Children's Cancer Center Heidelberg (KiTZ), German Cancer Research Center (DKFZ) and Heidelberg University Hospital, Heidelberg, Germany*

The full, final text of this abstract will be available at abstracts.asco.org at 5:00 p.m. ET on Thursday, May 28.

10504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase I trial of lorlatinib in patients with ALK-driven refractory or relapsed neuroblastoma: A New Approaches to Neuroblastoma Consortium study. *First Author: Kelly C. Goldsmith, Children's Healthcare of Atlanta, Emory University, Atlanta, GA*

Background: Lorlatinib, a potent ALK inhibitor, exerts unprecedented activity against neuroblastoma (NB) derived xenografts harboring common crizotinib-resistant *ALK* mutations, leading to a first in child phase I study. **Methods:** R/R NB patients (pts) > 12 months, with *ALK* mutations/amplification and prior ALK inhibitor (ALKi) treatment were eligible. Lorlatinib was administered in 28-day courses (C). For pts < 18 years, 5 dose levels (DL) (45, 60, 75, 95, 115 mg/m^2/day) were assessed. DL5 (115 mg/m^2/day) expansion is enrolling (cohort A1). For patients > 18 years, two DL (DL3a the adult RP2D of 100 mg/day and DL4a at 150mg/day) were assessed (cohort A2). Primary endpoint was dose-limiting toxicity (DLT) during C1 and neurocognitive toxicity through C2. Blood samples for circulating tumor DNA (ctDNA) were matched to radiologic restaging. **Results:** From 9/2017 to 1/2019, 33 eligible patients enrolled (13 with prior ALKi therapy), with median age (range) 5.5 years (2-17) on A1, 21.5 years (15-50) on A2. In A1, 3 pts each enrolled onto DL1-3, with no DLT's. 5/10 pts enrolled on DL4, with no DLT's. 1/3 on DL5 had a DLT of grade 3 diarrhea, with expansion ongoing. In cohort A2, 5 patients enrolled at 100 mg/day with no DLT's; 6 enrolled at 150 mg/day, with one DLT (grade 4 reversible psychosis). Most common treatment-related adverse events were weight gain (90%, grade 1-3), hyperlipidemia (90%, grade 1-3), concentration/memory impairment (23%, grade 1-2), peripheral neuropathy (13%; grade 1-2, A2 only), and peripheral edema (10%; grade 1, A2 only). Lorlatinib steady state exposure at DL3 and DL4 was in the range of exposures seen in adult lung cancer patients at the 100 mg and 200 mg DLs. In A1, 1/18 had partial response (PR), 3/18 had minor responses (MR), and 4/18 had stable disease (SD). Of pts with MR, 2/3 had PR of soft tissue and 1/3 had complete response (CR) by MIBG. In A2 pts, 1/10 had CR, 3/10 PR, and 3/10 MR; Notably, 2/3 with PR had CR by MIBG. Of the pts with MR, one had PR and one CR by MIBG. Responses occurred across dose levels, ALK mutations, and in ALKi pre-treated pts with median courses of 2 (1-24) on A1 and 10.5 (2-28) on A2. Serial ctDNA results showed mutant *ALK* variant allele frequency trajectories that correlated with clinical response and emergence of novel *ALK* mutations in *cis* that corresponded with disease progression. **Conclusions:** Inhibition of ALK-driven NB with lorlatinib occurs with manageable toxicity and objective anti-tumor activity. Prospective ctDNA allows for monitoring of disease and evolution of resistance. Clinical trial information: NCT03107988. Research Sponsor: Pfizer.

10505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Final analysis of phase I study of ceritinib in pediatric patients with malignancies harboring activated anaplastic lymphoma kinase (ALK). *First Author: Johannes H Schulte, Charite Berlin Campus Virchow-Klinikum, Berlin, Germany*

Background: Activation of anaplastic lymphoma kinase has been detected in several pediatric malignancies, including anaplastic large-cell lymphoma (ALCL), inflammatory myofibroblastic tumor (IMT), neuroblastoma and others. Preliminary findings from this phase 1, multicenter, dose-escalation study (NCT01742286) indicated a Maximum Tolerated Dose (MTD)/Recommended Dose for Expansion (RDE) of the potent oral ALK inhibitor ceritinib to be 510 mg/m^2 (fasted) and 500 mg/m^2 (fed) in pediatric patients (pts). Here, we report final safety, pharmacokinetics (PK) and efficacy results. **Methods:** Children aged ≥1 to <18 years with advanced, mostly pretreated, ALK-aberrant malignancies were enrolled in this study. Dose escalation was conducted to determine the MTD/RDE of ceritinib (primary objective), in both fasted and fed states, following which pts entered an expansion phase to evaluate safety, tolerability, and efficacy at the MTD/RDE. Secondary objectives were evaluation of safety, PK, and efficacy (overall response rate [ORR], duration of response [DOR] and progression-free survival [PFS]). **Results:** A total of 83 pts (median age, 8 years) with *ALK*-aberrant malignancies were enrolled into dose-escalation (n = 40) and expansion (n = 43) study periods. Of these, 55 pts (neuroblastoma, n = 30; IMT, n = 10; ALCL, n = 8; others, n = 7) were treated with ceritinib at MTD/RDE (510 mg/m^2 [fasted], n = 13; 500 mg/m^2 [fed], n = 42). Systemic exposure of ceritinib between the two doses was comparable, so data were pooled for efficacy assessment. The ORRs (95% CI) were 75% (34.9-96.8) for pts with ALCL, 70% (34.8-93.3) for IMT and 20% (7.7-38.6) for neuroblastoma. The median DOR was 15 months (95% CI: 5.8, 22.2) for the 6/30 pts with neuroblastoma who had confirmed CR or PR treated at fasted/fed MTD/RDE. Median DOR was not reached for those with ALCL and IMT. Most common adverse events (AEs) (N = 83; all-grades, all-causality, ≥50% of pts): vomiting (86.7%), diarrhea (78.3%), increased ALT (65.1%), increased AST (59.0%), nausea (56.6%), and abdominal pain (50.6%). Grade 3/4 AEs were observed in 80.7% of pts (mostly transaminase elevations) and were manageable. Six pts (7.2%) were discontinued from ceritinib due to a grade 3/4 AE (mostly transaminase elevation). **Conclusions:** Substantial activity was observed with ceritinib at the RDE in pts with IMT, ALCL and heavily pretreated neuroblastoma. The toxicity profile of ceritinib in children was manageable and similar to that previously reported in adults. Clinical trial information: NCT01742286. Research Sponsor: Novartis Pharmaceuticals.

10506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Dabrafenib + trametinib combination therapy in pediatric patients with BRAF V600-mutant low-grade glioma: Safety and efficacy results. *First Author: Birgit Geoerger, Gustave Roussy Cancer Center, Université Paris-Saclay, Villejuif, France*

Background: Low-grade gliomas (LGGs) are the most common brain tumors among children. Pediatric LGGs are often not surgically resectable and tend to demonstrate relapsed/remitting courses with current standard chemotherapy regimens. Moreover, radiation is often avoided due to its associated neurocognitive and endocrinologic sequelae. However, in pediatric patients (pts) with *BRAF* V600-mutant LGG, dabrafenib monotherapy has demonstrated meaningful clinical activity and acceptable tolerability (Hargrave et al, *Clin Cancer Res.* 2019; NCT01677741). Here we report the efficacy and safety of dabrafenib + trametinib (D+T) combination therapy in pediatric pts with previously treated *BRAF* V600-mutant LGG. **Methods:** This is a 4-part, open-label, multicenter, phase I/II study (NCT02124772). The limited dose-escalation (ESC) portion evaluated the D+T combination in pediatric pts (< 18 y) with recurrent/refractory *BRAF* V600-mutated solid tumors that were naive to MAPK pathway–targeted therapy. This was followed by a tumor cohort expansion (EXP), and the D+T combination was evaluated in *BRAF* V600-mutant LGG pts at recommended dose levels. Efficacy was determined by both investigator and independent review using the RANO criteria (for gliomas). Adverse events (AEs) were assessed per NCI-CTCAE v4.03. **Results:** Overall, 36 pediatric pts with LGG received D+T combination therapy (ESC, n = 16; EXP, n = 20); pooled efficacy data were available for both ESC and EXP, while LGG-specific safety data were available for EXP. At interim analysis (Aug 2019), 17 of the 20 pts in EXP remained on protocol therapy. Three pts withdrew/discontinued treatment because of AEs. Skin toxicity (95%) and pyrexia (75%) were the frequent AEs reported. No on-treatment deaths were reported. Across both ESC and EXP, the objective response rate (ORR) was 25% (95% CI, 12%–42%) per independent review (1 complete response [CR], 8 partial response [PR], 24 stable disease [SD], 2 progressive disease [PD], 1 unknown [UNK]) and 50% (95% CI, 33%–67%) per investigator review (2 CR, 16 PR, 17 SD, 1 UNK). However, ORR + SD was similar, with 92% and 97% of pts having SD or better per independent and investigator review, respectively. **Conclusions:** In pediatric pts with pretreated *BRAF* V600-mutant LGG, D+T combination therapy demonstrated clinical activity, with 92% of pts having SD or better by independent review using the RANO criteria. Pyrexia and skin toxicity were the common AEs; majority of these were low-grade and manageable. Clinical trial information: NCT02124772. Research Sponsor: Novartis.

10507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase I study of regorafenib in combination with vincristine and irinotecan in pediatric patients with recurrent or refractory solid tumors. *First Author: Michela Casanova, Pediatric Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: In pediatric patients with solid tumors, regorafenib demonstrated acceptable tolerability and preliminary anti-tumor activity. This phase 1 study evaluated regorafenib in combination with vincristine/irinotecan in pediatric patients with rhabdomyosarcoma (RMS) and other solid tumors. **Methods:** Patients with relapsed/refractory tumors received intravenous vincristine (1.5 mg/m^2, Days 1 and 8) and irinotecan (50 mg/m^2/day, Days 1–5) plus once-daily oral regorafenib (patients 6– < 24 months: 60 mg/m^2 escalating to 65 mg/m^2; patients 2– < 18 years: 72 mg/m^2 escalating to 82 mg/m^2) on either Days 1–14 (concomitant dosing) or Days 8–21 (sequential dosing) during each 21-day cycle. As per protocol, at least 50% of patients were required to have RMS. **Results:** At the time of the cut-off, of 21 treated patients (RMS, n = 12; Ewing sarcoma, n = 5; neuroblastoma, n = 3; Wilms tumor, n = 1), two had concomitant (72 mg/m^2) and 19 had sequential (72 mg/m^2, n = 6; 82 mg/m^2, n = 13) dosing. Median age was 10 years (1.5–17.0). Patients received a median of 3 cycles (1–17); dose reductions of irinotecan occurred in 62% of patients. Grade 3 dose-limiting toxicities were reported in both patients receiving concomitant dosing (peripheral neuropathy and liver injury; pain, vomiting, febrile aplasia) and one patient each in the sequential groups (rash and elevated AST; thrombocytopenia). Concomitant dosing was discontinued. The maximum tolerated dose and recommended phase 2 dose (RP2D) of regorafenib in the sequential combination was 82 mg/m^2. The most common grade ≥3 treatment-emergent adverse events were neutropenia (71%), thrombocytopenia (33%), leukopenia (29%), anemia (24%), and ALT increased (24%). The response rate was 38%, including 1 complete (RMS) and 7 partial responders (5 RMS, 2 Ewing sarcoma); 3 of whom had prior irinotecan. Six (4 with alveolar subtype) of 12 patients with RMS had a response. Nine patients (43%) had stable disease (maximum duration 17 cycles). After the cut-off, partial response was reported for two additional patients (1 RMS, 1 Ewing sarcoma). **Conclusions:** Regorafenib can be combined at its single agent RP2D of 82 mg/m^2 with standard-dose vincristine/irinotecan (with appropriate dose modifications) in pediatric patients with refractory/relapsed solid tumors in a sequential dosing schedule. Clinical activity was observed in patients with sarcoma. Clinical trial information: NCT02085148. Research Sponsor: Bayer.

10508 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase II study of antidisialoganglioside antibody, dinutuximab, in combination with GM-CSF in patients with recurrent osteosarcoma (AOST1421): A report from the Children's Oncology Group. *First Author: Pooja Hingorani, MD Anderson Cancer Center, Houston, TX*

Background: Treatment of patients with recurrent osteosarcoma (OS) is challenging and novel effective therapies are urgently needed. This study evaluated disease control rate (DCR) in patients with recurrent pulmonary OS, when treated with dinutuximab plus cytokine therapy as compared to a historical benchmark. The rationale for dinutuximab was the ubiquitous (> 95%) GD2 positivity in OS tumors and cell lines. **Methods:** AOST1421 was a single-arm phase 2 study. Patients with recurrent pulmonary OS in complete surgical remission were eligible. Patients received five cycles of dinutuximab 70mg/m^2/cycle with GM-CSF. Two different dinutuximab infusion schedules were used - 35mg/m^2/day over 20 hours (2-day) and 17.5mg/m^2/day over 10 hours (4-day) schedule. Primary end point was DCR, defined as proportion of patients event-free at 12 months from enrollment. Events were progressive disease or death within 12 months attributed to treatment or progression. The historical benchmark was AOST0221 with a 12-month DCR of 20% (95% CI 10-34%). Success was defined as ≥16/ 39 patients (> 40%) event-free at 12 months from enrollment. Secondary objectives included toxicity evaluation and dinutuximab pharmacokinetics (PK). **Results:** Forty-one patients were enrolled from Nov 2015 - Jan 2018. Thirty nine were eligible and evaluable (age 7-26 yr; median 15 yr). Data current to December 31, 2019 was used for analysis. Accrual rate was higher than expected (22.1 vs. 19.2 patients/ yr.) despite a concurrently open competing study. One of 136 administered therapy cycles met criteria for unacceptable toxicity when one patient receiving the 2-day schedule died after cycle 2 due to an unknown cause, attributed as probably related to protocol therapy. The protocol was revised to allow only the 4-day schedule. Other ≥ Grade 3 toxicities occurring in > 10 % participants were expected dinutuximab toxicities such as pain, diarrhea, hypoxia and hypotension. Dinutuximab did not demonstrate sufficient evidence of efficacy as 27/ 39 patients experienced an event for a DCR of 30.7% (95% CI 17- 47%). PK studies are pending and will be reported. **Conclusions:** Dinutuximab toxicity in adolescent and young adult OS patients was similar to younger patients. While GD2 remains a relevant target in OS, combination of dinutuximab with GM-CSF did not meet the targeted successful DCR in patients with completely resected tumor. Other strategies for targeting GD2 or dinituximab combination therapy may still be warranted. Clinical trial information: NCT02484443. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

10509 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Outcomes with reduced intensity therapy in a low-risk subset of children with National Cancer Institute (NCI) standard-risk (SR) B-lymphoblastic leukemia (B-ALL): A report from Children's Oncology Group (COG) AALL0932. *First Author: Reuven J. Schore, Children's National Health System and George Washington University School of Medicine and Health Sciences, Washington, DC*

Background: Post-hoc analysis of COG P9904 identified a low risk (LR) group of SR B-ALL patients aged 1-9.99 years with WBC < 50,000/μL, no CNS3, and either *ETV6/RUNX1* or double trisomies (DT) of chromosomes 4 and 10 with day 8 peripheral blood (PB) and day 29 marrow (BM) minimal residual disease (MRD) < 0.01% who had a 5-year event-free survival (EFS) of 97±2% and overall survival (OS) 98.8±0.8%. Outstanding results were also obtained for LR patients on COG AALL0331 using CCG-based ALL therapy. AALL0932 tested prospectively whether LR B-ALL patients could attain a 5-year EFS ≥95% with these regimens. **Methods:** Following a 3-drug induction, eligible AALL0932 LR patients had NCI SR B-ALL (no testicular leukemia, unfavorable genetics or Down syndrome) with DT or *ETV6/RUNX1* fusion, CNS1, no steroid pre-treatment, with Day 8 PB and Day 29 BM MRD < 0.01%. Between 2010-16, 603 LR patients were randomized to P9904-based regimen LR-M (n = 301) or CCG 1991/COG AALL0331-based regimen LR-C (n = 302). LR-M included 6 24-hour infusions of 1 gm/m^2 of methotrexate (MTX) with leucovorin rescue, but no anthracyclines or alkylating agents. Maintenance followed with daily 6-mercaptopurine (6-MP) and weekly oral MTX, and every 16 week 7-day pulses of dexamethasone (DEX) with vincristine (VCR) on days 1 and 8. Boys and girls were treated for 2.5 years from diagnosis. LR-C had no 24-hour MTX infusions, but included 2 Interim Maintenance (IM) phases with VCR and escalating IV MTX without leucovorin rescue given every 10 days for 5 doses, flanking an 8-week Delayed Intensification (DI) phase that included DEX, VCR, pegasparagase, doxorubicin (75 mg/m^2), cyclophosphamide (1 gm/m^2) and 8 doses of low-dose cytarabine (75 mg/m2/dose). LR-C Maintenance included daily 6-MP and weekly oral MTX with 5-day pulses of DEX and 1 dose of VCR given every 12 weeks. Girls received 2 years and boys 3 years of therapy from the start of IM I. **Results:** Both regimens achieved outstanding outcomes: 5-yr disease-free survival (±SE) 98.8%±0.8% for LR-M and 98.5%±0.9% for LR-C (p = 0.67). Both had 5-yr OS 100%. Therapies were well tolerated with higher rates of mucositis (12.9 vs 6.3%; p = 0.008) and allergic reactions (2.3% vs 0%; p = 0.02) on LR-C. **Conclusions:** AALL0932 demonstrated that application of stringent risk criteria can identify a favorable B-ALL subgroup almost certain to be cured with either LR-M or LR-C, allowing physicians and families to select the optimal treatment approach in the future. Clinical trial information: NCT01190930. Research Sponsor: U.S. National Institutes of Health, Other Foundation, Pharmaceutical/Biotech Company.

10510 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Outcomes in children with Down syndrome (DS) and B-lymphoblastic leukemia (B-ALL): A Children's Oncology Group (COG) report. *First Author: Karen R. Rabin, Texas Children's Cancer Center, Houston, TX*

Background: Patients with DS and B-ALL experience increased rates of relapse and toxicities. Here, we report results from 4 COG trials (2003-2018). **Methods:** We analyzed clinical, and outcome data for DS (n = 743) and non-DS (n = 21,703) patients age 1-30 enrolled on standard-risk (SR) trials AALL0331 and AALL0932 and high-risk (HR) trials AALL0232 and AALL1131. Initially, DS-ALL patients on AALL0232/AALL0331 experienced excess mortality, prompting enhanced supportive care and omission of induction anthracycline except for slow responders on AALL1131. Other modifications included: non-random assignment to treatment strata without investigational agents; leucovorin rescue after intrathecal methotrexate (MTX); equal maintenance length for boys and girls; every 12-week maintenance vincristine/steroid pulses; and reduced anthracycline and intravenous MTX for HR patients. **Results:** Across all 4 trials, DS and non-DS patients did not differ significantly in age, sex, initial WBC, or CNS status. DS-ALL patients had significantly higher end of induction (EOI) minimal residual disease (MRD) vs non-DS patients on both AALL0932 and AALL1131, but the difference persisted at end of consolidation (EOC) only on AALL1131, with fewer EOI MRD+ DS patients achieving EOC MRD < 0.01% (76.1 vs 88.0%, p = 0.001). 5-year EFS and OS were significantly poorer for DS vs non-DS across all trials (EFS 79.6+2.1% vs 86.3+0.3%, p < 0.0001; OS 86.5+1.8% vs 93.1+0.2%, p < 0.0001), as well as on each individual trial. In Cox regression analysis for all DS patients, inferior EFS was associated with several known risk factors (age > 10, EOI MRD >0.01%) but not with cytogenetics or CRLF2 status Induction death was more frequent in DS patients (3.4% vs 0.8%, p < 0.0001) as was death in remission (4.8+0.8% vs 1.8+0.1%, p < 0.0001). For death in remission, the increased frequency occurred pre-maintenance and in patients taken off protocol therapy, but not during maintenance, in contrast to prior reports. Grade >3 mucositis, infections, and hyperglycemia were significantly more frequent in DS patients on all trials. Grade >3 seizures were significantly more frequent in DS patients on HR but not SR trials (4.1% vs 1.7%. p = 0.001) and occurred in all phases pre-maintenance. **Conclusions:** Patients with DS and B-ALL continue to have inferior outcomes compared to non-DS, with increased relapse and toxicities. Less toxic approaches such as immunotherapies and targeted therapies hold promise to improve outcomes in both these areas. Research Sponsor: U.S. National Institutes of Health.

10511 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

CD19-targeted chimeric antigen receptor (CAR) T cells in CNS relapsed acute lymphoblastic leukemia (ALL). *First Author: Haley Newman, Children's Hospital of Philadelphia, Philadelphia, PA*

Background: CNS relapse of B-ALL is difficult to treat after cranial radiation or multiple relapses. Durable remissions of relapsed/refractory (r/r) B-ALL have been seen with CD19 CAR T cells; however, most trials excluded patients with active CNS disease. As we observed CAR trafficking into the CSF, we hypothesized that CD19 CAR T cells could control CNS B-ALL. **Methods:** We identified children and young adults with r/r CNS B-ALL treated on 4 clinical trials of CD19 CAR T cells, CTL019 or CTL119. NCT01626495 and NCT02435849 excluded active CNS disease, while the former in an amendment as well as NCT02374333 and NCT02906371 permitted active CNS disease controlled on therapy. All trials permitted CNS disease that cleared and excluded bulky intracranial disease that did not improve. We analyzed outcomes (CR, RFS) and safety. **Results:** We identified 65 patients 1-29y (median 10y) with r/r CNS B-ALL (CNS+) of 182 treated with CTL019/CTL119. There were no differences in age, sex, history of SCT or neurologic comorbidities in the CNS+ and CNS- cohorts. CNS+ patients were more likely to be in ≥2nd relapse (74% vs 46%, p < 0.01), to have received cranial radiation (58% vs 11%, p < 0.01), to have detectable CNS disease (p = 0.02) and less bone marrow disease pre-infusion (p < 0.01). At 1 mo post infusion, 62 (95%) CNS+ and 110 (94%) CNS- patients were in CR; 1 in each cohort died of sequelae of CRS and was inevaluable for response. All patients with CNS disease detected pre-infusion cleared by mo 3, including 9 in the CNS+ cohort [5 CNS2 (< 5 CSF WBC with blasts), 4 CNS3 (> 5 CSF WBC with blasts or exam/imaging evidence)] and 8 in the CNS- cohort (isolated CNS2 status pre-infusion). There was no difference in RFS (p = 0.28) in the CNS+ and CNS- cohorts [24-mo RFS: 61% (95% CI 46-73%) and 60% (95% CI 48-70%)]. There were 4 CNS relapses in the CNS+ cohort, and 1 in the CNS- cohort. Encephalopathy rate and grade was similar in the CNS+ and CNS- cohorts (52% vs 40% any grade; 12% vs 11% grade 3/4; p = 0.41). There were no deaths due to neurotoxicity (NT) and no statistically significant differences in incidence or severity of any NT or CRS in the CNS+ and CNS- cohorts. **Conclusions:** The CD19 CAR T cell therapies CTL019/CTL119 are effective at clearing CNS disease and inducing durable remissions in children and young adults with r/r CNS B-ALL. CNS relapse rates are low (< 3%). Most CD19 CAR T cell trials excluded patients with active CNS disease, primarily due to the risk of NT. We show that patients with r/r CNS B-ALL that is adequately controlled prior to infusion can be safely treated with CD19 CAR T cells, with no increased risk of NT. Clinical trial information: NCT01626495, NCT02435849, NCT02374333, NCT02906371. Research Sponsor: None.

10512 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Temsirolimus combined with etoposide and cyclophosphamide for relapsed/refractory acute lymphoblastic leukemia: Therapeutic advances in Childhood Leukemia Consortium (TACL 2014-001) trial. *First Author: Susan R. Rheingold, Children's Hospital of Philadelphia/Perelman School of Medicine, Philadelphia, PA*

Background: PI3K/mTOR signaling, a critical pathway in cell proliferation, metabolism, and apoptosis, is often dysregulated in acute lymphoblastic leukemia (ALL). A phase 1 trial of the mTOR inhibitor temsirolimus combined with etoposide and cyclophosphamide was performed in children with relapsed/refractory (r/r) ALL. **Methods:** Temsirolimus was administered intravenously (IV) on days 1 and 8 with cyclophosphamide 440 mg/m2 and etoposide 100 mg/m2 IV daily days 1-5. The starting dose level (DL) of temsirolimus was 7.5 mg/m^2 (DL1) with escalation to 10 mg/m^2 (DL2), 15 mg/m^2 (DL3), and 25 mg/m^2 (DL4). MRD was performed centrally. PI3K pathway inhibition was measured by phosphoflow cytometry (PFC) analysis of peripheral blood (PB) from treated patients (pts). **Results:** Sixteen heavily pretreated r/r ALL pts ages 2-19 years with marrow blasts $>$ 25% were enrolled; 15 were evaluable [10 B-ALL/5 T-ALL]. One dose-limiting toxicity (DLT) of grade (Gr) 4 pleural and pericardial effusions with pneumonitis/lung infection leading to Gr 5 cardiorespiratory arrest occurred in a pt treated at DL3. No further DLTs were seen in the DL3 expansion and DL4 cohorts. Gr 3/4 non-hematologic toxicities occurring in $\geq$ 3 pts included febrile neutropenia, elevated ALT, hypokalemia, mucositis, and tumor lysis syndrome and were independent of dose. Of 15 evaluable pts, 4 (27%; 2 B-ALL/2 T-ALL) had a complete response (CR) after cycle 1, comprised of 1 pt at each DL. Three had MRD $<$ 0.01%. Three pts (20%; 2 B-ALL/1 T-ALL) had partial response (PR). Overall response rate (CR+PR = ORR) was 47%. Pharmacodynamic PFC studies compared phosphoprotein levels pre (day 0) and post treatment (days 3-5) in 9 consenting pts with available PB. All tested pts showed basal activation of PI3K pathway signaling. Dose-dependent inhibition of mTOR targets phosphorylated (p) S6 and/or p4EBP1 was observed in 9/9 and 6/9 pts, respectively, following temsirolimus and chemotherapy treatment. Various patterns of compensatory upregulation of pPI3K, pmTOR, pAkt, and/or pERK was observed. **Conclusions:** Temsirolimus at 25 mg/m^2 combined with salvage etoposide and cyclophosphamide has an acceptable safety profile in high-risk pediatric patients with r/r ALL. Responses were observed at all DLs. mTOR target inhibition was achieved and appeared to correlate with dose level. Future testing of other PI3K/mTOR pathway inhibitors in combination with chemotherapy may be warranted with a goal of further increasing response in r/r ALL. Clinical trial information: NCT01614197. Research Sponsor: Pfizer IIB mechanism, Other Foundation.

10513 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Dexrazoxane and heart function among long-term childhood cancer survivors: A Children's Oncology Group study. *First Author: Eric Jessen Chow, Fred Hutchinson Cancer Research Center, Seattle, WA*

Background: Dexrazoxane (DRZ) has cardioprotective effects among doxorubicin (DOX) treated childhood cancer survivors up to 5 years after therapy. However, longer-term data are lacking. **Methods:** P9404, P9425, P9426, and DFCI 95-01 were randomized trials of acute lymphoblastic leukemia and Hodgkin lymphoma, where patients were randomly assigned to DOX$\pm$DRZ. P9754 enrolled osteosarcoma patients who all received DOX+DRZ. In all studies, DRZ was given as an intravenous bolus before DOX (10:1mg ratio). DOX doses ranged from 100-600 mg/m^2 across these 5 trials. A subset of COG institutions prospectively assessed cardiac function in long-term survivors from these trials, plus a matched group of osteosarcoma survivors treated with DOX alone. Echocardiograms (left ventricular [LV] Biplane ejection fraction [EF], shortening fraction [SF]) and blood biomarkers (b-type natriuretic peptides [BNP], N-terminal [NT] proBNP) were all analyzed centrally, with DRZ status masked. Lower LV function was defined as EF$<$50% or SF$<$30%. T-test, rank-sum, and multivariate regression adjusted for sex, cancer diagnosis age, current age, DOX dose, and chest radiotherapy were used to examine differences and associations by DRZ status. **Results:** Among 173 participants assessed (52% DRZ+; 54% male; mean DOX 294$\pm$96 mg/m^2) 17.6$\pm$2.4y since cancer diagnosis, DRZ+ participants were slightly younger (27.8 vs 29.6y, p=0.02), but baseline characteristics otherwise did not differ significantly by DRZ status. DRZ status was associated with higher FS (34.7$\pm$3.6% vs 33.4$\pm$4.3%, p=0.04) and EF (63.4$\pm$5.4% vs 61.4$\pm$5.5%, p=0.01), and lower BNP (median 10.4 pg/mL [IQR 6.0-18.0] vs 13.0 [IQR 6.0-28.2], p=0.03) and NT-proBNP (median 30.8 pg/mL [IQR 18.9-58.2] vs 47.1 [IQR 23.0-83.1], p$<$0.01). In stratified analyses, the cardioprotective effects associated with DRZ tended to be more pronounced in females (vs males) and those who received DOX $\geq$300 mg/m^2 (vs $<$300mg/m^2). Results from multivariate models were similar: DRZ was associated with higher SF (1.4% [95% CI 0.2, 2.6]) and EF (2.7% [95% CI 0.8, 4.6]), and reduced BNP (-4.0 pg/mL [95% CI -7.6, -0.4]) and NT-proBNP (-20.7 pg/mL [95% CI -33.5, -7.9]). Overall, DRZ was associated with a reduced risk of having lower LV function (odds ratio 0.27 [95% CI 0.08-0.96]). **Conclusions:** After $>$17y, childhood cancer survivors treated with DOX+DRZ had better LV systolic function and less myocardial wall stress compared with those treated with DOX alone. DRZ may preferentially benefit females and those treated with greater DOX doses. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

10514 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Cardiomyopathy risk among childhood cancer survivors of African ancestry and its molecular mechanisms. *First Author: Yadav Sapkota, St. Jude Children's Research Hospital, Memphis, TN*

Background: Cardiomyopathy occurs at significantly higher rates in survivors of childhood cancer than the general population, but few studies have evaluated racial/ethnic disparities. Utilizing whole-genome sequencing data in the St. Jude Lifetime Cohort (SJLIFE), we previously identified two risk loci on chromosomes 1 (rs6689879) and 15 (rs9788776) for ejection fraction (EF) and cardiomyopathy in survivors of African ancestry. The rs6689879*C was associated with 4.2% reduction in EF and 21.6-fold risk of cardiomyopathy and the rs9788776*G was associated with 5.6% reduction in EF and 46.8-fold risk of cardiomyopathy. However, molecular mechanisms behind these genetic associations are unknown. **Methods:** We assessed the risk of clinically-assessed/graded (per the National Cancer Institute Common Terminology Criteria for Adverse Events) cardiomyopathy in childhood cancer survivors of African ancestry (n = 301) by comparing them with those of European ancestry (n = 1870), adjusting for known cardiovascular risk factors including hypertension, abnormal glucose metabolism, hypercholesteremia, hypertriglyceridemia, sedentary behavior, risky alcohol drinking and smoking. Molecular mechanisms underlying the chromosome 1 locus was investigated using DNA methylation data in 265 SJLIFE survivors of African ancestry and gene expression profiles in human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) of breast cancer patients. **Results:** Multivariable analysis showed survivors of African ancestry had 1.46-fold (P= 0.067) and 2.43-fold (P= 0.0039) higher risks of grade 2-4 and grade 3-4 cardiomyopathy. Results from DNA methylation data showed rs6689879*C was correlated with hypomethylation of a probe (cg16996019) located within the promoter region of *PHTF1* (β = -0.10; P= 0.0014). Notably, the cg16996019 was also hypomethylated in survivors with cardiomyopathy (β = -0.15; P= 0.0028). These observations were further supported by upregulation (β = 0.45; P= 0.028) of *PHTF1* in hiPSC-CMs samples derived from doxorubicin-exposed breast cancer patients with and without experiencing cardiotoxicity (n = 3 each). **Conclusions:** Childhood cancer survivors of African ancestry are at higher risk of cardiomyopathy than those of European ancestry. Dysregulation of *PHTF1* may represent the molecular mechanism underlying the rs6689879-cardiomyopathy association. These findings have potential implications for long-term cardiac surveillance as well as up front cancer care for patients of African descent. Research Sponsor: U.S. National Institutes of Health, the Leukemia and Lymphoma Society and the American Lebanese Syrian Associated Charities, Memphis, Tennessee.

10515 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Underdiagnosis and undertreament of modifiable cardiovascular risk factors: A Childhood Cancer Survivor Study (CCSS) report. *First Author: Eric Jessen Chow, Fred Hutchinson Cancer Research Center, Seattle, WA*

Background: Survivors of childhood cancer exposed to cardiotoxic therapies are at increased risk of heart disease. Hypertension, dyslipidemia, and diabetes are modifiable cardiovascular risk factors (CVRFs) that synergistically increase this risk. Therefore, we aimed to determine the prevalence of and predictors associated with CVRF underdiagnosis and undertreatment in this population. **Methods:** CCSS participants at increased risk of heart disease due to prior cancer therapy were enrolled in an ongoing randomized intervention trial (NCT03104543) to improve CVRF identification and treatment. Participants completed a baseline survey (CVRF status, lifestyle habits, attitudes towards healthcare), anthropometry, and blood draw. Blood pressure, low density lipoprotein, triglyceride, glucose and Hgb A1c were measured and classified as normal/abnormal per standard clinical criteria. Multivariable logistic regression estimated odds ratios (OR [95% confidence intervals]) associated with predictors and risk of CVRF underdiagnosis and undertreatment. **Results:** As of January 2020, 522 participants (43% male) were available for analysis (47% response), with a median age 38y (range 20-65) and 28y (18-49) from original cancer treatment (75% anthracycline, 47% chest radiation). With mean measured BMI 27.3$\pm$6.5 kg/m^2, self-reported prevalence rates were hypertension 27%, dyslipidemia 33%, and diabetes 9%. While 90% of participants had a routine check-up $\leq$2y ago, 58% had a measured CVRF in the abnormal range. Specifically, among previously undiagnosed participants, we observed rates of abnormal blood pressure (26%), lipids (17%), and glucose tolerance (27%). Among those with pre-existing hypertension, dyslipidemia, and diabetes, 11%, 49%, and 54%, respectively, had measurements outside of the usual therapeutic target range. In multivariable analysis, BMI $\geq$25 kg/m^2 (vs $<$ 25) was associated with risk of underdiagnosis (OR 1.8 [1.2-2.8]). For undertreatment, significant adverse factors included older age ($>$ 35 vs $\leq$35y: OR 2.5 [1.2-5.1]), BMI $\geq$30 kg/m^2 (vs $<$ 25: OR 3.3 [1.7-6.4]), and greater perceived reliance on others for healthcare decisions (OR 1.7 [1.2-2.4]). Those with greater health-related self-efficacy were less likely to be undertreated (OR 0.5 [0.3-0.96]). **Conclusions:** CVRF underdiagnosis and undertreatment among childhood cancer survivors at increased risk of heart disease was common. Greater awareness among survivors and primary care providers and more aggressive control of CVRFs may mitigate this risk. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

10516 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Activity of front-line window therapy with temozolomide plus irinotecan in patients with primary multifocal Ewing sarcoma: ISG/AIEOP EW-2 protocol. *First Author: Asaftei Dorin Sebastian, Pediatric Onco-Hematology, A.O.U Città della Salute e della Scienza, University of Turin, Turin, Italy*

Background: The prognosis of patients with primary multifocal metastatic Ewing sarcoma (PMES) remains dismal. So far, combination with temozolomide and irinotecan (TEMIRI) was tested in patients with refractory or relapsed disease. This study evaluates the activity and the tolerability of TEMIRI as front-line treatment in PMES. **Methods:** In the study-period 2012-2018, a front-line window therapy with 2 courses TEMIRI (temozolomide 100 mg/sqm/day + irinotecan 50 mg/sqm/day for 5 days every three weeks) was introduced as amendment to the ISG/AIEOP EW-2 protocol *(EUDRACT#2009-011197-15,* Vers. 1.02*)* for patients with PMES. Main objective was to test the activity of TEMIRI evaluated by RECIST 1.1 criteria, with centralized revision of the radiological response. Secondary objectives included assessment of the toxicity profile and clinical benefit of the combination. A two-step study design by Simon was planned. **Results:** Thirty-four patients were enrolled. Median age at diagnosis was 19 years (range 3-55); males/females ratio was 2.4. Primary axial tumour was present in 24 (70%). After TEMIRI, RECIST response was as follows: partial response -20 (59%), stable disease -11 (32%), progression disease -3 (9%). After TEMIRI, amelioration in ECOG/Lansky score was achieved in 25/34 (73,5%), and reduction or disappearance of pain was observed in 31/34 patients (91%). TEMIRI toxicity was manageable: incidence of grade 3-4 nonhaematological and haematological toxicity was 3% and 3%, respectively (67/68 evaluable courses). At the time of the present analysis, 11 patients are alive; 7 of them are in complete remission and completed their treatment program (5-drug standard chemotherapy). With a median follow-up of 31 months (range 23-75), the 3-year survival estimate is 36,5%±0.09. **Conclusions:** Upfront TEMIRI x 2 courses showed an encouraging activity, with response rate 59% and deserves further evaluation combined with conventional treatments also in non-metastatic patients. In PMES new treatment strategies are urgently needed. Clinical trial information: NCT02727387. Research Sponsor: None.

10517 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Maintenance therapy with oral cyclophosphamide plus celecoxib in patients with metastatic Ewing sarcoma: Results of the Italian Sarcoma Group/AIEOP EW-2 study. *First Author: Nadia Puma, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: The prognosis of patients with metastatic Ewing sarcoma remains poor. The primary aim of the ISG/AIEOP EW2 Study (EUDRACT#*2009-011197-15*) was to evaluate the feasibility and efficacy of maintenance therapy with oral cyclophosphamide plus celecoxib. **Methods:** From June 1st 2009 to Nov 22nd 2019, 112 patients with metastatic Ewing sarcoma at onset entered the ISG/AIEOP EW2 study, consisting of induction chemotherapy, radiotherapy and/or surgery at the site of the primary tumor, a consolidation phase with high-dose busulphan/melphalan + autologous stem cell rescue, whole-lung irradiation (12-15Gy), and a maintenance phase of 180 days with cyclophosphamide 50 mg daily (35 mg/mq daily if age $<$ 14 years) plus celecoxib 400 mg twice daily (250 mg/mq twice daily if age $<$ 14 years). Exclusion criteria from the maintenance phase were disease progression, cardiac or gastro-intestinal comorbidity. For CTCAE v4.0 grade 3-4 toxicities a temporary interruption was planned. **Results:** Seventy-one patients were eligible and entered the maintenance phase. Median age was 16 years (range 13-41); sites of metastases were lung or single bone (n = 56) and multicentric metastatic spread (n = 15). Sixty-one patients terminated the maintenance phase, 4 patients are still on treatment, 1 patient interrupted the treatment due to auto-immune thrombocytopenia at 4 months, 5 patients were withdrawn throughout maintenance due to disease progression/relapse. The duration of maintenance therapy was 89% of the scheduled days, with a median suspension length of 12 days (range 1-44 days). Causes of temporary suspension were hematological toxicity (19 episodes), infections (12 episodes), gastrointestinal disorders (9 episodes), fluid retention/distal oedema (3 episodes), renal disorders (3 episodes). Median follow-up was 42 months. The 3-year EFS of patients who entered the maintenance phase was 0.79 $\pm$ 0.09 for lung or single bone, and 0.19 $\pm$ 0.11 for those with multicentric metastatic spread. **Conclusions:** This schedule of maintenance phase is feasible, despite previous intensive treatment. A longer follow-up is needed to monitor side effects and to evaluate clinical outcome of patients with lung or single bone metastases, while the outcome remains dismal for multicentric metastatic Ewing sarcoma. Clinical trial information: NCT02727387. Research Sponsor: None.

10518 Poster Discussion Session; Displayed in Poster Session (Board #405), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Tisagenlecleucel (Tisa) for relapsed/refractory (r/r) acute lymphoblastic leukemia (ALL): B2001X study focusing on prior exposure to blinatumomab (BLINA) and inotuzumab (INO). *First Author: Joerg Krueger, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada*

Background: B2001X (NCT03123939) is a multicenter global study of tisa to provide access to patients (pts) with r/r ALL including prior anti-CD19 therapy after enrollment ended in the pivotal ELIANA (NCT02435849) study. We report clinical outcomes and cellular kinetics in B2001X including pts with prior BLINA exposure or INO as bridging therapy (BT). **Methods:** Eligible pts ≤21 y at diagnosis with ≥2 relapse, refractory or post allogeneic transplant (alloSCT) relapse were enrolled globally. **Results:** As of Nov 4, 2019, 73 pts were enrolled; 67 received tisa. 91% received lymphodepletion. Among 65 pts ≥3 mo follow up (FU) or discontinued earlier (efficacy analysis set [EAS]) median FU was 9.6 mo (range [R] 0.2-16.5). Median age 10 y (R 2-33); prior alloSCT 61%; 15 pts had prior BLINA and 9 pts had INO as BT. Efficacy is summarized in Table. 13/14 relapsed pts were medullary (isolated or combined with extramedullary [EM]) and 1 EM; 9 within 6 mo including 4/5 who were CD19(+). 64% had CRS (G 3/4 13%/15%; Penn scale); 24% had neurologic events (G 3/4 9%/2%; CTCAE v4.03). 4 deaths ≤30 d: 2 early ALL progression, 1 fatal CRS with refractory ALL, 1 infection with multiorgan failure. Transgene level in peripheral blood: limited to no in vivo expansion in nonresponders (n=8) vs responders (n=42). Median duration of persistence (T last) of tisa was 272 d (R 27-379) in responders. In pts with CR/CRi, C_{max} (geo-mean [CV%]) and median T last were 9260 (124) copies/µg DNA and 154 d (R 28-349), respectively, in pts who received INO as BT (n=6) vs 38,500 (215) and 273 d (R 27-379), respectively, in pts with no INO as BT (n=36). **Conclusions:** Outcomes in B2001X remain consistent with ELIANA. In pts with prior BLINA or INO as BT, a trend toward suboptimal outcomes was observed but should be interpreted with caution due to small n, short FU and potential confounding factors. Clinical trial information: NCT03123939. Research Sponsor: Novartis.

Efficacy summary.

	Prior BLINA n=15	No Prior BLINA n=50	INO as BT n=9	No INO as BT n=56	All Pts in EAS n = 65 (Except for OS, N=67)
CR+CRi ≤3 mo, n (%) (95% CI)	10 (67) (38-88)	45 (90) (78-97)	6 (67) (30-93)	49 (88) (76-95)	55[a] (85) (74-92)
MRD (–) in CR/CRi pts, %	100	95	100	95	96
DOR	Not reached (NR)	NR	NR	NR	NR
DOR, % (95% CI)					
Mo 6	88 (39-98)	82 (66-91)	67 (20-90)	86 (70-93)	83 (69-91)
Mo 9	70 (23-92)	75 (57-86)	67 (20-90)	76 (58-87)	74 (57-85)
12 mo OS, % (95% CI)	53 (19-78)	91 (74-97)	71 (23-92)	85 (69-93)	83 (69-92)
Relapse in pts with CR/CRi at any time, n	2	12	4	10	14
CD19 status at relapse, n (–)/n (+)	2/0	7/5	1/3	8/2	9/5

[a]3 pts with no CR/CRi, 5 early progression, 2 deaths precluding disease evaluation.

10519 Poster Discussion Session; Displayed in Poster Session (Board #406), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Evaluation of CD22 modulation as a mechanism of resistance to inotuzumab ozogamicin (InO): Results from central CD22 testing on the Children's Oncology Group (COG) phase II trial of INO in children and young adults with CD22+ B-acute lymphoblastic leukemia (B-ALL). *First Author: Nirali N. Shah, Pediatric Oncology Branch, National Cancer Institute, Bethesda, MD*

Background: The COG AALL1621 phase 2 trial evaluated the efficacy of InO in children and young adults with relapsed/refractory CD22+ B-cell ALL. We report results of central surface CD22 expression on ALL and impact on response. **Methods:** Optional central CD22 testing was performed on bone marrow and/or peripheral blood at the NCI flow cytometry (FC) laboratory pre/post cycle 1. Percentage of blasts with CD22+ expression (CD22%) was measured by multiparameter FC and the BD Biosciences QuantiBRITE system quantified the CD22 site density by measuring CD22 antibody bound per cell (ABC). Comparison of ABC and CD22% between subgroups was based on Wilcoxon rank sum test or signed rank test as appropriate. Post-treatment CD22 assessments could only be performed on those with residual ALL. **Results:** Amongst 48 patients, 28 (58.3%) achieved a complete response (CR) or CR with incomplete count recovery. The median CD22 ABC, pre and post-cycle 1, was 2688 (range, 290-10715, n = 33) and 1098 (184-6822, n = 15) respectively. Amongst 27 subjects with paired pre/post samples, median pre-treatment CD22 ABC was lower in those with residual ALL (n = 13) than in those without residual ALL (ABC 1005 (290-8848) vs ABC 4123 (762-10715), p = 0.003). Baseline CD22% ranged more widely in those with residual ALL, median 99% (40-100%) vs. 99% (92.9-100%, no residual ALL) p = 0.025; and significant decreases in CD22% were seen compared to baseline in those with residual ALL, with median post-treatment CD22% 82% (1.4%-100%), p = 0.007. Amongst 3 subjects with baseline partial CD22% (40%, 79% and 83% partial CD22+ populations), post-cycle 1 evaluations revealed emergence of predominantly CD22 negative populations (6.5%, 34% and 48% CD22+, respectively), precluding eradication of minimal residual disease. Amongst those with *KMT2A* rearrangement, 2 of 4 had partial CD22 expression and 4 of 4 had low ABC ($<$ 1500). **Conclusions:** Baseline CD22 expression, specifically low CD22 ABC and partial CD22% were significantly associated with response to treatment, emerging as potential biomarkers for poor InO response. This is particularly relevant to patients with *KMT2A*rearrangement who may be predisposed to CD22 partial positivity and low ABC. Evolution of CD22 negative/dim disease post-therapy suggests CD22 modulation is a mechanism of resistance to InO. Response to InO monotherapy may be limited in those with baseline CD22 negative/dim populations. Clinical trial information: NCT02981628. Research Sponsor: Pfizer.

10520 Poster Discussion Session; Displayed in Poster Session (Board #407), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Comparison of chemotherapy dose intensity for AYAs on COG AALL1131 versus CALGB 10403. *First Author: Jennifer Lynn McNeer, University of Chicago, Chicago, IL*

Background: Outcomes for adolescents and young adults (AYAs) with acute lymphoblastic leukemia (ALL) are superior with pediatric-inspired therapy. CALGB 10403, the first US adult cooperative group prospective trial using a pediatric-inspired augmented BFM (ABFM)-based regimen, demonstrated feasibility and improved survival. We examined differences in drug delivery and targeted toxicities in AYAs who received the same therapy on C10403 vs the Children's Oncology Group (COG) study AALL1131. **Methods:** The proportion of AYAs receiving full dose (within 10% of protocol- specified) vincristine (VCR) and pegaspargase (PEG) during induction (IND), consolidation (CON), and delayed intensification (DI); the likelihood of selected grade ≥3 adverse events (AEs); and the impact of patient characteristics were compared in AYAs 16-30 years. Targeted AEs with analogous reporting requirements in both studies included hyperbilirubinemia, pancreatitis, sensory neuropathy, and GI/intracranial hemorrhage. Thrombosis, transaminitis and hyperglycemia were not comparably captured. Fisher's Exact test and logistic regression models were used for analyses. **Results:** After excluding AYAs removed from study after induction, 87 AALL1131 AYAs (accrued 2012-2016) and 188 C10403 AYAs (accrued 2007-2012) were analyzed with median ages of 17 (16-26) vs 22 (17-30) years, $p < 0.001$. There was no difference in the intensity of VCR delivery during IND, but in CON and DI, AALL1131 AYAs were more likely to receive all specified VCR (93.1% vs 81.9%, p = 0.02; 92.7% vs 72.1%, p = 0.01). Women were less likely to receive all specified VCR (OR 0.57, 95% CI 0.34-0.94, p = 0.03), and overweight/obese AYAs were somewhat less likely to receive all VCR compared to those considered normal weight (OR 0.88 and 0.59, p = 0.09). More C10403 AYAs were obese/overweight compared to AALL1131 AYAs (p = 0.04). There were no significant differences in dosing of PEG during IND/CON, but in DI AALL1131 AYAs were more likely to receive both doses (75.6% vs 57.1%, p = 0.03). No patient variables impacted delivery of PEG. There was no significant difference in grade ≥3 toxicities captured similarly on both studies. **Conclusions:** AYAs enrolled on AALL1131 were more likely to receive all protocol-specified VCR and PEG compared to those on C10403. Selected AE rates were comparable, suggesting that older AYAs do not tolerate doses of VCR and PEG for reasons other than toxicity, with body habitus as one potential variable. Further analyses to compare dose density, toxicities, and outcomes experienced by younger AYAs versus older are ongoing. Research Sponsor: U.S. National Institutes of Health, St. Baldrick's Foundation.

10521 Poster Discussion Session; Displayed in Poster Session (Board #408), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

OSTPDL1: A phase II study of avelumab, a monoclonal antibody targeting programmed death-ligand 1 (PD-L1) in adolescent and young adult patients with recurrent or progressive osteosarcoma. *First Author: Michael William Bishop, St. Jude Children's Research Hospital, Memphis, TN*

Background: Outcomes for recurrent osteosarcoma are poor and novel therapies are needed. Osteosarcoma has a high mutational burden with overexpression of PD-L1 in metastatic lesions, providing a rationale for testing immune checkpoint inhibitors in this population. We therefore evaluated the activity of the PD-L1 inhibitor avelumab in patients with recurrent or progressive osteosarcoma. **Methods:** We conducted a single-arm, open-label phase 2 trial at 4 collaborating institutions. Eligible subjects were ages 12 to ≤50 years with recurrent or progressive osteosarcoma and radiographic evidence of measurable disease. Subjects received avelumab 10 mg/kg intravenously every 2 weeks of 28-day cycles until disease progression or unacceptable toxicity. Primary endpoints were objective response rate (CR + PR according to RECIST v.1.1), and progression-free survival (PFS) at 16 weeks. Kaplan-Meier methods were used to estimate PFS. Secondary endpoints included toxicity. Correlative objectives included measurement of subsets of peripheral blood mononuclear cells and serum markers of immune activation, and measures of cell proliferation, co-inhibitory receptor expression on CD8 T cells, T cell repertoire, and epigenetic programming of T cells. **Results:** Between February 2017 and October 2019, 18 eligible subjects [67% male, median age 16.8 years (12.8-22.9)] were enrolled. Subjects had received median 3 prior systemic therapies (range 1-5). Sites of disease included lung/pleura (94%), bone (56%), and soft tissue (28%). Subjects received a median of 2 cycles (range 1-4) of avelumab. Median PFS was 8 weeks (95% CI 6.7-9.1). No objective responses occurred (17 with progressive disease), and the 16-week PFS was 0%. The most common adverse events (AEs) were alanine aminotransferase (ALT) elevation (17%), aspartate aminotransferase (AST) elevation, dyspnea, hyponatremia, and pain (each 11%). Treatment-related serious AEs (≥Grade 3) included dyspnea (n = 2), ALT/ALT elevation, hyponatremia, pericardial effusion and anemia (n = 1). Immune-related AEs included pneumonitis, Hashimoto thyroiditis, and pericardial effusion (all n = 1). One patient discontinued therapy after 1 dose due to grade 4 ischemic stroke, unrelated to avelumab. One death occurred on study due to rapid disease progression. **Conclusions:** Avelumab did not demonstrate activity in recurrent osteosarcoma. Correlative biology studies are ongoing to elucidate mechanisms of resistance to this therapy. Clinical trial information: NCT03006848. Research Sponsor: Pfizer, Other Foundation, American Lebanese Syrian Associated Charities.

10523 Poster Discussion Session; Displayed in Poster Session (Board #410), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Outcomes and toxicities in patients (pts) non-randomly assigned to immunotherapy Children's Oncology Group (COG) ANBL0032. *First Author: Ami Vijay Desai, University of Chicago Medical Center, Chicago, IL*

Background: Immunotherapy with the anti-GD2 antibody dinutuximab plus sargramostim (GM-CSF), aldesleukin (IL-2) and isotretinoin following consolidation therapy improved outcome for high-risk neuroblastoma (HRNBL) pts enrolled on COG ANBL0032. Randomization was halted in 2009; subsequent pts were non-randomly assigned to immunotherapy. Toxicities and survival were evaluated. **Methods:** HRNBL pts < 31 years old with a pre-autologous stem cell transplant (ASCT) response of ≥ partial response (PR) were eligible. Demographics, INSS stage, tumor biology, 1993 INRC pre-ASCT response and toxicities were summarized using descriptive statistics. Five-year (yr) EFS and OS from time of study enrollment were estimated. **Results:** From 2009-2015, 1,183 pts were non-randomly assigned to immunotherapy. 96.7% (n = 1,144) were ≥18 months old and 83.1% (n = 765/921) had stage 4 disease. 45.1% (n = 363/805) of tumors with known biology were *MYCN* amplified, 94.5% (n = 749/793) had unfavorable histology, and 54.9% (n = 397/723) were diploid. Pre-ASCT, 352 (29.8%) pts had complete response (CR), 418 (35.3%) had very good partial response (VGPR), and 413 (34.9%) had PR. 1,042 (88.1%) pts underwent a single and 141 (11.9%) underwent tandem ASCT. For the entire cohort, 5-yr EFS was 61.1±1.9% and 5-yr OS was 71.9±1.7%. 5-yr EFS and OS for pts ≥18 months of age with stage 4 disease (n = 746) were 58.4±2.3% and 71.0±2.1%. 5-yr EFS and OS were 82.3±4.8% and 86.7±4.2% among pts with stage 3 disease (n = 110). EFS but not OS was superior for those with a CR/VGPR pre-ASCT vs. PR (5-yr EFS: 64.2±2.2% vs. 55.4±3.2%, p = 0.0133; OS: 72.7±2.1% vs. 70.5±2.9%, p = 0.3811). There was a trend toward improved OS for those treated with tandem vs. single transplant (5-yr EFS: 65.9±4.3% vs. 60.4±2.1%, p = 0.1282; OS: 76.5±3.8% vs. 71.2±1.9%, p = 0.0704). Grade ≥3 toxicities (> 10% of pts) during GM-CSF and IL-2-containing cycles, respectively, included pain (15.6/11.4%), fever (15.1/32.7%), anemia (18.9/21.7%), thrombocytopenia (13.9/17.4%), lymphopenia (12.3/16.0%), and hypokalemia (13.3/25.2%). Additional Grade ≥3 toxicities (> 10% of pts) included hypoxia (10.1%) during GM-CSF-containing cycles, and anaphylaxis (12.0%), neutropenia (16.1%), hyponatremia (16.5%), and hypotension (13.8%) during IL-2-containing cycles. **Conclusions:** In this large cohort of HRNBL pts treated with immunotherapy, 5-yr EFS was 61.1%. Superior EFS was observed for pts with stage 3 disease and for those with CR/VGPR pre-ASCT. IL-2-containing cycles were associated with increased toxicity. Clinical trial information: NCT00026312. Research Sponsor: U.S. National Institutes of Health.

10524 Poster Discussion Session; Displayed in Poster Session (Board #411), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The first report of pediatric patients with solid tumors treated with venetoclax. *First Author: Kelly C. Goldsmith, Children's Healthcare of Atlanta, Emory University, Atlanta, GA*

Background: Dependence on the prosurvival protein B-cell lymphoma 2 (BCL-2) occurs in certain pediatric solid tumors, resulting in tumorigenesis and resistance to therapies. Venetoclax (VEN), an orally administered BCL-2-selective inhibitor, has preclinical anticancer activity in human-derived neuroblastoma models. Reported here are preliminary results from pediatric patients (pts) with recurrent or refractory (R/R) solid tumors treated with VEN monotherapy or VEN with cyclophosphamide and topotecan (Cy-Topo). **Methods:** This phase 1 open-label, 2-part study (NCT03236857) enrolled pts < 25 yr old with R/R malignancies; we report only on pts with solid tumors. Following a dose ramp-up, pts received 800 mg VEN (age/weight-adjusted adult equivalent) once daily for the first 8 wk; Cy-Topo was added optionally after wk 8. Dose-limiting toxicities (DLTs) were assessed during the first 21 days of VEN therapy or cycle 1 of VEN-Cy-Topo. Objectives included safety, toxicity, and preliminary efficacy. **Results:** As of Dec 17, 2019, 11 solid tumor pts were enrolled: neuroblastoma (n = 6), rhabdomyosarcoma (n = 2), Wilms' tumor, Carney-Stratakis syndrome, and low-grade fibromyxoid sarcoma (n = 1 each). Median age was 11 yr (range 3–22); median time on study was 6.9 mo (range 1.2–17.8). All pts experienced ≥1 treatment-emergent adverse event (TEAE); vomiting (72%; all grades) was most common. Grade ≥3 TEAEs were reported in 82% of pts; febrile neutropenia (64%), decreased blood cell count, and neutropenia (36% each) were the most common. Seven pts received 800-mg monotherapy for 8 wk; 3 of these pts did not receive Cy-Topo after monotherapy. Of the 7 pts who received VEN-Cy-Topo, 3 pts received 400 mg VEN with Cy-Topo. DLTs of grade 4 neutropenia/thrombocytopenia with delayed count recovery occurred in 2 pts on 800 mg VEN-Cy-Topo, necessitating a dose de-escalation (to 400 mg VEN). Grade 4 neutropenia occurred in 2 pts on 400 mg VEN with Cy-Topo, leading to the addition of myeloid growth factor to the therapy regimen. The best response after 8 wk of VEN monotherapy was stable disease (SD). Six pts were evaluable for tumor response with VEN-Cy-Topo; 1 neuroblastoma pt had a complete response after 5 cycles of 400 mg VEN, 4 pts had SD (3 on 800 mg and 1 on 400 mg VEN) and 1 (800 mg VEN) had progressive disease as best response. **Conclusions:** Continuous dosing of VEN with Cy-Topo was not tolerated due to cytopenias in 4/7 pts with solid tumors. Discontinuous dosing of VEN with Cy-Topo is being explored. Clinical trial information: NCT03236857. Research Sponsor: AbbVie, Inc.

10525 Poster Discussion Session; Displayed in Poster Session (Board #412), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase I study of tazemetostat, an enhancer of zeste homolog-2 inhibitor, in pediatric pts with relapsed/refractory integrase interactor 1-negative tumors. *First Author: Susan N. Chi, Dana-Farber Cancer Institute, Boston, MA*

Background: Absence of integrase interactor 1 (INI1) expression is a defining molecular feature of rhabdoid tumors (RT), epithelioid sarcoma (ES), and chordomas, inducing dependence on enhancer of zeste homolog-2 (EZH2). Tazemetostat (TAZ) is a selective EZH2 inhibitor approved by the FDA for treatment of patients (pts) ≥16 yrs with metastatic or locally advanced ES ineligible for complete resection. Data from a Phase 1 (Ph1) pediatric dose-escalation study (Ph1a) of TAZ were previously reported; herein we report interim efficacy and safety from the Ph1 pediatric dose-expansion study (Ph1b). **Methods:** NCT02601937 is a Ph1, multicenter study in pts 6 months – 18 yrs evaluating TAZ administered BID at 1200 mg/m^2 in Ph1b, per Ph1a recommendation. Ph1b cohorts enrolled pts based on tumor type: Atypical teratoid RT (ATRT), RT, and other INI1-negative tumors (including ES and chordoma). The Ph1b primary endpoint was overall response rate (ORR). Secondary endpoints included safety/tolerability, duration of response (DOR), and survival. **Results:** Ph1b has enrolled 47 pts who received TAZ oral suspension. Across all tumor types, ORR was 17% (Table). Responses were observed in ATRT (4/21), chordoma (2/4), and ES (2/7); 1 pt dosed at 520mg/m^2 and 7pts at 1200mg/m^2. In the ATRT cohort, 19% of pts responded to TAZ with a median DOR of 6.5 months. The median DOR has not yet been reached in the other cohorts, with ongoing responses in 3 pts. TAZ was generally well tolerated with no drug-related deaths. Most common adverse events (AE) include vomiting, nausea, and cough. During Ph1b enrollment, 1 pt with chordoma (dosed at TAZ 900 mg/m^2 for 15 months in Ph1a) developed a secondary malignancy (T-cell lymphoblastic lymphoma). In response, the pediatric recommended Ph2 dose was revised to limit exposure in pts without CNS involvement to 520 mg/m^2 TAZ (maximum dosing of 1 yr after response, pts to go off-treatment until disease progression). **Conclusions:** Interim results indicate TAZ is generally well tolerated in children with an AE profile similar to adults. Pt enrollment in the non-ATRT, INI1-negative cohorts is ongoing. TAZ shows promising anti-tumor activity in a subset of pediatric tumors, including ATRT, chordoma, and ES. Clinical trial information: NCT02601937. Research Sponsor: Epizyme, Inc.

	TOTAL[a] (n=47)	ATRT (n=21)	ES (n=7)	Chordoma (n=4)
ORR, %	17	19	29	50
Complete response, n	2	1	1	0
Partial response, n	6	3	1	2
Stable disease, n	9	3	3	0
Median DOR (range), months	-	6.5 (5.4–17.3)	NE[b] (5.5–12.8+)	NE[b] (3.6+ –17.1+)

[a]15 pts across additional tumor types did not show a response. [b]Not estimable

10526 Poster Discussion Session; Displayed in Poster Session (Board #413), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase I trial of pazopanib in combination with irinotecan and temozolomide (PAZIT) for children and young adults with advanced sarcoma. *First Author: Kieuhoa T. Vo, University of California, San Francisco, CA*

Background: Pro-angiogenic factors may represent therapeutic targets in sarcoma. Preclinical studies have demonstrated a potential additive or synergistic interaction between anti-angiogenic agents and chemotherapy. The purpose of this study was to determine the maximum tolerated dose (MTD), toxicities, pharmacokinetic (PK) and pharmacodynamics (PD) effects of PAZIT in patients with advanced sarcoma. **Methods:** Patients 6-30 years of age with relapsed/refractory sarcomas were eligible. In the initial dose escalation plan (A), patients received pazopanib PO (225-450 mg/m^2/dose) on Days 1-21 of 21-day cycles. Pazopanib was combined with fixed doses of irinotecan (IV 50 or PO 90 mg/m^2/dose) and temozolomide PO 100 mg/m^2/dose on Days 1-5. Due to DLTs, an amendment was made to the dose escalation plan (B) and patients received fixed doses of pazopanib PO (225 mg/m^2/dose) on Days 1-21 of 21-day cycles and reduced irinotecan doses (IV 25-37.5 or PO 45-67.5 mg/m^2/dose) and temozolomide PO 100 mg/m^2/dose on Days 1-5. Oral cephalosporin diarrhea prophylaxis was required. Dose escalation followed a 3+3 design. Correlative studies included PK (pazopanib, irinotecan) and PD (angiogenic factors, ctDNA) effects. **Results:** Sixteen patients were treated (median age 16 years, range 7-21). The dose levels in the table were evaluated. First cycle DLTs occurred at all dose levels (Table) and included diarrhea, pancreatitis, colitis, neutropenia, hypertension, deep vein thrombosis, and ALT increase. Due to excessive toxicity, an MTD could not be established. One patient with osteosarcoma had a partial response. Four patients had prolonged stable disease > 4 cycles, including 2 patients with Ewing sarcoma (5 and 6 cycles), rhabdomyosarcoma (9 cycles), and desmoplastic small round cell tumor (6 cycles). Mean±SD plasma exposures to pazopanib, irinotecan, and SN-38 in patients treated on dose level 1B (n = 4) on Day 4 were 601±83, 1.4±0.2 and 0.1±0.04 ug/mL*hr, respectively. Analyses of correlative studies are ongoing. **Conclusions:** Combination PAZIT therapy is not tolerable as evaluated at these doses/schedules. This study provides important toxicity data to inform future clinical trials using combination anti-angiogenic strategies in sarcoma. Clinical trial information: NCT03139331. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

Dose Level (mg/m^2/dose)	# of Evaluable Patients	# of Evaluable Patients with Cycle 1 DLTs
1A: pazopanib PO 350, irinotecan IV 50 or PO 90, temozolomide PO 100	5	2
-1A: pazopanib PO 225, irinotecan IV 50 or PO 90, temozolomide PO 100	5	2
1B: pazopanib PO 225, irinotecan IV 25 or 45, temozolomide PO 100	5	2

10527 Poster Discussion Session; Displayed in Poster Session (Board #414), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase I/II study of lenvatinib (LEN) plus everolimus (EVE) in recurrent and refractory pediatric solid tumors, including CNS tumors. *First Author: Filemon S. Dela Cruz, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Proangiogenic signaling pathways cooperate with mTOR-mediated regulation of cell growth and maintenance to drive development of many pediatric cancers. We report results of the phase 1 dose escalation for LEN + EVE in pediatric patients (pts) with recurrent solid and CNS tumors conducted by Children's Oncology Group. **Methods:** Dose escalation was conducted using a rolling-6 design. Pts received LEN + EVE orally once daily in continuous 28-day cycles. Dose determination was based on toxicity (CTCAE v4.03) during cycle 1. Pharmacokinetics (PK) of plasma LEN and EVE were monitored. **Results:** 17 pts were enrolled (9 male; 8 female). Median (range) age was 10 (3–21) years; 8 pts had CNS tumors. 17 were evaluable for dose-limiting toxicity (DLT). Enrollment started at dose level 1 (DL 1; LEN 11 mg/m^2 + EVE 3 mg/m^2) and, after treatment of 3 pts, was initially de-escalated to DL –1 (LEN 8 mg/m^2 + EVE 3 mg/m^2) due to DLT of proteinuria in 1 pt and self-resolving headache in another who, on review, did not meet the definition of DLT. No pts enrolled at DL –1 (n = 5) experienced DLT. Overall, DLTs were observed in 2 of the first 6 patients enrolled at DL 1: the initial pt with proteinuria and 1 more pt with hypertriglyceridemia and hypercholesteremia. Because 2 pts had reversible DLT of different categories not related to C_{max} or AUC, the DL 1 cohort was expanded to enroll an additional 6 pts, none of whom had DLT. Thus, 2/12 pts experienced DLT at DL 1. Overall, most common treatment-emergent adverse events (TEAEs; ≥ 50% of pts) were diarrhea, hypertension, hypertriglyceridemia, vomiting, abdominal pain, headache, and hypothyroidism. 47% of pts had ≥ 1 treatment-related TEAE grade ≥ 3; the most frequent was proteinuria (n = 2). On cycle 1 day 15, mean (SD) C_{max} (ng/mL) for LEN at DL –1 and DL 1, respectively, was 314 (150) and 359 (270), and mean (SD) $AUC_{0\text{-}8h}$ (hr • ng/mL) for LEN was 1570 (935) and 1780 (1100). Taking all toxicities and PK into account, no further dose escalation was recommended. Best overall response in pts with measurable disease was 2/11 stable disease, 7/11 progressive disease, and 2/11 not evaluable. **Conclusions:** The recommended phase 2 dose of LEN + EVE in children with solid and CNS tumors was LEN 11 mg/m^2 + EVE 3 mg/m^2, with maximum daily doses capped at 18 mg and 5 mg, respectively. The toxicity profile was no more than additive to single-agent therapy. PK exposure was comparable with children on single-agent LEN and to adults receiving LEN + EVE. Enrollment to the phase 2 portion (Ewing sarcoma, high-grade glioma, and rhabdomyosarcoma strata) is ongoing. Clinical trial information: NCT03245151. Research Sponsor: Eisai Inc., Woodcliff Lake, NJ, USA, and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., Kenilworth, NJ, USA.

10528 Poster Discussion Session; Displayed in Poster Session (Board #415), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Assisted reproductive technology outcomes in childhood cancer survivors: A report from the Childhood Cancer Survivor Study. *First Author: Kimberly W. Keefe, Brigham and Women's Hospital, Boston, MA*

Background: Some treatment exposures for childhood cancer reduce ovarian reserve. Registry-based evaluation has not been conducted for assisted reproductive technology (ART) outcomes of female survivors. **Methods:** The Childhood Cancer Survivor Study, a retrospective cohort of five-year survivors and siblings, was linked to the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS), which captures nationwide, CDC-required reporting of ART outcomes. We assessed live birth rate and relative risk (RR, 95% CI) as a function of treatment exposure, using generalized estimating equation to account for multiple ovarian stimulations per subject. **Results:** Among 9885 female survivors, 137 (1.4%; median age at diagnosis 10 years, range 0-20; 11 years of follow-up, 2-11) underwent 243 ART cycles (mean 1.8 cycles) and among 2419 siblings, 33 (1.4%) underwent 60 ART cycles (mean 1.8). Median age at autologous egg retrieval was 30 years (19-44) for survivors and 34 (24-43) for siblings. In the subset using autologous eggs (Table), 99 survivors underwent 155 ovarian stimulation cycles that resulted in 113 embryo transfers and 49 live births for a live birth rate of 32% per ovarian stimulation and 43% per transfer. Sibling live birth rate was 38% (p = 0.39 compared to survivors) per autologous ovarian stimulation and 53% (p = 0.33) per transfer. 38 survivors and 1 sibling underwent egg donor ovarian stimulation cycles. Two survivors used autologous eggs with gestational carriers and one cycle resulted in live birth. Cranial radiation therapy (RT) [RR 0.48 (0.27-0.87) p = 0.02] and pelvic RT [0.30 (0.14-0.66) p = 0.002], compared with no RT, resulted in lower RR of live birth in survivors. The likelihood of live birth after ART in survivors was not impacted by alkylator exposure [CED < 8000 mg/m2 vs. none: 1.14 (0.65-2.02); CED >8000 mg/m2 vs none: 1.07 (0.06-1.91)]. **Conclusions:** While live birth rates among survivors were lower compared with siblings, differences were not statistically significant. Pelvic and cranial RT were associated with a decreased likelihood of live birth, with no association with alkylator exposure identified. Research Sponsor: U.S. National Institutes of Health, Institutional funding from Brigham and Women's Hospital (Expanding the Boundaries Grant).

Diagnosis	Ovarian stimulations (N = 155)	Embryo transfer (N = 113)	Live birth per ovarian stimulation (N = 49)
Neuroblastoma	14	14	9(64%)
Bone cancer	15	10	7(47%)
Soft tissue sarcoma	9	5	4(44%)
CNS	12	8	5(42%)
Kidney (Wilms)	16	10	5(31%)
NHL	10	6	3(30%)
Leukemia	40	29	9(23%)
HD	39	31	7(18%)

10529 Poster Discussion Session; Displayed in Poster Session (Board #416), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Obstetrical and perinatal complications in survivors of childhood, adolescent, and young adult cancer: A population-based study. *First Author: Alina Zgardau, University of Toronto, Toronto, ON, Canada*

Background: Women who survive cancer diagnosed in childhood, adolescence or young adulthood may develop long-term health issues. Data are lacking on adverse reproductive outcomes such as infertility and obstetrical and perinatal complications. **Methods:** Using linked Ontario provincial cancer and obstetrical registries, we assembled a cohort of female cancer survivors diagnosed before age 21 years from 1985-2012. We matched survivors by age and geographic region to females without a prior cancer diagnosis. Outcomes included i) any recognized and past 20 weeks' gestation pregnancy; ii) perinatal complications; and iii) obstetrical complications (including a broad composite of severe maternal morbidity [SMM]). Multivariable Cox proportional hazard and modified Poisson models compared survivors to a non-cancer group and assessed demographic, diagnostic and treatment risk factors in survivors. **Results:** 3,486 survivors were matched to 17,428 women without prior cancer. Median age at cancer diagnosis was 12 years (IQR 5-16) and median follow-up was 26 years (IQR 21-32). 599 (17.2%) survivors had at least one recognized pregnancy compared to 3,885 (22.3%) women without prior cancer (Hazard Ratio [HR] 0.79, 95% Confidence Interval [CI] 0.7-0.9, $p < .0001$). Among those who had a recognized pregnancy, 581 (97.0%) survivors carried a pregnancy $>$ 20 weeks' gestation vs. 3791 (97.6%) in the non-cancer group (Relative Risk [RR] 1.0, CI 0.98-1.04). Factors significantly associated with a decreased likelihood of achieving at least one recognized pregnancy among survivors included brain tumour, cranial radiation, exposure to an alkylating agent or hematopoietic stem cell transplantation (HSCT). Among women who had a livebirth or stillbirth, survivors had a RR of 2.3 (CI 1.5-3.6) for SMM and 3.2 (CI 1.6-6.6) for cardiac morbidity. Factors associated with SMM among survivors included brain tumour and pre-existing kidney disease. Among livebirth pregnancies, cancer survivors were at higher risk of preterm birth (RR 1.6, CI 1.2-2.0), especially those who received an alkylating agent or HSCT. **Conclusions:** Survivors of childhood, adolescence or young adulthood cancer are less likely to achieve a recognized pregnancy compared to women without prior cancer. Those who carry a pregnancy >20 weeks' gestation are at higher risk for SMM and preterm birth. Fertility planning and counseling can be informed by cancer diagnosis and treatment, and high-risk obstetrical care is recommended for survivors at elevated risk of an adverse pregnancy outcome. Research Sponsor: CIHR, Restracomp SickKids Scholarship.

10530 Poster Session (Board #417), Fri, 8:00 AM-11:00 AM

Individual prediction of non-adherence to oral mercaptopurine (6MP) in children with acute lymphoblastic leukemia (ALL): Results from COG AALL03N1 study. *First Author: Anna Lynn Hoppmann, University of Alabama at Birmingham, Birmingham, AL*

Background: Poor adherence to 6MP (measured electronically [MEMS]) increases relapse risk in children with ALL (Bhatia et al. *JAMA Oncol* 2015). Adherence is difficult to assess clinically and non-adherers are more likely to over-report 6MP intake (Landier et al. *Blood* 2017). Key sociodemographic/clinical factors (Bhatia et al. *JCO* 2012) and red cell methyl-mercaptopurine (MMP, a 6MP metabolite) levels (Hoppmann et al. ASCO 2017) are associated with non-adherence and could potentially identify non-adherers. **Methods:** We developed a prediction model for 6MP non-adherence (MEMS adherence rate $<$ 90%), using receiver operating characteristic (ROC) analyses in 407 children with ALL receiving 6MP (mean age 7.7$\pm$4.4y; 68% males; 35% Caucasians, 34% Hispanics, 16% African Americans, 15% Asians). The cohort was divided into a training set (n = 250) and test set (n = 157) using stratified random sampling (stratified by race/ethnicity, gender, age and 6MP non-adherence). We used logistic regression with backward variable elimination, guided by change in area under ROC (AUC), to create a prediction model in the training set, using only clinical and sociodemographic variables (Clinical Model). We then generated a model that added 6MP dose-intensity (6MPDI)-adjusted red cell MMP levels to the Clinical Model (Final Model). All models were validated in the test set. **Results:** Predictors retained in the Training Clinical Model included: age, race/ethnicity, absolute neutrophil count, 6MPDI, family structure, and taking 6MP at the same vs varied time of day (AUC = 0.79; 95%CI 0.72-0.85). The Training Final Model (adding 6MPDI-adjusted MMP to the Clinical Model) yielded an AUC = 0.79 (95%CI 0.72-0.86). The Test Final Model (AUC = 0.79, 95%CI 0.69-0.88) showed significantly superior discrimination compared to the Test Clinical Model (AUC = 0.74, 95%CI 0.63-0.85; P = 0.002). Using a binary classifier with predicted probability of non-adherence $\geq$0.5, the Test Final Model had an accuracy of 79%, and positive and negative predictive values of 71% and 80%, respectively. **Conclusions:** We created, validated, and compared 2 risk-prediction models for 6MP non-adherence in children undergoing maintenance chemotherapy. While inclusion of red cell MMP levels provided superior discrimination in identifying non-adherent patients, the Clinical Model (without MMP levels) performed adequately well, and could be used in the clinical setting. Research Sponsor: U.S. National Institutes of Health.

10531 Poster Session (Board #418), Fri, 8:00 AM-11:00 AM

LAG-3 overexpression in pediatric Hodgkin lymphoma. *First Author: Scott Moerdler, Department of Pediatrics, Rutgers Cancer Institute of New Jersey, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ*

Background: The role of the PD-1/PD-L1 axis in Hodgkin Lymphoma (HL) has led to FDA approval for use of inhibitors in chemotherapy-refractory HL. Numerous additional immune checkpoints may be useful targets, but have not yet been evaluated in HL. LAG-3, a related checkpoint, has been demonstrated to be overexpressed on tumor infiltrating lymphocytes (TILs) of a variety of cancers with associated poor outcomes. LAG-3 is known to inhibit T cell proliferation and activation, representing a possible therapeutic pathway for anti-tumor immunity. However, LAG-3 has yet to be evaluated in pediatric cancers. The purpose of this study is to characterize the expression pattern and clinical significance of LAG-3 in pediatric HL using immunohistochemistry. **Methods:** Patient tumor samples from prior Children's Oncology Group clinical trials (AHOD0031) with matched patient outcome data containing 200 patient samples were obtained. 95% confidence intervals were calculated based on a range of observed prevalence of immune checkpoint expression. Using immunohistochemistry, paraffin embedded samples were tested for the expression of LAG-3 and PD-L1. Samples were stained for CD30 to better delineate Reed Sternberg cells from the remainder of the tumor microenvironment. Immune checkpoint staining was compared to positive controls of normal tonsil tissue, and negative controls of 3T3 cells. Expression intensity was scored by a Pediatric Pathologist. **Results:** 115 unique HL patient cases with evaluable HL tissue and correlating clinical outcome data were analyzed. Samples from 73/115 patients (63%) demonstrated positive LAG-3 staining, defined as over 10% of TILs expressing LAG-3. No demographic data including gender, race/ethnicity, age, or stage were significantly associated with LAG-3 expression. While not statistically significant there was a numerical difference in event free survival (EFS) and patients with LAG-3 expression demonstrated worse EFS. In terms of degree of LAG-3 expression, patients with the lowest positive expression were found to have the worst EFS, and those with highest expression demonstrated the best EFS. 97% of patient cases were found to be PD-L1 positive. 71/73 (97%) of patients who expressed LAG3 were also PDL1+, and 71/106 (67%) of PDL1+ cases were also LAG3+. LAG-3 and PD-L1 were found to be independent (p = 0.09). **Conclusions:** This project is innovative in its characterization of LAG-3 as an immune checkpoint target in pediatric HL. We hope that the information from this project will be used to support new clinical trials for pediatric patients with Hodgkin lymphoma. Research Sponsor: Children's Oncology Group.

10532 Poster Session (Board #419), Fri, 8:00 AM-11:00 AM

Change in cardiac function with CPX-351 in relapsed pediatric AML: A Children's Oncology Group (COG) report from AAML1421. *First Author: Kasey J. Leger, Seattle Children's Hospital, Seattle, WA*

Background: Anthracyclines (AC) are highly effective in treating acute myeloid leukemia (AML), but limited by cardiotoxicity (CTX). CPX-351, a liposomal preparation of daunorubicin (DNR) and cytarabine, may provide therapeutic benefit with less CTX. We evaluated acute changes in cardiovascular (CV) function and biomarkers after 1 cycle of CPX-351 in children with relapsed AML within the phase 1/2 study, AAML1421. **Methods:** Patients (pts) received 135 units/m^2/dose of CPX-351 on days 1, 3, and 5. Echocardiograms were centrally quantified at baseline (BL) and day 29 (end of cycle (EOC)). High sensitivity troponin (cTnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were measured at BL and days 5, 8, 15, 22, and 29. Differences between BL and post-CPX-351 echo/biomarker measurements were analyzed using pre-specified Wilcoxon signed rank tests. The relationship between EOC ejection fraction (EF) and clinical variables was assessed using repeated measures linear regression. **Results:** In 32 included pts, the median AC exposure prior to study entry was 337 mg/m^2 DNR equivalents. At baseline, markers of CV function and stress were abnormal (Table). Over 1 cycle, there was a statistically significant decrease in EF and circumferential strain (Table). NT-proBNP and cTnT did not increase significantly over time. In multivariable analysis, only increasing body surface area was significantly associated with lower EOC EF (b:-5.9, 95% CI -10.8,-0.9). Cancer therapy–related cardiac dysfunction, defined as $\geq$10% decline in EF to $<$ 50%, occurred in 6/32 pts at EOC. **Conclusions:** In this single arm study of AC pre-treated children, baseline abnormalities in CV function were common. CPX-351 was associated with a statistically significant decline in CV function without a rise in cardiac biomarkers. Absent a comparator population, it is not known how these cardiac trends compare to non-liposomal AC or non-AC salvage regimens. The COG AAML1831 trial will determine if CPX-351 offers cardioprotection compared to standard AC in pts with de novo AML. Clinical trial information: NCT02642965. Research Sponsor: Seattle Children's Center for Clinical & Translational Research Clinical Research Scholar Award, Other Foundation.

Changes in CV Parameters Following CPX-351.

Parameter	Baseline (BL)	End of Cycle (EOC) Day 29	Median Change from BL at EOC	p-value
Ejection Fraction	54% [48,57]	48% [44,51]	-3.3% [-7.8,0]	**< 0.001**
Global Longitudinal Strain	-16% [-18,-15]	-15% [-17,-12]	0.9% [-1.8,3.0]	0.30
Circumferential Strain	-25% [-30,-22]	-23% [-25,-19]	3.2% [0.5,6.6]	**0.027**
NT-proBNP (pg/mL)	231 [78,661]	167 [81,337]	-49 [-234,71]	0.37
cTnT (pg/mL)	7.7 [3,10.9]	8.9 [3,14.5]	0 [-1.2,5.6]	0.18

Median [interquartile range]

10533 Poster Session (Board #420), Fri, 8:00 AM-11:00 AM

Trends in conditional survival and predictors of late death in neuroblastoma. *First Author: Hannah Olsen, Dana–Farber Cancer Institute, Boston, MA*

Background: Significant advances in the treatment of neuroblastoma have been made in the past several decades. There are scant data examining how these improvements have changed over time and differentially affected conditional survival among high- and non-high-risk patient groups. **Methods:** We conducted a retrospective cohort study using the Surveillance, Epidemiology, and End Results Database. We analyzed clinical characteristics and survival outcomes for 4717 neuroblastoma patients. Kaplan-Meier methods were used to estimate overall survival (OS) and conditional overall survival (COS) conditioned on having survived 1, 2, or 5 years from diagnosis, with estimates compared between groups using log-rank tests. **Results:** Five-year OS was 41.46% (95% CI 38.77-44.13) for the high-risk group and 91.13% (95% CI 89.49-92.53) for the non-high-risk group. Both groups saw significant improvements in OS by decade ($p<0.001$). Five-year COS among 1-year survivors was 52.69% (95% CI 38.77-44.13) for the high-risk group and 96.75% (95% CI 95.57-97.62) for the non-high-risk group. One-year survivors in the high-risk group showed a statistically significant improvement in COS over time. No difference in COS was observed among 5-year high-risk survivors. There were no statistically significant changes in COS over time for 1- and 5-year survivors in the non-high-risk group. In the high-risk and non-high-risk groups, 82% and 32% of late deaths (>5 years from diagnosis) were attributable to cancer, respectively. Statistically significant adverse prognostic factors for late death were age >1 year at diagnosis, metastatic disease, and non-thoracic primary site (p=0.001). **Conclusions:** Improvements in COS over time have largely benefited high-risk patients, though they are still at higher risk for late death due to cancer when compared to non-high-risk patients. Age, stage, and primary site, but not treatment decade, influence outcomes among 5-year survivors. Research Sponsor: U.S. National Institutes of Health, Alex's Lemonade Stand Foundation.

Overall and conditional overall survival for 4,717 patients with neuroblastoma.

	All Patients		"High-Risk" Patients		"Non-High-Risk" Patients	
Years Survived	Estimated Overall Survival from Diagnosis* (%)	95% CI	Estimated Overall Survival from Diagnosis* (%)	95% CI	Estimated Overall Survival from Diagnosis* (%)	95% CI
0	69.83	68.39-71.21	41.46	38.77-44.13	91.13	89.49-92.53
1	79.26	77.86-80.57	52.69	49.54-55.73	96.75	95.57-97.62
2	87.50	86.26-88.63	67.00	63.53-70.22	98.39	97.45-98.98
5	95.11	94.09-95.97	85.90	81.94-89.05	99.00	98.08-99.48

10535 Poster Session (Board #422), Fri, 8:00 AM-11:00 AM

A phase I/II study of eribulin mesilate (ERI) plus irinotecan (IRI) in children with refractory or recurrent solid tumors. *First Author: Michela Casanova, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy*

Background: ERI is an inhibitor of microtubule dynamics. IRI is used to treat pediatric sarcomas. In the pediatric preclinical testing program, ERI was well tolerated and had promising activity compared with vincristine (a common chemotherapeutic for pediatric cancers) for various solid tumors (*in vivo* xenograft panels). **Methods:** Children with relapsed/refractory solid tumors (excluding active central nervous system tumors) were enrolled. Prior treatment with IRI was allowed. Dose escalation was conducted for 2 schedules with the primary objective (phase 1) of determining the maximum tolerated dose and the recommended phase 2 dose: (A) ERI 1.4 mg/m^2 IV infusion (Days 1 + 8 of 21-day cycle) + IRI 20 or 40 mg/m^2 IV infusion (Days 1–5 of 21-day cycle); (B) ERI 1.4 mg/m^2 IV infusion (Days 1 + 8 of 21-day cycle) + IRI 100 or 125 mg/m^2 IV infusion (Days 1 + 8 of 21-day cycle). Safety and pharmacokinetic parameters were assessed. **Results:** 13 patients (pts) were enrolled (median age: 9 years [range: 3–17]); 4 pts had rhabdomyosarcoma (RMS), 2 had non-RMS soft tissue sarcoma, 2 had Ewing sarcoma, 2 had hepatoblastoma, 2 had nephroblastoma, and 1 had neuroblastoma. Overall, 7 pts previously received IRI. No dose-limiting toxicities (DLTs) were reported for either schedule. At data cut-off (July 14, 2019), 4 pts (with Ewing sarcoma, neuroblastoma, RMS, or hepatoblastoma) continued treatment (A, n = 2; B, n = 2) and 9 pts discontinued treatment (primarily for radiographic progression, n = 7 [A, n = 4; B, n = 3]). All pts experienced ≥1 treatment-emergent adverse event (TEAE); the most common any grade TEAE was neutropenia (n = 10; A, n = 5; B, n = 5). 11 pts had grade ≥3 TEAEs (A, n = 6; B, n = 5); the most frequent grade ≥3 TEAE was neutropenia (n = 9; A, n = 5; B, n = 4). No pt withdrew ERI or IRI due to an AE; 3 pts had dose reductions for ERI (A, n = 1; B, n = 2) and 3 pts had dose interruption of ERI (A, n = 2; B, n = 1) due to AEs. No pt had dose reductions for IRI, and 3 pts had dose interruption of IRI (A, n = 2; B, n = 1) due to AEs. 3 deaths occurred; 2 deaths were the result of tumor progression (A, n = 1; B, n = 1), and the cause of 1 was unknown (B). 1 pt with neuroblastoma treated according to schedule A had a partial response. Systemic exposures of ERI, IRI, and SN-38 (IRI active metabolite) were similar between schedules and doses. **Conclusions:** No DLTs were observed. Toxicity was manageable. Administration of IRI treatment on Days 1–5 is widely used in pediatric cancers; enrollment for phase 2 is ongoing with treatment Schedule A (ERI 1.4 mg/m^2 Days 1 + 8 of 21-day cycle; IRI 40 mg/m^2 Days 1–5 of 21-day cycle). Clinical trial information: NCT03245450. Research Sponsor: Eisai Inc., Woodcliff Lake, NJ, USA.

10536 Poster Session (Board #423), Fri, 8:00 AM-11:00 AM

Risk factors in the HR-NBL-1/SIOPEN study in patients receiving dinutuximab beta (DB) based immunotherapy. *First Author: Ruth Lydia Ladenstein, St. Anna Children's Hospital and St. Anna Kinderkrebsforschung, Department of Paediatrics, Medical University Vienna, Vienna, Austria*

Background: We previously developed a risk factor model in HR-NBL1/SIOPEN patients treated without DB including age, LDH and metastatic site index (MSI). We tested if this score (Morgenstern, PBC 2018) would provide meaningful information in DB treated HR-NBL1/SIOPEN patients. **Methods:** High-risk patients (stage 4 ≥1yr.; stage 4 < 1yr. with MYCN amplification (MNA); stage 2, 3, 0-21y with MNA) received intensive induction, surgery, high dose therapy (HDT) and local radiotherapy (21Gy). Patients with a ≤9 months intervall till HDT/SCT, ≥ partial response prior and no progression received up to 5 cycles of 100mg/m^2 DB: as short-term (STI: 5 days) or long-term infusion (LTI: 10 days) ± 6 (STI) or 3 (LTI) x 10^6 IU/m^2 subcutaneous interleukin 2 (scIL2 over 2 x 5 days) followed by 2 weeks of 160mg/m^2 oral isotretinoin. **Results:** DB was used in 1018 patients [512 males; 89% Stage, 1% Stage 4s, 10% loc. MNA; 2.8 yrs median age at diagnosis] in 18 countries. STI was used in 61% patients, LTI in 39% and DB without scIL2 in 62% patients. 2-yrs. event-free (EFS)/overall survival (OS) was 0.65±0.02/0.78±0.01 and 5-yrs. EFS/OS of 0.56±0.02/0.63±0.02. 891/1018 patients were evaluable for risk factor analysis. EFS multivariate analysis included age, MSI, LDH ≥1250U/L, HDT typ, response prior DB, DB schedule and use of scIL2: only age > 1.5yrs.(p = 0.002) and MSI > 1 (p = 0.002) had independent prognostic prediction. If restricted to stage 4 only, LDH ≥1250U/L was also an independent factor (p = 0.049). Points were allocated in proportion to the log-cumulative hazard ratio (cHR): cHR for LDH > 1250U/L was 1.33 (score of 1), cHR for age > 5 years and metastatic site involvement (MSI) > 1 were 1.79 and 1.86 (scores of 2). Using the score (0 to 5) relevant risk groups can be identified: 5-yrs. EFS/OS for scores 0&1 are 0.80±0.06&0.77±0.04, score 2/3 are 0.58±0.03&0.57±0.04 and for scores 4/5 are 0.50±0.06&0.43±0.08. **Conclusions:** The score adds value in DB treatment groups as it differentiates prognostic subgroups facilitating decision making for future DB add on treatments. Clinical trial information: NCT01704716. Research Sponsor: EC grant No. QLRI-CT-2002-01768, Pharmaceutical/Biotech Company.

10537 Poster Session (Board #424), Fri, 8:00 AM-11:00 AM

Outcome in patients with refractory high-risk neuroblastoma. *First Author: Amir Bari Siddiqui, University of Chicago Medical Center, Chicago, IL*

Background: Outcome for high-risk neuroblastoma (HRNBL) patients (pts) with refractory disease at end of induction (EOI) is poor. The impact of therapies such as I-131-MIBG or irinotecan/temozolomide/dinutuximab (I/T/DIN) prior to autologous stem cell transplant (ASCT) on outcome is unknown. **Methods:** A multi-center, retrospective study of HRNBL pts diagnosed between 2008-2018 with refractory disease at EOI was conducted. Demographics, tumor biology, treatment response, and outcomes were abstracted. 3-year (yr) EFS and OS from time of diagnosis were estimated by the Kaplan-Meier method. **Results:** 3-yr EFS and OS were 54% and 79% for the 136 pts analyzed. 91 pts received no additional therapy prior to ASCT (Cohort 1); 32 pts received post-induction therapy prior to ASCT (Cohort 2); and 13 pts did not undergo ASCT (Cohort 3). The prevalence of metastatic disease in Cohort 1, 2, and 3 was 65%, 97%, and 85%. 3-yr EFS and OS were not statistically different between Cohort 1 (3-yr EFS and OS; 62% and 81%) and Cohort 2 [3-yr EFS and OS; 49% (p = 0.48) and 82% (p = 0.19)]. Outcome for Cohort 3 pts was significantly worse than Cohort 1 [3-yr EFS: 15% vs. 62% (p < .001); and 3-yr OS: 48% vs. 81% (p = 0.003)] and Cohort 2 [3-yr EFS: 15% vs. 49% (p < .001); and 3-yr OS 48% vs. 82% (p = 0.035)]. For Cohort 2 pts with metastatic disease, post-induction therapy included I/T/DIN (n = 12), MIBG (n = 16), MIBG plus I/T/DIN (n = 1), and other (n = 2). Metastatic disease response was observed in 10/12 (83%) pts who received I/T/DIN and 9/16 (56%) who received MIBG. MIBG plus I/T/DIN (n = 1) or MIBG with chemotherapy (n = 1) also induced response. Among the 21 pts with metastatic disease response, 3-yr EFS and OS were 69% and 94%; significantly better than Cohort 2 patients who did not respond to post-induction therapy [3-yr EFS and OS: 11% (p = 0.016) and 66% (p = 0.2)]. 6 Cohort 2 pts achieved a complete response (CR) in metastatic sites following I/T/DIN (n = 5) or MIBG (n = 1), and all are alive without relapse with median follow-up of 3.4 years (range 2.7-8.1). The single Cohort 3 patient who achieved a metastatic CR with I/T/DIN and did not undergo ASCT remains disease-free 2.4 years from diagnosis. **Conclusions:** Patient characteristics differed in the 3 Cohorts, reflecting the influence of refractory disease on treatment decisions. For Cohort 2 pts, outcome was better for those with metastatic disease at EOI who responded to post-induction therapy compared to those who did not. Pts who achieved a metastatic CR of refractory disease had excellent survival. Prospective studies testing the efficacy of I/T/DIN in pts with refractory metastatic disease at EOI are warranted. Research Sponsor: None.

10538 Poster Session (Board #425), Fri, 8:00 AM-11:00 AM

Rhabdomyosarcoma of the female genital tract: Long-term outcome and association with *DICER1* variation. *First Author: Rejin Kebudi, Istanbul University, Oncology Institute, Pediatric Hematology-Oncology, Istanbul, Turkey*

Background: Rhabdomyosarcoma (RMS) of the female genital tract is rare, accounting for 3.5% of cases of rhabdomyosarcomas. Germline *DICER1* mutations are associated with predisposition to pleuropulmonary blastoma and other tumors including sarcomas. Recently *DICER1*-associated RMS of the uterus/ovary has ben reported.. The aim of this study is to evaluate demographic characteristics, molecular pathogenesis, treatment and long term outcome of female genital tract rhabdomyosarcoma. **Methods:** Files of children with RMS of the female genital tract diagnosed at the Istanbul University, Oncology Institute during 1990-2019 were reviewed. Molecular genetic sequencing was performed by polymerase chain reaction amplification of genomic DNA extracted from the formalin-fixed, paraffin embedded tumors, followed by Sanger sequencing. Genetic testing for *DICER1* variants of the proband and family members was performed if *DICER1* mutation was detected in the tumor of the proband. **Results:** Of 210 RMS cases, 11 arose from the female genital tract. The median age at diagnosis was 52 months (10 months-15 years). Primary sites were vaginal (n = 5), uterus (n = 4), and ovary(n = 2). Presenting symptoms included vaginal mass (n = 6), vaginal bleeding (n = 5), and abdominal pain (n = 3). Four had group 1, five group 3, two group 2 disease and all received chemotherapy (vincristine, actinomycinD + cyclophosphamide).Three received radiotherapy; three underwent hysterectomy. *DICER1* mutation was detected in tumor tissue in three patients:[c.5113G > A (p.E1705K); c.5428G > T (p.D1810Y); c.1870C > T (p.Arg624Ter)] Genetic testing revealed germline *DICER1* pathogenic variation in two patients and their family members, one of whom had cystic nephroma in infancy and history of Wilms tumor in an uncle. They were referred for surveillance for the *DICER1* related diseases. A patient with metachronous bilateral ovarian RMS died. Two are married, one has children. The 5 year survival for RMS of the female genital tract was 85.7 % at a median follow-up of 34 (4-298) months. **Conclusions:** Rhabdomyosarcoma of the female genital tract is associated with a favorable prognosis, however some individuals undergo aggressive local therapies. Individuals with RMS of the female genital tract should be tested for *DICER1* pathogenic variation. The detection of a *DICER1* mutation in an individual or family members is important to facilitate surveillance for related tumors, so that they may be detected at the earliest possible stage, potentially increasing survival and decreasing risks of late effects. Research Sponsor: None.

10539 Poster Session (Board #426), Fri, 8:00 AM-11:00 AM

The role of autologous stem-cell transplantation in high-risk neuroblastoma consolidated by anti-GD2 immunotherapy: Results of 2 consecutive studies in a single referral institution. *First Author: Jaume Mora, Hospital Sant Joan de Déu de Barcelona, Barcelona, Spain*

Background: Treatment of high-risk NB within the major international cooperative groups (COG and SIOP) comprise intensive induction, consolidation with high dose chemotherapy and autologous stem cell rescue (ASCR) followed by anti-GD2 immunotherapy and isotretinoin as maintenance therapy. In the COG studies dinutuximab and cytokines (GM-CSF and IL-2) were used to treat patients in complete remission (CR) after ASCR whereas SIOPEN studies used dinutuximab-beta plus/minus IL-2 and included patients with responsive (no progression 109 days after ASCR) but refractory (skeletal metaiodobenzylguanidine positivity with three or fewer areas of abnormal uptake). **Methods:** Since December 2014, HR-NB patients referred to HSJD were eligible for consolidation with anti-GD2/GM-CSF immunotherapy in 2 consecutive studies (dinutuximab for EudraCT 2013-004864-69 and naxitamab for 017-001829-40) and naxitamab/GM-CSF compassionate use (CU) with or without prior ASCR. Patients were enrolled in 1st CR or with primary refractory bone/bone marrow (B/BM) disease. We accrued a study population of two groups whose consolidative therapy, aside from ASCR, was similar: anti-GD2 (dinutuximab or naxitamab) antibodies + GM-CSF and local radiotherapy. This is a retrospective analysis of their event-free survival (EFS) and overall survival (OS) calculated from study entry. **Results:** From Dec 14 til Dec 19, 67 study patients were treated with the COG (dinutuximab + GM-CSF+ IL-2 + RA) regimen (n = 21) in the HSJD-HRNB-Ch14.18 study or with Naxitamab and GM-CSF in the Ymabs study 201 (n = 12) or CU (n = 34). 23 patients were treated with primary refractory disease in the B/BM, and 44 in 1st CR. The 67 study patients included 13 (19%) treated following single ASCR and 54 following induction chemotherapy and surgery. Median follow-up for all surviving patients is 16.2 months. Two-year rates for ASCR and non-ASCR patients were, respectively: EFS 64% vs. 54% (p = 0.28), and OS 66.7% vs. 84% (p = 0.8). For the 44 pts in 1st CR, 2-year rates for ASCR and non-ASCR patients were, respectively: EFS 65% vs. 58% (p = 0.48), and OS 71% vs. 85% (p = 0.63). **Conclusions:** In this retrospective, single center study, ASCR did not provide survival benefit when anti-GD2 + GM-CSF based immunotherapy was used for consolidation after dose-intensive conventional chemotherapy. Research Sponsor: Ymabs Therapeutics and United Therapeutics, Institutional Funds.

10540 Poster Session (Board #427), Fri, 8:00 AM-11:00 AM

Tag-n-trak study: Preliminary analysis of an unselected biobank tumors with NTRK fusion transcript, the French SFCE society contribution. *First Author: Lauriane Lemelle, SIREDO Oncology Center (Care, Innovation and Research for Children and AYA with Cancer), Institut Curie, PSL University, Paris, France*

Background: *NTRK* (*Neurotrophic receptor tyrosine kinase)* fusion transcript was initially described in infantile fibrosarcoma (IFS) and is now known to be present in many other rare types of tumor with a lower incidence. The main objective of the study is to describe the presentation and outcome of unselected tumors with NTRK fusion transcript (NTRK-FTT) to better consider the role of TRK inhibitors (TRKi) in such entities. **Methods:** We selected patients (pts) from the Institut Curie biobank (adults and children) with NTRK-FTT and which were assessed by RT-qPCR then RNA sequencing in a prospective or retrospective process, between 2001 and 2019. **Results:** We identified 62 NTRK-FTT among 2119 screened tumors (2.2 cases/year with RT-qPCR and 6.9 cases/year with RNA seq after 2016), *NTRK3* (44 cases) (including 41 *NTRK3-ETV6*), *NTRK2* (9) or *NTRK1* (9). Most of pts had under 2 years (y) (74%) and only 7 pts were adults. We report preliminary analysis of clinical observation for the first 27 pts. Median age was 0.4 y [0-60.2]. Pathologic diagnosis was IFS (12 cases), various CNS tumors (4), atypical teratoid rhabdoid tumor (1), myofibroblastic inflammatory tumor (2), benign tumors (3), cellular congenital mesoblastic nephroma (2), lipofibromatosis like neural tumor, myxoïd liposarcoma, unclassifiable sarcoma (1 each). Two pts had metastatic tumors. Among all, 22 had surgery (1 mutilating), 15 chemotherapy, 4 radiotherapy, and 5 received TRKi, as second line treatment (2 pts) or ≥ third line (3 pts). After a median follow-up of 50 months [range, 1-155], 20/27 pts remained in complete remission, 3 had stable residue, and 4 had progressive disease (associated to 1 disease-related and 1 toxic deaths). Five-year OS is 88% [95%CI, 73.5-100] and 5y-EFS 59.5% [95%CI, 41.7-84.9]. **Conclusions:** This descriptive study showed that NTRK-FTT is rare (2.9%), encompasses a variety of different histotypes (n = 14). Systematic RNA sequencing allowed to depict 3.5 times more NTRK-FTT than targeted RT-qPCR. Overall outcome is favorable despite frequent tumor events. According to tumor type and the uncertainties regarding the long-term side effects of TRKi, the benefit/risk ratio must be carefully evaluated before using these drugs in first line. Research Sponsor: Bayer, Other Government Agency.

10541 Poster Session (Board #428), Fri, 8:00 AM-11:00 AM

A phase I study of simvastatin in combination with topotecan and cyclophosphamide in pediatric patients with relapsed and/or refractory solid and CNS tumors. *First Author: Thomas Cash, Aflac Cancer & Blood Disorders Center, Children's Healthcare of Atlanta; Department of Pediatrics, Emory University School of Medicine, Atlanta, GA*

Background: HMG-CoA reductase inhibitors (statins) can inhibit IL-6-mediated STAT3 activation, a critical pathway in pediatric CNS and solid tumors. Statins also inhibit tumor proliferation, angiogenesis, and restore apoptosis in preclinical pediatric solid tumor models. We therefore conducted a phase 1 trial of simvastatin in combination with topotecan and cyclophosphamide in children with relapsed/refractory (r/r) solid and CNS tumors. **Methods:** Eligible patients were 1-29 years of age with a r/r solid or CNS tumor. Simvastatin was administered orally twice daily on days 1-21, with topotecan 0.75 mg/m^2/dose IV and cyclophosphamide 250 mg/m^2/dose IV on days 1-5. Four dose levels (DLs) were planned: 140, 180, 225, 290 mg/m^2/dose. A 3+3 design was used to determine the maximum tolerated dose (MTD). Pharmacokinetic and pharmacodynamic analyses were performed. **Results:** The median (range) age of 14 eligible patients was 11.5 years (1 - 23). Diagnoses included neuroblastoma (N = 4), sarcoma (N = 7), and one each of malignant rhabdoid tumor of kidney, medulloblastoma, and Wilms tumor. Eleven DLT-evaluable patients received a median of 4 cycles (range: 1-6). There were 3 cycle 1 DLTs, grade 3 diarrhea and grade 4 creatine phosphokinase (CPK) increased at DL 1, and grade 4 CPK increased at DL 0 (100 mg/m2/dose). Grade 3/4 treatment-related cycle 1 adverse events occurring in ≥ 10% patients were neutropenia (100%), leukopenia (100%), thrombocytopenia (91%), lymphopenia (91%), anemia (55%), febrile neutropenia (55%) and CPK increased (18%). Best overall response was partial response in 1 patient and stable disease in four. Simvastatin and simvastatin acid C_{max} (geomean 82.5 and 12.6 ng/mL) and AUC_{0-6} (geomean 82.5 and 12.6 ng • h/mL) were comparable with reported pediatric literature values (C_{max} 3.5 and 0.4-2.1 ng/mL; AUC_{0-8} 10.7 and 3.8 ng • h/mL) after correction for the higher doses (3.77 vs 0.16 mg/kg) used in our study. Patient peripheral blood mononuclear cells showed maximum phospho-(p)STAT3 inhibition on Day 5, with recurrence by Day 21 despite continued simvastatin dosing. Plasma IL6 levels showed sustained IL6 inhibition with decrease to normal values by Day 21 in all patients, indicating potential on target effects. **Conclusions:** For this first-in-pediatrics trial of statins as anti-cancer therapy, the MTD of simvastatin with chemotherapy was 100 mg/m^2/dose. This combination was well-tolerated with predominantly hematologic toxicity and predictable DLTs related to simvastatin. Clinical trial information: NCT02390843. Research Sponsor: Pediatric Hematology Oncology Research Grant (PHORG), Aflac Cancer & Blood Disorders Center, Children's Healthcare of Atlanta.

10542 Poster Session (Board #429), Fri, 8:00 AM-11:00 AM

Phase II study of alisertib as a single agent in recurrent or progressive atypical teratoid rhabdoid tumors. *First Author: Santhosh Upadhyaya, St. Jude Children's Research Hospital, Memphis, TN*

Background: We conducted a Phase II study of alisertib, small-molecule inhibitor of Aurora A kinase, as single-agent treatment in patients < 22 y with recurrent or progressive atypical teratoid rhabdoid tumors (ATRT) (NCT02114229). **Methods:** Patients received alisertib once daily [80 mg/m^2 (enteric-coated tablets) or 60 mg/m^2 (liquid)] on Days 1–7 of a 21-day cycle for 2 y or until progressive disease (PD). Therapy was considered promising if $\geq$10 patients were without PD by MR imaging at 12 wk. Molecular groups were determined using Infinium Methylation EPIC BeadChips and the Heidelberg classifier. Alisertib plasma concentrations were measured in cycle 1, on Days 1 (single dose) and 7 (steady state) and analyzed using population-based modeling. **Results:** Data from 30 patients representing all 3 molecular groups [SHH (10/26), MYC (10/26), TYR (6/26), unknown (4/26)] was analyzed. One patient remains on therapy. The study did not meet the efficacy end point as only 8/29 patients were without PD after 12 wk, including 1 with partial response. Progression-free survival (PFS) was 31%$\pm$8.2% at 6 months and 15.8%$\pm$6.5% at 1 y. One- year overall survival (OS) was 42.1%$\pm$9.2%. One patient remained on treatment for $>$ 12 months, and another for $>$ 18 months. The median treatment duration was 44 days (range, 2–653 days). There was no difference in OS (p = 0.096) or PFS (p = 0.98) by molecular groups. Neutropenia was the most common adverse effect (77%). After single-dose alisertib, we observed higher mean maximum concentration (C_{max}) 10.1$\pm$3.0 μM and faster time to C_{max} (T_{max} = 1.2$\pm$0.7 h) in the 22 patients who received liquid formulation than those who received tablets (C_{max} = 5.7$\pm$2.4 μM, T_{max} = 3.4$\pm$1.4 h). Drug exposure did not differ between the formulations ($AUC_{0-\infty}$ = 58.6$\pm$25 h$\cdot\mu$M). Average apparent oral clearance was 2.32 L/h per m^2, which was about half that reported in adults. Serial CSF samples were collected in 2 patients; the CSF/plasma AUC ratios were 1.2%-2.7%. **Conclusions:** Although the study did not meet the efficacy end point, alisertib was well tolerated as a single agent in children with recurrent ATRT. A third of the patients demonstrated disease stabilization for $>$ 6 months. Treatment response beyond 1 y was seen in 2 patients Clinical trial information: NCT02114229. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

10543 Poster Session (Board #430), Fri, 8:00 AM-11:00 AM

Naxitamab, a new generation anti-GD2 monoclonal antibody (mAb) for treatment of relapsed/refractory high-risk neuroblastoma (HR-NB). *First Author: Jaume Mora, Pediatric Cancer Center Barcelona, Hospital Sant Joan de Déu, Barcelona, Spain*

Background: NB is a rare cancer but represents the most common extracranial solid tumor of childhood. Most HR-NB patients present with or develop metastatic disease typically in bone or bone marrow (BM). Despite advances in frontline multimodal therapy ~50% of patients relapse. Refractory or relapsed disease represents an unmet medical need. GD2 is an adhesion molecule abundantly expressed in NB. Naxitamab is a humanized anti-GD2 mAb with high receptor affinity. **Methods:** We evaluated naxitamab in HR-NB patients with disease in bone and/or BM, who were refractory to initial treatment(s) or who had insufficient response to therapy for progressive/relapsed disease. Patients were treated in an outpatient setting with naxitamab as a planned 30-minute i.v. infusion and s.c. granulocyte-macrophage colony-stimulating factor (GM-CSF). Patients received 3 infusions of naxitamab 3 mg/kg/dose during the first week of a treatment cycle repeated initially every 4 weeks. Patients were evaluated for safety (CTCAE V4.0) and efficacy (INRC, Park et al. 2017). **Results:** We report on 24 patients recruited from April 2018 with a data cut off in June 2019. At diagnosis, 21 patients were stage 4, 1 was stage 3, 2 were unknown. At study entry, 11 patients had metastases in bone, 1 in BM and 12 in both bone and BM. Overall objective response was 75% (18/24), with complete response (CR) in 67% (16/24) and partial response in 8% (2/24). Of the 13 patients with BM involvement at enrollment, 12 achieved CR in BM during trial therapy. 6 treatment-related SAEs were reported in 5 patients (anaphylactic reaction, pyrexia, and respiratory depression). **Conclusions:** Naxitamab is an anti-GD2 mAb under development for HR-NB. In addition to a high CR rate of 67% and an overall objective response rate of 75% in a high-risk patient population, naxitamab offers an unique option for treatment of patients in the outpatient setting. These data and convenience to patients are strongly supportive of further drug development. Clinical trial information: NCT03363373. Research Sponsor: Y-mAbs Therapeutics Inc.

10545 Poster Session (Board #432), Fri, 8:00 AM-11:00 AM

Deep learning for improved prediction of late-onset cardiomyopathy among childhood cancer survivors: A report from the St. Jude Lifetime Cohort (SJLIFE). *First Author: Fatma Gunturkun, University of Tennessee Health Science Center, Memphis, TN*

Background: Early identification of survivors at high risk for treatment-induced cardiomyopathy may allow for prevention and/or early intervention. We utilized deep learning methods using COG guideline-recommended baseline electrocardiography (ECG) to improve prediction of future cardiomyopathy. **Methods:** SJLIFE is a cohort of 5-year clinically assessed childhood cancer survivors including baseline ECG measurements. Development of cardiomyopathy was identified from clinical and echocardiographic measurement using CTCAE criteria (grade 3-4). We applied deep learning approaches to ECG, treatment exposure and demographic data obtained at baseline SJLIFE assessment. We trained a cascaded model combining a 12-layer 1D convolutional neural network to extract features from waveform ECG signals with a 2-layer dense neural network to embed features from other phenotypic data in tabular format to determine if use of deep learning with ECG data could improve prediction of cardiomyopathy. **Results:** Among 1,218 subjects (median age 31.7 years, range 18.4-66.4) without cardiomyopathy at baseline evaluation, 616 (51%) were male, 1,041 (85%) white, 157 (13%) African American and 792 (65%) were survivors of lymphoma/leukemia. Follow-up averaged 5 (0.5 to 9) years from baseline examination. Mean chest radiation dose was 1350 cGy (range 0 to 6,200 cGy) and mean cumulative anthracycline dose was 191 mg/m^2 (range o to 734 mg/m^2). A total of 114 (9.4%) survivors developed cardiomyopathy after baseline. A cascaded deep learning model built on a training set (N = 974 participants) classified cardiomyopathy in the test set (N = 244 participants) using both clinical and ECG data with a sensitivity of 70%, specificity of 73%, and AUC of 0.74 (95% CI 0.63-0.85), compared to a model using clinical data alone (sensitivity 61%, specificity 62%, and AUC 0.67, 95% CI 0.56-0.79). In subgroup analyses, models predicting cardiomyopathy within 0-4 years following baseline had a sensitivity, specificity, and AUC of 77%, 78%, and 0.78 (0.65-0.91), respectively. When predicting cardiomyopathy 5-9 years following baseline, model performance dropped to a sensitivity, specificity, and AUC of 70%, 70%, and 0.68 (0.50-0.87), respectively. **Conclusions:** Deep learning using ECG at baseline evaluation significantly improved prediction of cardiomyopathy in childhood cancer survivors at high risk for cardiomyopathy. Future directions will incorporate deep learning approaches to echocardiography to further improve prediction. Research Sponsor: None.

10546 Poster Session (Board #433), Fri, 8:00 AM-11:00 AM

Neuromuscular dysfunction and associated health/socioeconomic outcomes: A report from the Childhood Cancer Survivor Study (CCSS). *First Author: Rozalyn L Rodwin, Yale School of Medicine, New Haven, CT*

Background: Childhood cancer survivors are at risk for neuromuscular dysfunction. We estimated the prevalence and cumulative incidence of neuromuscular dysfunction in a cohort of childhood cancer survivors and examined associations with treatment exposures and health/socioeconomic outcomes. **Methods:** CCSS participants $\geq$5 years from cancer diagnosed between 1970-1999 (n = 25,583, 46.5% female, median [range] age 54.4 [15.1-57.6] years) and siblings (n = 5,044, 52.3% female, median [range] age 54.1 [32.5-57.0] years) were included. Neuromuscular dysfunction was identified by self-report of 1) motor dysfunction: impaired balance, tremor, or extremity weakness; 2) sensory dysfunction: impaired touch sensation. Multivariable analyses examined predictors of dysfunction by diagnosis. **Results:** Cumulative incidence of neuromuscular dysfunction was elevated at 20 years from diagnosis in survivors (24.3%, 95% CI 23.8-24.8; motor 18.2%, sensory 13.5%) versus siblings (8.9%, 95% CI 8.1-9.7). In survivors five years from diagnosis, motor dysfunction was associated with exposure to cytarabine (OR = 1.39, 95% CI 1.10-1.77) and spinal radiation (OR = 2.11, 95% CI 1.31-3.41) in acute lymphoblastic leukemia/non-hodgkin lymphoma (ALL/NHL), vinca alkaloids (OR 1.29, 95% CI 1.03-1.60) and brain radiation (OR = 1.58, 95% CI 1.35-1.85) in central nervous system tumors, and cytarabine (OR = 3.73, 95% CI 1.62-8.57) and non-brain/spine radiation (OR = 1.84, 95% CI 1.42-2.40) in bone/soft tissue tumors. Sensory dysfunction was associated with exposure to vinca alkaloids (OR = 3.45, 95% CI 1.06-11.22) in ALL/NHL, and platinum agents (OR = 1.31, 95% CI 1.03-1.67) and spinal radiation (OR = 3.71, 95% CI 1.24-11.11) in bone/soft tissue tumors. Survivors with neuromuscular dysfunction were at increased risk for adverse health/socioeconomic outcomes (Table). **Conclusions:** Neuromuscular dysfunction is a prevalent morbidity in childhood cancer survivors, associated with specific therapies within a particular diagnosis. Interventions are needed to identify and improve neuromuscular dysfunction given its association with adverse health/socioeconomic outcomes. Research Sponsor: None.

Health/socioeconomic outcomes in survivors with neuromuscular dysfunction compared with those without dysfunction.

	OR	95% CI
College or Higher Degree	0.72	0.67 – 0.78
Ever Employed	0.46	0.37 - 0.56
Anxiety	2.76	2.40 - 3.18
Depression	2.27	2.02 - 2.55
Obesity	1.15	1.06 - 1.24

Model adjusted for sex, race/ethnicity, age, presence of any grade 3/4 chronic condition

10547 Poster Session (Board #434), Fri, 8:00 AM-11:00 AM

Emotional distress, stress, and cardiovascular health in adult survivors of childhood cancer. *First Author: Margaret M. Lubas, St. Jude Children's Research Hospital, Memphis, TN*

Background: The contribution of emotional distress and stress to cardiac health in adult survivors of childhood cancer has not been reported, despite evidence of causal associations in the general population. **Methods:** Comprehensive medical assessments and standardized measures of depression, anxiety, post-traumatic stress disorder, and perceived stress were performed on 3,267 survivors in the St. Jude Lifetime Cohort (median [range] 29.9[18.0-64.5] years of age; 7.7[0-24.8] years at diagnosis; 49% female). Physical outcomes included hypertension, diabetes, dyslipidemia, cardiomyopathy, dysrhythmia (grades 2-4 per the NCI CTCAE criteria), myocardial infarction (grades 3-4), and metabolic syndrome (yes/no). Multivariable generalized linear models examined associations between these outcomes with any distress/stress, adjusted for demographics, cumulative anthracycline dose and thoracic radiation, physical activity, BMI, smoking, and alcohol intake. Unadjusted longitudinal associations between distress/stress and new onset cardiac conditions were examined among survivors who completed repeat medical assessment(s) (n = 1748; median follow-up = 3.9 years). New onset conditions were defined as a change from grade 0-1 at baseline to ≥ grade 2 at follow-up. **Results:** Survivor reported distress/stress (29% overall) was more prevalent in those with hypertension (28.2% vs 19.5%, $P< 0.001$), dyslipidemia (16.4% vs. 11.3%, $P< 0.001$), diabetes (9.4% vs. 6.9%, $P= 0.02$), and metabolic syndrome (32.2% vs. 23.2%, $P< 0.001$), but not among dysrhythmia, cardiomyopathy, and myocardial infarction. In separate multivariable models, distress/stress was associated with hypertension (RR = 1.24, 95% CI 1.07-1.43), dyslipidemia (RR = 1.29, 95% CI 1.03-1.61), and metabolic syndrome (RR = 1.35, 95% CI 1.17-1.54). Baseline distress/stress was associated with new onset hypertension (OR = 1.33, 95% CI 0.94-2.01), dyslipidemia (OR = 1.37, 95% CI 0.94-1.87), and dysrhythmia (OR = 2.78, 95% CI 1.12-6.91). **Conclusions:** Emotional distress/stress is associated with adverse cardiovascular health and may serve as an intervention target for improving cardiac health outcomes among survivors of childhood cancer. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

10548 Poster Session (Board #435), Fri, 8:00 AM-11:00 AM

Prediabetes and progression to diabetes among adult survivors of childhood cancer in the St. Jude Lifetime Cohort. *First Author: Stephanie Dixon, St Jude Children's Research Hospital, Memphis, TN*

Background: Cardiac death among survivors of childhood cancer occurs at > 10 times the rate expected in the general population. Modifiable cardiovascular risk factors, including diabetes, increase risk for major cardiac events in a near multiplicative fashion. Thus, prevention of progression from prediabetes to diabetes could improve long-term cardiac morbidity and mortality. However, little is known about prediabetes in survivors. **Methods:** Prevalence of prediabetes (fasting glucose 100-125 mg/dL or HbA1c 5.7-6.4%) and diabetes were assessed in 3529 5+ year survivors ≥18 years of age and compared to 450 community controls stratified by age and matched for race/ethnicity, sex, and BMI using Chi-squared statistics. Logistic regression estimated risk factors for prediabetes and cox proportional hazards regression for progression from prediabetes to diabetes among survivors with multiple visits, reported as odds (OR) and hazard ratio (HR), respectively, with 95% confidence intervals (CI). **Results:** Among 3529 survivors (median age 30 years, range 18-65), the prevalence of prediabetes overall was 29.2% (95% CI 27.7-30.7) and diabetes was 6.5% (5.7-7.3). In each age strata, survivors had significantly higher prevalence of prediabetes and diabetes than controls with over 50% of middle-aged survivors (35-44 years) having prediabetes or diabetes (Table). In a multivariable model, therapy-related risk factors for prediabetes included high pancreatic tail dose (≥20 Gy: 2.9 [1.8-4.8]) and moderate prescribed cranial radiation dose (OR [95% CI] > 0- < 20 Gy: 1.4 [1.1-1.8], 20- < 30 Gy: 1.4 [1.0-1.9]) independent of age, sex, race/ethnicity and BMI. Among 695 survivors with prediabetes and longitudinal follow-up, median 5.1 years, 68 (10%) progressed to diabetes. After adjustment for age, sex, race/ethnicity and BMI, risk of progression from prediabetes to diabetes was increased by the presence of insulin resistance (HR 4.9 [95% CI 2.3-10.6]) or prior treatment with hematopoietic cell transplant (HR 2.9 [1.1-7.7]) or total body irradiation (HR 4.6 [1.6-13.5]). **Conclusions:** Survivors of childhood cancer have a high prevalence of prediabetes and high rates of progression to diabetes. Strategies that prevent progression to diabetes should be considered to decrease diabetes risk and subsequent cardiac morbidity and mortality in this high-risk population. Research Sponsor: U.S. National Institutes of Health, Athe American Lebanese-Syrian Associated Charities (ALSAC).

	Prediabetes		Diabetes	
Age (years)	**Survivors %**	**Controls %**	**Survivors %**	**Controls %**
18-24	17.0	9.4	2.6	1.2
25-34	28.1	14.6	4.8	2.5
35-44	41.4	22.8	11.2	6.6
45-54	46.5	26.4	16.5	13.2
55-64	43.3	29.4	16.7	0.0

10549 Poster Session (Board #436), Fri, 8:00 AM-11:00 AM

Peripheral motor and sensory neuropathy in survivors of childhood central nervous system (CNS) tumors in the St. Jude Lifetime (SJLIFE) cohort. *First Author: Rozalyn L Rodwin, Yale School of Medicine, New Haven, CT*

Background: Survivors of CNS tumors are at risk for peripheral motor and sensory neuropathy. Chemotherapy's contribution to peripheral neuropathy has not been well studied in this population. We aimed to estimate the prevalence of peripheral neuropathy, and determine its association with tumor characteristics and treatment exposures. **Methods:** Within the SJLIFE cohort, survivors of CNS tumors (n = 363, median [range] age 24 [18-53] years, 43.3% female) ≥10 years from diagnosis and ≥ 18 years at evaluation completed in-person assessments for peripheral motor and sensory neuropathy (defined as abnormal motor or sensory subscales of the Modified Total Neuropathy Score). For comparison, matched community controls (n = 445, median [range] age 34 [18-70] years, 55.7% female) underwent the same assessment. Prevalence of ≥ grade 2 motor or sensory neuropathy was estimated by a modified Common Terminology Criteria for Adverse Events. Multivariable analyses adjusting for age, sex and race were used to identify associated disease and treatment characteristics. **Results:** Overall, 11.0% of survivors of CNS tumors versus 0.9% of controls had ≥grade 2 motor neuropathy ($p < 0.001$), and 15.7% of survivors of CNS tumors versus 2.3% of controls had ≥grade 2 sensory neuropathy ($p < 0.001$). Prevalence of motor and sensory neuropathy varied by diagnosis (Table). Vinca alkaloid exposure (OR 3.5, 95% CI 1.7-7.0) and infratentorial tumor location (OR 2.5, 95% CI 1.1-5.4, reference supratentorial location) were independent risk factors for sensory neuropathy. Infratentorial tumor location was also associated with an increased risk of motor neuropathy (OR 2.4, 95% CI 1.2-4.8). History of radiation and surgery were not significant independent risk factors for motor or sensory neuropathy. **Conclusions:** Prevalence of peripheral motor and sensory neuropathy was significantly higher in survivors of CNS tumors than in matched community controls. Survivors of CNS tumors would benefit from increased surveillance to identify and treat peripheral neuropathy, especially in those who received vinca alkaloids or had infratentorial tumors. Research Sponsor: St. Jude Children's Research Hospital is supported by the National Cancer Institute (U01 CA195547, M. Hudson, L. Robison, PIs), the Cancer Center Support (CORE) grant (P30 CA21765, C. Roberts, PI), and American Lebanese-Syrian Associated Charities (ALSAC).

Grade ≥2 motor and sensory neuropathy in survivors of CNS tumors by tumor histology.

	Motor Neuropathy (%)	Sensory Neuropathy (%)
Tumor Histology		
Astroglial (n = 182)	8.2	8.8
Craniopharyngioma (n = 30)	0.0	3.3
Ependymoma (n = 34)	14.7	14.7
Germ Cell (n = 12)	8.3	16.7
Medulloblastoma (n = 97)	18.6	33.0
Other (n = 8)	12.5	12.5

10550 Poster Session (Board #437), Fri, 8:00 AM-11:00 AM

Clinical and genetic risk factors for radiation-associated ototoxicity: A report from the childhood cancer survivor study and the St. Jude Lifetime Cohort. *First Author: Matthew R. Trendowski, The University of Chicago, Chicago, IL*

Background: Cranial radiation therapy (CRT) for pediatric cancer often results in ototoxicity in the form of hearing loss and tinnitus. We sought to identify clinical determinants and genetic risk factors for ototoxicity among adult survivors of pediatric cancer treated with cranial radiation. **Methods:** Relationships between age at last observation, sex, cumulative CRT dose and self-reported ototoxicity were evaluated for hearing loss and tinnitus among 1,991 (tinnitus) and 2,198 (hearing loss) survivors in the Childhood Cancer Survivor Study who received CRT. Logistic regression evaluated associations with non-genetic risk factors and comorbidities as well as SNP dosages in GWAS of CRT-related tinnitus (cases: 146; controls: 1,845) and hearing loss (cases: 270; controls: 1,928). **Results:** Males were more likely to report CRT-related tinnitus (9.4% vs. 5.4%; $p = 5.81\text{x}10^{-4}$) and hearing loss (14.0% vs. 10.7%; $p = 0.02$) than females after adjusting for dose and age at last observation. Survivors with tinnitus or hearing loss were more likely to experience persistent dizziness or vertigo (tinnitus: $p < 2.00\text{x}10^{-16}$; hearing loss: $p = 6.35\text{x}10^{-9}$), take antidepressants (tinnitus: $p = 0.02$; hearing loss: $p = 0.01$) and report poorer overall health (tinnitus: $p = 9.40\text{x}10^{-7}$; hearing loss: $p = 1.30\text{x}10^{-6}$) compared to survivors without tinnitus or hearing loss after age-adjustment. GWAS of CRT-related tinnitus revealed a prominent signal in chromosome 1 led by rs203248 ($p = 1.50\text{x}10^{-9}$), while GWAS of CRT-related hearing loss identified rs332013 ($p = 5.79\text{x}10^{-7}$) in chromosome 8 and rs67522722 ($p = 7.78\text{x}10^{-7}$) in chromosome 6 as approaching genome-wide significance. Replication analysis in an independent cohort of pediatric cancer survivors (SJLIFE) indicated that rs67522722, intronic to *ATXN1*, a gene associated with the neurodegenerative disorder spinocerebellar ataxia type 1, was significantly associated with CRT-related hearing loss ($p = 0.03$). Enrichment analysis and LD score regression with previous GWAS results of cisplatin-related hearing loss and tinnitus in testicular cancer survivors showed no detectable enrichment in genetic architecture with CRT-related hearing loss and tinnitus, respectively. **Conclusions:** Radiation-associated ototoxicity was associated with sex, several neuro-otological symptoms, increased antidepressant use and poorer self-reported health. GWAS of CRT-related hearing loss identified rs67522722 that was replicated in an independent cohort of pediatric cancer survivors. Research Sponsor: U.S. National Institutes of Health.

10551 Poster Session (Board #438), Fri, 8:00 AM-11:00 AM

Lung cancer as a subsequent neoplasm: A report from the Childhood Cancer Survivor Study (CCSS). *First Author: Taumoha Ghosh, University of Minnesota, Minneapolis, MN*

Background: Lung cancer has been reported as a subsequent neoplasm (SN) in childhood cancer survivors. We aimed to assess the prevalence of and risk factors for lung cancer in the CCSS. **Methods:** Among 25,654 five-year survivors participating in the CCSS, lung cancer was self-reported and then confirmed by pathologic record review. Cancer treatment exposures were evaluated including chemotherapy and chest radiation by field size (none, small, large) and in a dose group (0-10 Gy, 10-30 Gy, 30-40 Gy, and $>$ 40 Gy). Standardized incidence ratios (SIR) were calculated using rates from the Surveillance, Epidemiology, and End Results program. Hazard ratios (HR) were estimated for demographic and treatment variables using Cox proportional-hazards models. **Results:** Forty-two survivors developed subsequent malignant lung cancer (SIR 4.0, 95% CI 2.9-5.4), including 25 carcinomas, 7 mesotheliomas and 10 others. Two additional benign neoplasms were also identified. The cumulative incidence of lung SNs was 0.18% at 30 years (95% CI 0.10-0.25). Median time from primary diagnosis was 28 years (range 11-46); median age at diagnosis was 45 years of age (range 15-65). A multivariable model, including all covariates with a p-value $<$ 0.2 in univariate analysis, showed significant associations between lung cancer and older age at diagnosis (HR 10.5, 95% CI 1.4-76.4, for 15-21 years vs. 0-4 years), as well as with primary diagnoses (relative to leukemia, HR 8.7, 95% CI 1.1-66.0, for Hodgkin lymphoma; HR 20.7, 95% CI 1.3-331.0 for neuroblastoma; and HR 21.4, 95% CI 2.3-202.7, for bone cancer). In a treatment model, maximum chest radiation dose (HR 4.1, 95% CI 1.4-11.7, for 30-40 Gy; and HR 8.1, 95% CI 3.0-22.2, for $>$ 40 Gy, relative to 0-10Gy), but not sex, smoking status, or chemotherapy exposures, was associated with lung cancer. Notably, six survivors who developed lung cancer received no radiation and of these, five had a primary bone cancer. At the end of follow-up, 65.9% of survivors with lung cancer were deceased vs. 14.1% of survivors without lung cancer ($p < 0.001$). **Conclusions:** Survivors of childhood cancer are at increased risk for developing lung cancer associated with exposure to high doses of chest radiotherapy. To our knowledge, this is the first study to describe associations with neuroblastoma and bone cancer. Future studies to understand additional treatment-related risk factors beyond chest radiotherapy dose are needed. Research Sponsor: None.

10553 Poster Session (Board #440), Fri, 8:00 AM-11:00 AM

Treatment intensity and risk of chronic health conditions and late mortality among long-term survivors of Wilms tumor: A report from the Childhood Cancer Survivor Study. *First Author: Brent R Weil, Boston Children's Hospital, Boston, MA*

Background: Refinement in risk stratification has led to intensification of therapy for Wilms tumor (WT) patients with adverse prognostic factors. Chronic health conditions (CHCs) including cardiac conditions, subsequent malignant neoplasms (SMNs), and late mortality are known risks for WT survivors, however the impact of specific treatment regimens on these outcomes is largely unknown. **Methods:** Late mortality (all-cause and non-recurrence death $>$ 5 years from diagnosis), SMNs, and severity-graded CHCs (2 = moderate, 3 = severe, 4 = life-threatening, 5 = fatal) were assessed in 5-year WT survivors in the Childhood Cancer Survivor Study diagnosed from 1970-99. Survivors were categorized according to therapy received (Table). Cumulative incidence of mortality and standard mortality ratios (SMR) were estimated. Piecewise exponential models estimated rate ratios (RR) with 95% confidence intervals (CI). **Results:** Among 1507 survivors (median age at follow-up 26 yrs; range 6-55), 35-year cumulative incidence of all-cause mortality was 7.9% (SMR 2.9, CI 2.3-3.6) and 5.1% (SMR 1.9, CI 1.4-2.4) for non-recurrence mortality. RRs for developing any grade 2-5 CHC, grade 3-5 SMN, and grade 2-5 cardiac CHCs were higher for survivors compared to sibling controls (2.0, CI 1.8-2.3; 7.4, CI 5.0-10.8; 2.6, CI 2.2-3.1, respectively). Compared with VA and no RT, RR for non-recurrence late mortality and CHCs among survivors were higher for VAD + any RT, and for $\geq$ 4 drugs + any RT (Table). **Conclusions:** Administering increased-intensity therapy for WT is associated with increased late health consequences and non-recurrence late mortality, necessitating strategies to monitor and improve long-term health among survivors. Research Sponsor: National Institutes of Health.

RRs (95% CI) of mortality and CHCs among WT survivors by treatment*.

Treatment	N	All-cause late mortality	Non-recurrence late mortality	Any grade 2-5 CHC	SMN grade 3-5	Cardiac grade 2-5 CHC
Surgery only	32	1.1 (0.1-9.0)	1.5 (0.2-12.4)	0.8 (0.4-1.6)	3.0 (0.4-24.8)	1.0 (0.3-3.0)
VA no RT	677	1.0	1.0	1.0	1.0	1.0
VAD no RT	96	1.6 (0.5-4.7)	1.5 (0.4-5.3)	0.8 (0.5-1.2	0.8 (0.1-6.9)	1.1 (0.6-2.0)
VAD + ART no LRT	437	3.0 (1.7-5.4)	2.6 (1.3-5.1)	1.5 (1.3-1.9)	2.5 (1.0-6.1)	1.8 (1.3-2.5)
VAD + ART + LRT	95	3.0 (1.2-7.2)	2.7 (1.0-7.6)	1.7 (1.2-2.5)	8.4 (3.0-23.4)	2.2 (1.4-3.7)
≥ 4 drugs + any RT	170	6.5 (3.5-12.2)	3.8 (1.7-8.6)	2.0 (1.5-2.6)	4.2 (1.5-12.1)	2.6 (1.8-3.8)

*adjusted for sex, race, attained age. V, vincristine; A, actinomycin-D; D, doxorubicin; ART, abdominal radiotherapy; LRT, lung radiotherapy

10554 Poster Session (Board #441), Fri, 8:00 AM-11:00 AM

***HAGHL* genetic variants increase first fracture risk (FFR) in female childhood cancer survivors: A report from the Childhood Cancer Survivor Study (CCSS) and St. Jude Lifetime Cohort Study (SJLIFE).** *First Author: Cindy Im, University of Alberta, Edmonton, AB, Canada*

Background: Recent genome-wide association studies (GWAS) have reported substantial sex differences in the genetic architectures of bone-related phenotypes. We investigated sex-specific genetic determinants of FFR in survivors of childhood cancer. **Methods:** We performed sex-combined and sex-stratified GWAS for FFR using Cox regression models fitted on follow-up age in 2,453 long-term ($\geq$5 years) survivors in CCSS with ~5.4 million imputed SNPs (minor allele frequency, MAF$\geq$5%), with self-reported FFR defined by first fracture at any site after diagnosis. Replication analyses were conducted in an independent sample of 1,417 SJLIFE survivors with whole-genome sequencing and clinician-assessed FFR. All models were adjusted for relevant genetic (e.g., ancestry) and clinical (e.g., height, weight, treatment) factors. **Results:** Sex-combined and male-specific analyses yielded no associations with $P < 10^{-7}$. Among female CCSS survivors (N = 1,289, 33% $\geq$1 fractures), we discovered 7 genome-wide significant ($P < 5x10^{-8}$) SNP-FFR associations with strong evidence of sex effect heterogeneity ($P < 7x10^{-6}$) across 2 independent loci with no known associations with bone phenotypes. We replicated these associations in SJLIFE ($P \leq 0.05$) for 3 coding SNPs in the *HAGHL* gene (16p13.3), among which rs1406815 showed the strongest association (MAF = 20%, meta-analysis HR = 1.43, $P = 8.2x10^{-9}$; N = 1,935 women, 35% $\geq$1 fractures). We observed increased *HAGHL* SNP effects on FFR that corresponded with increasing head/neck (HN) radiation therapy (RT) dose (Table). Public *omics* data show replicated SNPs are associated with differential *HAGHL* expression in sex gland and musculoskeletal tissues (GTEx) and in osteoblasts treated with dexamethasone or prostaglandins (GRASP), suggesting sex-/therapy-specific biological pathways involving *HAGHL* SNPs for fracture are plausible. **Conclusions:** Novel associations between *HAGHL* genetic variants and FFR potentially reveal new sex- and therapy-specific biological mechanisms underlying bone-related health conditions in survivors of childhood cancer. Research Sponsor: U.S. National Institutes of Health.

rs1406815-FFR associations in female survivors stratified by HN RT dose.

	CCSS			SJLIFE		
HN RT strata	**N strata**	**HR (95% CI)**	**P**	**N strata**	**HR (95% CI)**	**P**
None	501	1.22 (0.95-1.57)	0.11	331	1.38 (1.03-1.85)	0.03
> 0 Gy	788	1.88 (1.54-2.28)	$2.4x10^{-10}$	315	1.14 (0.83-1.57)	0.43
> 24 Gy	195	3.05 (1.95-4.76)	$9.1x10^{-7}$	145	1.48 (0.85-2.57)	0.17
> 36 Gy	117	3.79 (1.95-7.34)	$8.2x10^{-5}$	61	3.08 (1.09-8.74)	0.03

10555 Poster Session (Board #442), Fri, 8:00 AM-11:00 AM

Frailty and neurocognitive decline in young adult survivors of childhood cancer: A longitudinal analysis from the St. Jude lifetime cohort. *First Author: AnnaLynn Williams, St. Jude Children's Research Hospital, Rochester, TN*

Background: Among young adult childhood cancer survivors, 8% meet the criteria for frailty, an aging phenotype associated with poor health. Frailty is associated with neurocognitive decline in the elderly general population, but this association has not been examined in young adult survivors of childhood cancer. **Methods:** Childhood cancer survivors (N = 845, mean [SD] age 30 [7] years, 22 [7] years post diagnosis, 52% male) were clinically evaluated for prefrailty/frailty (defined as $\geq$2/$\geq$3 of muscle wasting, muscle weakness, low energy expenditure, slow walking speed, exhaustion) and completed neuropsychological assessments at baseline and five years later. Linear regression models estimated mean differences in neurocognitive decline in prefrail/frail survivors *vs.* non-frail survivors adjusting for age, sex, race, CNS therapy (cranial radiation, intrathecal chemotherapy, neurosurgery), and baseline neurocognitive performance. *P*-values were adjusted for multiple comparisons using false discovery rate (FDR). **Results:** 18% and 6% of survivors were prefrail and frail at baseline. Baseline frailty was associated with declines in visual-motor processing speed, short-term memory, and sustained attention (Table). Prefrailty and frailty were associated with declines in focused attention and executive function (Table). No significant associations were observed between prefrailty or frailty and decline in global cognition, academics, motor processing speed, long-term memory, verbal learning, or verbal fluency despite significant baseline cross-sectional associations. **Conclusions:** Young adult prefrail and frail survivors had greater declines in attention and executive function compared to non-frail survivors, domains commonly associated with aging. These findings suggest that interventions designed to mitigate components of frailty may also mitigate or prevent neurocognitive decline. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

Mean decline in neurocognitive Z-scores relative to non-frail participants.

	Prefrail		Frail	
	β(95% CI)	***P***	**β(95% CI)**	***P***
Sustained attention	0.02 (-0.18, 0.21)	0.881	-0.43 (-0.75, -0.10)	0.053
Focused attention	-0.39 (-0.56, -0.22)	< 0.001	-0.61 (-0.89, -0.34)	< 0.001
Visual-motor processing speed	-0.09 (-0.20, 0.02)	0.248	-0.32 (-0.50, -0.13)	0.006
Short-term memory	-0.22 (-0.39, -0.05)	0.061	-0.48 (-0.76, -0.20)	0.006
Executive function	-0.29 (-0.49, -0.10)	0.018	-0.56 (-0.87, -0.25)	0.005

Adjusted for age, sex, race, CNS therapy, and baseline neurocognitive score. FDR adjusted p-values.

10556 Poster Session (Board #443), Fri, 8:00 AM-11:00 AM

Expression of the senescence biomarker *p16^{INK4a}* among childhood, adolescent, and young adult cancer survivors. *First Author: Andrew Brian Smitherman, UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC*

Background: The mechanism of accelerated aging among survivors of childhood, adolescent, and young adult cancer is not clearly understood. Cellular senescence may contribute to this process. We measured peripheral blood T lymphocyte *p16^{INK4a}* expression, a biomarker of cellular senescence and aging, among pediatric and young adult cancer survivors hypothesizing that *p16^{INK4a}* expression is higher due to chemotherapy exposure and among frail survivors. **Methods:** Two cohorts were enrolled from January 2018 to December 2019 at an academic medical center. One, a cross-sectional cohort of young adult cancer survivors and age-matched, cancer-free controls in whom we assessed *p16^{INK4a}* expression and clinical frailty. Frailty was measured with the modified Fried Frailty Index that evaluates skeletal muscle index, weakness, slowness, leisure energy expenditure, and exhaustion. A second cohort underwent prospective measurement of *p16^{INK4a}* expression before and after cancer chemotherapy. Eligibility among survivors and newly diagnosed patients required treatment with an alkylating agent, an anthracycline / anthracenedione, or both. Multivariable linear regression was used to model expression of *p16^{INK4a}* by patient age at assessment, treatment intensity, and frailty status. **Results:** The cross-sectional cohort enrolled 60 young adult survivors and 29 age-matched, cancer-free controls with median age 21 years and range 17-29 years for both groups. Survivors were a median of 5.5 years from end of treatment. The prospective cohort enrolled nine newly diagnosed patients (range 1-18 years). Expression of *p16^{INK4a}* was higher among young adult cancer survivors as compared to age-matched controls (9.6 v. 8.9 $\log_2$ p16 units, $p < 0.01$) representing a 25-year age acceleration in the survivors. Expression of *p16^{INK4a}* increased among newly diagnosed patients from matched pre- to post-treatment samples (7.3 to 8.9 $\log_2$ p16 units, $p = 0.002$). Nine survivors (16%) met criteria for being frail and had higher *p16^{INK4a}* expression as compared to robust survivors (10.5 [frail] v. 9.5 [robust] $\log_2$ p16 units, $p = 0.055$). **Conclusions:** Chemotherapy is associated with increased cellular senescence in pediatric and young adult cancer survivors as reflected in expression of *p16^{INK4a}* indicating an increase in molecular age following chemotherapy exposure. The large proportion of frail survivors in this study also exhibited higher levels of *p16^{INK4a}* suggesting that cellular senescence may be associated with early aging observed among these survivors. Research Sponsor: U.S. National Institutes of Health.

10557 Poster Session (Board #444), Fri, 8:00 AM-11:00 AM

Is it safe and worthwhile? A multi-site randomized clinical trial of FAmily CEntered (FACE) pediatric advance care planning for adolescents with cancer and their families. *First Author: Justin N. Baker, St. Jude Children's Research Hospital, Memphis, TN*

Background: Many clinicians express concern that pediatric ACP (pACP) is too distressful for families. We describe the effect of FAmily CEntered pACP for Teens with Cancer (FACE-TC) on families' self-reported experience. **Methods:** A 4-site, intent-to-treat, longitudinal, randomized clinical trial recruited adolescent/family dyads from hospital-based cancer-specialty clinics from 2016-2019. Adolescent/family dyads were screened/assented/consented/enrolled and randomized at a 2:1 ratio to either FACE-TC or Treatment as Usual control. FACE-TC is three weekly, 60-minute sessions with a certified facilitator (ACP survey; Next Steps: Respecting Choices Interview; Five Wishes advance directive). Satisfaction Questionnaire measured 7 positive (useful, helpful, load off my mind, satisfied, something I needed to do, courageous, worthwhile) and 6 emotional reactions (scared, hurtful, harmful, too much to handle, angry, sad). It was administered by a trained/blinded research assistant immediately following the Respecting Choices interview or 3 weeks post-baseline for controls. **Results:** Family participants were: primarily mothers (75%); mean age 46 years; 83% female; 82% white. Household income was ≤100% Federal poverty level for 26%; 58% had less than a Bachelor's degree. Attendance was 92% for three FACE sessions. FACE families (N = 116) compared to controls were more likely to report the study was "worthwhile" (97% vs. 86%, 0 = 0.0245); "useful" (97% vs. 83%, p = 0.0102); "helpful" (96% vs. 79%, p = 0.0079); and "something I needed to do" (84% vs. 55%, p = 0.0006). FACE families (Mean 28.1, SD 3.3) reported higher positive subscale scores than control families (Mean 24.9, SD 4.4) ($\beta = 2.98$, p = 0.0001). No significant differences were found for age, gender, race, household income, or adolescent on active treatment. There were no differences between FACE or control dyads on the 6 emotional reactions subscale score. **Conclusions:** Among a geographically, economically diverse families, FACE pACP was safe and worthwhile. Clinicians can be assured that a structured facilitated pACP intervention, although emotionally intense, did not unduly distress families who found the experience overwhelmingly worthwhile. Results fill the gap about how to successfully engage families in pACP with their adolescent child. Clinical trial information: NCT02693665. Research Sponsor: U.S. National Institutes of Health.

10558 Poster Session (Board #445), Fri, 8:00 AM-11:00 AM

Hospice use at end of life in children with cancer: The effect of insurance. *First Author: Emily E. Johnston, Stanford University Medical Center, Palo Alto, CA*

Background: The National Quality Forum has endorsed hospice care as a metric of high quality end-of-life (EOL) care for adults with cancer. Specific hospice-related quality metrics include hospice enrollment, hospice enrollment for ≥3d, and death outside of the acute care setting. These metrics have been examined extensively in adults and disparities related to a number of clinical and sociodemographic factors, including insurance, have been identified. However, for children with cancer, hospice utilization data is lacking. We addressed this gap by examining location of death and hospice utilization at EOL for children with cancer and determining whether these metrics varied with insurance status. **Methods:** We used national insurance claims data (Truven) to conduct a population-based analysis of patients with cancer who died between 2011 and 2017 at age 0-21y. The dataset was queried for hospice claims, inpatient claims, and location of death. The association between insurance (private vs. Medicaid) and 1) location of death, 2) hospice enrollment, and 3) days between first hospice claim and death was examined using multivariable regression analysis, adjusting for age at death, gender, and cancer diagnosis (hematologic malignancies vs. solid tumor). **Results:** A total of 1,492 children died at a mean age of 11y (SD: 6y); 56% were privately-insured, 56% were male, and 30% had hematologic malignancies. Overall, 58% died in the hospital (privately-insured: 54% vs. Medicaid: 63%). Forty-five percent enrolled in hospice (privately-insured: 46% vs. Medicaid: 43%) with 2% returning to the hospital to die after enrolling in hospice. The average time between first hospice claim and death was 3d (privately-insured: 10d vs. Medicaid: 2d, p = < 0.001). When compared to privately-insured children, children on Medicaid had similar likelihood of hospice enrollment (RR = 1.0, 95%CI = 0.6-1.8). However, children on Medicaid were more likely to die in the hospital (RR = 1.3, 95%CI = 1.1-1.4) and have fewer days between hospice enrollment and death if enrolled in hospice (IRR: 0.5, 95%CI = 0.3-0.8). **Conclusions:** In this first study to examine national hospice utilization in children with cancer, care varies significantly with insurance status. Children on Medicaid are more likely to die in the hospital and have shorter hospice enrollment duration than children with private insurance. Whether this variation represents EOL care preferences, provider biases, differences in quality and availability of hospice or home care to different insurers, or other barriers needs to be examined. Research Sponsor: Alex's Lemonade Stand and Leukemia Lymphoma Society.

10559 Poster Session (Board #446), Fri, 8:00 AM-11:00 AM

Prevalence and predictors of high-intensity end-of-life care among adolescents and young adults with cancer in Ontario: a population-based study using the IMPACT cohort. *First Author: Hallie Coltin, Division of Haematology/Oncology, The Hospital for Sick Children, Toronto, ON, Canada*

Background: End-of-life (EOL) care in adolescents and young adults (AYA) with cancer is poorly characterized, though this group may be at risk of elevated rates of high-intensity (HI) care and consequently, increased EOL suffering. Few population-based studies exist, and are limited by incomplete clinical information. AYA care patterns can vary by locus of care (LOC – pediatric v. adult), but LOC disparities in AYA EOL care are unstudied. **Methods:** We conducted a retrospective decedent population-based cohort study of all Ontario AYA diagnosed between 15-21 years of age with 6 prevalent primary cancers between 1992-2012, who died ≤5 years from diagnosis. Chart-abstracted clinical data were linked to health services data. The primary composite outcome (HI-EOL care) included any of: intravenous chemotherapy ≤14 days from death; > 1 emergency department visit ≤30 days from death; or > 1 hospitalization or intensive care unit (ICU) admission ≤30 days from death. Secondary outcomes included measures of the most invasive (MI) EOL care: mechanical ventilation ≤14 days from death, and death in the ICU. Factors associated with HI-EOL were examined. **Results:** Of 483 patients, 292 (60.5%) experienced HI-EOL care, 98 (20.3%) were mechanically ventilated ≤14 days from death, and 110 (22.8%) died in the ICU. Patients with hematological malignancies (v. solid tumors) were at greatest risk of HI-EOL care (OR, 2.3; 95CI, 1.5-3.5, $p < 0.01$), mechanical ventilation (OR, 5.4; 95CI, 3.0-9.7, $p < 0.01$), and death in an ICU (OR, 4.9; 95CI, 2.8-8.5, $p < 0.01$). AYA who died in a pediatric center were substantially more likely to experience MI-EOL measures compared to those dying in adult centers (mechanical ventilation, OR 3.2, 95CI 1.3-7.6, p = 0.01). Assessment of interactions showed LOC-based disparities widening over the study period (ICU death in pediatric v. adult centres: early period OR 0.9, 95CI 0.3-2.9, p = 0.91; late period OR 3.3, 95CI 1.2-9.2, p = 0.02; interaction term p = 0.04). AYA living in rural areas were also at higher risk of experiencing mechanical ventilation (OR, 2.0; 95CI, 1.0-3.8, p = 0.04) and death in ICU (OR, 2.1; 95CI, 1.1-4.0, p = 0.02). **Conclusions:** AYA with cancer experience high rates of HI-EOL care, with patients in pediatric centers and those living in rural areas at highest risk of MI-EOL care. Our study is the first to identify LOC-based disparities in AYA EOL care. Future studies should explore mechanisms underlying these disparities, including potential differences in palliative care services. Research Sponsor: Canadian Institutes of Health Research (CIHR), Other Foundation, Other Government Agency.

TPS10560 Poster Session (Board #447), Fri, 8:00 AM-11:00 AM

A phase II study of larotrectinib for children with newly diagnosed solid tumors and relapsed acute leukemias harboring TRK fusions: Children's Oncology Group study ADVL1823. *First Author: Theodore Willis Laetsch, University of Texas Southwestern Medical Center and Children's Health, Dallas, TX*

Background: In children, fusions of the *NTRK1/2/3* genes (TRK fusions) occur in soft tissue sarcomas, including infantile fibrosarcoma (IFS), congenital mesoblastic nephroma, high- and low-grade gliomas, secretory breast carcinoma, and papillary thyroid cancer. Rarely, TRK fusions also occur in Ph-like acute lymphoblastic leukemia and acute myeloid leukemia. Larotrectinib is a selective TRK inhibitor FDA-approved for the treatment of TRK fusion solid tumors in patients with no satisfactory alternative treatments or whose cancer has progressed following initial treatment. In children, larotrectinib demonstrated a 94% overall response rate (ORR) with a 12-month progression free survival rate of 75% (1). **Methods:** Patients <30 years with any newly diagnosed unresectable solid tumor or relapsed/refractory acute leukemia with TRK fusions are eligible. TRK fusions must be locally identified in a CLIA/CAP laboratory and are confirmed centrally using a targeted RNA sequencing panel. Patients with high-grade gliomas are excluded. Patients receive larotrectinib 100 mg/m^2/dose BID (max of 100 mg/dose) continuously in 28-day cycles. Patients with solid tumors who achieve CR will discontinue larotrectinib at the completion of at least 12 total cycles of therapy and 6 cycles after achieving CR. Those whose tumors become surgically resectable may undergo on study resection and discontinue therapy if an R0/R1 (IFS) or R0 (other tumors) resection is obtained. All other patients will receive 26 cycles in the absence of unacceptable toxicity or progressive disease. The primary endpoint is the ORR to larotrectinib according to RECIST 1.1 in children with IFS. The study uses a Simon 2-stage minimax design, and the regimen will be considered of sufficient interest if 16 of 21 (76%) patients with IFS demonstrate response. Patients with other solid tumors and leukemias will be analyzed in separate cohorts as secondary objectives. Correlative studies include serial sampling of circulating tumor DNA and neurocognitive assessments. This is the first Children's Oncology Group study to assign frontline therapy based on the presence of a molecular marker independent of histology, and the first clinical trial to evaluate larotrectinib for the treatment of leukemia. Enrollment began in October 2019 (NCT03834961). 1. Tilburg CMv, DuBois SG, Albert CM, et al: Larotrectinib efficacy and safety in pediatric TRK fusion cancer patients. Journal of Clinical Oncology 37:10010-10010, 2019 Clinical trial information: NCT03834961. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

TPS10561 Poster Session (Board #448), Fri, 8:00 AM-11:00 AM

A phase I study of Aurora kinase A inhibitor LY3295668 erbumine as a single agent and in combination in patients with relapsed/refractory neuroblastoma. *First Author: Steven G. DuBois, Dana-Farber/Boston Children's Cancer and Blood Disorders Center and Harvard Medical School, Boston, MA*

Background: Aurora kinase A (AurA) has been implicated in high-risk neuroblastoma, including roles stabilizing and increasing expression of MYCN protein. AurA impacts the function of MYCN in mediating transcription in a cell cycle dependent manner, suggesting that neuroblastoma and other *MYC/MYCN*-driven tumors may be sensitive to AurA inhibition. LY3295668 is a selective AurA inhibitor. The lack of AurB inhibitory activity is hypothesized to minimize on-target hematologic toxicity associated with AurB inhibition. The molecule's selectivity is intended to allow for continuous dosing at exposures associated with > 90% target inhibition at trough. In an analysis of LY3295668 antiproliferative effects in 560 cancer cell lines, neuroblastoma was among the most sensitive histologies tested. This screen also separately evaluated genomic predictors of response to LY3295668, with *MYC*/*MYCN* amplification identified as among the strongest predictors of sensitivity to this agent. LY3295668 is currently being evaluated in early phase adult trials. The current trial (J1O-MC-JZHD) was uniquely designed to hasten time to first-in-child oncology development for a rare unmet need of relapsed/refractory neuroblastoma patients. **Methods:** Study J1O-MC-JZHD (NCT04106219) is a multicenter, dual collaboration (NANT and ITCC), randomized, open-label, Phase 1 study of oral LY3295668 in children with relapsed/refractory neuroblastoma. A rolling 6 design will be followed for dose escalation in both a monotherapy cohort and a combination cohort testing LY3295668 together with cyclophosphamide and topotecan. The starting monotherapy dose will be equivalent to 80% of the adult maximum tolerated dose. Key eligibility criteria include recurrent/refractory neuroblastoma not amenable to curative treatment, age 2-21 years, mandatory archival tissue submission, ability to swallow capsules, and adequate hematologic and organ function. LY3295668 is administered in capsule form orally BID continuously. Primary objectives include assessments of safety and tolerability of study drug to identify RP2D as monotherapy and combination, and assess antitumor activity. Secondary objectives include assessment of the pharmacokinetic profile as monotherapy and in combination, and assessment of the relationship between study drug exposure and efficacy. Following determination of the RP2Ds, an expansion phase will randomize patients to monotherapy or to the combination arm. Enrollment began 16 Dec 2019 and is ongoing. Clinical trial information: NCT04106219. Research Sponsor: Eli Lilly & Co.

11000 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Trainee and workforce diversity in hematology and oncology: Ten years later what has changed? *First Author: Ana I. Velazquez Manana, University of California, San Francisco Medical Center, San Francisco, CA*

Background: The diversification of the healthcare workforce has been identified as a strategy to address health disparities and increase patient-physician trust. A prior review of diversity among oncology fellows up to 2010, showed an increase in female representation over 17 years, but no change in underrepresented minorities (URM). We aim to assess the changes in hematology and oncology (HO) fellowship diversity over the last decade and how this compares to our workforce. **Methods:** Publicly available registries were used to assess differences among female and URM HO fellows, HO fellowship applicants, internal medicine (IM) academic faculty, IM residents, medical school graduates (MSG), and the US population in 2019. These were compared to the 2016 HO practicing physicians. Changes in URM and female HO fellow representation from 2009 to 2019 were assessed. Data was analyzed using binomial tests and simple linear regression models. **Results:** Female representation among HO fellows (43.8%) was increased when compared with HO practicing physicians (+11.8%, $p < 0.0001$) and IM faculty (+3.2%, $p = 0.0079$); no difference from IM residents or HO applicants. Female HO fellows were underrepresented when compared with MSG (-4.0%, $p = 0.0014$) and US population ($P < 0.0001$). Hispanic HO fellows (6.1%) had increased representation when compared to IM faculty (+2.7%, $p < 0.0001$), but were underrepresented when compared to IM residents (-2.2%, $p = 0.0012$) and US population ($p < 0.0001$). The proportion of Hispanic HO fellows was no different when compared to HO practicing physicians, HO applicants, and MSG. African American (AA) fellows (3.8%) were underrepresented when compared to IM residents (-2.0%, $p = 0.0005$), HO applicants (-1.7%, $p = 0.0465$), MSG (-2.4%, $p = 0.0001$), and US population ($p < 0.0001$). AA fellows were increased when compared to HO practicing physicians (+1.5%, $p = 0.0002$), but no different than IM faculty. Asian HO fellows were increased when compared to IM residents, MSG, and US population. Over the last 10 years there has been no significant change in the proportion of AA or female HO fellow representation, with a decreasing trend in Hispanics (-0.14% per year, $p = 0.04$).**Conclusions:** The current state of diversity in HO workforce still requires attention. Despite ongoing efforts, females, AA, and Hispanics continue to be underrepresented. The decreasing trend in Hispanic representation and clear differences in diversity between HO fellowships and IM residencies calls for action among fellowship programs and national societies to increase URM engagement and recruitment. Research Sponsor: None.

11001 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

A comprehensive analysis of the demographics and citation-based productivity of radiation oncologists practicing at comprehensive cancer centers. *First Author: Shearwood McClelland, Indiana University School of Medicine, Indianapolis, IN*

Background: Academic radiation oncology represents a constantly changing landscape. We sought to determine the demographic makeup of the current academic radiation oncology workforce. **Methods:** Internet searches of the 51 National Cancer Institute-designated Comprehensive Cancer Centers were conducted in September 2019. The Scopus database was subsequently searched in December 2019 to ascertain the h-index for each radiation oncologist. H-indices were analyzed by faculty rank (junior faculty versus associate professor versus full professor) and gender. Variables were coalesced for statistical analysis using Fisher's exact test and two-tailed t-tests. **Results:** Analysis of 993 radiation oncologists revealed that 53.6% are junior faculty, 24.8% are associate professors, and 21.7% are full professors. The average radiation oncologist has been an MD for 19.6 years; 32.5% (232/993) are women, and less than 5% (47/993) are underrepresented minorities (URM). Of the 51 department chairs, 11.8% are women and 5.6% are underrepresented minorities. Women are significantly underrepresented among full professors (odds ratio = 1.78; $p = 0.010$) and departmental chairs (odds ratio = 3.80; $p = 0.0007$); there was no significant difference for assistant professorship ($p = 0.067$) nor associate professorship ($p = 0.348$). The overall mean h-index for all faculty was 17.64. Mean h-index was 8.21 for junior faculty, 18.46 for associate professors, and 40.05 for full professors; these differences were statistically significant ($p < 0.0001$). The overall mean h-index was 19.35 for men (n = 668) and 14.11 for women (n = 323); this difference was statistically significant ($p < 0.0001$). **Conclusions:** The majority of academic radiation oncologists are assistant professors; fewer than 5% are underrepresented minorities. Men comprise more than two-thirds of the workforce, and are significantly overrepresented at the full professor (by 78%) and departmental chair (by 280%) levels in academic radiation oncology. The average radiation oncologist at a comprehensive cancer center has published more than 17 manuscripts cited at least 17 times. Contrary to previous findings comparing male and female residents, the difference in academic productivity by gender among faculty was statistically significant. These findings provide objective data to assess the radiation oncology academic workforce and provide a useful benchmark to measure change going forward. Research Sponsor: None.

11002 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Caring for transgender cancer patients: Shortcomings of medical education. *First Author: Ernesto Gil Deza, Insituto Oncologico Henry Moore, Buenos Aires, Argentina*

Background: Caring for transgender patients requires specific knowledge and skills. Medical schools spend less than 5 hours on average training for treatment of LGBT patients (Obedin-Maliver, JAMA, 306 (9), 971). This paper assesses the knowledge on the topic and skills of postgraduate Oncology students from Universidad del Salvador at the Observational Standard Clinical Examination (OSCE) 2019 (JCO 34 (15), Abstract e18150, 2017). **Methods:** At one of the stations of OSCE 2019, students had thirty minutes to complete a clinical record of a simulated transman patient with ovarian cancer stage IIIC. Based on the real case of Robert Eads, actors were trained with the documentary on his life "Southern Comfort". Students were assessed on: A) knowledge of the transman condition, B) use of preferred gender pronoun by the patient, C) discontinuation of testosterone treatment, D) recommendation of genetic study, E) treatment of ovarian cancer according to NCCN guidelines, F) moral discomfort with LGBT patient care. All interviews were filmed or recorded by an observer. All films, recordings and clinical records were reviewed to rate the students' performance. **Results:** A total of 25 postgraduate Oncology students took the OSCE 2019. Assessment: A) 5/25 (20%) lacked knowledge of the transman condition, B) 3/25 (12%) did not use the patient's preferred gender pronoun, C) 17/25 (68%) discontinued testosterone, D) 23/25 (92%) requested genetic study, E) all students treated ovarian cancer according to NCCN guidelines, F) none expressed moral discomfort with LGBT patient care. **Conclusions:** 1) It is feasible to assess the knowledge and skills required for treatment of transgender patients in Oncology. 2) We found shortcomings of student's medical training regarding transgender patients: one in five did not understand the patient's condition, three did not use the patient´s preferred gender pronoun during the interview and more than half suspended the necessary hormone therapy for their condition. 3) This emphasizes the need to deepen our medical and communication skills in order to assist the transgender population and should be included in future ASCO-ASH milestones for specialty accreditation. Research Sponsor: None.

11003 Poster Discussion Session; Displayed in Poster Session (Board #260), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Social media use among NCI designated cancer centers: Where is the diversity? *First Author: Ana I. Velazquez Manana, University of California, San Francisco, San Francisco, CA*

Background: The NCI-Designated Cancer Centers (NCC) are recognized for their leadership, research, and education of health care professionals (HCP). NCC are required to study and improve cancer disparities in their communities. Since the introduction of social media (SM), online platforms have become a source of health information and peer support among patients with cancer, leading to its adoption by NCC across the nation. We aimed to analyze the use of SM among NCC and how the racial/ethnic (RE) diversity represented in their SM messaging compares to their communities. **Methods:** We reviewed all original SM posts from adult NCC-specific Facebook (FB) and Twitter (TW) pages between 1/1/2019 to 12/31/2019. Basic laboratory NCC pages and retweets were excluded. A 1-year time period was selected to account for variation during health campaigns months. We analyzed each post's language and content, and the gender and RE of individuals presented in images and videos (IV). Content was categorized into: screening, clinical trials, HCP, or patient story. Data was analyzed using chi-square and Wilcoxon signed-rank tests. **Results:** We reviewed the FB and TW pages of 56 NCC. The median account age was 10 years for FB and 9 years for TW with a median number of followers of 9,861 and 6,066, respectively. The median number of posts per NCC was 250 in FB and 332 in TW. Only 5 NCC posted in a non-English language (range 1 – 5 posts). Among SM IV, >60% of pages displayed females in ≥50% of their posts, African Americans (AA) were presented in 12-14% and Hispanics in 5%. When compared to their city demographics, Whites and Asians were significantly over-represented while Hispanics and AA were under-represented in NCC's SM messaging (Table). When compared to the US census, over-representation of Asians and under-representation of Hispanics persisted. Cities with ≥20% AA or Hispanics displayed a higher proportion of IV presenting the respective RE group ($p<0.05$). Content was not associated with RE makeup. **Conclusions:** By analyzing the IV posted by NCC on 2 SM platforms, we identified that Hispanics and AA were under-represented in NCC's SM messaging. Furthermore, SM outreach for non-English speakers was abysmal. Equitable visual representation of diverse RE in NCC's SM messaging has the potential to serve as a tangible means to demonstrate cultural competency and close the gap in cancer disparities. Research Sponsor: None.

	US census (%)	City demographics NCI CC (mean %)	Facebook (mean %)	p-value	Twitter (mean %)	p-value
White	60	43	62	< 0.0001	61	< 0.0001
AA	13	23	14	< 0.0001	12	< 0.0001
Hispanic	18	10	4	< 0.0001	5	< 0.0001
Asian	6	9	11	0.0033	14	< 0.0001

11004 Poster Discussion Session; Displayed in Poster Session (Board #261), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Feasibility of developing a Twitter journal club for hematology/oncology education. *First Author: Elizabeth Henry, Loyola University Medical Center, Maywood, IL*

Background: Medical trainees are increasingly utilizing social media platforms for professional development, networking and education. Twitter chats (TC) are a growing tool to engage health professionals in virtual multi-institutional, cross-discipline discussions. A meta-analysis of Twitter as a tool in residency education demonstrated high rates of satisfaction and concept retention. Despite rapid uptake, few studies address needs for social media use and implementation in graduate medical education. **Methods:** We created a Twitter account (@HOjournalclub) and registered a certified hashtag (#HOJournalClub) with healthcare symplur. For each monthly TC, a specific tumor type and relevant publication was selected. This information was disseminated and amplified to reach trainees on Twitter. A content expert was invited to each TC to provide additional commentary. During TCs, participants answer questions based on domains of critical journal appraisal. Qualitative and quantitative analysis was performed. Basic demographics and tracked hashtag use to measure impressions, participants, and tweets per TC were gathered. Responses were collated and general themes were assessed. Participants were surveyed on ease of participation, article accessibility, and prior use of social media for education. **Results:** Since inception, @HOJournalClub has grown to >650 followers. Most are US-based (83%) medical trainees or healthcare professionals. Additional followers are in South America, Africa, UK, Europe, Middle East, India, East Asia and Australia. Gender is evenly distributed (51% male, 49% female.) Five #HOJournalClub chats have been held to date. Each attracted a mean of 30 participants, generating a mean of 217 tweets. Chats garnered a mean of 270,000 impressions (221,000-319,000) in the 48h after TC. Most participants accessed the chat in real time, with a small subset responding at alternate times. This asynchronous use has enhanced international participation. In post-TC surveys, majority of respondents report being new (48%) or sporadic (48%) users of TCs. Survey participants reported TC participation increased interaction with others in the field, improved literature appraisal skills and led to changes in clinical practice. **Conclusions:** Implementation of a Twitter-based journal club is feasible and attracts participation from trainees, promoting engagement and networking. It represents a novel educational tool for engagement in multi-institutional, multi-national and cross-discipline discussion of relevant hematology/oncology literature. Research Sponsor: None.

11005 Poster Discussion Session; Displayed in Poster Session (Board #262), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Effect of video-based patient education on pancreatic cancer knowledge and behavior. *First Author: Wendy Turell, PlatformQ Health, LLC, Needham, MA*

Background: Treatment outcomes for pancreatic cancer are optimized when patients/caregivers are engaged, informed and supported participants in their care. However, challenges exist regarding care engagement, disease and treatment related education, and the attainment of adequate psychosocial support. To address these needs, we created video-based patient education activities with the National Pancreas Foundation to empower patients/care with information and resources on pancreatic cancer facts, diagnosis, medical management, and strategies to minimize side effects and maximize quality of life. **Methods:** One 1-hour patient education activity was broadcast live and online, followed by on-demand release, in 2018-2019 at CancerCoachLive.com and via Facebook Video for 12 months. Features included panel discussions, slides, live polling and Q&A, and video vignettes of real patient experiences. Knowledge-focused test questions were administered at 3 time points (pre-activity, immediate post-activity, and 2-mos [follow-up] post). Behavioral and communication-focused questions were also asked at follow-up. Data from these questions, live poll responses, and learner-submitted questions pre-event and during live Q&A were analyzed to determine engagement, lessons learned and continuing patient needs. **Results:** In total, 6,276 patients took part in the activity. Patient questions prior to and during the activity focused on basic knowledge about pancreas gland function, tumor development, disease escalation, and medical management. In-session polling results revealed that prognosis and life expectancy were the top concerns for participants. Two months post-education evaluation showed: 33% reported improved communication with their healthcare providers (HCPs) regarding pancreatic cancer; 46% reported improved feelings of being more "in-control" of health care decisions; 25% reported improved care behaviors for their health. Reports of improved HCP communication were specific to: side effect management, clinical trials availability, treatment option knowledge, and confidence related to engaging in discussions. Knowledge improvements were observed for 3 of 4 questions related to facts about the pancreas, pancreatic cancer, and treatment. **Conclusions:** Patient/caregiver education on pancreatic cancer yields gains in knowledge and behavior, improves patient/caregiver engagement, improves treatment decision-making, and maximizes quality of life. Research Sponsor: Celgene.

11006 Poster Discussion Session; Displayed in Poster Session (Board #263), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Innovation in resident oncology education: Switching from an inpatient ward rotation to a hybrid model of inpatient consultations and outpatient clinics. *First Author: Jennifer King, Indiana University School of Medicine, Indianapolis, IN*

Background: Interest in pursuing a career in oncology has decreased among internal medicine residents completing an inpatient oncology rotation. Over several years, our institutional data at Indiana University School of Medicine reflected lower resident satisfaction with the oncology inpatient ward rotation compared to other rotations. **Methods:** A hybrid model of inpatient consultations and outpatient clinics replaced the traditional inpatient oncology rotation at our institution. Over a six-month period preceding and following the change in format, residents completed anonymous rotation assessments and rated their experiences on a 5-point Likert scale (low 1 to high 5). Areas assessed included: patient load, educational value of patient mix, quality of didactics and teaching, quality of patient care delivery, adequacy of time for reading, and overall educational quality of the rotation. **Results:** The hybrid oncology rotation (8 respondents out of 10 residents approached) was rated as significantly superior to the traditional ward format (15 respondents out of 16 residents approached) in six out of eight areas. Improvements in the perceived quality of patient care delivery (p=0.139) and quality of didactics (p=0.058) were also observed without reaching statistical significance. The balance of inpatient and outpatient experiences with the hybrid rotation was highly rated (4.5 ± 0.5). **Conclusions:** The implementation of a hybrid oncology rotation was associated with perceived improvement in educational value, patient mix, and time for reflection and study without apparent compromise in the quality of patient care delivery. Research Sponsor: None.

Comparison of resident ratings of the oncology rotation before and after the implementation of a new hybrid format of inpatient consultations and outpatient clinics.

	6-month period preceding implementation of new format (n=15)	6-month period following implementation of new format (n=8)	*p-value*
Number of admissions/consultations /patient contacts	4.2 (0.5)	4.625 (0.5)	0.044*
Educational value of patient mix	3.73 (1.1)	4.5 (0.5)	0.018*
Inpatient/outpatient balance		4.5 (0.5)	
Adequacy of time for reading/study	3.67 (0.9)	4.625 (0.5)	0.003*
Overall quality of faculty teaching	3.93 (0.8)	4.75 (0.3)	0.003*
Quality of patient care delivery system	4.33 (0.7)	4.625 (0.5)	0.139
Relevance of material to learner	4.08 (1)	4.83 (0.4)	0.018*
Quality of didactic education (teaching sessions)	4.08 (1)	4.67 (0.5)	0.058
Overall rating of rotation	3.93 (0.7)	4.75 (0.3)	0.002*

11007 Poster Discussion Session; Displayed in Poster Session (Board #264), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Design-based bone marrow biopsy training. *First Author: Sam Brondfield, University of California, San Francisco, CA*

Background: Hematology/oncology fellows must achieve bone marrow biopsy proficiency. However, a cost-effective, high-fidelity system to practice these procedures has not been described. Other specialties utilize 3D printing to practice procedures. Using design thinking, we developed, implemented, and evaluated a bone marrow biopsy training session with 3D pelvis models. **Methods:** We printed two models using an NIH template and optimized them through iterative prototyping. We covered a hole at the intended biopsy site with a replaceable cap simulating cortical bone, used cork as medullary bone, and used sand and water as marrow. Caps of two densities simulated softer and harder bone. Fellows could lift silicone skin pads to view anatomy. A flat base minimized movement. In July 2019, we conducted a one-hour practice session ("3D session") with eight fellows during orientation. After an anatomy review, fellows practiced biopsies using the models with faculty feedback. Fellows also attended a one-hour session with a hematologist demonstrating a biopsy on a patient ("patient session"), the only session offered in previous years. We used a t-test to compare course ratings and pre/post-orientation self-assessed comfort with biopsies (5-point scales). Six months later, we surveyed attendings about fellow biopsy skill and success rate compared to prior years. S.B. conducted a content analysis of a focus group with four fellows and email feedback from one fellow. **Results:** Fellows rated the 3D and patient sessions highly (4.50 vs 4.75, p = 0.51). Procedural comfort improved significantly after orientation (2.13 to 3.63, p = 0.03). Attendings noted no difference between the 2019 fellows and prior years. Fellows called the 3D session "helpful" and "high-yield." They praised the opportunity to practice repeatedly with high-fidelity anatomy, rehearse mechanics, receive feedback, and internalize anatomy and muscle memory for later recall. Fellows noted that the model did not allow for patient positioning practice and that the denser cap was too hard. Fellows suggested incorporating a female pelvis and more soft tissue. **Conclusions:** We developed, implemented, and evaluated a design-based bone marrow biopsy training session. Though we did not find outcome differences compared to traditional training, 3D printing represents a feasible, cost-effective, and high-fidelity educational tool. 3D sessions, in conjunction with patient sessions, may augment understanding of anatomy and provide opportunities for practice and feedback. Future iterations should incorporate user feedback to optimize model fidelity and utility. Research Sponsor: None.

11008 Poster Discussion Session; Displayed in Poster Session (Board #265), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Enhancing cancer literacy among Appalachian Kentucky middle and high school students. *First Author: Lauren Hudson, University of Kentucky Markey Cancer Center, Lexington, KY*

Background: Kentucky has the highest rates of overall cancer incidence and mortality in the United States and the Appalachian region of the state experiences the highest burden of the disease. Poor health behaviors, poverty, poor health care access, low education levels, and low health literacy drive the cancer disparities in Kentucky. Inadequate health literacy is associated with lower participation in preventive measures, which can increase one's risk of developing cancer. Increasing cancer literacy among youth represents an opportunity to potentially decrease cancer disparities across Kentucky. In a recent study, we piloted a cancer education intervention in Kentucky middle and high schools to determine if such an intervention could enhance students' cancer literacy. Through the study, we documented a significant increase in students' short-term cancer literacy levels (Hudson L. et al. *Journal of Cancer Education*, in press). **Methods:** This quantitative survey research study aims to examine the long-term effects of the cancer education intervention on the cancer literacy of Kentucky middle and high school students. An online pretest cancer literacy survey consisting of 10 items was administered to a new set of 164 participants from six new schools, followed by the delivery of a cancer education presentation. Immediately following the presentation, participants took a posttest with identical items to the pretest. A follow-up identical test is being administered 3 months after the initial intervention to determine participants' longer-term knowledge retention. **Results:** Replicating our prior work, significant ($p < 0.0001$) increases in both average and median percent of correctly marked items (average: pretest = 50% versus posttest = 77%; median: pretest = 50% versus posttest = 80%) and scores on each individual question were observed immediately following the intervention. Additionally, the average rating as to how the intervention influenced students considerations toward encouraging a family member or friend to change their habits following the intervention was 8 (1 = extremely unlikely;10 = extremely likely). **Conclusions:** This work demonstrates an increase in cancer literacy levels after the educational intervention and indicates that the information motivates participants to share cancer prevention information with others. A follow-up survey will measure participants' longer term knowledge retention levels. These data may suggest that a school-based educational intervention can change behaviors that can lower cancer incidence and mortality rates. Research Sponsor: U.S. National Institutes of Health.

11009 Poster Discussion Session; Displayed in Poster Session (Board #266), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Burnout among oncology physician assistants (PAs) from 2015 to 2019. *First Author: Eric Daniel Tetzlaff, Fox Chase Cancer Center, Philadelphia, PA*

Background: Changes in the demand and delivery of healthcare have led to a significant increase in employment of PAs in Oncology (Onc). These changes may also increase PAs risk of burnout, a syndrome characterized by a high level of emotional exhaustion (EE) and/or depersonalization (DP). This study was initiated to explore temporal changes in burnout & the PA workforce. **Methods:** Using the same methods from 2015, a national survey of Onc PAs was conducted in 2019. Survey items (n = 74) examined personal and professional characteristics, collaborative practice (CP), team structure, organizational context (OC), and burnout. OC was assessed using Areas of Worklife Survey (AWS) domains: workload, control, reward, community, fairness, & values. Low AWS domain score indicated a workplace mismatch (WM). Burnout was assessed with the Maslach Burnout Inventory. Change in burnout was examined with repeated measures logistic regression. **Results:** 234 out of 917 PAs (25.5%) completed the full survey. Respondents were mostly female (86%), married/partnered (78%), in Med Onc (71%), and practicing in the outpatient setting (67%). Burnout increased from 34.8% in 2015 to 48.7% in 2019 [odds ratio for burnout, 2019 vs 2015 = 1.92 (95%CI 1.40-2.65), $p < .001$]. Adjustment for workforce variables did not explain the increase in burnout. Among 2019 respondents, increased hours worked ($p = .003$), sub-specialty ($P = .018$), less time (%) spent on direct patient care ($p = .007$), practicing below full extent of education and training ($p = .048$), dissatisfaction with CP ($p < .001$), and perceptions of poor collaborative physician leadership ($p < .001$) were associated with higher rates of burnout. No difference in burnout was seen for personal or team characteristics, practice setting, years in onc, or # of patient visits. AWS scores were lower for PAs with burnout vs. without burnout ($p < .001$). PAs with a WM had a higher rate of burnout for each AWS domain ($p < .001$); most common WMs were fairness (44%) and workload (43%). **Conclusions:** The rate of burnout for Onc PAs has significantly increased and is now at levels of nearly 50%. Burnout in Onc PAs related to WM in workload is common, significant, & not explained by patient volume alone. The causes of burnout are multifactorial and additional research is needed in this at risk group. Research Sponsor: Association of Physician Assistants in Oncology, U.S. National Institutes of Health.

	2015 (n = 250)	2019 (n = 234)
Burnout Overall	87 (34.8%)	114 (48.7%)
EE (High)	76 (30.4%)	102 (43.6%)
DP (High)	44 (17.6%)	52 (22.2%)
Burnout by sub-specialty		
Med Onc	73/188 (38.8%)	88/165 (53.3%)
Surg Onc	9/30 (30.0%)	18/39 (46.2%)
Rad Onc	2/13 (15.4%)	1/12 (8.3%)
Other	3/19 (15.8%)	7/18 (38.9%)

11010 Poster Discussion Session; Displayed in Poster Session (Board #267), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Identifying burnout in young oncologists: The sooner the better. *First Author: Elena Elez, Medical Oncology Department, Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain*

Background: Professional burnout is an important issue for the healthcare systems with potentially relevant consequences in the quality of patient care. Young oncologists are a special risk population, due to high workload, academic pressure and other specific factors related to cancer care. Work life and lifestyle factors are related with burnout levels and may define specific interventions to reduce and prevent burnout. **Methods:** A survey based on the validated Maslach Burnout Inventory Human Services Survey for Medical Personnel (MBI-HSS MP) was conducted. Additional questions to explore work life and lifestyle factors were included. We studied potential burnout amongst young Spanish oncologists (residents and oncologist in the first 5 years of professional performance). Statistical analyses, including linear regression, were carried out to test the relations between overall burnout score and work and lifestyle factors. **Results:** We obtained 243 responses to the survey. The sample was representative in terms of age, sex, geographic region, professional profile (residents and young oncologists) and a homogeneous distribution per year of residence (final participation rate was of 26.6%). Regarding 5 Burnout profiles, 32.1% of the participants were classified as Ineffective, 25.1% as Burnout, 21% as Engaged, 17.3% as Overextended and 4.5% as Disengaged. Percentage of Burnout profile is higher in medical oncology residents (28.24%) than in young oncologists (19.79%). The highest percentage of burnout profile was observed in the second-year residents (35,71%) and gradually decreases, in parallel to an increase in the engaged profile. The multivariable linear regression analysis showed a significant correlation between not having a good work life balance and adequate vacation time and the burnout score. **Conclusions:** Burnout affects a significant number of young oncologists with significantly different profiles and differences across regions. Adapted interventions to the most frequent profiles and at different stages of the training and professional career may be necessary particularly at the early beginning. Actions towards achieving a better work and personal life balance and stress management could be effective. These results are the basis for the prospective part of our study that aims to design an intervention and to assess its efficacy in this population. Research Sponsor: Spanish society of medical oncology.

11011 Poster Discussion Session; Displayed in Poster Session (Board #268), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Results of emotional burnout study among oncologists in Russia. *First Author: Tatiana Semiglazova, NMIC N.N.Petrov, St. Petersburg, Russian Federation*

Background: Emotional burnout (EB) is a syndrome caused by chronic work-related stress. This is a non-adaptive reaction to chronic stress resulting from professional activities and leading to the depletion of emotional and personal resources. Oncologists have high burnout risk, because involuntarily involved in the negative experiences of patients and get emotional stress. So it is important to develop measures to prevent EB for medical oncologists. Aim: The aim is to study the prevalence and severity of EB among oncologists and to develop preventive measures. **Methods:** A screening survey of the Russian Society of Clinical Oncology (RUSSCO) was conducted among 389 oncologists in various regions of Russia. The Maslach Burnout Inventory and online self-administered questionnaire were used. The questionnaire was sent out in November 2019. The questionnaire was based on a multi-factor model, which includes the following components: emotional exhaustion, depersonalization, reduction of professional achievements. **Results:** The average age of the respondents was 49.5 years, 61% of them were female. Chemotherapists made up 47.5%, 28% were surgeons, 8.5% were radiotherapists, 7% were diagnostic profile specialists, administrators made up 3%, 14.5% of the respondents had related specialties: clinical psychologists, pathologists, palliative care doctors. 30% of respondents had scientific degree. The results of the study were the following. 71.6% of specialists have expressed EB syndrome; 28% at EB formation stage, 1% have no signs of EB. There wasn't a significant difference in EB rates across oncologists of various specialties. All stages of EB were identified. Female specialists are more likely to have manifestations of EB. EB severity was the same for doctors of inpatient and outpatient care. The extreme mode of work did not show significant differences of EB among both male and female specialists. First 5 years and more than 15 years of professional activity are most vulnerable to development of EB. EB was least affected by specialists over 65 years old with extensive experience. **Conclusions:** Hight level of EB was revealed among oncologists. Study results should be used during EB prevention, development of psychotherapeutic assistance and in educational programs. Research Sponsor: None.

11012 Poster Discussion Session; Displayed in Poster Session (Board #269), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The Matilda effect: Under-representation of women in hematology and oncology awards. *First Author: Shruti R Patel, Mayo Clinic, Rochester, MN*

Background: The proportion of women in the field of hematology and oncology (H&O) has increased over recent decades, but representation by women in leadership positions remains a challenge. Our aim was to examine representation of winners of recognition awards by gender and race from the major international hematology and oncology societies. **Methods:** Published award recipients from the seven major H&O societies were reviewed, with 26 years of data included (1994-2019). Awardee demographics and academic rank were collected and included in the analysis. Gender was determined based on awardee full name and verified by public data. Chi-square and Cochran-Armitage tests were used to analyze the data. **Results:** Over the past 26 years, 942 awards were presented at the 7 major H&O societies. We excluded 27 gender specific awards from the analysis. Of the 915 awardees included in analysis, award recipients were overwhelmingly men (77.9%) and non-Hispanic white (84.7%). Gender breakdown by society is described in table. ESMO and ASTRO represented the lowest distribution of women at 9.1% and 11.1%, respectively. Women awardees received 30.3% of the awards categorized as humanistic and education-related, while only receiving 16.0% of awards in the basic sciences category ($p<0.01$). The Cochran-Armitage test demonstrated an upward trend in the number of women awardees, from 10% between 1994-1998 to 25.6% between 2014-2019 (p=0.0004). Over the past five years, the average proportion of women medical oncologists was 35.6% per the AAMC. In this time period, women oncologists have received only 24.0% of all awards, suggesting the awardees included in the study period do not represent the proportion women in the field (p=0.00424). Black, Hispanic, and Asian awardees represented 3.7%, 3.3%, and 6.8% of the total awardees, respectively. Of the 64 Black and Hispanic awardees, 60.9% of the awards were for investigating healthcare disparities and only 4.6% were given for basic science research. **Conclusions:** During our study period, women physicians and investigators were less likely to receive recognition awards from the seven major H&O societies compared to men. We also observed a considerable low proportion of minority awardees in all oncology subspecialties. While the proportion of women awardees has increased over time, significant underrepresentation remains. Research Sponsor: None.

Society	Women (%)	Men (%)
ASCO	54 (27.8)	140 (72.2)
ASTRO	7 (11.1)	56 (88.9)
AACR	50 (22.1)	176 (77.9)
ASH	44 (23.2)	146 (76.8)
EHA	8 (20.5)	31 (79.5)
ESMO	6 (9.1)	60 (90.1)
SSO	33 (24.1)	104 (75.1)

11013 Poster Discussion Session; Displayed in Poster Session (Board #270), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Gender differences in faculty rank and subspecialty choice in academic medical oncology. *First Author: Laura Graham, University of Washington, Seattle, WA*

Background: The gender gap in the United States healthcare field has been closing. In 2000 women made up 45% of medical school matriculants and by 2017 outnumbered men. Based on our personal observations at academic meetings, however, we hypothesized that gender differences persist in faculty rank and subspecialty choice in academic medical oncology. **Methods:** We created a database of medical oncologists at the top 15 cancer centers as ranked by the *U.S News and World Report* in 2019. We identified all medical oncology faculty in the subspecialty fields of breast, gastrointestinal (GI), genitourinary (GU) and thoracic oncology from institution websites (12/2019-1/2020). Faculty working only at satellite clinics (i.e. non-research appointments), and the few faculty in more than one subspecialty group, were excluded. Gender (determined by pictures), subspecialty and academic rank were recorded based on data from institution websites and professional social networking sites. Proportions of men and women in each subspecialty and at each faculty rank were calculated; odds ratios (OR) and χ^2 tests were used for comparisons. **Results:** 346 men and 244 women were identified as subspecialty medical oncologists, comprising 59% and 41% of faculty members, respectively. Gender representation by subspecialty and academic rank are shown in the Table. Breast oncology had more women oncologists than men (OR 2.9, $p < 0.001$); GU oncology had fewer women (OR 0.3, $p < 0.001$). The representation of women and men was comparable at the lower academic ranks (instructor, assistant and associate professors). But at the top rank of full professor, only 31% were women (OR 0.54, $p = 0.001$). Notably, even in breast oncology, the one subspecialty with a greater proportion of women, women still comprised a lower proportion of full professors than men. **Conclusions:** Gender differences persist in academic medical oncology. At the top 15 US cancer centers, gender differences are seen in subspecialty representation, with more men in GU oncology and more women in breast oncology. Fewer women than men achieve the rank of full professor, even in breast oncology. Additional research is needed to explore the causes of, and contributors to, these differences as well as their impact. Research Sponsor: U.S. National Institutes of Health.

Professor Rank, N (%)	Male (n =346)	Female (n =244)	All (n = 590)
Full	116 (33)	52 (21)	168 (28)
Associate	78 (23)	70 (29)	148 (25)
Assistant	112 (32)	85 (35)	197 (33)
Instructor	40 (12)	37 (15)	77 (13)
Subspecialty Choice,N(%)			
Breast*	71 (21)	110 (45)	181 (31)
GU*	95 (27)	27 (11)	122 (21)
Thoracic	71 (21)	52 (21)	123 (21)
GI	102 (29)	66 (27)	168 (28)

*$p < 0.05$

11014 Poster Discussion Session; Displayed in Poster Session (Board #271), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Gender variation in clinical activity and Medicare payments among medical oncologists and hematologists. *First Author: Manojna Konda, The University of Arkansas for Medical Sciences, Little Rock, AR*

Background: While physician sex has been shown to impact salary even after adjusting for productivity, gender-based differences in clinical activity and reimbursement for oncologists and hematologists are not completely understood. We evaluated the differences in Medicare reimbursement for male and female physicians in medical oncology and hematology. **Methods:** A retrospective analysis using Centers for Medicare & Medicaid Services Physician and Other Supplier Public Use File (POSPUF) for the year 2017 was performed to identify charges and total payment information for individual oncologists and hematologists. Mean values were compared using two-sample t-test, and the medians were compared by Wilcoxon rank-sum test. **Results:** A total of 8553 oncologists and hematologists (2710 women and 5843 men) were included in the POSPUF in 2017. Female physicians submitted a mean of 16,754 fewer charges (95% CI, −19,696 to −13,812; $P < .0001$), collected a mean of $173,632 less in revenue (95% CI, −201,184 to −146,080; $P < .0001$), and submitted a mean of 5.65 fewer unique billing codes (95% CI, - 6.69 to - 4.61; $P < .0001$) compared to their male counterparts. Women represented 219 of the 1069 most highly productive oncologists and hematologists (20.4%) and collected a mean of $281,263 (95% CI, −417,517 to −145,008; $P < .0001$) less than similarly productive men. **Conclusions:** This study suggests that female oncologists and hematologists submit fewer Medicare charges and receive lower Medicare payments compared to male providers. Even among similarly productive hematologists and oncologists, women collected less revenue than men. Further research is required to explore causes for this difference. Research Sponsor: None.

Number of charges, payments, and unique billing codes in 2017.

Variable		Total, No. (%)	Mean (SD)	Mean Difference (95% CI)	*P* Value	Median (IQR)	Median *P*Value
Charges, No.	All	318,517,087	37,240 (74,149)	NA	NA	2176 (42,000)	NA
	Women	69,905,377 (22.1)	25,795 (55,478)	−16,754 (−19,696 to −13,812)	<0.0001	1,066 (23,414)	<0.0001
	Men	248,611,710 (77.8)	42,549 (80,823)	NA	NA	3,359 (52,236)	NA
Payments, $	All	3,378,143,718	394,966 (696,989)	NA	NA	89,481 (438,595)	NA
	Women	748,906,486 (21.9)	276,349 (517,373)	−173,632 (−201,184 to−146,080)	<0.0001	59,520 (261,406)	<0.0001
	Men	2,629,237,233 (78.1)	449,981 (759,912)	NA	NA	108,894 (522,317)	NA
Unique Billing Codes, No.	All	868	22.16 (23.3)	NA	NA	10 (31)	NA
	Women	496 (57.1)	18.30 (21.43)	− 5.65 (− 6.69 to − 4.61)	<0.0001	7 (26)	<0.0001
	Men	832 (95.8)	23.95 (25.35)	NA	NA	13 (34)	NA

11015 Poster Session (Board #272), Fri, 8:00 AM-11:00 AM

Stress related to electronic health record (EHR) use among oncology trainees: A quality improvement study to optimize information gathering. *First Author: Teja Ganta, Icahn School of Medicine at Mount Sinai, New York, NY*

Background: Poor EHR usability is associated with physician burnout [1]. Oncology providers are tasked with coordinating data from multiple sources/tabs within an EHR (biomarkers, genetic data, imaging, etc.) to make treatment plan decisions. It is hypothesized that oncology trainees will have decreased stress using an EHR tool to optimize data gathering. **Methods:** This single-institution quality improvement study aims to decrease the time and stress associated with navigating the EHR to review/document laboratory data among first-year clinical oncology fellows rotating on consult services at The Mount Sinai Hospital as measured by self-reported survey data. An EHR tool was built that pulls into the note a drop-down list of user-selectable laboratory panels grouped according to hematologic/oncologic disease presentations. A survey was sent to all fellows in the program to assess attitudes toward the EHR. All 1st-year fellows were given access to the EHR tool as they are the ones who primarily rotate on consult services. After 3 months, a follow-up survey was sent to 1st-year clinical fellows to assess satisfaction with the EHR intervention. **Results:** For the baseline survey, there are a total of 17 respondents (response rate 77%). 70.6% of fellows believe using the EHR increases their level of stress. The most prevalent reasons cited for frustrations with the EHR are "Hard to read other providers' notes" (82.4%), "Gathering information from multiple different pages" (76.5%), "Increased documentation requirements" (76.5%), "Inability to quickly navigate the system" (64.7%). For the follow-up survey targeting 1st-year fellows, there are a total of 6 respondents (response rate 100%). 5 fellows tried the EHR tool at least once. Of those 5 fellows, 100% use it daily in clinical practice while on consult services, believe it makes notes more legible, believe it saves time spent in chart review, and believe it decreases their stress associated with navigating the EHR. **Conclusions:** A majority of clinical oncology fellows believe that the EHR contributes to their stress. The reasons cited suggest that interventions that optimize note-writing and chart-reviewing may decrease stress. The majority of fellows who used this EHR tool believe the tool improved their efficiency and stress levels. This suggests more widespread use of this tool among oncology clinicians may contribute to wellness although further studies to increase utilization must be taken. Research Sponsor: None.

11016 Poster Session (Board #273), Fri, 8:00 AM-11:00 AM

Is burn-out-syndrome a problem among oncology workers? Incidence and effective tools to achieve improvement. *First Author: Alberto Jacobo Cunquero Tomas, Medical Oncology Department, Consorcio Hospital General Universitario de Valencia, Valencia, Spain*

Background: Burn-Out Syndrome (BOS) is defined by (1) emotional and physical exhaustion; (2) cynicism and depersonalization; and (3) no personal nor professional fulfillment. It affects up to 78% of oncology-related workers (doctors, nurses and nurse-assistants, among others). This may decrease quality in both patient assistance and institutional processes. However, there is lack of resources for its diagnosis and management. Our objective is to: (1) determine the incidence of BOS in our team; (2) analyze potential causes; and (3) decrease in 20% the percentage of BOS affected workers. **Methods:** From October 2018 to November 2019, 20 nurses and nurse-assistants participated. Process map and Ishikawa fish-bone diagram were design to analyze BOS potential causes and to design appropriate interventions after Priority/pay-off matrix description. To do so, participants were asked to fulfill a personal detail questionnaire at the beginning, and adapted versions for the GHQ-12 and Maslach Index questionnaires after each intervention. To track the improvement process, a PDSA cycle was fulfilled and re-evaluated overtime. Project developed through the ASCO Quality Training Program and the Fundación ECO support. **Results:** Population main characteristics: 87% women, 47-year-old median age. 12 nurses, 6 working in the clinic. 90% with more than 5 years of experience in Oncology. At baseline, 75% healthy (GHQ-12), BOS cause risk: exhaustion 70%, depersonalization 45%, fulfillment 55%. Two interventions developed to improve exhaustion BOS risk: (1) ergonomy tips; and (2) self-assessment and self-help tools. 9 subjects lost after 2nd intervention. After interventions, 34% exhaustion risk reduction and 100% healthy workers (GHQ-12). **Conclusions:** After two interventions, we have achieved an improvement of 34% lowering the risk of suffering BOS among our workers. Health perception improved to 100%. The loss of 9 subjects after the 2nd intervention may be a bias when interpreting the final results. Giving the appropriate tools to medical oncology workers helps reduce BOS risk significantly Research Sponsor: None.

11017 Poster Session (Board #274), Fri, 8:00 AM-11:00 AM

The experience of first-year hematology and oncology fellows after implementing a wellness chief fellow at an academic cancer center. *First Author: Sherise C. Rogers, Division of Medical Oncology, Department of Internal Medicine, The Ohio State University Comprehensive Cancer Center, Columbus, OH*

Background: Hematology & Oncology trainees are high risk for burnout. Risk factors include early stage in career, female gender and isolation. From previous assessment, the program discovered that the feeling of isolation was a problem experienced by our trainees. Our first-year fellows are challenged with multiple acclimations and the intense demands of inpatient service. As a result, we developed the leadership position of Wellness Chief Fellow to address the specific needs of this population during academic year 2019. **Methods:** The Wellness Chief (WC) is a third-year Hematology and Oncology Fellow with good communication skills and knowledge of resources at the academic cancer center. The WC gave a Wellness lecture during first-year orientation to emphasize the prioritization of personal wellbeing throughout fellowship. The WC developed a list of wellness resources within the hospital system and local community and shared these with the fellows. The WC also provided quarterly one-on-one confidential mentoring to first year fellows. These meetings were informal and semi-structured. Topics included adjusting to the academic center and their new fellowship role, moving to a new city, current support system, clinical and research mentorship, life challenges and self-care. Mid-year, the first-year fellows were surveyed regarding their experience. **Results:** Eight fellows participated in one-on-one mentoring and 5 completed a mid-year evaluation. 4/5 fellows were new to the city. All trainees felt that mentoring helped them adjust to fellowship. 4/5 stated that they found a clinical mentor and 3/5 have a research mentor and started a research project. 4/5 acknowledged that they have a friend in the fellowship program and 5/5 stated that they do have someone to go to if they were experiencing a challenging life event. All fellows reported gaining something valuable after each mentoring session. 3/5 subjectively experienced burnout within 6 months of the fellowship program. One person stated they experienced burnout once per week and 2 reported monthly burnout. **Conclusions:** A Wellness Chief Fellow can buffer the effects of isolation within the first-year fellowship experience by providing mentoring and resources during a challenging acclimation period. Research Sponsor: None.

11018 Poster Session (Board #275), Fri, 8:00 AM-11:00 AM

Storytelling as a means of improving community and decreasing burnout in a large academic cancer center. *First Author: Sherise C. Rogers, Division of Medical Oncology, Department of Internal Medicine, The Ohio State University Comprehensive Cancer Center, Columbus, OH*

Background: Burnout is highly experienced amongst physicians who care for patients with cancer. Workplace isolation is a risk factor for burnout. The field of oncology is growing at a rapid pace and many cancer centers are expanding to meet the demands of patient care and research. Prior assessments revealed that our hematology and oncology fellows were experiencing feelings of isolation and disconnection, which was likely reflected from our greater academic community. **Methods:** The traditional art of storytelling has been used to offer guidance, teaching, new perspective taking and understanding of self. The concept of "My Story", an interactive storytelling lecture series was developed to address the following objectives at a large academic cancer center: 1) Promote connection and decrease isolation amongst the cancer sub-specialties 2) Increase fellow-faculty interaction for mentorship, 3) provide an outlet to discuss sensitive topics such as burnout, grief, unexpected patient outcomes, medical errors, work- life balance, career transitions, personal struggles, and bias. A faculty member was identified to tell their unique story for a special lecture. Fellows and faculty members from hematology, oncology, radiation-oncology, neuro-oncology, gynecology-oncology, and surgical oncology were invited. All audience members were encouraged to ask questions and engage in discussion. A survey was distributed after the inaugural event for evaluation. **Results:** A total of 56 people attended the inaugural event. There were 14 fellows, 9 faculty members and 33 others, which included basic scientists and advance practice providers. 17 individuals completed our post survey, which included 6 faculty members, 4 fellows, 1 nurse practitioner, 1 student and 5 others. On a scale from 1-10 (mean scores reported), participants rated the experience 7.5 for enjoyment, 6.6 for sense of connection with the group, 6.0 for inspiring them to make new connections with others and 6.8 when asked if they left with new tools to assist with personal challenge. **Conclusions:** A lecture series that invites multidisciplinary cancer physicians and surgeons to discuss personal career and life challenges can be beneficial to addressing burnout, decreasing isolation and improving connection and community at a large academic cancer center. Research Sponsor: None.

11019 Poster Session (Board #276), Fri, 8:00 AM-11:00 AM

Reflection rounds to facilitate resilience in hematology/medical oncology fellows. *First Author: Erica C. Nakajima, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

Background: Given the prevalence of burnout among medical oncologists (40-60% in the literature), education on burnout risk factors, recovery, and prevention are needed urgently in training curricula for medical oncology fellows. Care of patients with cancer is increasingly complex, and often can seem overwhelming to new trainees. Debriefing as a resiliency skill to develop self-reflection and identify coping strategies may provide a durable way to navigate these complexities. Optimization of fellowship Reflection Rounds (RR) was selected as a fellow-led quality improvement (QI) project for the current academic year. **Methods:** A QI team including the APD and representatives from all levels of fellowship training was assembled. Feedback regarding previously unstructured, monthly, hour long faculty-facilitated RR for first year fellows was reviewed. Topics with associated readings were selected and paired with fellow-nominated faculty based on the most common recurring themes. The QI team administered the Stanford Professional Fulfillment Index (PFI) to all fellows at the midway point of the academic year. RR were re-structured to include a chaplain with trainee communication expertise and a chief fellow to participate the sessions to assess changes in trainee engagement. Repeat assessment of the Stanford PFI is planned for the end of the academic year. **Results:** Topics identified for discussion included handling bias, futile care, patient communication, end of life care, and work-life balance. 26 fellows completed the Stanford PFI including nine 1st year fellows, 13 2nd year fellows, and 6 3rd year fellows. Survey results revealed emotional and/or physical fatigue as areas of greatest need for improvement in fellow well-being with 27% of fellows reporting "moderate" emotional or physical exhaustion. **Conclusions:** RR provides a safe and effective forum to develop peer debriefing and self-refection as resiliency skills within hematology/medical oncology fellowship training. Optimization of RR will continue as fellows become more involved in planning and implementation of curricular improvements to promote resiliency and enhance wellness. Research Sponsor: None.

11020 Poster Session (Board #277), Fri, 8:00 AM-11:00 AM

Exploring glocalization in the construction and implementation of global curricula. *First Author: Meredith Elana Giuliani, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Despite proposed advantages of global oncology curricular harmonization including physician mobility and improving the quality of care the challenges and unintended consequences require greater study. The aim of this study was to problematize the concept and implementation of global oncology curricula and their relationship to local contexts of power and culture. **Methods:** Fourteen international participants involved in the development and implementation of global oncology curricula completed in-depth, one-on-one semi-structured interviews lasting 40-60 minutes. Snowball sampling was employed. The participant sample was representative of different geographic regions, genders and professional scopes of practice to ensure diverse perspectives were sought. Through iterative analyses, using an abductive approach, the study team discussed and reviewed the data and made revisions through collaborative analysis to enhance comprehensiveness and to improve credibility. In the final analysis the meaning and implication of the themes were discussed yielding a conceptual analysis. **Results:** Our data have articulated 5 key challenges for global curricula including 1) Ambiguous or conflicting perspectives on the purpose and scope of Global Oncology Curricula 2) Insufficient representation of diverse perspectives and realities in the creation of the final curricula 3) A rigid conceptualization of competency requirements 4) A mismatch between the curricular requirements and local context and 5) The influence of power relationships and decision makers. Leveraging the strengths of diversity including fostering representation, addressing power differentials and factoring local contexts may be an approach to mitigating these challenges. **Conclusions:** Global oncology curricula may serve important advocacy roles within the healthcare system. Leveraging diversity may positively impact the common challenges in the construction and implementation of global oncology curricula. Research Sponsor: None.

11021 Poster Session (Board #278), Fri, 8:00 AM-11:00 AM

Effect of participation in the annual Immuno-oncology Young Investigators' Forum (IOYIF) on the competency and performance of young researchers. *First Author: Joan B. Fowler, Creative Educational Concepts, Lexington, KY*

Background: Advancing the fight against cancer involves many types of research across different disciplines and professions, from PhD-trained scientists to medical oncology physicians. The IOYIF is a competitive academic research program where oncology junior faculty, clinical and post-doctoral fellows who are pursuing a career in academic research in IO are invited to submit an abstract of their unpublished, original research to a panel of expert judges for assessment. **Methods:** Performance and confidence change were objectively assessed by analyzing pre- and post-test results before and after the presentation of research. Statistical testing between pre- and post-participation were conducted via chi square analysis with a priori significance set at 0.05. **Results:** Participants experienced an improvement in mean abstract score following participation in the forum. The mean abstract score improvement was statistically significant for All Participants ($P< 0.001$) and all sub-groups ($P< 0.001$), with the sole exception of Clinician Scientists. Overall, PhD/Postdoctoral Research participants demonstrated the most improvement. The mean abstract score improvement was statistically significant for those who attended presentation coaching ($P< 0.001$) as well as for those that did not ($P= 0.001$); the magnitude of improvement was greater among those who attended coaching. Participant self-reported mean confidence scores increased with statistical significance from pre- to post-participation in the forum ($P< 0.001$); this increase was noted across all participants and all sub-groups, and was observed in relation to both presentation skills and research defense. Young Investigators reported that lack of experience with grant writing is the most significant barrier they face to obtaining grant funding; they also listed lack of mentorship/guidance in publishing as a prominent barrier. **Conclusions:** This analysis demonstrates that an IO research forum designed for young investigators can improve the performance and confidence of these scientists. These findings highlight the robust, multifaceted impact of the IOYIF on advancing the professional development of the next generation of IO researchers. Identification of barriers demonstrates the tangible value of the IOYIF in providing needed mentorship to further research efforts, deliver axioms of grant writing guidance, and bridge the gap young researchers face in obtaining funding and publishing their work. Research Sponsor: AstraZeneca.

11022 Poster Session (Board #279), Fri, 8:00 AM-11:00 AM

Introduction of a patient communication course to postgraduate oncology training in Russia. *First Author: Maxim Kotov, National Medical Research Center of Oncology N.N.Petrov, St. Petersburg, Russian Federation*

Background: Communication skills are an obligatory part of postgraduate oncology education in European and Western countries and its benefits for doctors, patients, and the healthcare system are well-known. However, teaching efficient patient communication is challenging in developing countries where the paternalistic model is still spread and medical professionals are unaware that these skills are lacking. We hypothesize that a short simulation-based course for oncology residents introduces communication skills and raises awareness about its value. **Methods:** A 2-day communication course based on the Calgary-Cambridge model was taught to a cohort of PGY2 oncology residents. Lectures, seminars, and clinical simulations emphasizing a patient-centered approach, including open questions, active listening, identifying patient concerns, empathy, summarizing, and bad news delivery were conducted by certified teacher. A simulation exam was administered to those who completed the communication course and those who did not complete the course. Scores (max. 130) from two clinical scenarios assessed by the examiner, actors, and participant were compared between groups. **Results:** Ten PGY2 residents completed the course and seven did not complete the course. Medians scores for the first scenario given by the examiner, actor and resident were 99 (IQR: 90 – 122), 125 (IQR: 122 – 127) and 102 (IQR: 91 – 108) for course participants and 15 (IQR: 7-35), 18 (IQR: 12-34) and 61 (IQR: 41-83) for non-participants, respectively. Medians scores for the second scenario were also higher in participant group: 113.5 (IQR: 100-117), 107 (IQR: 98-118) and 104 (IQR: 99-112) vs. 22 (IQR: 12-50), 18 (IQR: 10 - 44) and 66 (IQR: 43-81), respectively. Four (40%) course participants and seven (100%) non-participants evaluated themselves higher than the examiner and actor. **Conclusions:** A short patient communication course for young oncologists effectively improves communication skills and provider self-awareness in developing countries. Research Sponsor: None.

11023 Poster Session (Board #280), Fri, 8:00 AM-11:00 AM

Oncology fellows' survivorship clinic: An opportunity for education and multidisciplinary care delivery. *First Author: Hira Latif, Medstar Washington Hospital Center, Washington, DC*

Background: Cancer survivors in the U.S. are expected to exceed 20 million by 2026. Most fellows do not receive formal training in survivorship during oncology fellowship despite cancer survivorship comprising 2% of the American Board of Internal Medicine's Oncology examination and the recent accreditation standards related to survivorship care from the Commission on Cancer. **Methods:** We developed a survivorship curriculum and a multidisciplinary survivorship clinic staffed by a medical oncologist and physiatrist in September 2018. Oncology fellows rotated during their ambulatory block and completed surveys assessing skills and perceptions of competence at the beginning and end of the academic year. **Results:** 8 fellows completed the pre-survey and 6 of them completed the post-survey. While only a quarter had delivered a survivorship care plan/treatment summary prior to starting clinic, all fellows had delivered these (median=2, range=2-8) at the end of the year. Most fellows had seen survivors of breast, colorectal and hematologic malignancies prior to starting clinic; few had seen survivors with lung (12.5%), GU (0%) or head and neck (25%) cancer. These numbers increased, particularly with fellows' seeing survivors of GU (50%) and head and neck cancers (100%) at the end of the year. Prior to the rotation less than half the fellows had assisted with managing cancer survivors' treatment consequences or provided continuity of care through a multidisciplinary team. Similarly, only 25% had counseled cancer survivors with psychosocial concerns. On the post-survey, 100% of fellows reported practicing and feeling experienced in these domains. Post- survey showed improvement in self-reported competence levels in caring for cancer survivors (see Table). **Conclusions:** Participating in a survivorship clinic has a positive impact on oncology fellows' experience and competence in caring for cancer survivors. Future directions are geared toward expansion of fellows' skills to include areas related to cardiovascular and physical medicine. Research Sponsor: None.

Median scores for fellows' self-reported level of competence in caring for cancer survivors using a Likert scale of 1-5. (1: very unskilled to 5: very skilled).

	Pre-Survey	Post-Survey	P- Value
Provide current cancer information at the appropriate level	3	4	0.070
Provide a treatment summary and survivorship care plan	2	4	0.028
Identify people at high risk of cardiovascular complications due to their cancer treatment	3	4	0.064
Work with a multidisciplinary specialty team to provide continuity of care	2	4.5	0.038

11024 Poster Session (Board #281), Fri, 8:00 AM-11:00 AM

Student loan debt and visa status influence on career choices for hematology and medical oncology fellows in the United States. *First Author: Karam Al-Issa, Indiana University School of Medicine, Indianapolis, IN*

Background: There are multiple factors influencing future career plans for US hematology/oncology fellows. The objective of this study is to evaluate the effects of student loan debt and visa status as potential factors affecting their career choices. **Methods:** A total of 159 US hematology/oncology fellowship programs were contacted, program directors forwarded the survey to current hematology/oncology fellows and recent graduates (classes of 2019, 2018 and 2017). The survey consisted of 13 questions regarding their student loan debt and visa status, research experience, initial career plan, current career for graduates, the influence of student loan debt and visa status on their career decisions (academic, private practice, industry), and whether or not their training programs had resources or mentorship to help them deal with those factors. We used a scale of 1-5 to determine how much each factor affected career choice (1 = extremely unaffected, 5 = extremely affected). **Results:** A total of 220 physicians have participated, 177 (80.5%) fellows and 43 (19.5%) graduates. For graduates, 35% had student loans during fellowship, 40% of them thought that their loans affected their career choice with a score of 4-5. 93% of graduates with student loans answered that they weren't aware of resources/mentorship to address their loans effect on their career. 44% of graduates were on J1/H1 visa during training, 74% of them thought that their visa status affected their career choice with score of 4-5. 63% of graduates who were on visa answered that they weren't aware of resources/mentorship to address visa status as a factor influencing their career options. For current fellows, 51% have student loans, one third of them thought that their loans affected their career choice with score 4-5. 77% of fellows with student loans answered that they weren't aware of resources/mentorship to address their loans effect on their career. 16% of current fellows are on J1/H1 visa, 66% of them thought that their visa status is affecting their career choice with score 4-5. 62% of fellows who are on visa answered that they weren't aware of resources/mentorship to address visa status as a factor influencing their career options. **Conclusions:** Hematology/oncology fellows report that student loan debt and visa status are important factors affecting their career decisions. The majority of hematology/oncology fellows in this survey weren't aware of resources or mentorship to help deal with these factors. Mentors need to be aware of these factors to help fellows achieve their career goals. Research Sponsor: None.

11025 Poster Session (Board #282), Fri, 8:00 AM-11:00 AM

Just-in-Time Teaching (JiTT) screencasts for the resident inpatient oncology service: A pilot study evaluating feasibility and effectiveness. *First Author: Patrick Kuhlman, Wake Forest School of Medicine, Winston-Salem, NC*

Background: Just-in-Time Teaching (JiTT) screencasts have been viewed positively in some undergraduate and graduate medical settings. JiTT screencast effectiveness has not yet been evaluated for medical trainees in the inpatient adult hematology/oncology setting. Objectives: Our pilot study's goal was to identify relevant learning objectives, to assess feasibility of screencast development, and to optimize screencast delivery. **Methods:** To identify key clinical topics, a mixed methods approach first utilized institutional retrospective data (6/1/2018-6/30/2019) to determine the most common inpatient medical problems followed by qualitative interviews of teaching faculty and senior residents. The following six topics were identified for inclusion: 1. Metastatic disease to spine 2. Brain metastases 3. Oncologic emergencies 4. Cancer associated venous thromboembolism 5. Hematologic emergencies 6. Sickle cell disease: inpatient management For each topic, a literature review was performed to develop teaching points which were then refined with input from clinician experts. Each screencast went through several rounds of edits by faculty and trainees prior to submission to the instructional design team for final editing. Screencast length ranged from 13 – 25 minutes (mean of 18 minutes). Qualitative and quantitative feedback was obtained from residents by structured focus group session and online surveys. **Results:** All residents reported that educational content was "just right." The series of 6 screencasts was completed within 2 months of dedicated fellow research time. Preferred screencast length was 10-20 minutes and preferred viewing speed was 1.5x original speed (7/10). All residents reported that a screencast database would be a helpful resource for future clinical rotations. All residents (n = 10) reported that screencasts improved medical oncology knowledge base and will improve care provided to cancer patients. **Conclusions:** Creation of a screencast series was feasible for a hematology-oncology fellow. Systematic identification of key clinical topics led to materials which were confirmed by faculty and trainees to be important for internal medicine medical education on inpatient oncology services. This pilot data indicate that JiTT screencasts may be an effective educational intervention and directly informed a randomized educational research study which is currently enrolling participants. Research Sponsor: Wake Forest Comprehensive Cancer Center Pilot Funds.

11026 Poster Session (Board #283), Fri, 8:00 AM-11:00 AM

Optimizing management of glioblastoma: Educational impact on clinicians. *First Author: Michelle Arielle Worst, Medscape LLC, New York, NY*

Background: Glioblastoma multiforme (GBM) is a rare, malignant tumor of the central nervous system (CNS) with poor prognosis. Nearly all patients experience recurrence due to GBM's heterogeneity and there is currently no standard approach to treatment. Despite having few targeted agents with demonstrated efficacy, molecular testing is utilized due to its value in improving diagnostic accuracy and prognostic stratification. Moreover, recent data has shown an increase in promising data with regards to treating GBM using various mechanisms. Because of the clinical conundrum GBM poses and the lack of available treatment options, clinicians are challenged to stay current with new data and how best to integrate new agents into treatment paradigms. The objective of this study was to assess the changes in oncologists' and pathologists' knowledge through participation in education regarding optimal GBM treatment. **Methods:** The educational activity was a 30-minute online, video discussion segmented into 3 parts with synchronized slides and 2 faculty. Educational effect was assessed with a repeated pairs pre-/post-assessment study with a 3-item, multiple choice, knowledge questionnaire and one confidence assessment question. For all questions, each participant served as his/her own control. Pre- and post-assessment scores were compared to determine the relative changes in the proportion of correct responses. A chi-square test assessed statistical significance at the $P < 0.05$ level. The activity launched 26th June 2019; data were collected until 19th August 2019. **Results:** Overall significant improvements were seen after education for oncologists (N = 62, $P < .001$) and pathologists (N = 67, $P < .01$). The relative improvement was 67% for oncologists and 45% for pathologists (pre-/post-assessment average correct response rates were 30%/50% and 29%/42%, respectively). Following the activity, 55% of oncologists and 51% of pathologists had a measurable improvement in confidence in their ability to differentiate among late-stage investigational agents for GBM based on mechanism of action. **Conclusions:** Participation in an online, CME intervention consisting of a series of video discussions, totaling 30-minutes, resulted in statistically significant improvements in knowledge and confidence of oncologists and pathologists, that may lead to improvements in clinical care. As new data and agents emerge, new educational activities are necessary to reinforce knowledge, close persistent gaps, and increase oncologists' and pathologists' confidence in this clinical setting. Research Sponsor: Bayer.

11027 Poster Session (Board #284), Fri, 8:00 AM-11:00 AM

Lung cancer screening knowledge in four internal medicine university programs. *First Author: Samuel Urrutia Argueta, Indiana University, Indianapolis, IN*

Background: Low density CT (LDCT) screening reduces lung cancer specific and all-cause mortality in high risk populations. However, it remains underutilized. Screening discussions often start in primary care clinics of which nearly 30% are occupied by residents. Recognizing gaps in knowledge in early medical training may translate into a higher utilization of LDCT screening. **Methods:** To evaluate knowledge about lung cancer screening in Internal Medicine (IM) residents at 4 academic programs we distributed a survey to assess population at risk, mortality benefits, comparison between LDCT, colonoscopy and mammogram, and a knowledge self assessment. **Results:** 166 out of 360 (46%) IM residents at the 4 institutions participated, including 42% PGY-1, 30% PGY-2, and 28% PGY-3. Residents attained an average of 2.9 correct responses out of 7 (43.1%), without any statistically significant difference among programs. PGY-1 residents performed better than PGY-2 and PGY-3 (p=0.022). 36% correctly identified the appropriate population for screening. 90% correctly indicated that LDCT screening results in a cancer specific mortality reduction. 59% correctly indicated that LDCT results in all-cause mortality reduction. 7.7% answered that women stand to benefit the most from screening. 66% correctly answered that LDCT underperforms colonoscopy regarding mortality reduction. 22% answered correctly that LDCT outperforms mammography in reducing mortality. 65% of residents perceived their knowledge to be average or lower. **Conclusions:** LDCT knowledge is deficient among the residents studied. PGY-1 residents performed significantly better than their upper level peers. There were no significant differences among institutions. Research Sponsor: None.

Residents recognized their knowledge deficits.

Knowledge about lung cancer screening	PGY-1		PGY-2		PGY-3		p
	n	%	n	%	n	%	
	70		50		46		
General knowledge*	3.15 (1.08)	42.10%	3.14 (1.1)	30.1	2.6 (1.16)	27.7	0.022
USPSTF target population							
Correct answer	23	33	15	30	20	43	0.64
Incorrect answer	8	11	3	6	5	11	
Incorrect answer	33	47	27	54	19	41	
Incorrect answer	6	9	5	10	2	4	
Cancer-specific mortality benefit							
Yes	63	90	47	94	38	83	0.19
All-cause mortality benefit							
Yes	45	64	27	55	17	38	0.02
Subgroup of most benefit							
Hispanics	2	3	1	2	3	7	0.32
Women**	5	7	6	12	3	7	
Coal miners	8	11	6	12	1	2	
Patients with COPD	37	53	30	61	29	63	
Blacks	18	26	6	12	10	22	
Comparison to colonoscopy							
Better	10	14	8	16	10	22	0.79
Same	14	20	9	18	6	13	
Worse**	45	65	33	66	30	65	
Comparison to mammogram							
Better**	22	32	10	20	5	11	0.046
Same	17	25	21	42	20	43	
Worse	29	43	19	38	21	46	

* Number of correct responses divided by number of total questions (SD)
**Correct answer

11028 Poster Session (Board #285), Fri, 8:00 AM-11:00 AM

Practice gaps and challenges integrating new immuno-oncology agents in the treatment of cancer patients in the United States: A mixed-method study. *First Author: Neal E. Ready, Duke University School of Medicine, Durham, NC*

Background: Previous research has indicated challenges integrating new immuno-oncology agents (IOAs) and predictive immune biomarkers into practice. Barriers, clinical gaps and underlying causalities explaining these challenges, however, are poorly understood. **Methods:** A mixed-methods educational needs assessment was conducted with physicians from 6 specialties (oncology, interventional radiology, pathology, pulmonology, emergency medicine and rheumatology), clinical pharmacists, physician assistants and advanced nurse practitioners involved in the care of cancer patients in the United States. Semi-structured interviews and discussion groups were thematically analyzed to identify challenges, barriers and underlying causalities. Qualitative findings subsequently informed the development of online surveys, which served to quantify findings. The following findings pertain to oncologists. **Results:** A total of 660 health care providers participated in the study, in which 17 interviews and 88 surveys were completed with oncologists. Seventy-two percent reported sub-optimal knowledge of the interactions between IOAs and the tumor's micro-environment, while 62% reported sub-optimal skills determining which IOA to select based on this information. Oncologists reported sub-optimal knowledge of best practices for using IOAs to treat cancer in presence of an autoimmune disease (74%-80% depending on condition), and sub-optimal skills weighing the risks and benefits of prescribing IOAs for these profiles (66%-77%). In addition, 50% of oncologists reported feeling overwhelmed by the volume of new IOAs being made available. Many oncologists expressed doubts regarding the clinical benefit (59%) and innovative nature (43%) of emerging IOAs. Finally, 46% reported limited skills identifying viable treatment options based on pharmacodiagnostic test reports. Barriers to having predictive biomarkers inform treatment decisions included sub-optimal communication between specialists regarding specimen requirements and desired biomarker information. **Conclusions:** This study demonstrates the need to further support healthcare professionals as they face challenges integrating new IOAs and predictive immune biomarkers into practice. Given the wide array of IOAs becoming available each year, addressing the knowledge, skills, confidence and attitude gaps identified in this study could help improve health care delivery and potentially optimize outcomes for cancer patients. Research Sponsor: Bristol-Myers Squibb Company.

11029 Poster Session (Board #286), Fri, 8:00 AM-11:00 AM

GI oncology molecular tumor board: Fostering collaboration and clinical education for personalized therapy. *First Author: Joseph Elan Grossman, Beth Israel Deaconess Medical Center, Boston, MA*

Background: In recent years, genomic profiling has become standard of care for several gastrointestinal (GI) cancers. In addition to standard of care indications, comprehensive genomic profiling has led to novel and expanded applications of targeted therapy, chemotherapy, and immunotherapy and facilitated identification of potential clinical trials. A GI molecular tumor board (MTB) was developed with a goal of improving understanding of the biological effects of genomic alterations and their therapeutic implications to enhance personalized therapy. **Methods:** Foundation Medicine (FM) collaborated with physicians in the GI oncology group of an academic medical center to develop a GI MTB starting March 2019. As of December 2019, 27 GI oncology cases were presented where FoundationOneCDx testing was performed and a clinical question was posed. Cases were discussed by faculty, fellows, research staff, and a clinical genomic scientist and oncologist from FM. Impacted signaling pathways and biomarkers were discussed for each case alongside clinical content so that physicians could consider therapeutic options and clinical trials. Presenting faculty were asked to complete a questionnaire for each case presented to assess the impact of the MTB discussion on clinician knowledge and patient-level treatment recommendations. **Results:** Of 27 questionnaires sent to 7 providers, 17 (63%) were completed. Respondents indicated that as a result of the MTB, the treatment plan was changed in 2 cases (12%), reinforced in 9 cases (53%) and in 6 cases (35%) there was no effect. On a Likert scale of 1-4 where 1 is "rare/poorly" and 4 is "great" mean scores were as follows: Did this MTB help you understand the biological effects of the main genomic alteration(s) reported in the case presented? 3.3. Did this MTB help you understand the possible therapeutic implications of the main genomic alterations in the case presented? 3.3. Did this MTB improve your understanding of the role of next generation sequencing and comprehensive genomic profiling in making treatment decisions? 3.4. **Conclusions:** The results of our questionnaire indicate that treatment decisions were changed in a minority of cases based on the MTB. In most cases, clinical decision making was reinforced and understanding of the biological effects of genomic alterations and their therapeutic implications were improved. Based on this feedback we will continue to refine and integrate the GI MTB into clinical care for patients with GI malignancies, and share our experience locally with other disease groups. Research Sponsor: None.

11030 Poster Session (Board #287), Fri, 8:00 AM-11:00 AM

Perceptions of research training in a hematology/oncology fellowship program. *First Author: Stephanie L Pritzl, University of Wisconsin Department of Medicine, Madison, WI*

Background: Current research training in Hematology/Oncology (Heme/Onc) fellowship is typically limited to mentoring relationships, which are highly variable due to the absence of standardized training for mentors and different perceptions of successful mentor-mentee relationships. Formal research productivity assessment is challenging and lacking in our current educational framework. **Methods:** Electronic surveys were developed to assess research training during fellowship at the University of Wisconsin (UW). Surveys were sent to current Heme/Onc fellows (n = 9), members of fellowship leadership (n = 4), and core research faculty (n = 5) with prior successful mentorship to trainees. **Results:** Surveys were completed by 6 fellows, 3 fellowship leadership, and 5 core research faculty. Both faculty and trainees recognized the research mentor-mentee relationship to be critical, with 5/6 (83%) fellows and 3/5 (60%) core research faculty identifying research mentors as the most meaningful training source. However, despite 5/6 (83%) fellows having a research mentor identified, there were large variations in the perceived level of proficiency in core research topics. While 3 fellows felt only slightly prepared in basics of clinical trial design, 1 fellow felt very prepared and 2 felt somewhat prepared. Furthermore, 2 fellows each felt very prepared, somewhat prepared, or not at all prepared in assembling grant components. There was also variable confidence reported by core research faculty in the ability of trainees to obtain funding and conduct independent research after fellowship, with 1 extremely confident, 2 somewhat confident, and 2 only a little confident. All individuals surveyed recognized manuscript publication, abstract presentation, and grant acquisition as important measures of research productivity. Beyond that, however, only 1/5 (20%) core research faculty and 0/3 (0%) fellowship leadership noted using rubrics for critical review of trainee academic progress despite 3/6 (50%) fellows believing that such rubrics were being used for their evaluation. **Conclusions:** The divergent experiences identified among research mentors and mentees and the lack of clearly defined metrics of research productivity highlights the need for a more standardized educational framework and formative evaluation tools. These identified needs have led to a pilot program at UW that intends to create a professional learning community for research mentors, define competencies for research training, and design a research training portfolio and accompanying assessment rubric. Research Sponsor: University of Wisconsin Department of Medicine 2019-2020 Medical Education Innovation Grant.

11031 Poster Session (Board #288), Fri, 8:00 AM-11:00 AM

Assessing impact of inpatient rotations on resident interest in hematology-oncology. *First Author: Bilal Farooqi, Comprehensive Hematology Oncology, Brandon, FL*

Background: Working as a hematologist-oncologist is rewarding yet challenging. As cancer cases increase, there is a growing need to recruit more oncologists. It has been hypothesized that earlier exposure to oncology may improve resident interest in the field. This is often achieved by rotations on inpatient oncology wards, which represents only a small subset of the clinical work typical in hematology-oncology. We looked to assess whether early exposure to an inpatient oncology rotation impacts pursuit of this career path. **Methods:** Categorical interns in Internal Medicine at the University of Florida during year 2017-2018 were surveyed anonymously before and after their inpatient oncology rotation. Confidential identifiers were used to pair surveys. Similar surveys were used in the cardiology and gastroenterology rotations to allow for comparison. The survey included descriptor words to choose when describing the field. These words were categorized as either positive or negative. **Results:** Thirty-three interns were surveyed. Seventeen surveys were able to be paired (52% response rate) in oncology. Cardiology had 15 paired survey responses and gastroenterology had 13 paired responses. Using a 4-point Likert scale, interest in hematology-oncology decreased overall from 3.12 to 2.82 ($p = 0.059$) while interest in pursuing a fellowship remained the same. Stress levels were increased slightly from 2.30 to 2.05 ($p = 0.564$). Cardiology also saw a decrease in interest in the field from 3.53 to 2.93 ($p = 0.007$) but also an increase in pursuing fellowship from 2.20 to 2.60 ($p = 0.014$) and decreased stress from 3.13 to 2.67 ($p = 0.020$). Gastroenterology saw a decrease in interest in the field as well from 3.46 to 2.92 ($p = 0.020$). Interest in pursuing a fellowship and stress levels were not significantly different for gastroenterology. Field descriptors including "challenging," "scared," and "excited" decreased the most while "confident," "inspired," and "motivated" increased the most when describing hematology-oncology. **Conclusions:** While interest in this field was negatively impacted, stress levels associated with the field decreased. Furthermore, field descriptors were generally more positive and optimistic in the post-rotation setting. Though not statistically significant, these findings suggest that interns see oncology as less stressful and feel more capable after inpatient exposure during intern year. As much of hematology-oncology practice is outpatient, increasing intern exposure in this area may further improve perception and recruitment to the field. Research Sponsor: None.

11032 Poster Session (Board #289), Fri, 8:00 AM-11:00 AM

Delivery of cancer survivorship education to community health care professionals. *First Author: Ashley Pariser, Yale Smilow Cancer Center, New Haven, CT*

Background: Cancer survivorship care is an integral part of oncology care. Although oncologists overwhelmingly demonstrate a desire to be a part of their cancer survivors' care and management, only 60% of oncologists feel comfortable promoting healthy lifestyle behaviors, screening and prevention care. There is currently no standard of care for survivorship care education and data evaluating current educational models is limited. **Methods:** Project ECHO (Extension for Community Healthcare Outcomes) utilizes telehealth to promote long-distance learning and sharing of best practices. We utilized the Project ECHO model to deliver a survivorship curriculum in 6 hourly, bi-weekly sessions from October 2019 to December 2019. The curriculum was aligned with the 4 central tenets of survivorship care and was developed based on a needs assessment. Recruited participants included registered nurses (RN), registered dietitians (RD), advanced practice providers (APP), radiation oncologists and medical oncologists. Participants were enrolled in either a local ECHO curriculum or a national ECHO curriculum. Local Connecticut participants were invited to participate in semi-structured interviews to evaluate their experience. **Results:** Eight participants including 3 MDs, 1 APP, 1 SW and 3 RNs from 3 community oncology clinics in suburban Connecticut enrolled in the local ECHO curriculum. Twenty-eight participants including 17 RDs, 2 MDs, and 3 APPs from 13 hospital and community practices enrolled in the national ECHO curriculum. Four participants (50%) agreed to participate in semi-structured interviews. Motivations to participate included ease of participation and interest in survivorship. Participants described a positive experience, citing a well-structured curriculum and sense of community as highlights. Two participants described the sessions as empowering, leading to more discussions and engagement with survivors. All participants described an increased awareness of resources available for cancer survivors. Areas for improvement included greater assistance with technology and session time management. Concomitant patient care was the most cited barrier to participation. **Conclusions:** This pilot study is the first to demonstrate the feasibility of the Project ECHO model for delivering cancer survivorship education to community oncology providers. Further research evaluating the correlation between improved provider knowledge and survivorship care outcomes is needed. Research Sponsor: None.

11033 Poster Session (Board #290), Fri, 8:00 AM-11:00 AM

Use of oncology electronic learning resources to learn about geriatric oncology. *First Author: Tina Hsu, University of Ottawa, Ottawa, ON, Canada*

Background: Despite the aging population driving cancer growth, oncology trainees receive little training in geriatrics. While electronic resources, such as ASCO University, may help meet this gap, use of available geriatric oncology (GO) modules is low. We sought to understand why by exploring how oncology trainees currently learn about GO, their preferred methods for learning about GO, and their attitudes towards e-learning and geriatrics. **Methods:** Canadian medical oncology residents and recent graduates were electronically surveyed about the following domains: demographics, self-directed learning practices, use of electronic resources, perceived facilitators and barriers to e-learning, and geriatric oncology teaching. Descriptive statistics were used to analyze the data. **Results:** Respondents (n = 47) were mostly aged < 35 (66%). Respondents felt that learning about older adults was important (mean 4.3±1.0 out of 5) and generally felt comfortable caring for them (mean 3.9±0.9 out of 5) despite minimal training in geriatrics.Almost half (48.9%) received 0-2 hours of teaching in GO during residency, with the majority (59.6%) receiving teaching in clinic, 36.2% through lectures and 21.3% via seminars. Respondents also learned about GO through reading journal articles (42.6%), modelling in clinic (36.2%), reading a textbook (19.2%) or attending a conference (19.2%). Respondents preferred to learn about GO through on-site lectures (46.8%), dinner meetings (42.6%), case discussion (42.6%) and attending conferences (38.3%). Although overall respondents highly valued electronic learning (mean 4.3±0.75 out of 5), only a minority (8.5%) had received GO teaching electronically using e-modules and only 23.4% respondents were aware of e-learning resources in GO. In contrast most respondents (83%) had used an e-learning resource to learn about oncology. The most common oncology e-resources used were ASCO University (61.7%), Oncology Education (61.7%), and ASCO meeting videos (44.7%). **Conclusions:** Although oncology trainees value and commonly use e-learning resources, e-learning is not a common or preferred way to learn about GO, potentially due to lack of awareness about these resources. Future research will explore whether the current methods of educating oncology learners about older adults are appropriate and sufficient, as well as how trainees value and prioritize learning about topics that are not included in the formal curricula. Research Sponsor: Royal College Robert Maudsley Fellowship for Studies in Medical Education, Department of Innovation in Medical Education (DIME) Health Professions Education Research Grant.

11034 Poster Session (Board #291), Fri, 8:00 AM-11:00 AM

Setting focus on oncology in a German undergraduate medical training program: Our experience with a longitudinal elective *Interdisciplinary Oncology*. *First Author: Stefanie Zschaebitz, Department of Medical Oncology, National Center for Tumor Diseases, Heidelberg University Hospital, Heidelberg, Germany*

Background: Compared to other academic disciplines such as social sciences and humanities, medical school curricula leave limited opportunities to meet individual interests of students. **Methods:** To allow students to set an individual focus in their MD education, and to promote a sound scientific basis, n = 11 longitudinal electives ("tracks") were introduced within the Heidelberg Curriculum Medicinale (HeiCuMed) in 2017. The volume of additional training consists of 2 weekly lectures hours for at least 1.5 years of training. Participation in the program has been on a voluntary basis until 2019 and now is obligatory for every student. **Results:** n = 141 students are currently enrolled within the track "Interdisciplinary Oncology (IO)". More than n = 50 optional courses are offered each semester covering oncologic subjects such as scientific methods in cancer research, ethical issues in research and clinical practice, communication and clinical skills training. The modular system of the IO elective allows for a wide selection of topics for participating students but also poses a challenge for graded assessments. **Conclusions:** Conducting a modular elective including graded assessments is feasible. The longitudinal track IO has a high voluntary participation rate and very positive feedback from students. This indicates that our teaching concept is very well suited to address the call for increased choice and specialization in medical curricula in Germany. Research Sponsor: None.

11035 Poster Session (Board #292), Fri, 8:00 AM-11:00 AM

Effect of live education targeted to genetic counselors on knowledge and competence. *First Author: Vanessa Carranza, Creative Educational Concepts, Lexington, KY*

Background: Rapid advancements in genomics and sequencing technologies have presented a growing need for experts in the field of genetics to translate results and optimize patient care. As knowledge regarding DNA mutations and the technology to properly detect them continuously advances, it will be vital that genetic counselors play a larger role in the oncology healthcare team. **Methods:** These activities were designed to target genetic counselors involved in the diagnosis, management and genetic counseling of patients who have or are at risk for DDR-mutated cancers, attending live symposia at the 2018 & 2019 American College of Medical Genetics & Genomics Annual Meeting. Learning and knowledge was objectively assessed by analyzing pre- and post-test results before and after the educational activities. To determine retention of knowledge over time, follow-up assessments were sent to participants after each live activity. Assessment questions in the form of case studies were utilized to gauge whether participants translated knowledge into practice at follow-up. Statistical testing between pre- and post-tests and from pre-test to follow-up were conducted via chi square analysis with a priori significance set at 0.05. **Results:** Evaluations were collected from N = 275 (onsite) participants. Improved learners, as determined by significant ($P < 0.05$) increases in correct responses, were observed in several specific topic areas: When to consider germline testing (2018 participants: 53.33% pre-test vs. 87.5% post-test; 2019 participants: 42.55% pre-test vs. 84.72% post-test). Patients most likely to benefit from a PARP inhibitor based on genetic testing results (2018 participants: 50% pre-test vs. 93.75% post-test; 2019 participants: 75.49% pre-test vs. 94.37% post-test). However not all improvement was sustained at follow-up: When it is appropriate to consider germline testing (2018 participants: 64.44% at follow-up – not significant ($P = 0.138$); 2019 participants: 85% at follow-up ($P < 0.001$). Patients most likely to benefit from a PARP inhibitor based on genetic testing results (2018 participants: 68.89% at follow-up – not significant ($P = 0.140$); 2019 participants: 65% at follow-up – not significant ($P = 0.329$). **Conclusions:** This analysis shows that live accredited education can significantly improve the knowledge and competence of genetic counselors in multiple areas surrounding the use of germline testing to guide treatment recommendations. Results also suggest that ongoing education in clinically appropriate scenarios is warranted. Research Sponsor: AstraZeneca.

11036 Poster Session (Board #293), Fri, 8:00 AM-11:00 AM

Micro-learning: A new approach to upskilling and professional development on the management of patients on immunotherapy. *First Author: Helen Winter, Bristol Cancer Institute, Bristol, United Kingdom*

Background: Advances in cancer management are rapidly evolving . The introduction of immunotherapy across many tumour types and the potential of effector T cell therapies for patients requires upskilling in the wider health care team. This requires developing learning aimed at understanding the new mechanisms of action, potential side effects and how we educate and manage our patients receiving these therapies. **Methods:** Five stand alone micro-learning sessions on Immunotherapy were designed aimed at the acquisition of new skills and knowledge in a concise and targeted way. These sessions covered the key areas identified by the Systemic Therapy Day and Acute Oncology Units. These topics developed covered: What is Immunotherapy (IO) (its not chemo); How to interpret thyroid function for patients on IO; Get to know your Cortisol levels and adrenal insufficiency in patients with IO; Proactive management of IO Colitis; Liver function for patients on IO. These were delivered and evaluated during the working day in brief bite-sized sessions. **Results:** Attendance at formal training sessions - including annual study days and monthly study sessions are not keeping pace with the requirements for upskilling of staff. We present the evaluation of micro-learning delivered within the working day in short sessions. **Conclusions:** In the era of precision medicine, immunotherapy and effector T cell therapies a new approach to learning and upskilling in the wider health care team is needed. An integrated approach to learning on-the -job with short micro-learning sessions may embed the acquisition of new skills. More importantly, vocational education seeks to change habits, behaviour and culture. This needs to be accessible and flexible to adapt to the current patterns of work. Research Sponsor: None.

11037 Poster Session (Board #294), Fri, 8:00 AM-11:00 AM

Developing South Asia's first structured head and neck surgery multicenter fellowship initiative. *First Author: Shamit Chopra, Patel Hospital, Jalandhar, India*

Background: Despite high head neck cancer incidence in South Asia, there exist few fellowship programs, which are limited by lack of structure, review processes and standard curricula. Our aim was a regionwide multicenter head and neck fellowship initiative to address the above limitations. **Methods:** A 10-member task force was constituted in January 2018 under the aegis of the Foundation for Head and Neck Oncology. First phase: Initial curriculum drafted by incorporating region-specific perspectives, aided by multiple source documents. Candidate eligibility criteria outlined, accommodating multiple pertinent disciplines and an international applicant base. Format for a structured entrance examination, and a mandatory/desirable rotation schedule were developed. Second Subcommittee(SC) phase: Creation of a web portal (www.fhnofellowship.org) by Outreach SC, approval of applicant centers by Accreditation SC, layout of exam structure by the Examination SC, and defining a rank order list-driven match process by the Match SC. Third phase: Development of standard documentation including suggested bibliography, log book format, recommended grand rounds topics, common minimum criteria for fellowship graduation. A common entrance exam was conducted in Feb 2019, which incorporated written screening, center-candidate interactions, objective interview, and the merit-based institution-fellow match. **Results:** Total number of applicants: 92, the majority Oral Maxillofacial Surgeons(83.7%). Seventeen fellows matched in the first cycle, the initial and 6-month program compliance 94.1% and 88.2% respectively. More eligible institutions accredited(36.8% increase) prior to the second cycle in Nov 2019, during which 19 fellows(11.8% increase) were matched. An interim review was done in Oct 2019, and periodic reviewing set at 6-month intervals. Planned fourth phase: Objective center/candidate feedback, surgical video repository, online training schedule, develop the fellowship exit examination, and expand outreach to other countries. **Conclusions:** Owing to high head neck cancer incidence in the subcontinent, anatomic complexity, need to balance outcomes/toxicities and requirement of expert multidisciplinary care; structured head neck fellowship training is imperative. Despite inherent challenges of concept and implementation in a diverse multicultural resource-limited setting, we foresee the application of region-relevant perspectives helping us achieve the objective of furthering subspecialty head neck training in South Asia. Research Sponsor: None.

11038 Poster Session (Board #295), Fri, 8:00 AM-11:00 AM

Customized social media-based oncology education. *First Author: Udaykumar Punukollu, Nizam's Institute of Medical Sciences, Hyderabad, India*

Background: Social media has profoundly impacted our professional lives. Quick access to reliable sources of information and engaging with like-minded experts certainly aids in professional development. The purpose of this study is to assess the perception of oncology experts towards social media based education and to develop a platform based on their feedbacks for constructive engagement of the professionals and to improve educational outcomes. **Methods:** Based on Kirkpatrick 4 level model, 15 questions were designed for oncology experts. We collected responses through online surveys and by distributing the questionnaires at oncology events. Based on the results obtained, we developed a customised social media application for oncologists in android version. User experience design was done in InVision Studio and Model View Presenter (MVP) design pattern was used in software development. Beta testing of the application was done with 50 experts and questionnaire was given to them at the end of beta testing period to compare the technical advantages of our mobile application with their currently preferred social media platform for oncology based education. **Results:** Among 311 responders, medical oncologists, radiation oncologists, surgical oncologists, hemato oncologists and oncopathologists constituted 45%, 29%, 16%, 7% and 3% respectively. Only 14% clearly denied that social media has improved educational outcomes. Eighty seven percent felt that they lack adequate knowledge in other areas of expertise and 67% of the oncologists were not well informed about the latest oncology updates. Only 60% could actively engage in interdiscliplinary collaboration due to reasons unspecified. When asked about the best way to learn a topic of interest, majority opined it through peer discussion with experts pertaining to that topic of interest. The two major problems faced by experts while seeking social media based education is academic discussions being unorganised and non-academic discussions unwelcomed. After considering these feedbacks, a mobile application in android version was developed. At the end of beta testing, 96% reported a technical advantage of our customised application over their preferred social media based oncology education. **Conclusions:** A minimum viable product has been developed after considering the feedbacks received from oncologists of various sub-specialities. Such a customised social media application is more appealing when easily applicable across low and middle income countries and in a manner that allows addition of local language options without changing the application software. Research Sponsor: None.

11039 Poster Session (Board #296), Fri, 8:00 AM-11:00 AM

Quality and reliability of online video information of breast cancer in Spanish. *First Author: Fernando Cristobal Diaz, University of Texas Rio Grande Valley, Harlingen, TX*

Background: Online health information is a central part of how patients learn about a cancer diagnosis. Involving patients in shared decision making is associated with better outcomes. Previous studies have identified a lack of high-quality, reliable online material related to cancer in English using validated tools. As the number of Spanish speaking people in the US, and globally, continues to grow, it is important that high-quality, reliable information is available in Spanish. No studies have evaluated online breast cancer informational videos in Spanish. **Methods:** A search using the phrase "cancer de mama" (translation: "breast cancer") was conducted on YouTube. The first 200 video URLs were included for study with duplicates, non-Spanish, and non-informational videos excluded. The videos were characterized by several variables, including year of upload, country of origin, content discussed, views, likes, dislikes, and typology group ("Personal", "Professional", "Health Portal", etc.). The quality and reliability of these videos were examined by measuring Global Quality Scale (GQS), a 5-point DISCERN score, and JAMA scores. **Results:** 173 videos met inclusion criteria in the study. The majority of the videos which discussed signs and symptoms were uploaded by a 'commercial' typology, risk factors mainly uploaded by 'health portals' (21%), and treatment options by 'professionals' (50%). Relatively few videos have discussed reconstruction, survivorship, and breast cancer in men. 57% of these videos were uploaded prior to 2017, 36% by different personnel followed by government/news agency (25%), and professionals (23%). There was no significant difference between number of views (p-value: 0.526) and likes (p-value: 0.122) among the five typology groups. Professional videos had the highest average GQS (2.55), DISCERN score (1.90), and JAMA score (2.05). Personal videos had the lowest average GQS (1.98) and DISCERN score (1.06). GQS, DISCERN, and JAMA scores were all statistically significantly different between each typology. **Conclusions:** The majority of online breast cancer videos in Spanish are older than 3 years and produced outside the US. They are generally of poor quality and reliability, although higher in professional videos. Given the lack of current, high-quality, and reliable informational videos available, needs assessments should be conducted to identify the most useful learning resources for Spanish-speaking patients. Specialists should consider uploading educational videos to improve the paucity of high-quality, reliable information online. Research Sponsor: None.

11040 Poster Session (Board #297), Fri, 8:00 AM-11:00 AM

Content analysis of pancreatic cancer conversations on Twitter: What matters most to users? *First Author: Udhayvir Singh Grewal, Louisiana State University Health Sciences Center, Shreveport, LA*

Background: Social media has an important role in addressing medical misinformation by connecting the global community of health care professional (HCP), cancer patients and advocates. We evaluated the content and dynamics of discussions around pancreatic cancer (PC) on Twitter to identify subtopics of greatest interest to these users. **Methods:** We used online analytical tool (CREATION Pinpoint) to quantify Twitter mentions (tweets and re-tweets) related to PC between 1/2018 to 12/2019. Keywords, hashtags, word combinations and phrases were used to query for PC mentions. HCP profiles were identified using machine learning and then human verified and remaining user profiles were classified as general public (GP). Data from conversations were analysed and stratified qualitatively (using e.g keywords/combinations/phrases) into 5 categories; 1) prevention (P), 2) survivorship (S), 3) treatment (T), 4) research (R), and 5) policy (Po). We analysed the impact of PC awareness month (PCAM) and celebrity PC diagnosis on the overall level of conversations. **Results:** Out of 1,258,028 mentions on PC, 313,668 unique mentions were classified into the 5 categories. We found that HCP discuss PC research more than the GP, while GP are more interested in treatment. PCAM did not increase mentions by HCP in any of 5 categories while GP mentions over 2 years, increased temporarily in all categories except prevention. HCP mentions did not increase with celebrity PC diagnosis. Alex Trebek's diagnosis increased GP mentions on survivorship, while Ruth Ginsburg's diagnosis increased conversations on treatment (Table). **Conclusions:** Twitter mentions between HCP and GP around PC are not aligned. The HCP conversation was mainly limited to research while GP were more interested in treatment. PCAM temporarily increased GP conversations around treatment, research, survivorship and policy but not prevention. Future studies should address which factors determine how celebrity diagnoses drive conversations. Research Sponsor: None.

Month	P-HCP	P-GP	S-HCP	S-GP	T-HCP	T-GP	R-HCP	R-GP	Po-HCP	Po-GP
Jan 18	62	620	132	1276	435	3409	405	4005	0	2
March 18	76	547	98	2805	347	3498	372	3151	2	37
May 18	65	649	158	1576	438	4841	424	3162	1	17
July 18	35	248	95	1073	244	2811	255	2629	0	3
Sept 18	36	250	122	1046	246	2441	392	2780	0	1
Nov 18	106	802	297	4137	552	13428	460	4907	3	52
Jan 19	60	390	178	1350	337	3365	506	2844	0	1
March 19	83	692	271	10724	595	5930	605	5195	0	28
May 19	116	902	171	1965	565	9929	503	3169	2	18
July 19	40	1965	144	795	428	3782	444	2948	4	25
Aug 19	176	941	221	3842	562	36267	388	4635	6	21
Sept 19	65	333	193	1759	272	6813	452	3580	1	21
Nov 19	99	674	280	5405	456	7385	644	8206	2	50

11041 Poster Session (Board #298), Fri, 8:00 AM-11:00 AM

Patterns of Twitter use among trainees in hematology-oncology related areas. *First Author: Miguel Gonzalez Velez, Mayo Clinic Arizona, Phoenix, AZ*

Background: Twitter (TW) is an essential tool in the medical community. Few studies have examined the use of TW by medical trainees. We aimed to assess its utilization among trainees in hematology-oncology related areas (HORAs). **Methods:** 576 training programs in HORAs were obtained. We contacted a potential pool of 3,142 trainees. A 50 item survey was distributed between 2/2019-5/2019, focusing on: demographics, professional use, attitudes toward TW, and patient interactions. Responses were analyzed using parametric descriptive statistics. **Results:** 442 responses (14% response rate) were received; 203 (46%) used a TW account for professional activities. See table for demographics. The most common reasons for using TW were: continuous education (73%), dissemination of information (62%), and networking (62%). > 80% of users have positive views on using TW for: promoting academic discussions (92%), trainees education (89%), and conference networking (83%). 50 (25%) have used TW for collaborations, with abstracts and papers being the most common (20%). Most agreed or strongly agreed that TW: is a useful education tool (89%), and might be useful for career advancement (85%). The most common challenges were: the value of TW content can be decreased by irrelevant content and biased sources (64%), not peer-reviewed (51%), and difficulty searching information (50%). 68% considered that programs should promote the engagement of trainees, but only 21% reported instruction in the use of TW. 83% agree or strongly agree that TW is useful for physicians and patient interactions, but 82% have concerns about legal repercussions. **Conclusions:** Almost half of trainees in HORAs use TW for professional activities. The most common uses are for education, dissemination of information and networking. Most trainees that use TW have positive views regarding education and academic collaborations. Use of Twitter may strengthen trainees' education, provide mentorship opportunities, and promote career advancement. Challenges on TW use should continue to be addressed. Research Sponsor: None.

Gender	**n = 442, %**
Female	211, 47%
Male	231, 53%
Specialty	
Medical H-O	264, 56%
Pediatric H-O	82, 21%
Radiation Oncology	38, 8%
Other	58, 15%
Race	
Asian	139, 31%
African American	19, 4%
Hispanic	21, 5%
White	246, 56%
Other	17, 4%
Training Program	
Academic Center	418, 94%
Community/Academic	7, 2%
Community/Private	4, 1%
Other	13, 3%
Future Career Plan	
Basic Science	19, 4%
Clinician-Educator	121, 27%
Clinician-Investigator	173, 39%
Private Practice	93, 21%
Undecided	34, 8%
TW account	
Yes	285, 64%
Professional	203, 46%
No professional	82, 18%
No	157, 36%

11042 Poster Session (Board #299), Fri, 8:00 AM-11:00 AM

Females as surgical oncologists in Taiwan: A nationwide population-based study. *First Author: Weiming Cheng, Taipei City Hospital, Taipei, Taiwan*

Background: Operations for malignancy are stereotypically viewed as the field of men, especially in eastern countries. In recent decades, more and more women devoted themselves to be surgical oncologists. However, they face many challenges, especially when they treating patients with sex organ-related malignancies. In the present study, we compared the disparities between female and male surgical oncologists in urology, general surgery, and gynecology by analyzing a nationwide, population-based database in Taiwan. **Methods:** National Health Insurance covers more than 99.6% of population in Taiwan. The system's claim data are released as the National Health Insurance Research Database. One of its database, the Longitudinal Health Insurance Database 2000, contains all the original data of one million randomly-selected beneficiaries enrolled in year 2000. We recruited the yearly inpatient and outpatient service volumes, oncological surgical volumes, revenue, and sex ratio of patients of each female and male attending general surgeons, gynecologists, and urologists with practice more than five years from 1995 to 2013. The differences of these factors between male and female physicians in each specialty were compared with Mann-Whitney U-test. $P < 0.05$ was viewed as statistically significant. **Results:** There are 13, 87, and 191 female urologists, general surgeons, and gynecologists included, accounting for 6.7%, 7.0%, and 51.3% of physicians in each specialty in Taiwan respectively. Female urologists and general surgeons had significantly more female patients ($p = 0.004$ and < 0.001 respectively). Female urologists had insignificantly less patient service numbers, oncological surgical volumes, and revenues ($p = 0.285$, 0.718, 0.077 respectively), while female general surgeons and gynecologists performed worse than corresponding male physicians (all p value < 0.001). Of noted, female general surgeons have significantly less patient service (66.0 ± 57.1 vs. 94.8 ± 98.9 patients, $p < 0.001$) and total surgical volumes (2.30 ± 2.50 vs. 3.28 ± 3.33 surgeries, $p = 0.001$) but more oncological surgeries (0.33 ± 0.64 vs. 0.17 ± 0.41 surgeries, $p = 0.003$); however, there is no differences after exclusion of surgeries for breast cancer (0.07 ± 0.22 vs. 0.12 ± 0.32 surgeries, $p = 0.057$). **Conclusions:** Patients tend to seek medical help from same-sex physicians in Taiwan. Females could have a comparable career with males in urology, while gender inequality remains significant in general surgery and gynecology. Female surgical oncologists may have advantages in breast cancer treatment. Research Sponsor: None.

TPS11043 Poster Session (Board #300), Fri, 8:00 AM-11:00 AM

Building resilient oncologists: A feasibility study of a resiliency curriculum for hematology oncology fellows. *First Author: Monica Sheila Chatwal, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Rates of burnout and career dissatisfaction have declined slightly, but remain high among oncologists (Berg, AMA 2020). As hematology oncology fellows prepare to join this workforce, the ACGME now mandates wellness be a part of their training curriculum. Yet, there are few, if any, structured and effective programs specifically for these trainees. Based on feedback from our prior mindfulness-based wellness curriculum, we created a more varied and comprehensive resiliency program with the use of our institutional resources to incorporate and evaluate as part of our fellowship curriculum (ASCO, Abstract 10508), and potentially expand to other fellowships. **Methods:** This is a single-center, non-randomized, pilot project to assess the feasibility, acceptability, and impact of a resiliency training program. All hematology oncology fellows at our institution were eligible for enrollment, and participation was voluntary. A total of seven monthly, 1 hour sessions were conducted through the academic year. Each session focused on a particular topic - alternative forms of wellness through art and music, self care, mindfulness and stretching, reflective writing, and healthy boundaries and work life integration - which have all been studied individually in wellness and burnout with positive results. Sessions were co-led by a peer and "expert" guest speakers from our training institution. Participants completed questionnaires pre and post-program, and feedback evaluations after each session. Questionnaires included the Perceived Stress Scale (PSS), Five Facet Mindfulness Questionnaire (FFMQ), Connor Davidson Resiliency Scale (CDRS-10), and modified Maslach Burnout Inventory (MBI), as well as demographics and open response questions. The primary aim was feasibility (enrollment, completion, and compliance rates), and the secondary aim was acceptability (usefulness of the intervention). Examination of stress, mindfulness, resiliency, and burnout were exploratory. Enrollment and data collection are complete, with 18 of 29 (62%) eligible participants consented. Data analysis is in process. Research Sponsor: University of South Florida Graduate Medical Education Grant, Moffitt Cancer Center Genitourinary Department Funding.

11500 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Comparison of two chemotherapy regimens in Ewing sarcoma (ES): Overall and subgroup results of the Euro Ewing 2012 randomized trial (EE2012). *First Author: Bernadette Brennan, Royal Manchester Children's Hospital, Manchester, United Kingdom*

Background: In 2010, different chemotherapy regimens were standard in Europe and the USA for newly diagnosed ES. In the absence of novel agents to investigate, comparison of these two strategies was considered worthwhile. **Methods:** Newly diagnosed localised or metastatic ES patients aged 5-50 were eligible. Patients were randomized to receive either the European regimen (Arm A) of VIDE (vincristine [V], ifosfamide [I], doxorubicin [D] and etoposide [E]) induction and VAI or VAC (V, actinomycin D and I or cyclophosphamide [C]) consolidation or the USA regimen (Arm B) of compressed VDC/IE induction and IE/VC consolidation. The primary outcome measure was event-free survival (EFS); secondary outcomes included overall survival (OS) and toxicity. The design was Bayesian with interpretation based on posterior probabilities (with non-informative priors) – i.e. probability that true hazard ratio (HR) < 1.0 given the data [Pr(HR$<$1.0| data)], with 95% credible intervals (CrI) reported. HRs were obtained from Cox models adjusted for baseline stratification parameters. Heterogeneity tests (HT) were used to investigate whether the treatment effect differed according to baseline parameters. Analysis was intention-to-treat. **Results:** Between December 2013 and May 2019, 640 patients were randomised (320 to each arm) from 10 European countries. Baseline stratification factors were: sex (58% male; 42% female); age (41% $<$14 years; 59% 14+ years); disease type (74% localised, 17% lung/pleural metastasis, 9% other metastasis); tumour volume (56% $<$200 ml, 44% $>$200 ml); country (37% UK, 31% France, 32% other). Median follow-up was 1.7 years. The HRs (95% CrI) were 0.70 (0.51, 0.95) for EFS and 0.64 (0.42, 0.96) for OS in favour of Arm B, with posterior probabilities of 98% for both that Arm B was better. Subgroup analyses showed no evidence that this benefit differed depending the baseline features, with no HT being close to significance (table). There were no major differences in acute toxicity: 68% of patients in Arm A experienced serious adverse events and 67% in Arm B. **Conclusions:** VDC/IE chemotherapy is superior to VIDE for both EFS and OS, with no excess toxicity. This benefit is consistent across all baseline stratification parameters. Clinical trial information: ISRCTN92192408. Research Sponsor: Cancer Resaerch UK and European Union FP7 grant.

Heterogeneity tests for baseline stratification subgroups.

	HT p-value	
Outcome measure	**EFS**	**OS**
Parameter		
Gender	0.65	0.91
Age	0.18	0.82
Disease type	0.36	0.56
Tumour volume	0.56	0.35
Country	0.63	0.50

11501 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Efficacy of add-on treosulfan and melphalan high-dose therapy in patients with high-risk metastatic Ewing sarcoma: Report from the International Ewing 2008R3 trial. *First Author: Uta Dirksen, Pediatrics III, West German Cancer Center, University Hospital Essen, German Cancer Consortium (DKTK), Essen, Germany*

Background: Ewing 2008R3 (EudraCT2008-003658-13) was conducted in 12 countries. It evaluated the effect of treosulfan and melphalan high dose chemotherapy followed by re-infusion of autologous hematopoietic stem cells (HDTreoMel) on event-free (EFS, primary endpoint) and overall survival (OS) in high-risk Ewing Sarcoma (EwS). **Methods:** Phase III, open label, prospective, multi-center, randomized controlled clinical trial. Eligible patients (pts) had disseminated EwS with metastases to bone and/or other sites, excluding pts with only pleuropulmonary metastases. Pts received 6 cycles of VIDE induction and 8 cycles of VAC consolidation therapy. Patients were randomized to receive additional HDTreoMel chemotherapy or no further treatment (control), They were further stratified by number of bone metastases (1, 2-5, $>$ 5). One-sided adaptive inverse-normal 4-stage design, changed after the 1st interim analysis via Müller-Schäfer method. Initial sample size 185 pts, type I error rate 2.5%, power 80%. **Results:** 109 pts were randomized between 2009 and 2018: 55 were randomized to HDTreoMel. With a median follow-up of 3.3 years, the primary endpoint EFS was not significantly different between HDTreoMel and control in the adaptive design (HR 0.85, 95% CI 0.55-1.32, intention-to-treat). 3-year (3y) EFS was 20.9 % (95% CI 11.5-37.9%) in HDTreoMel and 19.2 % (95% CI 10.8-34.4%) in control pts. Results were similar in the per protocol collective. Subgroup analyses showed that independent of treatment, male patients had a worse outcome than female patients: 3y EFS 13.3% (95% CI 5.7-31.1%) vs 25.2% (95% CI 15.5-40.8%); p = 0.07. Patients aged $<$ 14 had a better outcome when treated in the HDTreoMel group: 3y EFS 39.3% (95% CI 20.4-75.8%) vs 9% (95% CI 2.4-34%); p = 0.016; HR 0.40 (0.19-0.87). These effects were similar in the per protocol collective. Severe toxicities of hematology, gut, general condition and infection were more pronounced in the HDTreoMel group ($p < 0.05$). **Conclusions:** In patients with very high risk EwS, additional HDTreoMel was of no benefit for the entire cohort of patients. HDTreoMel may be of benefit for children age $<$ 14. This observation is supported by comparable results from a non-randomized trial EE99 R3 (Ladenstein et al. JCO, 2010). Clinical trial information: NCT00987636. Research Sponsor: German Cancer Aid.

11502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Results of the second interim assessment of rEECur, an international randomized controlled trial of chemotherapy for the treatment of recurrent and primary refractory Ewing sarcoma (RR-ES). *First Author: Martin G. McCabe, University of Manchester, Manchester, United Kingdom*

Background: Five-year survival of RR-ES is about 15%. Several chemotherapy regimens are used, but without robust evidence. rEECur, the first randomised controlled trial in this setting, is defining a standard of care, balancing efficacy and toxicity. **Methods:** Patients aged 4 to 50 with RR-ES and fit to receive chemotherapy were randomised between topotecan & cyclophosphamide (TC), irinotecan & temolozomide (IT), gemcitabine & docetaxel (GD) or high-dose ifosfamide (IFOS). Primary outcome measure was objective response (OR) after 4 cycles by RECIST 1.1. Secondary outcomes included PFS, OS and toxicity. A probability-based Bayesian approach was used with multiple pairwise comparisons. At the first interim analysis patients allocated to GD had worse OR and PFS than the other arms and accrual to the GD arm was halted. The second interim assessment was planned to determine which arm should be closed when at least 75 evaluable patients had been recruited to the remaining arms and evaluated for the primary outcome measure. **Results:** 366 patients (87% RECIST-evaluable), recruited between 18/12/14 and 17/12/19, were randomised to TC (n=124), IT (118), GD (72) and IFOS (53). Median age was 20 years (range 4-49). Patients had: refractory disease (19%), first recurrence (66%), $>$ first recurrence (14%). Initial disease site was bone in (66%). Sites of progression were: primary site only (16%) pleuropulmonary only (32%), other metastatic (52%). At median follow up of 9.2 months, outcome in the IT arm was: response rate 20%, median PFS 4.7 months (95% CI: 3.4 to 5.7), median OS 13.9 months (95% CI: 10.6 to 18.1). The table shows, for each pairwise comparison of IT with the other open arms (randomly labelled A and B to maintain blinding), the probabilities that OR, PFS and OS were better for X than for each other arm (RR = risk ratio, HR = hazard ratio). For OR, PFS and OS, all comparisons favoured arms A and B. The main grade 3/4 adverse events (% patients with an event) for IT (left hand values) compared with A and B pooled were: vomiting (6% v 1%), nausea (6% v 0%), diarrhoea (17% v 0%), fatigue (3% v 1%) and febrile neutropenia (3% v 24%). **Conclusions:** The first randomised trial in RR-ES has shown that IT, used as a control arm in planned and ongoing randomised phase II studies in RR-ES, is less effective than A and B in achieving tumour shrinkage or prolonging PFS and OS. The remaining two arms are continuing to recruit patients. Clinical trial information: ISRCTN36453794. Research Sponsor: Cancer Research UK, European Commission, German Cancer Aid, Finnish Children's Cancer Foundation, Australia & New Zealand Children's Haematology & Oncology Group, Australia & New Zealand Sarcoma Association.

	OR	PFS	OS
Pairwise comparison	**Pr(true RR >1)**	**Pr(true HR <1)**	**Pr(true HR <1)**
IT v A	41%	7%	32%
IT v B	44%	33%	38%

11503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Three versus one year of adjuvant imatinib for high-risk gastrointestinal stromal tumor (GIST): Survival analysis of a randomized trial after 10 years of follow-up. *First Author: Heikki Joensuu, Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland*

Background: Adjuvant imatinib improves recurrence-free survival (RFS) when administered after surgery to selected patients with operable gastrointestinal stromal tumor (GIST). It is uncertain whether overall survival (OS) improves, since imatinib improved OS in only one of the 3 large randomized trials conducted, and in this trial (the Scandinavian Sarcoma Group XVIII/German trial; SSGXVIII/AIO; NCT00116935) the statistical significance for OS remained borderline. The objective of the present analysis was to evaluate long-term OS of patients who participated in the SSGXVIII/AIO trial. **Methods:** SSGXVIII/AIO is an open-label, randomized (1:1), multicenter phase 3 trial. Four hundred patients who underwent macroscopically complete surgery for GIST with a high estimated risk for recurrence according to the modified National Institutes of Health Consensus Criteria were accrued between February 2004 and September 2008. Imatinib was scheduled to be administered 400 mg/day orally for either 12 months or 36 months after surgery. The patients were scheduled to be followed up for 10 years after study entry. Imaging of the abdomen was carried out periodically. The primary end point was RFS; the secondary objectives included OS and treatment safety. **Results:** The median follow-up time was 119 months. In the Intention-To-Treat Population 194 RFS events and 96 OS events were recorded. In the 36-month group, 5-year and 10-year RFS was 71.4% and 52.5%, and in the 12-month group, 53.0% and 41.8%, respectively (HR 0.66, 95% CI 0.49-0.87; P = .003). In the 36-month group, the 5-year and 10-year OS rates were 92.0% and 79.0%, and in the 12-month group, 85.5% and 65.3%, respectively (HR 0.55, 95% CI 0.37-0.83; P = .004). In the Efficacy Population, from which 15 patients who did not have GIST in central pathology review and 24 patients who had intra-abdominal metastases removed at surgery were excluded, 10-year OS was 81.6% in the 36-month group and 66.8% in the 12-month group (HR, 0.50, 95% CI 0.32-0.80; P = .003). No new safety signals were detected. **Conclusions:** About 50% of deaths can be avoided during the first decade of follow-up after surgery with 3-year imatinib treatment as compared to 1-year treatment. Clinical trial information: NCT00116935. Research Sponsor: Novartis.

11504 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Results of a randomized phase II/III study comparing perioperative adriamycin plus ifosfamide and gemcitabine plus docetaxel for high-grade soft tissue sarcomas: Japan Clinical Oncology Group study JCOG1306. *First Author: Kazuhiro Tanaka, Oita University Faculty of Medicine, Yufu, Oita, Japan*

Background: Our previous phase II study for high-grade soft tissue sarcomas (STS), JCOG0304, suggested long-term favorable effects of perioperative adriamycin plus ifosfamide (AI) on survival of STS patients. We have also reported in 2015 ASCO Annual Meeting that a phase II/III trial to confirm the non-inferiority of perioperative gemcitabine plus docetaxel (GD) to AI for high-grade STS (JCOG1306) had been started. We herein report the results of JCOG1306 at the early termination by the preplanned second interim analysis. **Methods:** Patients with operable, FNCLCC grade 2/3 STS primary tumor (T2bN0M0 or anyTN1M0, AJCC 7th edition) or first local recurrent tumor in the extremities or trunk were randomized to AI or GD. Chemotherapy consisted of adriamycin 60 mg/m^2 plus ifosfamide 10 g/m^2 for AI or gemcitabine 1,800 mg/m^2 plus docetaxel 70 mg/m^2 for GD. The treatments were repeated for 3 courses preoperatively and 2 courses postoperatively in a 3-week interval. The primary endpoint in phase III part was overall survival (OS). Planned sample size was 140 with a one-sided alpha of 0.1, power of 0.7 and a non-inferiority margin of 8% at 3-year OS, assuming 3-year OS of AI to be 85% and that of GD as 87%. The patient accrual has started in February 2014 and finished in September 2018. **Results:** A total of 143 patients were enrolled and included in the efficacy analysis. Seventy and 73 patients were assigned to AI and GD, respectively. At the second interim-analysis on December 2019, the estimated 2-year OS was 94.3 % (95% confidence interval (CI) 83.4–98.1) in AI and 91.6 % (80.9–96.4) in GD (hazard ratio (HR) 2.55, 95% CI 0.67–9.78). The estimated 2-year progression-free survival was 81.9 % (95% CI: 69.5–89.7) in AI and 64.0 % (51.1–74.4) in GD (HR 2.32, 95% CI 1.22–4.39). There were no treatment-related deaths in both groups. The most common Grade 3 or higher adverse events in AI were neutropenia (88.4%), anemia (49.3%), and febrile neutropenia (36.2%), whereas those in GD were neutropenia (79.5%), febrile neutropenia (17.8%), and alanine aminotransferase (9.6%). Based on the result of this analysis, the Data Monitoring and Safety Committee of JCOG recommended terminating the study since the point estimate of HR was above the prespecified allowable HR of 1.61. **Conclusions:** Although the toxicities were modest in GD, non-inferiority of GD to AI could not be confirmed. In the perioperative chemotherapy for high-grade STS in the extremities and trunk, AI remains the standard regimen. Clinical trial information: UMIN000013175. Research Sponsor: National Cancer Center Research and Development Fund [grant number 29-A-3], AMED [grant number JP18ck0106336].

11505 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Preliminary results of a phase II study of neoadjuvant checkpoint blockade for surgically resectable undifferentiated pleomorphic sarcoma (UPS) and dedifferentiated liposarcoma (DDLPS). *First Author: Christina Lynn Roland, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: is a randomized, phase II non-comparative trial evaluating the efficacy of neoadjuvant checkpoint blockade [nivolumab (N) or ipilimumab/nivolumab (I/N)] in patients (pts) with surgically resectable retroperitoneal DDLPS or extremity/truncal UPS treated with concurrent neoadjuvant radiation therapy (RT, UPS only). **Methods:** Primary endpoint was pathologic (path) response. Secondary endpoints were safety, RECIST response, recurrence-free survival, overall survival and patient-reported outcomes. Biospecimens (tumor, blood, fecal microbiome) at baseline, on therapy, and at time of surgery were collected and will be assessed for immune-based prognostic biomarkers. We assessed correlation between radiographic and pathologic response by linear regression. Correlative analyses includes assessment of tumor PD-L1 expression, characterization of tumor immune infiltrates by multiplex immunohistochemistry, and transcriptomic and genomic analyses. **Results:** Of the 25 pts enrolled; 24 are evaluable for response (14 DDLPS, 9 UPS). Clinical activity was variable by histologic subtype and treatment with RT. Median path response in the UPS cohort was 95% [95% CI 85–99] and was similar between the N/RT and I/N/RT groups (Table). Median path response in the DDLPS cohort was 22.5% [95% CI 85–99; Table]. Median change in tumor size (radiographic response) was -4% and +9% in the UPS and DDLPS cohorts, respectively. There was no correlation between path response and radiographic response (R^2 0.0309; p = 0.43). Of 8 pts with path response $\geq$ 85%, there was 1 partial response, 5 stable disease and 2 progressive disease by RECIST criteria. There was 1 delay to surgery due to grade 3 hyperbilirubinemia (Arm B). There was no difference in toxicity between N/RT and I/N/RT. **Conclusions:** N/RT and I/N/RT have significant clinical activity in UPS; more than expected compared to historic controls. Toxicity profiles were as expected and the majority of patients underwent resection without delay. Larger studies evaluating N/RT in UPS are warranted given the significant path response in this cohort. RECIST was not associated with path response and better markers of on-treatment clinical activity are needed. Correlative analyses that may guide combination strategies are ongoing and will be presented at the meeting. Clinical trial information: NCT03307616. Research Sponsor: Bristol Myers Squibb.

11506 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A single-arm multicenter phase II trial of doxorubicin (Doxo) in combination with trabectedin (Trab) given as first-line treatment to patients with metastatic/advanced uterine (U-LMS) and soft tissue leiomyosarcoma (ST-LMS): Final results of the LMS-02 study. *First Author: Patricia Pautier, Medical Oncology Department, Institut Gustave Roussy, Villejuif, France*

Background: U-LMS and ST-LMS are rare tumors with poor prognosis when locally advanced or metastatic, and with moderate chemosensitivity. Overall response rates (ORR) given in the 1st-line setting do not exceed 50% for U-LMS and 35% for ST-LMS with a mean response duration of 3- 6 months without impact on overall survival (OS). In 2015 we reported very encouraging results of the LMS-02 study (NCT02131480) with ORR of 59.6% in U-LMS, and 39.3% in ST-LMS with manageable toxicity (Pautier; Lancet oncol 2015). Herein, we report the updated results of progression-free survival (PFS) and final results of overall survival (OS). **Methods:** Patients (pts) received 60 mg/m^2 intravenous Doxo followed by trabectedin 1.1 mg/m^2 as a 3-hour infusion on Day 1 and pegfilgrastim on Day 2, repeated every 3 weeks for up to 6 cycles. Surgery for residual disease was permitted. Patients were stratified into U-LMS and ST-LMS groups. **Results:** Overall, 108 patients with LMS with a median age of 59 years and mostly metastatic disease (85%) were enrolled. Of those, 77 patients (71.3%) have received all 6 cycles of treatment, and 20 patients (18.5%) had metastasis resection. With a median follow-up of 7.2 years (95% CI: 6.9 - 8.2), the overall median PFS was 10.1 months (95% CI: 8.5 - 12.6), being 8.3 months (95 CI: 7.4 - 10.3) and 12.9 months (95% CI: 9.2 - 14.1) in U and ST group, respectively. Median OS was 34.4 months (95% CI: 26.9 - 42.7), being 27.5 months (95% CI: 17.9 - 38.2) in U-LMS and 38.7 months (95% CI: 31.0 - 52.9) in ST-LMS group. The median OS among the 20 pts with surgery was not reached vs 31.6 months in the population without surgery (95% IC: 23.9 - 35.4). **Conclusions:** The Doxo +Trab combination is an effective 1st-line therapy for pts with LMS, with promising PFS and OS results and an acceptable safety profile. Merely for comparison, the most recent results of Doxo alone in metastatic LMS, given in 1st-line setting in a phase III ANNOUNCE trial conducted during the same period, reported median PFS of 6.9 months, and median OS of 21.9 months (ASCO 2019 LBA3). Results of the LMS04 trial (NCT02997358), a randomized phase III study comparing this combination vs Doxo alone in 1st-line therapy in metastatic LMS are pending. Clinical trial information: NCT02131480. Research Sponsor: Pharmamar laboratory.

11507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A Ib/II study of the combination of lenvatinib (L) and eribulin (E) in advanced liposarcoma (LPS) and leiomyosarcoma (LMS) (LEADER). *First Author: Tom Wei-Wu Chen, National Taiwan University Hospital, Taipei City, Taiwan*

Background: For advanced LPS and LMS, the two most common histologies in soft tissue sarcoma, there are limited treatment options that readily balance efficacy and toxicity. Patients (pts) treated with E had an improved median overall survival (OS) in a phase III randomized study compared to dacarbazine but with an unsatisfactory 4% objective response rate (ORR). Early studies of L, a multi-targeted anti-angiogenic inhibitor, had suggested efficacy in sarcoma pts. We hypothesized that the combination of anti-angiogenic agent and chemotherapy could potentiate treatment benefit and aimed to explore the safety and efficacy of L + E in advanced LMS and LPS. **Methods:** LEADER was a single-arm phase Ib/II study for advanced adult LMS and LPS pts who had received no more than 2 lines of systemic chemotherapy. The phase Ib part (starting dose: L 18mg/day, E 1.1mg/m^2) had been reported and the recommended phase 2 dose (RP2D) was determined at L 14mg/day and E 1.1mg/m^2 D1, D8 every 21 days. The primary endpoint of the phase II part was ORR by RECIST 1.1, secondary endpoints included ORR by Choi criteria, progression-free survival (PFS), 6-month PFS rate, and OS. With $\alpha = 0.05$ and 80% power, the pts needed for stage I and total of the Simon 2-stage design was 13 and 27 pts, respectively. **Results:** As of Jan 22, 2020, 20 pts (F/M 13/7) had been treated with at least one cycle of L + E; 14 were LMS (5 uterine, 9 non-uterine) and 6 were LPS (4 dedifferentiated, 2 myxoid round cell). The median age was 51 (range 29-73); the median lines of treatment(s) received before enrollment was 1 (range 0-3). 18 pts were evaluable for primary endpoint: the ORR by RECIST 1.1 was 27 % (5/18) (95% CI 10-53%). The ORR by Choi criteria was 67 % (12/18) (95% CI 41-87%). With 8 PFS events, the median PFS and 6-month PFS rate was 56 weeks (95% CI 25-not reached) and 72%, respectively. There were no OS events. The ORRs by RECIST 1.1 between different L starting doses were not significantly different (18mg 33% (2/6) vs 14mg 25% (3/12), p = 0.7). 15 pts experienced at-least one grade (gr) 3 or 4 adverse event (AE); gr 3 or 4 AEs occurred in $>$ 1 pts included (% of phase Ib, % of phase II pts) hypertension (n = 4) (67%, 0%); hand-foot-syndrome (n = 4) (50%, 7%), proteinuria (n = 3) (0%, 25%), febrile neutropenia (n = 2) (17% vs 5%), neutropenia (n = 6) (50% vs 25%). The RP2D was associated with overall lower gr3/4 AEs except for proteinuria. **Conclusions:** L + E had shown promising efficacy in advanced LMS and LPS. L at 14mg/day had a better AE profile without compromising activity. The exploratory biomarker study of LEADER is ongoing. Clinical trial information: NCT03526679. Research Sponsor: Eisai.

11508 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A phase II study of MEK162 (binimetinib [BINI]) in combination with imatinib in patients with untreated advanced gastrointestinal stromal tumor (GIST). *First Author: Ping Chi, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: ETV1 and KIT are lineage-specific master transcriptional and signaling survival factors in GIST. In preclinical models, dual lineage targeting of ETV1 by MEK inhibition with BINI and KIT by imatinib are synergistic in suppressing GIST tumorigenesis and progression. This single-arm phase II study is designed to test the efficacy of the BINI+imatinib as a first-line treatment in patients (pts) with advanced GIST. **Methods:** Adult pts with untreated advanced GIST received imatinib (400mg daily) plus BINI (30mg twice daily), 28-day cycles. The primary endpoint (EP) was RECIST1.1 objective response rate (ORR) (complete response [CR]+partial response [PR]). The study was designed to detect a 20% improvement in the ORR of imatinib alone (unacceptable rate of 45%; acceptable rate of 65%). A sample size of 44 patients was required, using an exact binomial test, one-sided type I error of 0.08 and type II error of 0.1. Confirmed PR in $>$ 24 pts would be considered positive. Secondary EPs included RR by Choi and EORTC criteria, resectability conversion rate (RCR), progression free survival (PFS), overall survival (OS) and long-term AEs. Correlatives included characterization of tumor genomics by MSK-IMPACT, cfDNA by MSK-ACCESS, ETV1 protein levels and transcriptomes and signaling inhibition. **Results:** At data cutoff of Jan 31, 2020, 38/39 pts with advanced GIST of all genotypes, including 3 *KIT/PDGFRA*-wild type GIST pts, were evaluable for primary EP. Median age 60 (range 29-78), 29% female. 26/38 pts with confirmed PR; Best ORR was 68.4% (two-sided 95% CI, 51-83%; one-sided 90% CI, 57-100%). 8/9 pts became resectable after treatment; RCR was 88.9% (95% CI, 52-100%). 13 pts remain on trial (2-159 weeks [wks]). 9 pts discontinued trial due to disease progression (11-159 wks); one pt progressed within 3 months, indicating primary resistance. Grade 3/4 toxicity included CPK elevation (asymptomatic, 61%), neutrophil decrease (11%), maculopapular rash (8%), anemia (8%). No unexpected toxicities observed. Correlation of outcome with MSK-IMPACT, MSK-Access and paired tumor biopsies will be presented. **Conclusions:** This study met its primary endpoint. BINI plus imatinib is highly effective in treatment-naive advanced GIST, with expected and manageable long-term treatment-associated toxicities. The combination strategy warrants further evaluation in direct comparison with imatinib in the frontline treatment of GIST. Clinical trial information: NCT01991379. Research Sponsor: Both Array/Pfizer and NIH OPD/FDA.

11509 Poster Discussion Session; Displayed in Poster Session (Board #397), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase II multi-arm study of durvalumab and tremelimumab for advanced or metastatic sarcomas. *First Author: Neeta Somaiah, Department of Sarcoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: The combination of durvalumab (D), (anti- PD-L1) and tremelimumab (T), (anti-CTLA-4), was evaluated to determine activity in specific sarcoma subtypes (NCT02815995). We report final results of the clinical efficacy, safety and correlatives. **Methods:** Pts $\geq$12 yrs, with advanced/metastatic sarcoma, were enrolled based on subtype: LPS, LMS, angiosarcoma (AS), UPS, synovial sarcoma, osteosarcoma, ASPS, chordoma, and other sarcomas. Pts received D 1500mg and T 75mg every 4 wks for 4 cycles followed by D alone every 4 wks for up to 12 months (mo) unless the patients experienced unacceptable toxicity or disease progression. Re-treatment was allowed if progression occurred after stopping therapy within the next 12 mo. The primary end-point was PFS at 12 wks (RECIST). Secondary objectives included safety, response rates (irRC and RECIST) and survival. Biopsies were collected at baseline and at 6 wks for flow, PD-L1, multiplex IHC staining and sequencing. **Results:** Baseline characteristics of the 57 pts who received treatment are listed in the Table. Median OS for all pts was 20.8 mo (95% CI: 11.7, NR), the 12-mo survival was 63% (95% CI: 52%, 78%) and the 24-mo survival was 45% (95%CI: 33%, 61%). The mPFS for all pts was 4.5 mo (95% CI: 2.8, 6.9). The PFS at 12 wks for all pts was 51% (95%CI: 37%, 63%), PFS at 12 mo was 28% (95% CI: 18%, 43%), and PFS at 24 mo was 25% (95% CI: 16%, 41%). The 12 wk PFS was lowest for the LPS cohort (6 pts) at 16% (95% CI: 1%, 52%), and highest for the ASPS cohort (10 pts) at 90% (95% CI: 47%, 99%). PRs by irRC were observed in ASPS (5/10), chordoma, (1/5), UPS (1/5), and cutaneous AS (1/1), and 14 pts completed 12 mo of therapy. 14 pts (24.6%) experienced grade $\geq$3 related AEs (colitis, nausea, cardiac dysfunction, thyroiditis, pneumonitis, hepatitis, myositis, anemia and fatigue). Clinical benefit correlated with tumors with an inflamed phenotype; based on higher than median density of 3 major categories of tumor infiltrating lymphocytes (TIL): CD3+, CD3+CD8+, CD3+CD8+GZB+, seen in the 36 paired biopsies. **Conclusions:** In addition to histology (ASPS, cutaneous AS, UPS, chordoma), a higher TIL immune score can help predict clinical benefit. Clinical trial information: NCT02815995. Research Sponsor: Medimmune- AstraZeneca.

Characteristic	No. (%)
No. of pts	57
Median age, yrs (range)	48 (22 - 77)
Sex	
Male	31 (54)
Female	26 (46)
Performance status	
1	35 (61)
2	21 (37)
3	1 (2)
Prior lines of therapy	
Median (range)	2 (0 - 6)
None	5 (9)
1 - 2	24 (42)
≥3	28 (49)
Sarcoma Cohorts	
LPS	6 (10)
ASPS	10 (17.5)
Chordoma	5 (9)
Osteosarcoma	5 (9)
Undifferentiated pleomorphic sarcoma	5 (9)
Synovial sarcoma	5 (9)
Leiomyosarcoma	5 (9)
Angiosarcoma	5 (9)
Other tumors	11 (19)

11510 Poster Discussion Session; Displayed in Poster Session (Board #398), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Association of immune-related adverse events (irAEs) with improved clinical outcome in sarcoma patients treated with immune checkpoint blockade (ICB). *First Author: Evan Rosenbaum, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: IrAEs are associated with improved clinical outcomes after treatment with ICB in select epithelial malignancies. We hypothesized that sarcoma patients (pts) treated with ICB who developed an irAE would have improved outcomes compared to pts who had no irAE. **Methods:** Adverse events (AEs) from 3 sarcoma-specific ICB trials (nivolumab plus NKTR-214, pembrolizumab plus epacadostat, and pembrolizumab plus T-VEC) were reviewed. AEs probably or definitely related to ICB were classified as immune- or non-immune-related by the principal investigator. Endpoints of interest included best overall response (BOR) by RECIST 1.1 (complete response [CR]/partial response [PR]), durable clinical benefit (DCB; CR/PR/stable disease [SD] $\geq$ 16 weeks), and progression-free survival (PFS). Outcomes were stratified by the presence or absence of $\geq$ 1 irAE of any grade and by grade 1-2, grade 3-4, or no irAE (three-category comparison). **Results:** A total of 124 pts received ICB on these studies. Median pt age was 56 (range: 13-90); 53% were male; all but one pt had a performance status of $\leq$ 1. BOR was PR in 12 pts, SD in 41, and PD in 69. 2 pts were not evaluable. 40 pts (32%) had $\geq$ 1 irAE of any grade, 6 of whom had a grade 3-4 irAE. The most common irAEs ($\geq$ 5% of pts) were rash (15%), arthralgia (11%), myalgia (9%), pruritis (8%), and hypothyroidism (6%). The proportion of pts with a CR/PR was higher in pts with than without an irAE (18% vs. 6%, respectively; P = 0.058). A significantly higher proportion of pts with an irAE had DCB compared to those without (53% and 29%, respectively; P = 0.017). The median PFS of pts with an irAE was 16.6 months compared to 10.6 in those without (P = 0.013). The proportion of pts with a grade 3-4 irAE and a CR/PR was highest (33%) compared to pts with grade 1-2 (15%) or no irAE (6%) (P = 0.048). More pts with grade 3-4 irAE achieved DCB (67%) than grade 1-2 (50%) or no irAE (29%) (P = 0.027). Median PFS was 22.6, 15, and 10.6 weeks in the grade 3-4, grade 1-2, and no irAE groups, respectively (P = 0.047). **Conclusions:** Approximately one-third of advanced sarcoma pts with ICB-based immunotherapy developed an irAE. As reported previously in select carcinomas, sarcoma pts with irAEs were more likely to have clinical benefit than those without irAEs. Further research is needed to understand the mechanism behind this association and to validate these findings prospectively. Research Sponsor: None.

11511 Poster Discussion Session; Displayed in Poster Session (Board #399), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A multicenter phase II study of nivolumab +/- ipilimumab for patients with metastatic sarcoma (Alliance A091401): Results of expansion cohorts. *First Author: James Lin Chen, The Ohio State University, Columbus, OH*

Background: In the open-label multicenter phase II study, A091401, nivolumab (N) and nivolumab+ipilimumab (N+I) demonstrated a confirmed response rate (RR) of 5% and 16%, respectively in patients (pts) with advanced sarcoma (D'Angelo SP et al Lancet Oncology 2018). Responses occurred in undifferentiated pleomorphic sarcoma (UPS), myxofibrosarcoma, leiomyosarcoma, sarcoma not otherwise specified and alveolar soft part sarcoma. Here, we report efficacy of N and N+I, in each of 3 expansion cohorts [gastrointestinal stromal tumor (GIST), UPS and dedifferentiated liposarcoma (DDLS)]. **Methods:** Pts refractory to $\geq$ 1 regimen(s) were randomized (non-comparative) to receive either N [N (3 mg/kg q2W)] or N+I [N (3 mg/kg Q3W x4, then Q2W) plus I (3 mg/kg q3W x4)]. The primary endpoint was 6 month confirmed RR (RECIST v1.1). For UPS and DDLS, 2 confirmed responses in the 1st 12 evaluable pts was needed (85% power, 1-sided alpha=0.15, 5 v 25% RR). For GIST, a confirmed response in the 1st 9 evaluable pts expanded enrollment to 24 (80% power, 1-sided alpha=0.10, 5 v 20% RR). Other endpoints: adverse events (AEs, TRAEs), progression-free and overall survival (PFS, OS), and correlatives. **Results:** See table. **Conclusions:** Neither N or N+I lead to confirmed responses in GIST. In DDLS and UPS, the primary response endpoint was met with N+I but not with N alone (RR 14% for N+I vs. 7% and 8% for N alone). For the GIST cohort TRAE was higher with N+I, holding enrollment as required per protocol. There remains a pressing need to determine genomic and clinical biomarkers of response, resistance and toxicity. Correlative analyses (whole exome sequencing, multiplex IHC and RNAseq) are in progress. Support: U10CA180821, U10CA180882; ClinicalTrials.gov Identifier: NCT02500797. Research Sponsor: U.S. National Institutes of Health.

	GIST (n=18)		DDLS (n=24		UPS (n=24)	
Treatment	N	N+I	N	N+I	N	N+I
Evaluable	9	9	12	12	12	12
Design						
Median age (range)	69 (41-79)	62 (40-81)	62 (27-82)	59 (46-68)	64 (34-85)	60 (44-84)
% female	20	46	53	36	36	53
% ≥3 regimens	80	46	33	43	50	40
%≥ Grade 3 TRAE	10	46	20	14	15	14
6mth RR n%, (CI)	0, 0% (0-31%)	0, 0% (0-28%)	1, 7% (0.2-32%)	2, 14% (2-43%)	1, 8% (0.2-36)	2, 14% (2-43%)
Response Duration[b]	-	-	4.5	8.3 & 13.1	14.6	7 & 7.6
Median PFS[b]	1.5 (1.3-10)	2.9 (1.4-NE[c])	4.6 (3.2- NE)	5.5 (2.8 -NE)	1.5 (1.4- NE)	2.7 (1.5 -NE)
Median OS[b]	9.1 (4.9-NE[c])	12.2 (6-NE)	8.1 (7-NE)	13.1 (9.1-NE)	6.6 (2.4-17.6)	NE (5.1-NE)

a) Confidence interval b) In months c) Not estimable.

11512 Poster Discussion Session; Displayed in Poster Session (Board #400), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Survivin-responsive conditionally replicating adenovirus for patients with advanced sarcoma demonstrated potent and long-term efficacy and high safety in a phase I clinical trial. *First Author: Satoshi Nagano, Kagoshima University, Kagoshima, Japan*

Background: Whereas one of oncolytic viruses (OVs), inducing selective tumor killing and systemic anti-tumor immunity, was approved by FDA in 2015, the best OV that more safely and efficiently treats intractable cancers has not been successfully developed. By our platform technology to efficiently construct next-generation OVs, *i.e.*, "conditionally replicating adenoviruses (CRAs) that target and/or treat tumor cells with multiple factors" (m-CRAs), we identified that among candidates, survivin-responsive m-CRAs (Surv.m-CRAs) exhibited the most potent antitumor efficacy and cancer selectivity (*i.e.*, safety) in preclinical studies (*Cancer Res*, 2005 *et al.*). Here we present the data of First-In-Human phase I clinical trial of Surv.m-CRA-1 for musculoskeletal tumors (MST). **Methods:** This single-arm, open label study included 9 patients with unresectable and advanced MST. Patients underwent a single intratumoral injection of either 1×10^10 viral particle (vp) (low), 1×10^11 vp (mid) or 1×10^12 vp (high). The primary endpoints were safety and tolerability. The secondary endpoints included the local control of treated tumor at one month, defined by RECIST and Choi criteria, analysis of dissemination of Surv.m-CRA-1, serum cytokine and adenoviral antibody. Long-term follow-up was done in some patients. **Results:** Four patients (44.4%) had grade 3 or higher adverse events, including lymphopenia, leukocytopenia and mildly elevated liver transaminase in 2, 1 and 1 patient, respectively. Virus excretions, including second peak of viremia from viral replication in tumor, were observed in 1, 2 and 3 patients of low, mid and high dose, respectively. Out of 9 patients, 5 PR, 3 SD and 1 PD by Choi, and 8 SD and 1 PD by RECIST were observed. During follow-up, another 1 and 2 patients became PR by Choi and RECIST, respectively. Of note, long-term PR (over 2 years) after a single injection of Surv.m-CRA-1 was achieved in two chordoma cases in low dose. **Conclusions:** Surv.m-CRA-1 was well tolerated and showed antitumor activity for prolonged periods against advanced MST. We about to start Phase I/II study of multiple injections of Surv.m-CRA-1 for advanced solid tumors in two-arms for musculoskeletal tumors and pancreatic cancer. Clinical trial information: R000026464. Research Sponsor: Japan Agency for Medical Research and Development.

11513 Poster Discussion Session; Displayed in Poster Session (Board #401), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Defining the role of neoadjuvant systemic therapy in high-risk retroperitoneal sarcoma: A multi-institutional TARPSWG study. *First Author: William W. Tseng, Department of Surgery, Division of Breast, Endocrine and Soft Tissue Surgery, Keck School of Medicine, University of Southern California, Los Angeles, CA*

Background: Surgery is the mainstay of treatment for patients with retroperitoneal sarcoma (RPS), but this can be challenging, and recurrence rates are high. Novel treatment approaches are needed. In this study, we sought to 1) determine the frequency and potential predictors of radiologic tumor response and 2) assess clinical outcomes in patients with primary high risk RPS who were treated at sarcoma referral centers with neoadjuvant systemic therapy followed by surgery. **Methods:** Clinicopathologic data was retrospectively collected for eligible patients treated from 2008-2018 at 13 institutions within the Transatlantic Australasian Retroperitoneal Sarcoma Working Group (TARPSWG). For each patient, preoperative objective response (RECIST1.1) was reported by each institution. Univariable and multivariable logistic models were performed to determine predictors of response. Kaplan-Meier plots were constructed for overall survival (OS) and cumulative incidences of local recurrence (LR) and distant metastasis (DM). **Results:** In total, 158 RPS patients were included in this study. A median of 3 cycles (IQ range 2-4) of neoadjuvant systemic therapy were given. No complete responses were observed. Partial response (PR) was seen in 37 patients (23%), stable disease (SD) in 88 (56%) and progressive disease (PD) in 33 (21%). Subtype-specific differences were seen including PR in 5 out of 11 (45%) patients with undifferentiated pleomorphic sarcoma. Overall, higher number of cycles given was positively associated with PR ($p = 0.005$). No other factors including receipt of neoadjuvant radiation therapy were predictive of PR. All patients underwent complete (R0/R1) resection with a major complication (Clavien-Dindo $\geq$3) rate of 23%. Differences in OS were observed based on preoperative response type ($p = 0.005$). In grade 3 dedifferentiated liposarcoma, patients who received adriamycin-ifosfamide versus another regimen had decreased LR and improved OS. In leiomyosarcoma, patients who received adriamycin-DTIC versus another regimen had a higher PR rate (37% vs. 16%), decreased LR, DM and improved OS. Limited by low numbers, these subtype-specific data did not reach statistical significance. **Conclusions:** In patients with high risk RPS, response to neoadjuvant systemic therapy is overall modest and may be regarded as an indicator of disease biology to predict survival after surgery. Subtype-specific regimens should be further validated and incorporated into prospective trials of neoadjuvant systemic therapy in RPS (e.g. STRASS2). Research Sponsor: None.

11514 Poster Discussion Session; Displayed in Poster Session (Board #402), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Trabectedin and radiotherapy in soft-tissue sarcoma (TRASTS) study: An international, prospective, phase II trial in localized myxoid liposarcoma—A collaborative Spanish (GEIS), Italian (ISG) and French (FSG) group study. *First Author: Alessandro Gronchi, Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: Myxoid liposarcoma (ML) exhibits especial sensitivity to trabectedin (T). In prospective series, T showed responses in 44% of patients (pts) with ML. ML is also sensitive to radiation therapy (RT) and preclinical data suggested radiosensitizing properties of T. Preoperative short-course of T with concurrent low-dose RT was conducted in a multicenter, European, phase I/II trial. We present here the data from the phase II part in pts with centralized diagnosis of locally advanced, resectable ML. **Methods:** Pts received 3 cycles (C) of T in combination with RT (45 Gy) in 25 fractions (1.8Gy/fraction). The phase I part of the study had the classic 3+3 design. Dose Levels for T were: -1 (1.1 mg/m^2), 1 (1.3 mg/m^2) and 2 (1.5 mg/m^2) Results were already reported (EClincalMedicine 2019;9:35-43) and the dose selected for the phase 2 part was 1.5 mg/m2. RECIST responses were evaluated preoperatively at week 10. Surgical specimens were processed for histologic changes and residual tumor. **Results:** From July 2016 to September 2019, 47 pts (M/F 31/16) with median age 43y (18-77) and median tumor size 11 cm (3-25 cm), 20 low and 24 high grade (3 not available) were enrolled in the phase II part of the study. The major grade 3/4 toxicities were neutropenia (21.3%), ALT (14.9%), GGT (8.5%) and AST (8.5%) elevation. There were no deaths due to toxicity. 43/47 patients received the planned 3 preoperative T cycles. All pts completed RT. 1 patient started RT before the first cycle of T and was excluded from the analysis. All pts were evaluable for response: 14 achieved PR (30%), 32 SD (70%). All pts underwent surgery (37 [86%] R0/ 5 [12%] R1/ 1 [2%] R2/ 3 not available). Median viable residual tumor was 10% (0-90) with 23/43 pts (53%) with $\leq$ 10% viable remaining tumor. Of them 6/43 (14%) had complete responses. At a median FU of 18 months (3-41) one pt developed local recurrence and 2 distant metastases. No deaths were observed. The corresponding 2-yr disease-free survival and overall survival were 97% (95% confidence interval 95-100) and 100%. **Conclusions:** T in combination with RT was feasible and well tolerated in the preoperative setting. The activity of the combination compares favorably with the administration of T/RT alone. This regimen could potentially become an alternative to anthracycline+ifosfamide concurrent to RT in high risk localized ML. Clinical trial information: NCT02275286. Research Sponsor: PharmaMar.

11515 Poster Discussion Session; Displayed in Poster Session (Board #403), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A randomized phase II study of gemcitabine (G) alone or with pazopanib (P) in refractory soft tissue sarcoma (STS). *First Author: Christopher W. Ryan, Oregon Health & Science University, Knight Cancer Institute, Portland, OR*

Background: Both G and P are active single-agents in the treatment of STS. We hypothesized that the anti-VEGF-R activity of P could augment the efficacy of G and conducted this study of G+P vs G+placebo (0). **Methods:** In this multi-center, double-blind study, eligibility included metastatic STS with receipt of 1–3 prior systemic regimens inclusive of an anthracycline. Patients (pts) were stratified by sarcoma subtype (liposarcoma (LPS) vs. other) and study site, then randomly assigned 1:1 to receive G 1000 mg/m2 IV over 30 minutes on days 1 and 8 every 21 days plus either P 800 mg PO or matching 0 daily. The primary endpoint was progression-free survival (PFS). **Results:** 54 pts were accrued from 2012–2019, Accrual was halted prior to the planned N of 80 due to withdrawal of funding. There were no differences in pt characteristics between the two arms including age (median = 60), sex (M/F 52/48%), histology (LPS 30%, leiomyosarcoma 26%, UPS 15%, synovial 11%, other 17%) and number of prior systemic therapies (median = 1). With a median follow-up of 19.1 months, PFS favored G+P and was significant using the Gehan-Wilcoxon test which favorably weighs earlier events (table). The response rate was 6.9% on the G+P arm and 8.0% on the G+0 arm; response rate was 22% for LPS treated with G+P. The most common grade $\geq$3 AEs (G+P v G+0) were: neutropenia (41% vs 40), hypertension (17% v 4), anemia (7% v 12). One patient died of hepatic failure on the G+P arm. **Conclusions:** This study demonstrated improved PFS with G+P as compared with G alone. Early termination limited statistical power. G+P is active in LPS, although P regulatory labeling currently limits use for LPS. Clinical trial information: NCT01532687. Research Sponsor: Novartis and Glaxo Smith Kline, U.S. National Institutes of Health.

	G+P (N = 29)	G+0 (N = 25)	Gehan-Wilcoxon p-value	Log Rank p-value
PFS (months) Median [95% CI]	4.5 [3.0, 8.5]	1.6 [1.4, 4.3]	0.017	0.162
LPS (N = 16)	8.9 [4.3, NA]	1.5 [1.0, NA]	0.195	0.511
Other (N = 38)	4.4 [3.0, 8.3]	2.2 [1.4, 4.6]	0.079	0.26
Clinical Benefit (PR+SD)	66% [45.7, 82.1]	40% [21.1, 61.3]	0.06*	
LPS	78% [40.0, 97.2]	29% [3.7, 71.0]	0.10**	
Other	60% [36.1, 80.9]	44% [21.5, 69.2]	0.30*	

*proportions test; **exact proportions test

11516 Poster Discussion Session; Displayed in Poster Session (Board #404), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Long-term follow-up for duration of response (DoR) after weekly *nab*-sirolimus in patients with advanced malignant perivascular epithelioid cell tumors (PEComa): Results from a registrational open-label phase II trial, AMPECT. *First Author: Andrew J. Wagner, Dana-Farber Cancer Institute, Boston, MA*

Background: Malignant PEComa is a rare, aggressive sarcoma, with no approved medical treatment. Cytotoxic chemotherapies have limited benefit for patients with advanced disease. The AMPECT trial measured the effects of *nab*-sirolimus (ABI-009) and is the first prospective study in advanced malignant PEComa. *nab*-Sirolimus is a nanoparticle albumin-bound mTOR inhibitor with significantly higher intratumoral drug levels, mTOR target suppression, and anti-tumor activity in animal models versus other mTOR inhibitors. This report presents long-term follow-up of DoR after the primary analysis. **Methods:** Patients (N=34) received *nab*-sirolimus (100mg/m^2 IV, weekly, 2/3 weeks) until progression or unacceptable toxicity. Primary endpoint: ORR by IRR. Key secondary endpoints included DoR, PFS6, OS, and safety. Exploratory endpoints included correlation of tumor genotype and outcome. The sample size of 30 efficacy-evaluable patients was based on an estimated ORR of 30% and the lower bound of the 95%CI of ORR to exclude values less than 14.7%. The primary analysis was conducted when all patients were treated ≥6 months (May 22, 2019). This report updates the primary response analysis and DoR with an additional 8.5-month of follow-up. **Results:** As of Feb 06, 2020, of the 31 efficacy-evaluable patients, the confirmed ORR by IRR was 39% (12/31, 95%CI: 21.8, 57.8), with 1 complete response (CR) and 11 partial responses (PR), 52% stable disease (SD, 16/31, with 10/16 SD ≥12 weeks), and 10% progressive disease (3/31); the disease control rate (CR+PR+SD ≥12 weeks) was 71%. PFS6 was 71% (95%CI: 47.7, 85.1). The majority of responses (67%) were reached at the first post-baseline scan at week 6, with a median time to response of 1.4 months (95%CI: 1.3 to 2.8). The median DoR by IRR was not yet reached (range 5.6-38.7+ months; calculated median 22.2+ months) with 8/12 (67%) responders still on treatment for >1 year and 5/12 (42%) >2 years. Mutational analysis available for 25 patients identified that TSC2 loss-of-function mutations significantly correlated with response; 8/9 (89%) patients with TSC2 had a confirmed response. **Conclusions:** Responses of advanced malignant PEComa to *nab*-sirolimus were highly durable and occurred in 39% of patients based on independent review. The high disease control rate with manageable toxicities suggest that *nab*-sirolimus is effective and represents an important new treatment option for these patients. Clinical trial information: NCT02494570. Research Sponsor: Aadi Bioscience, Other Government Agency.

11517 Poster Discussion Session; Displayed in Poster Session (Board #405), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase II study of oraxol in the treatment of unresectable cutaneous angiosarcoma. *First Author: Vinod Ravi, The University of Texas MD Anderson Cancer Center, Department of Sarcoma Medical Oncology, Houston, TX*

Background: Oraxol is a combination of oral paclitaxel and a novel oral P-glycoprotein inhibitor, HM30181A. Cutaneous angiosarcomas are highly aggressive malignant tumors with poor prognosis. Currently there is no FDA-approved treatment. **Methods:** This is an open label study evaluating the activity, safety and tolerability of Oraxol 205mg/m^2 administered orally, once daily, for 3 consecutive days per week. Planned treatment is for 25 weeks. Subjects included in this study had not received prior therapy with a taxane and did not have metastatic disease. Tumour response was evaluated at 6 weekly intervals using RECIST and photography. A Simon two stage design was used. **Results:** 18 of 24 enrolled patients (pts); male/female 11/7; median age 77 years (range 56-93), were evaluable at time of analysis. Subjects were recruited during an 18 month period, from Aug-2018 to Jan-2020. Best objective response rates were: CR 22% (n = 4), PR 11% (n = 2), SD 67% (n = 12), PD 0%. 42% of pts with SD had durability > 13 weeks (range 13-25). Median PFS was 38 weeks. All pts remain alive at time of reporting. Furthermore, 5 pts (28%) who had inoperable lesions were deemed operable after Oraxol and received surgical resection. Oraxol was generally well tolerated. Most common adverse events (AEs) G>3 were: diarrhea (n = 1), fatigue (n = 3), neutropenia (n = 9), leucopenia (n = 5), lymphopenia (n = 5). Serious AEs were G3 pneumonia in 2 subjects and G4 neutropenia in 2 subjects, one of which was febrile. All events fully resolved. Neuropathy was uncommon: n = 2 (G1 = 1 @ day 10, G2 = 1 @ day 64). Dose reductions were recorded in 7 subjects. 2 subjects discontinued treatment due to AEs; both asymptomatic pneumonitis seen on CT, which recovered after discontinuation. Following the initial positive results, the protocol has been amended to change the maximum recruitment of subjects from 25 to 43. **Conclusions:** Oraxol provides an orally administered treatment option for angiosarcoma, with a high and durable clinical benefit rate (CR + PR+ long SD). It is generally well tolerated even in an older patient population; particularly with respect to the the low incidence of neuropathy compared to IV paclitaxel. Recruitment is ongoing. Clinical trial information: NCT03544567. Research Sponsor: Athenex Inc.

Complete Response (CR)	Partial Response (PR)	Stable Disease (SD)	Progression
4 (22%)	2 (11%)	12 (67%)	0 (0%)

11518 Poster Discussion Session; Displayed in Poster Session (Board #406), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase II single-arm study of nivolumab and ipilimumab (Nivo/Ipi) in previously treated classical Kaposi sarcoma (CKS). *First Author: Alona Zer, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: CKS is a mesenchymal neoplasm associated with HHV8 infection. Though recombinant INFa is approved for treatment of AIDS-related KS, data is limited regarding the role of immune modulation in CKS therapy. Based on favorable responses in viral-induced cancers, we hypothesized that CTLA-4 and PD-1 blockade can induce tumor regression in CKS. We present pre-planned interim analysis of a phase II study of Nivo/Ipi in previously treated progressive CKS. **Methods:** CKS pts with progressive disease after > 1 line of systemic therapy and measurable disease received nivolumab 240mg d1,15,28 and ipilimumab 1mg/kg d1 q42 days until progression or toxicity. The primary endpoint was overall response rate (ORR) evaluated clinically, radiologically (RECIST) and metabolically (FDG-PET). Secondary endpoints include 6-months progression free survival rate (PFS) and safety. Exploratory endpoints included PD-L1/MMR by IHC, DNAseq (596 genes)/RNAseq (whole transcriptome) of tumor and matched blood specimens to explore CKS genomic traits and IO correlates: TMB and MSI status, MMR and PD-L1 protein expression, and immune gene transcript expression (PD-1, PD-L1, CTLA-4, and others) (Tempus Labs, Chicago, IL, USA). **Results:** Fifteen patients were enrolled and evaluable (Apr18-Jan20). Median age 72.5 (61-81), all male. At a median FU of 15.7 mo ORR as per RECIST was 66% (9 pts PR, 1 pt CR, 2 pts SD, 3 pts NE). Clinical ORR was 87% and metabolic ORR was 60%. Median PFS was not reached, 6mo PFS rate was 85% and 1y PFS rate was 75%. The safety profile was as expected with all pts experiencing G1 toxicity, 3 pts with G2 toxicity (1 hepatic, 2 asymptomatic lipase increase) and 2 pts with G3 toxicity (1 colitis, 1 asymptomatic lipase increase). One SAE was reported (TIA considered not related to therapy) and treatment was discontinued in 3 pts. Correlative results are available for 8 pts showing a trend for copy number loss in genes with tumor-suppressive activity (FOXA1, ELF3), no PDL1 expression, low TMB, microsatellite stability, but marked overexpression of CTLA-4, PD-1, PDL-1, CD40, OX40 and LAG3 RNA immune transcripts. **Conclusions:** The interim analysis of this prospective phase II study of nivolumab and low-dose ipilimumab demonstrates promising activity in progressive CKS, with 66% ORR and a 6mo PFS rate of 85%. Toxicity profile is as expected in this class of drugs. Correlative studies are preliminary, but warrant further investigation into genomic traits and immune gene expression profiles. Clinical trial information: NCT03219671. Research Sponsor: BMS.

11519 Poster Discussion Session; Displayed in Poster Session (Board #407), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A pilot study evaluating the safety, tolerability, and efficacy of doxorubicin and pembrolizumab in patients with metastatic or unresectable soft tissue sarcoma. *First Author: Michael B. Livingston, Levine Cancer Institute, Atrium Health, Charlotte, NC*

Background: Doxorubicin has been the traditional standard therapy for treatment of advanced soft tissue sarcoma (STS). The addition of cytotoxic agents leads to increased toxicity with minimal improvement in efficacy. Pembrolizumab monotherapy has demonstrated activity and tolerability in previous study of advanced STS. This study combined pembrolizumab with doxorubicin to determine safety and efficacy in the frontline setting. **Methods:** This single-center, single-arm, phase 2 trial enrolled subjects with unresectable or metastatic STS and no prior anthracycline therapy. Subjects were treated with pembrolizumab 200 mg IV and doxorubicin 60 mg/m2 (75 mg/m2 dose escalation per investigator discretion) IV every 3 weeks. The primary endpoint of safety, based on Bayesian stopping rules, evaluated if the severe or life-threatening treatment emergent adverse event (TEAE) rate exceeded 0.55. Secondary endpoints included overall survival (OS), objective response rate (ORR), and progression free survival (PFS). Efficacy and safety were based on RECIST 1.1 and CTCAE v 4.0, respectively. Kaplan-Meier methods evaluated time to event outcomes. **Results:** From 4/2017 to 12/2019, 30 subjects (53% female, median age 61.5 years, 10 patients > 70 years (33%)) were enrolled in the study with 6 (20%) patients still on treatment and 27 evaluable for response. The most common histologic subtypes were leiomyosarcoma (33%) and liposarcoma (23%), and a majority of patients demonstrated high grade disease (60%). Current analysis shows a median follow-up of 9.9 months. One subject experienced a stopping rule event (grade 3 autoimmune disorder). ORR was 33% (95% CI 17-54%), with documented disease control in 78% (95% CI 57.7-91.4%) of patients. Eight (30%) patients achieved a partial response, one (4%) patient achieved a complete response and 12 (44%) patients had stable disease. Preliminary results demonstrate median PFS of 6.9 months (PFS-6 mo: 52%) and median OS of 15 months (OS-6 mo: 81%) compared to historical PFS-6mo of 4.6 months and OS of 12.8 months with doxorubicin alone.[1] Most common grade 3+ TEAEs included neutropenia (11 [37%]), febrile neutropenia (6 [20%]), anemia (5 [17%]), and nausea (4 [13%]). Molecular and biomarker analysis is currently in progress. **Conclusions:** The combination of pembrolizumab with doxorubicin has manageable toxicity and preliminary promising activity in the treatment of anthracycline-naive advanced soft tissue sarcomas. Ref: 1. Lancet Oncol. 2014 Apr; 15(4):415-23. Clinical trial information: NCT03056001. Research Sponsor: Merck Sharp & Dohme Corp.

11520 Poster Discussion Session; Displayed in Poster Session (Board #408), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

SAINT: Results of an expanded phase II study using safe amounts of ipilimumab (I), nivolumab (N), and trabectedin (T) as first-line treatment of advanced soft tissue sarcoma [NCT03138161]. *First Author: Erlinda Maria Gordon, Sarcoma Oncology Research Center, Santa Monica, CA*

Background: Sarcoma cells are most immunogenic earlier in the disease. Hypothesis: Immune checkpoint inhibitors would be most effective when given as first-line therapy. **Methods:** Eligible patients include previously untreated male or female patients, ≥ 18 years of age with locally advanced unresectable or metastatic soft tissue sarcoma (STS), with measurable disease by RECIST v1.1. Immune checkpoint inhibitors I (1 mg/kg i.v. q 12 weeks) and N (3 mg/kg i.v. q 2 weeks) were given with T (1.2 mg/m2 i.v. q 3 weeks), a tumoricidal agent that depletes growth-promoting macrophages in the tumor microenvironment. Primary endpoint: Objective response rate by RECIST v1.1; Secondary endpoints: (1) Progression-free survival (PFS) at 6 months, (2) Overall survival (OS) at 6, 9, 12, 24, and 48 months, and (3) Incidence of adverse events. **Results:** Efficacy analysis: There were forty-one evaluable subjects. Best overall response rate was 19.5%; disease control rate 87.8%. The median OS was >12.5 months; median PFS was >6.0 months (6-month OS rate: 75%; 6-month PFS rate: 50%). Safety analysis: Grade 3 TRAEs include fatigue (n = 5), increased TSH (n = 3), decreased TSH (n = 1), adrenal insufficiency (n = 1), hyperglycemia (n = 1), dehydration (n = 1), hyponatremia (n = 2), bipedal edema (n = 2), increased AST (n = 8), increased ALT (n = 19), increased ALP (n = 2), increased CPK (n = 3), port site infection (n = 2), psoriasis exacerbation (n = 1), anemia (n = 6), thrombocytopenia (n = 2), and neutropenia (n = 2). Grade 4 TRAES include neutropenia (n = 1), thrombocytopenia (n = 2), and increased CPK (n = 2). **Conclusions:** These data suggest that combinatorial therapy with Ipilimumab, Nivolumab and Trabectedin (1) may have synergistic activity in achieving disease control, and (2) is safe with manageable toxicity for patients with previously untreated STS. Clinical trial information: NCT03138161. Research Sponsor: Bristol-Myers-Squibb.

Efficacy analysis of evaluable patients.

Best Overall Response RECIST v1.1 (n = 41)	Median PFS mos. (Range)	Median OS mos. (Range)
3 CR*, 5 PR, 28 SD, 5 PD	>6.0 (1 – 22)	>12.5 (1 – 23)

*One surgical CR

11521 Poster Session (Board #409), Fri, 8:00 AM-11:00 AM

Differential genomic landscape of clinically advanced/metastatic chordomas (mChor) based on primary tumor site. *First Author: Jonathan Keith Killian, Foundation Medicine, Cambridge, MA*

Background: We queried whether comprehensive genomic profiling (CGP) could differentiate genomic alteration (GA) differences in mChor based on tumor site of origin **Methods:** 111 mChor FFPE tissues were sequenced using a hybrid-capture based CGP method to evaluate all classes of genomic alterations (GA). Tumor mutational burden (TMB) was determined on up to 1.1 Mbp of sequenced DNA and microsatellite instability (MSI) was determined on 114 loci. **Results:** 27 clivus (Cliv), 12 cervical (Cerv), 10 thoracic (Thor) and 44 lumbosacral (Sacr) mChor were compared (Table). A separate set of 18 mChor were submitted as metastasis biopsies with no primary tumor site available (Unk). mChor was generally more common in men with Sacr tumors. Cliv patients were significantly younger (p = 0.00002). GA/tumor was highest in Sacr at 2.9 and lowest Thor at 1.5. All (100%) mChor were MSI stable and the TMB was low (< 5 mut/Mb) for all cases. *CDKN2A* and *CDKN2B* mutation frequencies were highest in Sacr (52% and 46%, p = 0.009 and 0.0109). Potentially actionable GA in *PTEN* were highest in Thor and Sacr. *PTCH1* GA were seen in Cliv and Cerv and *PBRM1* GA potentially associated with immune-oncology (IO) drug response were present in all groups. Additional noteworthy targets were seen in all groups but were found in less than 11% of cases throughout the study (Table). **Conclusions:** Genomic profiles of our mChor cohort differ based on the site of tumor origin in the axial spine. Sacr appear to have the highest frequency of GA and the greatest number of potentially targetable GA. Although MSI and TMB biomarker results do not predict responsiveness, a significant *PBRM1* GA frequency in all groups raises the possibility of IO drug benefit for some patients. Research Sponsor: Foundation Medicine Inc.

	All (111)	Clivus/ Skull Base (27)	Cervical (12)	Thoracic (10)	Lumbo-sacral (44)	Metastasis Bx 1^0 Unknown (18)
Gender female/ male	32%F/ 68%M	44%F/ 56%M	33%F/ 67%M	50%F/ 50%M	16%F/84%M	39%F/61% M
Age Median (range) years	56 (10-85)	43 (10-72)	57 (16-75)	63 (18-83)	57 (21-85)	56 (33-79)
GA/Tumor	2.3	1.9	2.3	1.5	2.9	1.7
CDKN2A	37%	22%	42%	30%	52%	22%
CDKN2B	31%	19%	42%	0%	46%	22%
PTEN	11%	0%	8%	20%	16%	11%
PBRM1	10%	4%	10%	13%	7%	22%
PTCH1	2%	4%	8%	0%	0%	0%
Other Noteworthy Targets < 11% of cases	See Subtypes	*TSC2, EGFR, PIK3CA*	*CDK4, CDK12, ERBB3*	*CDK4, ERBB3,*	*KIT, EGFR, BRCA1/2, TSC1/2, PDGFRA, BRAF, PIK3CA*	*CDK4, BRCA2*
Median TMB	1.2	1.2	2.4	1.7	0.9	0.9

11522 Poster Session (Board #410), Fri, 8:00 AM-11:00 AM

IMMUNOSARC: a collaborative Spanish (GEIS) and Italian (ISG) sarcoma groups phase I/II trial of sunitinib and nivolumab in advanced soft tissue and bone sarcoma: Results from the phase II part, bone sarcoma cohort. *First Author: Emanuela Palmerini, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy*

Background: Herein, we present the results of the cohort on advanced bone sarcoma patients of the phase II part of the IMMUNOSARC study (NCT03277924), a European multicentre phase I-II trial aimed at investigating the activity of the combination of sunitinib (SU) and nivolumab (NI) in selected advanced sarcoma subtypes. **Methods:** Adult, pretreated, progressing patients, ECOG 0-1, with a diagnosis of osteosarcoma, high-grade bone sarcoma, Ewing sarcoma, chondrosarcoma or dedifferentiated chondrosarcoma were eligible. SU 37.5 mg/day as induction was given days 1-14 and then reduced to 25mg/day continuously. NI was administered at 3 mg/Kg every 2 weeks from week 3. SU-NI was maintained up to progression or intolerance. Primary end-point was progression-free survival rate (PFSR) at 6 months (H1: PFSR 6-months: 15%). Secondary end-points: overall survival (OS), objective response rate (ORR) by RECIST v 1.1 and toxicity. **Results:** From Nov 2017 to Dec 2018, 40 eligible patients were included: (M/F = 27/13), median age 47 years (range 21-74), ECOG 0 in 11 (27%) cases, 36 (90%) were metastatic, 4 (10%) locally advanced. Histology: 17 osteosarcomas (43%), 14 chondrosarcomas (35%) (4 dedifferentiated), 8 Ewing sarcomas (20%), 1 bone undifferentiated pleomorphic sarcoma (2%). PFSR at 6 months based on local evaluation was 32%. At a median FU of 12.5 months (2-26), median PFS was 3.7 months (95% IC 3.4-4) while median OS was 14.2 months (95%CI: 7.1-21.3). OS rate at 3 and 6 months were 87% and 73%, respectively. ORR by RECIST: 1 CR (2.5%) (1 patient with dedifferentiated chondrosarcoma, lasting 22 months and on going), 1 PR (2.5%) (1 patient with osteosarcoma, lasting 5.7 months), 22 SD (55%, lasting > 6 months in 45% of the cases) and 16 PD (40%). G3/5 toxicities are detailed in Table. **Conclusions:** The trial met its primary endpoint in the cohort of patients with advanced bone sarcoma, with > 30% of patients free from progression at 6 months. Preplanned tumor microenvironment genomic, exploratory analysis on pre and post-treatment tumor samples is on going. Clinical trial information: NCT03277924. Research Sponsor: Pfizer, Bristol-Myers Squibb, Matteo Amitrano Onlus.

Grade 3-5 side effects in 40 patients with bone sarcoma after sunitinib and nivolumab.

Toxicity	Grade 3-4	Grade 5
Neutropenia	4 (10%)	0
Anaemia	4 (10%)	0
ALT/AST increased	3 (7.5%)	0
Fatigue	2 (5.0%)	0
Oral mucositis	2 (5.0%)	0
Thrombocytopenia	1 (2.5%)	0
Dysphagia	1 (2.5%)	0
Gastric haemorrhage	1 (2.5%)	0
Malaise	1 (2.5%)	0
Thromboembolic event	1 (2.5%)	0
Pneumonitis (toxic death)	0	1 (2.5%)

11523 Poster Session (Board #411), Fri, 8:00 AM-11:00 AM

Efficacy of maintenance therapy with zoledronic acid in patients with localized Ewing sarcoma: Report from the international Ewing 2008 trial. *First Author: Uta Dirksen, Pediatrics III, West German Cancer Center, University Hospital Essen, German Cancer Consortium (DKTK), Essen, Germany*

Background: Ewing 2008R1 (EudraCT2008-003658-13, Sponsor UKM) was conducted in 12 countries. It evaluated the effect of zolendronic acid (ZOL) maintenance therapy on event-free (EFS, primary endpoint) and overall survival (OS) from randomization in standard risk Ewing Sarcoma (EwS). **Methods:** Phase III, open label, prospective, multi-center, randomized controlled clinical trial. Eligible patients (pts) had localized EwS with either good histological response to induction chemotherapy and/or small tumors (< 200ml). Pts received 6 cycles VIDE induction and 8 VAI (male) or 8 VAC consolidation (female) and were randomized to receive either 9 cycles of maintenance ZOL or no further treatment (control;ctrl). ZOL cycles started parallel to the 6^{th} consolidation cycle. Randomization was stratified by tumor site (pelvis/no pelvis). Two-sided adaptive inverse-normal 4-stage design, changed after the 1^{st} interim analysis via Müller-Schäfer method. Initial sample size 448 pts, type I error rate 5%, power 80%. **Results:** 284 pts were randomized between 2009 and 2018 (142 ZOL / 142 ctrl). With a median follow-up of 3.9 years, the primary endpoint EFS was not significantly different between the ZOL and ctrl group in the adaptive design (HR 0.74, 95% CI 0.43-1.28, intention to treat). 3-year (3y) EFS rates were 84.0% (95% CI 77.7-90.8%) for ZOL vs 81.7% (95% CI 75.2-88.8%) for ctrl. Results were similar in the per protocol collective. Cause-specific HR for local recurrence in ZOL was csHR 0.30 (95% CI 0.08 -1.09; p = 0.07), for metastatic progress/ new metastases csHR 1.0 (CI 0.5-2.2), for combined relapse/progress csHR 0.3 (95% CI 0.1-1.7), for second malignancies csHR 4.0 (95% CI 0.45-36.1) compared to ctrl. The 3y OS was 92.8% (95% CI 88.4-97.5%) for ZOL and 94.6% (95% CI 90.9-98.6%) for ctrl. For ZOL the 5y OS was 87.3% (95% CI 80.7-94.5%) and 89% (95% CI 83.7-95.9%) for ctrl. Noticeable more renal, neurological and gut toxicities were observed for ZOL ($p < 0.05$), with severe renal toxicities occurring more often in the ZOL arm (p = 0.003). **Conclusions:** In patients with standard risk localized Ewing Sarcoma there is no benefit from maintenance treatment with zoledronic acid, but significant side effects were observed. Clinical trial information: NCT00987636. Research Sponsor: German Cancer Aid.

11524 Poster Session (Board #412), Fri, 8:00 AM-11:00 AM

Correlation of response with progression-free (PFS) and overall (OS) survival in relapsed/refractory Ewing sarcoma (RR-ES): Results from the rEECur trial. *First Author: Keith Wheatley, University of Birmingham, Birmingham, United Kingdom*

Background: Survival for RR-ES at 5 years remains < 15%, so novel treatments are needed. Almost all Phase II trials for RR-ES use response as the primary outcome measure. It is unclear whether response is a valid surrogate for survival outcomes. **Methods:** Patients (pts) were eligible if they had RR-ES and were evaluable for imaging response (primary outcome) if they had measurable disease by RECIST 1.1. The randomization was initially between four chemotherapy regimens: topotecan-cyclophosphamide, irinotecan-temozolomide, gemcitabine-docetaxel (GD), high-dose ifosfamide. Response was assessed after 2, 4 (primary) and 6 cycles of therapy and was classified as complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD). PFS and OS were secondary outcomes. Survival from each assessment point by response status was analyzed, by Cox models, with hazard ratios (HR) given for PR v. SD and CR+PR v. SD. **Results:** From 2015-19, 241 pts with response data were entered. The relationship between response status and PFS and OS is shown in the table (HR < 1.0 indicates better outcome for PR or CR+PR than SD). Both PFS and OS were similar for pts with PR or CR+PR compared to those with SD. OS was inferior for patients with PD (all $p < 0.01$) (PFS is by definition zero for patients with PD at that timepoint). Small numbers mean CR results are not reliable. Results were consistent across all treatments and between refractory and relapsed disease. At the first interim assessment the GD arm was dropped, with risk ratios for response compared to the other three arms (blinded as still open) of 0.3, 0.5 and 0.5. If a new outcome – disease control (CR+PR+SD) – is defined, the risk ratios are 0.7, 0.8 and 0.7; i.e. still inferior for GD, but less so. **Conclusions:** Response does not correlate with survival outcomes in RR-ES, so considering PR, or even CR, a success and SD a failure when evaluating treatments may be misleading. We propose PFS as a better primary outcome for future trials and it will be introduced as such in the rEECur trial. Clinical trial information: ISRCTN36453794. Research Sponsor: European Union FP7 grant.

Survival (% at 1 year) by response status.

	Response category				HR (95% CI)	
Assessment after	**CR**	**PR**	**SD**	**PD**	**PR v. SD**	**CR+PR v. SD**
Cycle 2: N (%) pts	4 (2)	50 (21)	121 (50)	66 (27)		
PFS %	0	26	20	0	0.8 (0.6-1.2)	0.9 (0.6-1.3)
OS %	75	66	69	21	1.2 (0.7-1.8)	1.1 (0.7-1.8)
Cycle 4: N (%) pts	8 (5)	49 (30)	71 (44)	33 (21)		
PFS %	13	32	22	0	0.9 (0.6-1.4)	0.9 (0.6-1.4)
OS %	63	69	81	22	1.6 (0.9-2.7)	1.5 (0.9-2.5)
Cycle 6: N (%) pts	13 (14)	39 (41)	32 (34)	10 (11)		
PFS %	37	26	14	0	0.8 (0.5-1.4)	0.7 (0.4-1.2)
OS %	70	77	74	50	1.0 (0.5-2.1)	0.7 (0.4-1.4)

11525 Poster Session (Board #413), Fri, 8:00 AM-11:00 AM

A phase II study of anlotinib in treating patients with relapsed or metastatic primary malignant bone tumor. *First Author: Lina Tang, Affiliated Sixth People's Hospital, Shanghai Jiaotong University, Shanghai, China*

Background: Primary malignant bone tumors are rare forms of cancer and include mainly bone sarcomas, which are categorized into 3 common types based on tissue origin: osteosarcoma, chondrosarcoma and Ewing sarcoma. A phase II trial was designed to explore the anlotinib activity in patients with relapsed or metastatic primary malignant bone tumor. **Methods:** Eligible pts were received 12mg of anlotinib once daily, 2 weeks on and 1 week off until progression or unacceptable toxicity. Key-eligibility criteria were aged 14-70 years, histologically confirmed diagnosis of osteosarcoma, chondrosarcoma, bone derived malignant fibrous histiocytoma, giant cell tumor, Ewing sarcoma and PNET, confirmed previous chemotherapy failure, ECOG 0-1(0-2 for amputation pts), required at least one measurable lesion. We observed PFS, OS, ORR, DCR and AE in this study. **Results:** From August 2018 to April 2019, 42 pts were included. Of 42 efficacy-evaluable pts, 25 were man, median age was 28 (14-68) years. There were 29 pts of osteosarcoma, 9 pts of chondrosarcoma, 3pts of Ewing sarcoma and 1 pt of bone derived malignant fibrous histiocytoma. The progression-free rate at 12 weeks ($PFR_{12weeks}$), ORR and DCR were 71.3%, 9.52% and 78.57%. Median PFS was 5.26 months (95%CI = 3.48-8.44) . Median OS was 11.40 months (95%CI = 10.09, [ ). Median PFS of osteosarcoma and chondrosarcoma was 4.83 months (95%CI = 3.48, 7.13) and 2.76 months (95%CI = 1.31, [ ) respectively. The most common Gr 3-5 anlotinib-related AEs were hypertension (19.05%), hypertriglyceridemia (9.52%), hand-foot syndrome (7.14%), and proteinuria (4.76%). **Conclusions:** The phase II study shows a promising activity of anlotinib in patients with relapsed or metastatic primary malignant bone tumor and an acceptable toxicity. Clinical trial information: NCT03527888. Research Sponsor: None.

11526 Poster Session (Board #414), Fri, 8:00 AM-11:00 AM

Preliminary evaluate the safety and efficacy of anlotinib in advanced sarcoma patients in multi-line therapy. *First Author: Yao Weitao, Hen Nan Cancer Hospital, The Affiliated Cancer Hospital of Zheng Zhou University, Zhengzhou City, China*

Background: Patients with advanced bone and soft tissue sarcoma are mostly treated with chemotherapy, but the effect is poor. Anlotinib hydrochloride is a multi-targeted receptor of tyrosine kinase inhibitors (TKI), which has demonstrated therapeutic effects on a variety of sarcoma subtypes, and is approved for the treatment of advanced soft tissue sarcomas in China. **Methods:** This is a single-arm, prospective, single-center clinical study. The included criteria were patients with pathological diagnose of bone and soft tissue sarcoma, at least one measurable lesion (according to RECIST 1.1), failed of more than first-line therapy (except for alveolar soft tissue sarcoma) in the last 6 months, with the normal function of main organs. All patients received anlotinib for more than 1 month. The primary study endpoint was objective response rate (ORR). Disease control rate (DCR) and side effects was also calculated. **Results:** At the latest follow up in Jan. 20th, 2020, a total of 31 patients were enrolled. The median age of the patients was 38 (8-79) years. The main subtypes included osteosarcoma (25.8%), undifferentiated pleomorphic sarcoma (19.4%), synovial sarcoma (16.1%), fibrosarcoma (12.9%). 83.9% of patients received for at least third-line therapy of anlotinib. The oral administration time was 1.5-15 months, with the average of 4.34 months. The ORR was 29%. The DCR was 77.4%. Patients who had received other TKI drugs had an ORR of 20% and a DCR of 70% in 10 cases (32.2%) in this group. mPFS and mOS have not been reached. Adverse events were mainly in grades I and II, including 6 (19.4%) of anorexia or diarrhea, 5 (16.1%) of pain, 4 (12.9%) of hand-foot syndrome, 3 (9.7%)of hypertension, fatigue and mucosa ulcer each. One case had hypertension in grades III. **Conclusions:** Anlotinib has shown a definite effect in the treatment of advanced sarcomas. Effectiveness can also be observed in patients who have failed in other targeted therapy. The adverse events are minor and can be tolerated. Clinical trial information: NCT04223583. Research Sponsor: None.

11527 Poster Session (Board #415), Fri, 8:00 AM-11:00 AM

A randomized, double-blind, phase II clinical trial of GI-6301 (yeast-brachyury vaccine) versus placebo in combination with standard of care definitive radiotherapy in locally advanced, unresectable, chordoma. *First Author: Peter Joseph DeMaria, National Cancer Institute at the National Institutes of Health, Bethesda, MD*

Background: Chordoma is a rare neoplasm of the notochord that overexpresses brachyury, a transcription factor associated with epithelial-to-mesenchymal transition, metastasis, poor prognosis, and chemotherapy resistance. GI-6301 is a recombinant yeast-brachyury vaccine shown to demonstrate brachyury-specific immunogenicity, excellent safety profile, and some evidence of clinical activity in patients with chordoma in a previous phase I trial. Radiation therapy (RT) can modulate the tumor to become an immunostimulatory milieu. Preclinical studies have shown a synergistic effect combining RT with vaccine, thus prompting this clinical trial evaluating the combination of GI-6301 with RT in chordoma (NCT02383498). **Methods:** Adults with locally advanced, unresectable chordoma were treated on a randomized, double-blind, placebo controlled, phase 2 clinical trial. Patients received 3 doses of GI-6301 (80 x 107 yeast cells) vs placebo followed by photon or proton RT, followed by GI-6301 vs placebo until disease progression. Primary outcome was overall response rate (ORR) defined as a complete response or partial response in the irradiated tumor site at 24 months. Immune assays were conducted to evaluate immunogenicity. Due to slow accrual, an unplanned interim analysis was undertaken. **Results:** 24 pts were randomized and treated between May 2015 and September 2019. Vaccine was well tolerated with no dose reductions or treatment discontinuation. Treatment-related serious adverse events included: nausea/emesis (2); fatigue (2); dehydration (2); diarrhea (1); radiation necrosis (1); stroke (1); sepsis (1). There was no difference in ORR between the two arms. Pre-existing brachyury-specific T-cells were detected in the majority of patients but did not correlate with response to therapy. Most patients developed T-cell responses during therapy, regardless of treatment arm. **Conclusions:** There was no difference in ORR between the two arms. GI-6301 was well tolerated with toxicities related to RT, not vaccine. The trial was stopped early due to low conditional power for finding a statistical difference at the planned end of accrual, based on findings to date. Future studies will define utility of vaccines targeting brachyury in chordoma. Clinical trial information: NCT02383498. Research Sponsor: U.S. National Institutes of Health.

		Vaccine	**Placebo**
Study	Randomized	11	13
Population	Evaluable	9	13
Tumor Location	Clival	4	6
	Other	5	7
Overall Response	PD	5	8
	SD	3	4
	PR	1	1
	CR	0	0
	ORR	1	1

11528 Poster Session (Board #416), Fri, 8:00 AM-11:00 AM

Increased pathological complete response rate with neoadjuvant denosumab in locally advanced giant cell tumor. *First Author: Gabriela Monte Tenorio Taveira, Hospital do Câncer de Pernambuco, Recife, Brazil*

Background: Giant cell bone tumor corresponds to 5% of bone tumors, has an osteolytic pattern and mainly affects long bone epiphyses in young adults. Despite being considered benign, it can metastasize and is treated as a locally destructive tumor, since it causes pain, limited joint movement and impaired function, with a risk of pathological fractures. The use of denosumab for surgical downstaging and reduction of recurrence is being studied, but the standard of treatment is still surgical. **Methods:** 15-year experience in monitoring 40 patients at the Cancer Hospital of Pernambuco-BR, who used neoadjuvant denosumab. They received Denosumab 120mg on D1, D8 and D15 as attack phase and subsequent maintenance with 120mg monthly. **Results:** The 40 patients made an average of 10 doses of neoadjuvant denosumab. Mostly located in the femur (41%) and tibia (23%), but with rare disorders in talus or orbit. Metastasis occurred in 6%, with site in lung and bones. Most were women (62%) around 21-40 years old, with Capanacci III classification at 72%. In this group, 28 had locally advanced disease and 12 had unresectable or metastatic disease. After using neoadjuvant denosumab, 75% have already had a biopsy, of which 63% (19/30) had a complete pathological response in biopsy. Of the patients with no post-denosumab neoplasia, 26% (5/19) had recurrence after medication and surgical procedure. Neoadjuvant treatment with denosumab, a monoclonal antibody that binds to RANKL, has been shown to benefit from histological response and surgical downstaging. We found 63% of complete pathological response in the 30 patients who underwent biopsy after medication, with bone sclerosis and hypocellular fibrous tissue as the main finding. Of these, 26% had disease recurrence after surgery. These data follow the international standard of disease recurrence rate, which is around 30%. **Conclusions:** We hope that the use of neoadjuvant desonumab will be more widespread and that it will be able to perform surgical downstaging, allowing less invasive and morbid procedures. Thus achieving greater joint preservation at the expense of a disease recurrence rate similar or less than standard surgical treatment. Research Sponsor: None.

11529 Poster Session (Board #417), Fri, 8:00 AM-11:00 AM

Maximum tumor dimension and tumor volume as prognostic factors in patients with newly diagnosed localized Ewing sarcoma (ES)- a report from the Children's Oncology Group (COG). *First Author: Leo Mascarenhas, Children's Hospital Los Angeles, University of Southern California, Keck School of Medicine, Los Angeles, CA*

Background: Maximum tumor dimension > 8 cm. and large tumor volume have been reported to be adverse prognostic factors in patients with ES but have not been prospectively evaluated in the context of a phase 3 clinical trial with interval compressed chemotherapy. **Methods:** COG AEWS1031 (NCT01231906) was a randomized phase 3 clinical trial comparing interval compressed chemotherapy regimens in patients with newly diagnosed localized ES of bone and soft tissue. A correlative objective of AEWS1031 was to evaluate tumor size and volume as prognostic factors. Institution-reported dimensions of the primary tumor from baseline imaging were prospectively collected. For inclusion in this analysis, patients had to have at least 1 tumor dimension reported for tumor size analyses and dimensions in 3 axes for tumor volume analyses. Maximum dimension was dichotomized as less than vs. > / = 8cm. Tumor volume was dichotomized as less than vs. > / = 200 mL. Event-free (EFS) and overall survival (OS) from enrollment were calculated using Kaplan-Meier methods and compared between groups using a two-sided log-rank test. Hazard ratios (HR) and confidence intervals (CI) were calculated using the Cox model. **Results:** The 5-year EFS and OS of the 629 eligible patients was 78% (95% CI: 75-81%) and 87% (95% CI: 84-90%) respectively and there was no significant difference in both EFS and OS between the randomized interval compressed chemotherapy arms of AEWS1031. 590 of 629 (94%) patients were evaluable for maximum tumor dimension and 307 (52%) had tumors > / = 8 cm. Patients with tumors > / = 8 cm were at significantly increased risk for EFS events (p = 0.016) with estimated 5-year EFS of 73.7% (95% CI: 68.1 vs.78.4%) vs. 82.9% (95% CI 77.7-87.1%) for patients with tumors < 8 cm [HR: 1.53 (1.08-2.17)]. For tumor volume, 586 of 629 patients (93%) were evaluable and 180 (31%) had tumors > / = 200 mL. Patients with tumor volume > / = 200 mL were at significantly increased risk for EFS events (p = 0.003) with estimated 5-year EFS of 70% (95% CI: 62.3-76.4%) vs. 81.6% (95% CI: 77.2-85.2%) for patients with tumors < 200 mL [HR: 1.69 (1.2-2.39)]. **Conclusions:** Maximum tumor dimension and tumor volume as defined are both prognostic in patients with newly diagnosed localized ES treated with interval compressed chemotherapy. Clinical trial information: NCT01231906. Research Sponsor: U.S. National Institutes of Health.

11530 Poster Session (Board #418), Fri, 8:00 AM-11:00 AM

Characterizing the landscape of genomic variants in high-risk pediatric osteosarcoma. *First Author: Amanda Marinoff, Dana–Farber Cancer Institute, Boston, MA*

Background: Survival rates for patients with metastatic and/or recurrent osteosarcoma are poor, and treatment strategies have remained unchanged for more than three decades. Genomic characterization can identify new treatment strategies and improve risk stratification. To date, sequencing studies of osteosarcoma have focused on newly diagnosed patients. We present one of the first reports of osteosarcoma genomics in a high-risk cohort. **Methods:** 92 samples from 92 patients were sequenced in a CLIA/CAP laboratory with a targeted NGS panel test. Patients were enrolled in one of two studies. The PROFILE study enrolls all patients seen at Dana-Farber Cancer Institute, and the GAIN study enrolls patients with metastatic and/or recurrent cancer at 11 institutions. Sequencing was performed using primary tumor samples at biopsy and/or from sites of metastasis when available. **Results:** 33 patients were enrolled on the PROFILE study, and 59 were enrolled on GAIN. Diagnostic stage was available for 65 (67%) of patients. 37% had metastatic disease at diagnosis. The 3-year overall survival (OS) was 71% for the entire study population, 56% for patients with metastatic disease at diagnosis, and 81% for patients with initially localized disease. The presence of metastases at diagnosis was significantly associated with poor outcome ($p < 0.0087$) and was the only independent clinical prognostic factor identified. Genomic analysis revealed frequent alterations in TP53 (37%), RB1 (15%), CDKN2A (13%), MYC (12%), CDKN1A (12%), ATRX (10%), and CCND3 (8%). Patients whose tumors had MYC amplification (defined as ≥ 6 copies) had a 3-year OS of 39% compared with a 3-year OS of 76% in the absence of MYC amplification, a difference with borderline statistical significance ($p = 0.051$). **Conclusions:** In the first study to examine genomic alterations detected by targeted gene panel sequencing in a CAP-certified laboratory in a large population of pediatric patients with higher risk osteosarcoma, the most frequently occurring events were similar to those found in prior reports. MYC amplification, reported as a possible poor prognostic factor in other studies, was present in 12% of patients and was associated with a worse OS, though this finding did not reach statistical significance. Research Sponsor: Institutional/ Philanthropic.

11531 Poster Session (Board #419), Fri, 8:00 AM-11:00 AM

Genomic analysis of advanced malignant soft tissue tumors to suggest effect of genome-wide loss-of-heterozygosity of germline mutations/variants on anti-PD-1 immunotherapy response and survival of the patients. *First Author: Katsuhito Takahashi, Kameda Medical Center, Center for Multidisciplinary Treatment of Sarcoma, Department of Sarcoma Medicine, Kamogawa, Japan*

Background: Malignant soft tissue tumor is a rare cancer with few therapeutic options. Although recent genomic characterization of soft tissue sarcoma revealed massive CNA and an excess of polygenic burden of pathological germline variants, their clinical and therapeutic significance remains to be understood. **Methods:** We recruited 155 patients with malignant soft tissue tumors (135 female and 20 male, mean age 51, 100 LMS, 19 LPS, 4 ESS, 3 UPS, 3 AS, 3 MPT, 3 GIST and others) of confirmed metastasis/recurrence. Whole exome sequencing was performed as reported in 2018ASCO. The MSI status was analyzed by PCR. Tumor immune microenvironment was assessed by immunohistochemistry. **Results:** Of the 595 COSMIC genes, heterozygous germline mutations/variants of the genome-wide 0-44 genes (av. 9.7/tumor) showed somatic loss-of-heterozygosity (LOH) with allele frequency of more than 70%. Patients with less than 33% LOH (n=53) in the total of somatic and LOH mutations showed improved 5-year survival rate compared with those (n=102) with more LOH (71% vs 52%, p=0.037). LMS (n=100) had higher value of LOH mutations than other tumors (n=55)(av. 55.5 vs 31.2%, $p<0.001$). Two patients with bone metastasis, one from liver undifferentiated sarcoma (case 1) and the other from uterine LMS (case 2) were identified as MSI-High and resultant higher TMB of 6.48 and 6.60/Mb, respectively than 1.47/Mb in av. Tumors from both cases had de novo mutations of MMR deficiency as EXO I (A153V) and WRN (S1120F) in case 1 and MSH2 (G674D) in case 2. Case 1 with pleural dissemination was treated with 5 cycles of Pembrolizumab (200mg/body, d1 q3weeks) but was progressive disease, while case 2 had no evaluable lesion after surgical removal of bone metastasis. Number of CD8+ T-cell infiltration (TIL), one of the best parameter with response to PD-1 blockade, was much higher in case 2 than in case 1 (av. 907 vs 290/mm^2). Case 2 had no LOH mutations while case 1 had 37% LOH with more total mutations in tumor (16.1 vs 85.9/Mb). Higher values of LOH (av. 67 vs 19%) were clearly correlated with decreased density of CD8+TIL in tumor tissues (av. 9.6 vs 429/mm^2, n=5, p=0.018). **Conclusions:** Our results, for the first time, suggest that in malignant soft tissue tumors, accumulation of genome-wide LOH of germline mutations/variants, from which self-antigens could be generated, may influence tumor immune microenvironment, and thus influence immunotherapy response and survival of the patients. Research Sponsor: Japan Sarcoma Association Fund for Promotion of Genomic Medicine of Rare Cancers, The Osaka Foundation for The Prevention of Cancer and Lifestyle -related Diseases Research Grant.

11532 Poster Session (Board #420), Fri, 8:00 AM-11:00 AM

Outcomes of patients (pts) with advanced gastro-intestinal stromal tumors (GIST) treated with multi-kinase inhibitors other than imatinib (IM) as first-line treatment. *First Author: Alice Boileve, Institut Gustave Roussy, Villejuif, France*

Background: IM is the standard first-line therapy in advanced GIST, with a median progression-free survival (PFS) of 30 months. Recent multi-kinase inhibitors (MKIs) such as nilotinib, dasatinib or masitinib have been tested as first-line therapies in phase II/III studies. This might theoretically result in increased PFS (by the addition of a new line of treatment), or in early emergence of resistance to approved MKIs. **Methods:** A retrospective chart review was performed in GIST pts who received investigational MKIs (in phase II/III trials) as first-line treatment, followed by IM as second line. Data on demographics, molecular profile, PFS, and overall survival (OS) were collected in two French referral centers. **Results:** Of 47 pts, (57% females), 22 (47%) had a *KIT* exon 11 mutation, one a *KIT* exon 9 mutation (2%), one a *PDGFR* D842V mutation (2%). Five patients were wild-type for *KIT* and *PDGFR*. The mutational status was unknown in 18 pts (38 %). From 2005 to 2011, 21 pts (45%) received masitinib, 18 (38%) received dasatinib and 8 pts (17%) received nilotinib. Median PFS on first-line treatment was 18.9 months [95%IC: 9.0-26.0]. Median time-to-failure (TTF) with IM was 19.7 months [95%IC: 14.8-53.4]. Median time to second relapse was 50.2 months [95%IC: 31.2-92.2]. Thirty-five patients (74.5%) were dead at the end of follow-up. The median OS from time of initial diagnosis was 5.9 years [95%IC: 4.5-8.2]. **Conclusions:** GIST pts who received MKIs other than IM as first-line treatment and IM as second-line had a time to second relapse longer than that observed historically with IM in first line. This suggests that using MKIs other than IM in first line does not decrease IM efficacy in second line. Further comparative studies are needed to confirm these findings, but this is encouraging to further develop studies with other MKIs in the first line setting. Research Sponsor: None.

11533 Poster Session (Board #421), Fri, 8:00 AM-11:00 AM

Role of adjuvant imatinib dose in radically resected GIST harboring KIT exon 9 mutations. *First Author: Bruno Vincenzi, Policlinico Universitario Campus, Bio-Medico, Rome, Italy*

Background: Gastrointestinal stromal tumors (GIST) with a driver mutation in *KIT* exon 9 (Ex9) represent about 10% of all newly diagnosed cases. In the metastatic setting, Ex9-mutated GIST patients benefit from higher doses of imatinib (800 mg/day vs standard 400 mg/day). The additional therapeutic benefit from a higher dose of imatinib in the adjuvant setting in this molecular subgroup has not been confirmed. **Methods:** We retrospectively identified 105 patients (pts) with resected Ex9-mutated GIST treated with adjuvant imatinib (800 mg/day or 400 mg/day) in 15 different European centers. Disease-Free Survival (DFS) and Imatinib Failure-Free Survival (IFFS) were calculated and analyzed according to the daily dose of imatinib and relevant clinical and pathological variables. Kaplan–Meier curves were used to estimate survival in univariate analyses, and the log-rank test was used to compare the groups. Hazard Ratios (HR) with 95% confidence intervals (CI) were calculated using a univariable Cox model. A multivariate Cox regression model was also performed. **Results:** Of the 105 pts who met the inclusion criteria, 69 (65.7%) were treated with 400 mg/day and 36 (34.3%) with 800 mg/day. The risk score (AFIP-Miettinen criteria) between the two dose groups was not statistically different (P = 0.29). Median DFS was 73.0 months (mo) in the 400 mg/day group and 61.9 mo in the 800 mg/day group (HR = 0.82, 95% CI: 0.47-1.47; *P* = 0.50). Median IFFS was 156.8 mo in the 400/day mg group and 117.4 mo in the 800 mg/day group (HR = 0.66, 95% CI: 0.34-1.29; *P* = 0.19). In a multivariable analysis, the variables statistically associated with DFS were mitotic count, the longest tumor diameter and the duration of adjuvant therapy. Mitotic count and the duration of adjuvant therapy were also associated with IFFS. Importantly, the daily imatinib dose was not associated with survival in either analysis (Table). **Conclusions:** This is the largest reported cohort of pts with Ex9-mutated GIST treated with either the 400 mg/day or the 800 mg/day dose of adjuvant imatinib. Although retrospective in nature, the data confirm the prognostic value of mitotic count and suggest that patients with Ex9-mutated GIST derive no additional survival benefit from the 800 mg/day dose. Research Sponsor: None.

Multivariable Cox regression.

	DFS		IFFS	
	HR	***P* value**	**HR**	***P* value**
Number of mitoses	**5.03**	**< 0.001**	**7.89**	**0.001**
Duration of adjuvant treatment	**0.96**	**0.01**	**0.95**	**0.01**
Max. tumor diameter	**1.10**	**0.04**	1.00	0.85
Tumor rupture	1.73	0.18	2.20	0.11
Site of GIST	1.20	0.34	1.42	0.17
Sex	1.23	0.50	1.36	0.42
Age at diagnosis	1.02	0.17	1.00	0.79
Adjuvant imatinib dose	*0.75*	*0.41*	*1.20*	*0.67*

11534 Poster Session (Board #422), Fri, 8:00 AM-11:00 AM

Laparoscopic versus open surgery for gastrointestinal stromal tumor in esophagogastric junction: A multi-center, retrospective cohort analysis with propensity score matching. *First Author: Wenjun Xiong, Guangdong Provincial Hospital of Chinese Medicine, the Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China*

Background: Laparoscopic resection is increasingly performed for Gastrointestinal stromal tumor (GIST). Nevertheless, laparoscopic approach for the GIST located in the esophagogastric junction (EGJ-GIST) represent a surgical challenge. This study aims to investigate the efficacy of laparoscopic surgery and open procedure for EGJ-GIST through the propensity score matching (PSM) method. **Methods:** Between April 2006 and April 2018, 1824 patients underwent surgery were finally diagnosed with primary gastric GIST at four medical centers in South China. EGJ-GIST was defined as a GIST with an upper border of less than 5 cm from the EG line. Among them, 228 patients were identified and retrospectively reviewed with regard to clinicopathological characteristics, operative information and long-term outcomes. The PSM methods was used to eliminate the selection bias. **Results:** After PSM, 102 cases, consisted of 51 laparoscopic (LA) and 51 open surgery (OP), were enrolled. The match factors contained year of surgery, gender, age, BMI, tumor size, mitotic rate, recurrence risk and adjuvant tyrosine kinase inhibitors treatment. The LA group was superior to the OP group in operative time (108.5±56.5 vs. 169.3±79.0 min, $P < 0.001$), blood loss (54.6±81.9 vs. 104.9±156.4 ml, $P = 0.042$), time to liquid intake (3.1±1.8 vs. 4.3±2.2 d, $P = 0.003$), hospital stay (6.0±2.3 vs. 9.9±8.1, $P = 0.001$), and postoperative complication (5.9% vs. 25.5%, $P = 0.006$). The median follow-up was 55 (range, 2-153) months in the entire cohort. No significant differences were detected in either the relapse-free survival (RFS, $P = 0.109$) or overall survival (OS, $P = 0.113$) between two groups. The 1-, 3-, and 5-year RFS in the LA and OP groups were 100.0%, 95.5%, 91.0% and 100.0%, 90.8%, 85.7%, respectively. The 1-, 3-, and 5-year OS in the LA and OP group were 100%, 95.6%, 91.3% and 100.0%, 91.1%, 85.4%, respectively. **Conclusions:** Laparoscopic surgery for EGJ-GIST is associated with the advantages of shorter operative time, reduced blood loss, shorter time to liquid intake and shorter length of stay, all without compromising post-operative outcomes and long-term survival. Research Sponsor: None.

11535 Poster Session (Board #423), Fri, 8:00 AM-11:00 AM

Quality of life (QoL) and self-reported function with ripretinib in ≥4th-line therapy for patients with gastrointestinal stromal tumors (GIST): Analyses from INVICTUS. *First Author: Michael C. Heinrich, Portland VA Health Care System and OHSU Knight Cancer Institute, Oregon Health & Science University, Portland, OR*

Background: Ripretinib is a novel switch-control tyrosine kinase inhibitor (TKI) that broadly inhibits KIT and PDGFRA kinase signaling through a dual mechanism of action. In INVICTUS (NCT03353753), a randomized, double-blind, placebo-controlled trial of ripretinib in ≥4th-line advanced GIST, ripretinib reduced the risk of disease progression or death by 85% vs placebo and had a favorable overall safety profile in patients previously treated with ≥3 prior TKIs. **Methods:** As part of the INVICTUS trial, patient reported outcome (PRO) measures were collected using EQ-5D-5L (EQ5D) and EORTC QLQ-C30 (C30). In prespecified and additional analyses, ANCOVA models were built to compare changes from baseline to cycle 2 day 1 (C2D1) for PRO measures within the ripretinib and placebo arms and determine the difference between treatment arms. PRO measures included the EQ5D visual analogue scale (VAS) and the C30 physical functioning (PF) and role functioning (RF) scales (all scores range from 0–100; higher scores are better). The C30 overall health and overall QoL questions were also assessed (scores range from 1–7; higher scores are better). Fixed effects included treatment arm, number of previous anticancer treatments (3 vs ≥4), and ECOG score at baseline (0 vs 1/2). **Results:** Overall, 129 patients were randomized and 128 received treatment (85 to ripretinib 150 mg QD; 43 to placebo). All PRO p-values are nominal, and no statistical significance is being claimed. VAS scores improved an average 3.7 points from baseline to C2D1 with ripretinib vs an average decline of 8.9 with placebo (P = 0.004; improvement or no change, 67% vs 41% of patients, respectively). Similarly, the average PF score improved 1.6 points with ripretinib and decreased 8.9 with placebo (P = 0.004; improvement or no change, 68% vs 44%). RF scores also improved an average of 3.5 points with ripretinib vs a decrease of 17.1 with placebo (P = 0.001; improvement or no change, 77% vs 50%). For the overall health and overall QoL questions, scores increased with ripretinib an average of 0.20 and 0.28, respectively, and decreased 0.78 and 0.76 with placebo (both P = 0.001; improvement or no change, 74% vs 47% and 79% vs 59%, respectively). **Conclusions:** Based on the 5 PRO measures assessed, when compared with placebo and best supportive care, ripretinib provided patient-benefit in advanced GIST with PRO measures of role and physical function, VAS, overall health, and overall QoL remaining stable. Clinical trial information: NCT03353753. Research Sponsor: Deciphera, LLC.

11536 Poster Session (Board #424), Fri, 8:00 AM-11:00 AM

Lower-dosing ponatinib in pre-treated GIST: Results of the POETIG phase II trial. *First Author: Johanna Falkenhorst, Department of Medical Oncology, University Hospital Essen, West German Cancer Center, University Duisburg-Essen, Essen, Germany*

Background: Despite long-lasting responses to imatinib most metastatic gastrointestinal stromal tumors (GIST) eventually progress and subsequent treatments are associated with limited duration of disease control. Ponatinib is a potent KIT inhibitor with a strong activity against secondary mutations in exon 17, including the highly resistant D816 mutations of KIT. Based on the dose-depending toxicity profile we sought to evaluate the safety and activity of lower dosing (30mg) ponatinib in pretreated patients with KIT-mutant GIST. We here report safety data for the whole cohort and first efficacy data for the last line cohort within a planned interim analysis. **Methods:** This multicenter phase 2 trial (NCT03171389) recruited patients with advanced, unresectable GIST progressing after imatinib (Cohort A/B: absence/presence of KIT Exon 13/14 mutations by plasma sequencing) or imatinib, sunitinib and regorafenib (Cohort C). Patients were treated with 30mg oral ponatinib daily in 4-week-cycles. The primary endpoint was the clinical benefit rate at 16 weeks as measured by mRECIST1.1 criteria. **Results:** At the cutoff date of 31st Jan 2020, 39 patients were evaluable for safety analysis (25 male, 14 female, median age 60 (38-86) years). Median duration of treatment was 65 (14-699) days. 66.7% of all patients observed Grade 3/4 adverse events (AEs), most common were pain (10/39), hypertension (6/39), GGT or lipase increase (both 5/39), and fever (3/39). One AE of special interest was observed (myocardial infarction, rated not related to study drug) and 20/39 patients experienced at least 1 severe AE (6/39 possibly related to ponatinib). Within the last line cohort, 20 patients were evaluable for efficacy. Clinical benefit rate was 35% (CI 15.4-59.2%). Median progression-free survival was 86 days with single patients yielding long-lasting responses (75% quartile 210 days, maximum: 420 days). **Conclusions:** Treatment with ponatinib was tolerable at a dose of 30mg qd with a toxicity profile comparable to other TKIs used in GIST. The majority of grade 3/4 AEs were hypertension or asymptomatic increases of laboratory values and thromboembolic events were rare. In a heavily pretreated patient population that lacks alternative treatment options the clinical activity was notable. An updated analysis including predictive biomarkers will be presented. Clinical trial information: NCT03171389. Research Sponsor: Arbeitsgemeinschaft Internistische Onkologie, Germany, Pharmaceutical/ Biotech Company.

11537 Poster Session (Board #425), Fri, 8:00 AM-11:00 AM

Identification of SDHA germline mutations in sporadic SDHA mutant gastrointestinal stromal tumors (GIST): The need of a genetic counselling. *First Author: Margherita Nannini, Medical Oncology Unit, Sant'Orsola-Malpighi Hospital, Bologna, Italy*

Background: SDH-*deficient* GIST, as defined by the loss of expression of SDHB, account up to about 10% of all gastric GIST and generally affect younger population. Germline mutations in SDHB, SDHC, and SDHD occur in about 20–30% of SDH-*deficient*, that may be referred to a hereditary condition known as hereditary GIST-paraganglioma syndrome (Carney-Stratakis Syndrome), whereas germline SDHA mutations have been rarely described in apparently sporadic cases. Currently, even germline testing is recommended for SDH-*deficient* GIST, there are no clear guidelines for genetic counselling and follow-up of SDH*x* mutation carriers and relatives, especially for SDHA mutant GIST not yet linked to well-defined hereditary syndrome. The aim of this work was to study the SDHA gene in the normal DNA of patients with SDHA mutant GIST. **Methods:** Thirteen patients carrying SDHA-mutant GIST were studied (8F/5M). Median age of diagnosis was 45,9 years (range 25-74). All GIST were located in the stomach and 3 patients out 13 presented a metastatic disease. In all cases except one, the GIST was the only cancer presentation and no personal or familial history of cancer was revealed. All cases were negative for SDHB immunohistochemistry. Germline mutations were identified through Sanger sequencing of SDHA in the normal counterpart. **Results:** Germline mutations were identified in all patients for which normal counterpart was available: 4 cases harboured truncating mutations (S384X, R31X and W119X); 5 cases carried pathogenic missense mutations (G233V, R171H, R589Q, G257A and R600Q) and 2 cases had splice site alterations (c.457-3_457-1 delCAG and c.456+9 C > T). In 8 cases the tumor DNA showed the loss of the corresponding wild-type allele, while in the other 3 cases compound heterozygosity for an additional somatic mutation was detected (R589W, R451C,and R171C). In 2 patients, unfortunately, normal DNA was not available, however both tumours carried two mutational hits on SDHA (one with heterozygous G419R and E564K, and one with homozygous R585Q). Of note, 5 patients presented un-usaul SDHA related clinical characteristics as were not young adult (> 50 years-old) or no multifocal GIST. **Conclusions:** We demonstrated that germline SDHA mutations are highly frequent in SDHA-*deficient* GIST. Therefore, although a clear syndrome has not been defined, genetic counselling and follow-up of SDHA mutation carriers and relatives should be clarified. Research Sponsor: None.

11538 Poster Session (Board #426), Fri, 8:00 AM-11:00 AM

Long-term results of selective internal radioembolization (SIRT) to control progressive liver metastases of gastro-intestinal stromal tumors (GIST) beyond treatment with tyrosine kinase inhibitors (TKI). *First Author: Peter Hohenberger, Division of Surgical Oncology and Thoracic Surgery, Mannheim University Medical Centre, University of Heidelberg, Mannheim, Germany*

Background: Liver and peritoneum are the main area of metastatic spread in GIST. Liver resection does not play a role for hepatic metastases in comparison to f.e. colorectal cancer. If hepatic metastases are the only or major area of tumor progression and are resistant to available TKIs due to a missing mutation in *KIT/PDGFRA/SDH* ('wildtype') or after treatment with 1st/2nd/3rd/4th line therapy, interventional radioembolization with yttrium-90 (^{90}Y) microspheres are promising treatment options, as radiation doses as high as 200Gy can be applied locally. We analyzed the long-term results of SIRT with respect to hepatic-progression-free survival (HEP-PFS) in a consecutive cohort of patients.. **Methods:** From 1/2008 to 1/2018, 25 pts (12f, 13m) with biopsy proven liver metastases of GIST which were the only (n = 13) or the dominant site of progression (n = 12) were treated by SIRT. Median age at GIST diagnosis had been 51.8 yrs and when receiving SIRT was 57.6yrs (range, 18–75yrs). The mutational status was 'wildtype' (n = 7, 2 NF-1), exon 11 (n = 7), exon 11+2nd mutation (n = 6), exon 9 (n = 3), exon 9+2ndmut (n = 1), and, exon 13 (n = 1). All patients except of two had prior TKI therapy: 1 line n = 3, 2 lines n = 11, 3-4 lines n = 9. Follow-up after SIRT was done via dynamic MRI and contrast-enhanced (CE)-CT, the median follow-up is 30.6 mos (range, 12-100mos) and all patients were followed until death. **Results:** The median hepatic-progression free survival (HEP-PFS) after SIRT was 17 months (range, 5-53+, 95%CI 11.8-22.1 mos). Of the patients with concomitant extrahepatic disease, the extraHEP-PFS was median 10 months. Twelve patients received next-line TKI therapy for progressive extrahepatic disease, whereas six patients required this for progressive liver metastases. When comparing the results according to the mutational status, patients with a 'wildtype' tumor showed a better median HEP-PFS of 19 mos (range, 12-53+, 95%CI 16.7-21.2 mos.) in comparison to *KIT* exon 9/11/13 mutated patients with only 14 months (range, 4-34 mos., 95%CI 6.5-21.4 mos), $p < 0.11$ (Wilcoxon). **Conclusions:** 90Y radioembolization (SIRT) offers a safe and effective treatment for patients with liver metastases of GISTs being the dominant site of tumor progression and with no drug treatment options available. In patients known to have no mutation in *KIT/PDGFRA* (wt, also NF-1 associated) it looks whether the results might be even more promising and SIRT could be used in early treatment lines. Research Sponsor: None.

11539 Poster Session (Board #427), Fri, 8:00 AM-11:00 AM

Safety profile of ripretinib, including impact of alopecia, and Palmar-Plantar Erythrodysesthesia Syndrome (PPES) on patient-reported outcomes (PROs), in ≥ fourth-line advanced gastrointestinal stromal tumors (GIST): Analyses from INVICTUS. *First Author: Suzanne George, Dana-Farber Cancer Institute, Boston, MA*

Background: Ripretinib is a novel switch-control TKI that broadly inhibits KIT and PDGFRA kinase signaling. In INVICTUS (NCT03353753), a randomized, double-blind, placebo (PBO)-controlled trial of ripretinib in ≥4th-line advanced GIST, ripretinib reduced the risk of disease progression or death by 85% vs PBO with a favorable overall safety profile. Common (> 20%) adverse events (AEs) included, but were not limited to, alopecia and PPES. Exploratory analyses evaluated the impact of alopecia and PPES on quality of life (QoL). **Methods:** Patients (pts) with advanced GIST previously treated with at least imatinib, sunitinib, and regorafenib were randomized (2:1) to ripretinib 150 mg QD or PBO. AEs were graded using CTCAE v4 and PROs collected using EQ-5D-5L (EQ5D) and EORTC QLQ-C30 (C30). Repeated measures (RM) models assessed the impact of alopecia and PPES on 5 PROs (EQ5D visual analogue scale; and C30 physical functioning, role functioning, and the overall health and overall QoL questions) within the ripretinib arm. Fixed effects were sex, alopecia/PPES, and ECOG scores at baseline. **Results:** 128/129 randomized pts received treatment (85 ripretinib 150 mg QD; 43 PBO). Alopecia, regardless of causality, occurred in 44 (51.8%) on ripretinib (34 [40.0%] grade 1; 10 [11.8%] grade 2) and 2 (4.7%) on PBO (both grade 1). PPES occurred in 18 (21.2%) on ripretinib (11 [12.9%] grade 1; 7 [8.2%] grade 2); none on PBO. The median times in days to first occurrence and worst severity grade with ripretinib were 57.0 and 62.5 for alopecia; 56.5 and 57.0 for PPES. The RM models showed a slight trend towards improvement in PRO score over time for pts with alopecia; the only association reaching a P-value of < 0.05 was between alopecia and increased overall QoL. None of the associations between PPES and PRO scores reach $P < 0.05$. All PRO p-values are nominal, and no statistical significance is being claimed. **Conclusions:** Ripretinib had a favorable overall safety and tolerability profile. When stratified by alopecia and PPES, patient-reported assessments of function, overall health, and overall QoL were maintained over time. For both alopecia and PPES, onset and maximum severity occurred almost simultaneously, indicating that these events generally did not progressively worsen. These results suggest that alopecia and PPES are manageable and do not have a negative effect on function, overall health, and QoL. Clinical trial information: NCT03353753. Research Sponsor: Deciphera, LLC.

11540 Poster Session (Board #428), Fri, 8:00 AM-11:00 AM

A phase II trial of the DNA methyl transferase inhibitor, SGI-110 (Guadecitabine), in children and adults with SDH-deficient GIST, pheochromocytoma, and paraganglioma, and HLRCC-associated kidney cancer. *First Author: Mary Frances Wedekind, Pediatric Oncology Branch, NCI, NIH, Bethesda, MD*

Background: Loss of activity of the Krebs cycle component succinate dehydrogenase (SDH) complex is a mechanism of tumorigenesis in SDH-deficient cancers. Accumulation of the metabolite succinate inhibits α-ketoglutarate-dependent dioxygenases leading to DNA hypermethylation. Guadecitabine is a small molecule DNA methyltransferase inhibitor. We conducted a Phase II study to test the hypothesis that guadecitabine will impact tumor growth by reversing DNA hypermethylation in tumors with Krebs cycle abnormalities (NCT03165721). Study Objectives: Our primary objective was to assess the clinical activity of guadecitabine in patients with SDH-deficient GIST, PHEO/PGL, and HLRCC-associated renal cell carcinoma. Secondarily, we desired to evaluate the toxicities of patients on treatment with guadecitabine. **Methods:** We conducted a single site, open label, phase II study using a small optimal two-stage design to evaluate response in SDH-deficient GIST, PHEO/PGL, and HLRCC-associated renal cell carcinoma. Patients >12 years of age received guadecitabine subcutaneously at 45mg/m^2/day for 5 consecutive days on a 28-day cycle. Activity via imaging response was assessed utilizing RECISTv1.1. Toxicities were graded using version 4.0 of the NCI Common Toxicity Criteria. All patients were included in analysis. **Results:** We enrolled nine patients (6F:3M) with an age range of 18-57 years. Seven patients had SDH-deficient GIST (78%), one patient with paraganglioma (11%), and one with HLRCC-associated renal cell carcinoma (11%). No patients had a complete or partial response. Five patients came off study due to progression (56%) with one death due to disease progression in the patient with HLRCC-associated renal cell carcinoma (11%). Three patients (33%) withdrew due to lack of response with stable disease. One patient was withdrawn due to investigator's discretion (11%). Toxicities possibly, probably, or definitely related to drug included grade 3 leukopenia (11%) febrile neutropenia (11%), grade 3-4 neutropenia (22%) requiring dose reductions, grade 3 hypertension (11%), grade 2 lung infection requiring hospitalization (11%). **Conclusions:** In this single site, open label, phase II study in patients with SDH-deficient GIST, PHEO/PGL, and HLRCC-associated renal cell cancer guadecitabine was tolerated by the majority of patients. No complete or partial responses were observed. Clinical trial information: NCT03165721. Research Sponsor: U.S. National Institutes of Health.

11541 Poster Session (Board #429), Fri, 8:00 AM-11:00 AM

Primary adult retroperitoneal sarcoma (RS): Comprehensive genomic profiling (CGP) study. *First Author: Andrea Necchi, Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: We performed CGP on 315 cases of RS to discover targetable genomic alterations (GA) and their potential impact on potential targeted and immunotherapy (IO) selection. **Methods:** FFPE tissues from 315 clinically advanced RS tissues underwent hybrid-capture based CGP (DNA and RNA). Tumor mutational burden (TMB) was determined on up to 1.2 Mbp of sequenced DNA, and tumor cell PD-L1 expression was determined by IHC (Dako 22C3) (low = 1-49%; High = >50% tumor cell staining). **Results:** 155 liposarcomas (LPS), 74 leiomyosarcomas (LMS), 46 pleomorphic sarcomas (PLS), 7 solitary fibrous tumors (SFT), 6 malignant peripheral nerve sheath tumors (MPNST), 5 synovial sarcomas (SS) and 5 dendritic follicular cell sarcomas (DFCS) were studied; 17 cases were excluded. Median age was 59. There were 5.1 GA/tumor, none were MSI-high, median TMB was low at 2.4; PD-L1 IHC staining was low-positive in 21% and high-positive in 5%. MPNST patients were younger (median 28 years vs. 59 years). LPS was more frequent in men and LMS in women. LPS had more GA/tumor than LMS, with DFCS having the highest and SS the lowest. *TP53* and *RB1* GA were the highest in LMS and *CDK4/6* and *MDM2* GA the highest in LPS. Molecular targets in mTOR pathway were most frequently altered. Targetable gene fusions in *ALK*, *ROS1* and *NTRK1-3* were rare. Non-targetable fusions in *HMGA2* (LPS and some PLS), *STAT6* (SFT) and *SS18* (SS) were also identified. **Conclusions:** RS in our cohort are predominantly composed of LPS, LMS and PLS and we identified a small proportion with "actionable" genomic targets on CGP, albeit in association with uncertain mTOR pathway inhibitor benefit and uncommon targetable kinase fusions. Our analysis suggests that a small subset of RS may respond to immunotherapy based on putative biomarker expression. Research Sponsor: Foundation Medicine Inc.

	LPS	LMS	PLS (NOS)	SFT	MPNST	SS	DFCS
N	155	74	44	7	6	5	5
Female gender	42%	78%	49%	57%	33%	60%	60%
Median age	60	60	57	52	28	39	56
GA/tumor	6	3.4	5.2	6	5.7	2.6	7.4
TP53	5%	66%	26%	29%	33%	0	0
RB1	1%	32%	9%	0	0	0	0
NF1/NF2	1%	1%	4%	0	83%	0	0
PIK3CA	2%	3%	0	0	17%	20%	0
ESR1	12%	0	0	14%	0	0	0
CDKN2A	< 1%	1%	15%	0	83%	0	0
CDKN2B	< 1%	1%	11%	0	83%	0	0
CDK4/6	89%	0	28%	14%	0	0	20%
PTEN	2%	12%	9%	0	0	0	20%
MDM2	91%	1%	30%	14%	17%	0	20%
ALK	1%	0	0	0	0	0	0
ROS1	1%	1%	0	0	0	0	0
NTRK1-3	1%	1%	2%	0	17%	0	0
Median TMB (mut/Mb)	1.6	3.2	2.4	0.8	4.8	0.8	0.8
PD-L1 IHC Low Positive	25%	10%	33%	0	0	0	0
PD-L1 IHC High Positive	3%	0%	16%	0%	0%	0%	20%

11542 Poster Session (Board #430), Fri, 8:00 AM-11:00 AM

Phase I study results of APG-115, a MDM2-p53 antagonist in Chinese patients with advanced liposarcoma and other solid tumors. *First Author: Xing Zhang, Melanoma and Sarcoma Medical Oncology Unit, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: APG-115 is a potent, small-molecule MDM2 inhibitor and immune modulator with promising antitumor activities in various tumors, especially those wild-type *TP53* with MDM2 amplification (*TP53*^{wt}+MDM2 amp). To better delineate safety, optimal dosage, and potential target population, we report updated results. **Methods:** Patients with advanced liposarcoma and other solid tumors received APG-115 (100-200 mg) orally every other day for 21 days of a 28-day cycle. The primary endpoints were safety and tolerability. Efficacy (assessed by RECIST v1.1), pharmacokinetics (PK) and pharmacodynamics (PD) have also been analyzed. **Results:** Enrollment of this Phase I study (CTR20170975) was completed. As of January 7, 2020, 21 patients (14 liposarcomas, 2 synovial sarcomas, 2 adenoid cystic carcinomas, 1 chondrosarcoma, 1 osteosarcoma, 1 rhabdomyosarcoma) were treated in 3 dose levels of APG-115: 100 mg (n = 11), 150 mg (n = 8) and 200 mg (n = 2). The median number of cycles of APG-115 was 2 (0; 6). Two DLTs were observed at 200 mg, thrombocytopenia and febrile neutropenia. The most common treatment-emergent adverse events (TEAEs) (≥20%) included leukopenia, thrombocytopenia, neutropenia, anemia, increased blood creatinine, hypercholesterolemia, hypertriglyceridemia, hypoalbuminemia, vomiting, and nausea. The incidence of TEAEs was much lower at 100 mg. Serious AEs occurred in 5 patients (23.8%) which were assessed as possibly drug related by investigators. In 20 efficacy-evaluable patients, there was 1 patient with a partial response, 12 patients with stable disease, and 7 patients with progressive disease, yielding a disease control rate (CR, PR, SD) of 61.9%. Among the 13 patients (9 liposarcomas) who benefited, 11 had *TP53*^{wt} and 7 had *TP53*^{wt}+MDM2 amp, including one liposarcoma patient (150 mg) who had a PR, she was kept-up over 10 months, even though the treatment was discontinued for over 5 months, indicating the host immune modulatory effects of APG-115. Another patient with liposarcoma (100 mg, *TP53*^{wt}+MDM2 amp) had 28.5% tumor shrinkage at cycle 4 and remained on treatment. PK results showed an approximately dose-proportional increase in exposure on Day 1. PK-PD analyses showed the serum macrophage inhibitory cytokine-1 (MIC-1) increased with increased APG-115 exposure. **Conclusions:** The phase I data have demonstrated that APG-115 monotherapy was well tolerated, with minimal toxicity at 100mg (RP2D), and conferred encouraging anti-tumor activities in patients with liposarcomas. Clinical trial information: CTR20170975. Research Sponsor: Ascentage Pharma (Suzhou) Co., Ltd. Suzhou, China.

11543 Poster Session (Board #431), Fri, 8:00 AM-11:00 AM

Prognostic role of MRP1 in localized high-risk soft tissue sarcoma (STS): Translational research associated to randomized phase III trial (ISG-STS 1001). *First Author: Javier Martin Broto, Virgen del Rocio University Hospital, Institute of Biomedicine Research (IBIS)/CSIC/Universidad de Sevilla, Seville, Spain*

Background: The ceiling-drug effect seen for most active drugs in STS could be related, partially, to multidrug resistance mechanisms (MDRM). We previously reported the independent prognostic role for RFS and OS of MRP1 in high-risk localized STS of limbs and trunk-wall treated with epirubicin and ifosfamide (Mol Cancer Ther.2014 13(1):249-59). A translational study was carried out within the randomized phase III trial of epirubicin plus ifosfamide vs histotype-tailored neoadjuvant chemotherapy (NCT01710176), to investigate MRP1 prognostic value using the trial population as validation set. **Methods:** Patients enrolled in the trial were invited to participate, through the informed consent, to this analysis. IHC used QCRL-1 (Santa Cruz biotechnology) MRP1 monoclonal antibody. TMAs were built on the highest-grade area of each tumor, being the procedure blinded for clinical data. MRP1 expression was grouped as low (≤ 25% positive cells) vs high (> 25% positive cells) expression. For data analysis, patients were grouped as A) epirubicin plus ifosfamide control arm and B) histotype-tailored experimental arm. Drugs used in group B were: gemcitabine-docetaxel (UPS), gemcitabine-DTIC (LMS), trabectedin (High-grade (HG) myxoid LPS), ifosfamide-etoposide (MPNST) and high-dose ifosfamide (SS). Prognostic value of MRP1's extension was analyzed using Cox's proportional hazard regression. A p-value < 0.05 was considered statistically significant. **Results:** 175 patients were analyzed (median age 49; males 61%) with median follow-up of 4.66 y. Group A (n = 88) included HG-myxoid LPS (27%), SS (25%), UPS (24%), LMS (12%) MPNST (10%) and others (2%); group B (n = 87) included UPS (38%), SS (24%), HG-myxoid LPS (20%), LMS (10%) and MPNST (8%). MRP1 high extension was distributed as follows: 48% (A) and 57% (B). High MRP-1 expression showed significantly worse prognosis for disease-free survival (DFS) (HR 2.71 (1.31-5.62) p = 0.007) and a trend towards worse OS (HR = 2.75 (0.97-7.81) p = 0.058) in group A. No correlation was seen between MRP-1 expression and DFS (p = 0.384) or OS (p = 0.665), in group B. **Conclusions:** MRP1 overexpression was related to significant worse prognosis in 2 prospective randomized series of high-risk, localized, STS treated with neoadjuvant epirubicin and ifosfamide. These agents are both substrate of MRP1; this could add rationale for a possible predictive role, as MDRM, for the two most active drugs in STS. A trial combining epirubicin, ifosfamide and MRP1 inhibitor is currently under design. Research Sponsor: European Union grant (Eurosarc FP7 278472).

11544 Poster Session (Board #432), Fri, 8:00 AM-11:00 AM

SAR-096: A phase II trial of ribociclib in combination with everolimus in advanced dedifferentiated liposarcoma (DDL), and leiomyosarcoma (LMS). *First Author: Sujana Movva, Fox Chase Cancer Center, Philadelphia, PA*

Background: Inhibition of CDK4 is being studied in a variety of sarcomas, especially dedifferentiated liposarcoma (DDL) where prolonged progression free survival has been noted. Exposure to CDK4 inhibitors in Rb+ leiomyosarcoma (LMS) cell lines leads to decreased cell proliferation, and increased senescence, and G0/G1-phase arrest. When combined, ribociclib a CDK4 inhibitor and everolimus, an mTOR inhibitor show synergistic growth inhibition in multiple tumor models. **Methods:** Patients (pts) were enrolled to one of two cohorts: DDL or Rb+ LMS. LMS pts were required to have 1 prior line of therapy; DDL pts required no prior therapy. There were no limits to prior therapies in either group. Progression on prior therapy and measurable disease by RECIST 1.1 was also required. Ribociclib was given at 300 mg daily for 21/28 days and everolimus was given continuously at 2.5 mg daily in 28 day cycles. The primary endpoint was progression free rate at 16 weeks. A Simon two-stage design was utilized and if at least 8 out of 24 pts were progression free at 16 weeks, the treatment was declared promising for the cohort. Here in we present data on the LMS cohort. **Results:** Twenty-four LMS pts, 83% (n = 20) female, 58% (n = 14) uterine primary were treated. Median prior lines of therapy was 3.5 (range 1-9). Of 22 pts with complete data, 6 (27.2%) met the primary endpoint of non-progression at 16 weeks. Median PFS was 19.6 weeks (range 2.8-84), with progression as best response occurring in 13 pts. There were no objective responses. Five pts who had progressive disease on multiple lines of therapy experienced prolonged progression free survival (23-84 weeks). Grade 3-4, toxicities included neutropenia (29%), thrombocytopenia (12.5%) and leucopenia (12.5%) being most common. Tissue samples pre and on therapy as well as blood were collected in 21 and 18 pts respectively to evaluate pharmacodynamic changes. **Conclusions:** Final data on the primary endpoint for the LMS cohort is pending; it is notable that several heavily pre-treated LMS pts experienced prolonged progression free survival for $>$ 9 months. Updated results and biology correlatives will be presented. Clinical trial information: NCT03114527. Research Sponsor: Novartis, U.S. National Institutes of Health.

11545 Poster Session (Board #433), Fri, 8:00 AM-11:00 AM

Genomic landscape of angiosarcoma: A targeted and immunotherapy biomarker analysis of 143 patients. *First Author: Andrea P. Espejo Freire, University of Miami-Sylvester Comprehensive Cancer Center, Jackson Memorial Hospital, Miami, FL*

Background: Targeted therapies for angiosarcoma (AS) patients have limited efficacy. Although significant responses to immunotherapy (IO-therapy) have been observed in cutaneous AS, its efficacy across all types of AS is not known. Herein, we describe genetic and molecular biomarkers of AS in order to propose potential therapeutic options. **Methods:** We retrospectively reviewed 143 AS tumors profiled by Next-Generation Sequencing (NGS) 592-gene panel (Caris Life Sciences,Irving, TX, USA). Whole transcriptome sequencing (WTS) was performed on 53 tumors. Mutations and copy number amplifications (CNAs) were analyzed and grouped by pathway. Biomarkers potentially associated with response to IO-therapy (TMB-High [$\geq$10/Mb], MSI-High, and PD-L1 [IHC $\geq$ 2+ and 5%]) were also analyzed. AS subtypes based on primary tumor site were compared. P-values were corrected using a Benjamini & Hochberg method. **Results:** Sample median age was 67 (range 22-89), 61% were female, and 29% were classified as metastatic/recurrent. The most commonly mutated genes were TP53 (29%), ARID1A (17%), POT1 (16%), and ATRX (13%); MYC CNA was found in 23% of cases. IO-therapy markers were present in 36.4% of cases (TMB-High in 26%, PD-L1+ 21.8%, MSI-High 0.7%). Pathway alterations were detected in 86% of AS cases. By pathway, TP53 was altered in 31%, cell cycle 30%, DNA damage repair (DDR) 21%, RAS 18%, PI3K 15% and chromatin remodeling 14%. By site, head/neck (HN) AS had the highest rate of IO-therapy markers (65%, $p < 0.05$) [TMB-High (63%, $p < 0.0001$)], TP53 mutation (51%, $p = 0.07$), and POT1A mutation (41%, $p < 0.01$). MYC CNA was highest in breast (63%) and extremity (40%) AS ($p < 0.0001$). DDR alterations were present in 56% ($p = 0.09$) of cutaneous AS and ranged from 12-27% in other subtypes (not significant, NS). RAS and PI3K alterations ranged from 6-27% across all subtypes (NS). **Conclusions:** Our findings suggest differential angiosarcoma biology across primary sites. HN AS had more frequent markers of potential IO-therapy response, as well as DDR alterations. Next in frequency, we found ARID1A which is possibly associated with overactive EZH2, a target of tazemetostat. MYC amplification suggests a role targeting cell cycle via cyclin-dependent kinase or bromodomain inhibitors in breast and extremity ASs. Finally, RAS and PI3K are mutated in a low percentage of cases, explaining the limited benefit of tyrosine kinase inhibitors in AS. Future AS clinical trials should be designed with consideration of primary site, IO-therapy response biomarkers, and activated pathway. Research Sponsor: None.

11546 Poster Session (Board #434), Fri, 8:00 AM-11:00 AM

Immune-checkpoint genes as predictive biomarkers of trabectedin in advanced soft-tissue sarcoma (STS): A Spanish Group for Research on Sarcomas (GEIS) translational study. *First Author: David Silva Moura, Group of Advanced Therapies and Biomarkers in Sarcomas, Institute of Biomedicine of Seville, Ibis/Hospital Universitario Virgen Del Rocío/Csic/Universidad De Sevilla, Seville, Spain*

Background: Despite several second-line options are accessible for the treatment of advanced STS, there is a lack of predictive biomarkers available to support the rational selection of these drugs. Trabectedin specifically targets mononuclear cell lineage (macrophages and monocytes) that ultimately could inhibit tumor angiogenesis. Moreover, trabectedin seems to induce the expression of immune-checkpoint proteins (e.g. PD-L1); however, the predictive value of these factors remains unknown. We present the analyses of immune-checkpoint genes (*CD274*, *CD86*, *CTLA4*, *HAVCR2*, *LAG3* and *PDCD1*) and *CD163*, *CD4*, *CD68* and *CD8A* expression as potential predictive factors of response to trabectedin in a subset of STS patients of the GEIS registry. **Methods:** Selection criteria included patients with STS, pretreated with at least 2 lines in the advanced setting (one line being trabectedin), with paraffin block available and ethic committee's approval. Direct transcriptomics was performed using HTG Molecular Oncology Biomarker Pathway panel (HTG Molecular Diagnostics, Inc.; Tucson, AZ, USA), following manufacturers' instructions. Data analyses were performed taking into account the median Log2 of expression of each gene and by correlating it with progression-free survival (PFS) for trabectedin, and overall survival measured from the starting date of trabectedin treatment (OS). **Results:** Among 387 registered patients, fitting with the inclusions criteria, 139 cases were used for gene expression analyses, as the discovery set. Patients had median age of 52 years, 54% were females and had a median follow-up from diagnosis of 44 months. High expression of *CD274* (PD-L1) was significantly associated with better PFS of trabectedin (5.4 *vs.* 3.0 months; p= 0.006). Similar results were obtained with high expression of *CTLA4* and *LAG3*: 6.0 vs 3.1 months; $p = 0.005$ and 5.4 vs 2.7 months; $p = 0.042$, respectively. Expression of *CTLA4* and *LAG3* showed no significant impact in OS; whereas *CD274* high expression showed a trend towards better OS (17.9 vs 10.2 months; $p = 0.077$). Also, no significant correlation was achieved for *CD163*, *CD4*, *CD68*, *CD8A*, *CD86* and *HAVCR2*; *PDCD1* (PD-1) showed a trend towards better PFS of trabectedin, $p = 0.114$. **Conclusions:** The expression of selected immune-checkpoint genes exhibited a potential predictive value for trabectedin in advanced STS. Validation studies (at the transcriptional and protein level) are currently ongoing to confirm their potential predictive role. Research Sponsor: Spanish Group for Research on Sarcomas (GEIS).

11547 Poster Session (Board #435), Fri, 8:00 AM-11:00 AM

Cardiac safety of trabectedin monotherapy and in combination with pegylated liposomal doxorubicin in patients with sarcomas and ovarian cancer. *First Author: Robin Lewis Jones, Royal Marsden Hospital/Institute of Cancer Research, London, United Kingdom*

Background: Trabectedin (T) is an established option as monotherapy for advanced soft tissue sarcomas (STS; Leiomyosarcomas and Liposarcomas in the USA) and in combination with pegylated liposomal doxorubicin (PLD) for recurrent ovarian cancer (ROC). This retrospective analysis evaluated the cardiac safety profile in over 1500 patients (pts) from clinical trials administering T monotherapy for STS or in combination with PLD (T+PLD) for ROC. **Methods:** Integrated cardiac safety data was analyzed from ten Phase 2 trials and one Phase 3 trial in STS (T) and two Phase 3 ROC trials (T+PLD). Cardiac-related treatment-emergent adverse events (TEAEs) were summarized using MedDRA terminology and by Kaplan-Meier analysis for time-to-event variables. Subgroup analyses were performed for cardiac-related TEAEs, including any significant decrease in LVEF. **Results:** Integrated data on T monotherapy included 982 pts (Table). Of these, 110 (11.2%) pts who received $\geq$1 dose of T experienced a cardiac-related TEAE, including tachycardia (3.1%), palpitations (1.5%), LVEF decrease (1.3%), sinus tachycardia (1.0%), and/or congestive cardiac failure (1.0%). A multivariate analysis revealed factors associated with increased risk to be cardiovascular medical history (risk ratio [RR]: 1.90; 95% CI: 1.24-2.91; p = 0.003) and age $>$ 65 years (RR: 1.78; 95% CI: 1.12,2.83; $p = 0.014$). Cardiac-related TEAEs were reported in 78 (12.6%) of 619 pts receiving T+PLD (Table). Incidence of cardiac-related TEAEs was greater with T+PLD compared with PLD monotherapy (12.6% vs 5.6%). A multivariate analysis showed that pts were at increased risk for experiencing cardiac-related TEAEs when treated with T+PLD compared to PLD monotherapy (RR: 2.70; 95% CI: 1.75,4.17; $p < 0.0001$) and when there was a history of prior cardiac medication (RR: 1.88; 95% CI: 1.16,3.05; $p = 0.010$). **Conclusions:** Although infrequent, patients receiving T after prior anthracyclines or in combination with PLD are at risk for cardiac dysfunction, and appropriate clinical awareness and monitoring is encouraged to optimize patient outcomes. Research Sponsor: Janssen.

Number of patients exposed to study treatment and safety analysis sets.

Study	No. Patients in Safety Analysis	
Monotherapy	Trabectedin	Dacarbazine
Phase 3 SAR-3007 LMS/LPS (STS) trial	378	172
Ten Phase 2 Studies	604	-
Integrated Data (SAR-3007+Phase 2)	982	-
Combination Therapy	Trabectedin+PLD	PLD
OVA-301	333	330
OVC-3006	286	282
Integrated Data (OVA-301+OVC-3006)	619	612

PLD, pegylated liposomal doxorubicin.

11548 Poster Session (Board #436), Fri, 8:00 AM-11:00 AM

A phase Ib study of ribociclib in combination with doxorubicin in advanced soft tissue sarcomas (aSTS). *First Author: Lara E. Davis, Oregon Health and Science University, Portland, OR*

Background: aSTS are typically treated with single agent doxorubicin (dox). CDK4 inhibitors such as ribociclib (ribo) may have a role in treating STS, which frequently rely on hyperphosphorylation of Rb to evade the Rb checkpoint. We hypothesized that dox efficacy could be increased by inhibiting Rb phosphorylation with a short course of ribo, then removing ribo to permit cell cycle progression prior to dox, thus potentiating the DNA-damaging effects of dox. **Methods:** Open label, dose-finding study of ribo and dox in dox-naïve patients (pts) with Rb+ aSTS. Rb status determined by IHC. Primary objective to determine the recommended phase 2 dose (RP2D). Secondary objective of antitumor activity. Pts received ribo 400-600 mg PO QD x7d followed by 72h rest before dox 60-75 mg/m2 IV, q21d. Pts free from progression of disease after 6 cycles continued on ribo maintenance at 600 mg QD q3/4wk. Dose-limiting toxicity (DLT) period was cycle 1, with target toxicity rate of 30% using a modified toxicity probability interval (mTPI) design. Growth factor support was not allowed during DLT period. **Results:** 9 screened pts were ineligible by Rb status. 16 pts enrolled with 15 evaluable for dose determination (7 dedifferentiated LPS, 8 other subtypes). 4 of 7 pts treated at starting dose level (400 mg ribo, 75 mg/m2 dox) had a DLT; all febrile neutropenia. 1 of 8 pts treated at dose level -1 (400 mg ribo, 60 mg/m2 dox) had a DLT of gr4 anemia. Febrile neutropenia events occurred during cycle 1, when growth factors were prohibited. Toxicity was similar to historical dox AEs (Table). Two partial responses for overall response rate (ORR) of 13%. Five (33%) were progression-free at 18 wks. Correlative studies ongoing. **Conclusions:** This study determined a RP2D of ribo 400 mg with dox 60 mg/m2 when used in combination for the treatment of aSTS. Clinical trial information: NCT03009201. Research Sponsor: Novartis.

Number (%) of pts with grade 3-4 AEs attributed to treatment.

AE	All grades	Gr ≥3
Anemia	9 (56%)	1 (6%)
Febrile neutropenia	4 (25%)	4 (25%)
Lymphocyte count decreased	10 (63%)	4 (25%)
Mucositis oral	5 (31%)	1 (6%)
Neutrophil count decreased	10 (63%)	8 (50%)
Platelet count decreased	6 (38%)	1 (6%)
White blood cell decreased	12 (75%)	8 (50%)

11549 Poster Session (Board #437), Fri, 8:00 AM-11:00 AM

Comparison of different systemic therapeutic regimes in resectable high-risk soft tissue sarcoma: Results of a network meta-analysis. *First Author: Jan Haussmann, Heinrich Heine University, Düsseldorf, Germany*

Background: The treatment of high-risk soft tissue sarcoma of the trunk or the extremities consists of surgical resection with risk-adapted radiation therapy. Further treatment options which can significantly improve local and systemic tumor control including chemotherapy are not well established. Due to the heterogeneity of disease different systemic approaches as well as their application during different time points have been attempted. **Methods:** We conducted a literature search for randomized clinical trials in the treatment of localized, resectable high-risk soft tissue sarcoma comparing different treatment modalities according to the PRISMA guidelines. We extracted published hazard ratios and number of events for the endpoints of overall and disease-free survival (OS; DFS) as well as local and distant recurrence-free interval (LRFI; DRFI). The different modalities were compared in a network meta-analysis against the defined standard treatment surgery ± radiotherapy using the inverse-variance heterogeneity model (ivhet) with the help of the Microsoft Excel add-in Meta-XL V5.3. **Results:** The literature search identified 25 studies including 3489 patients. The network analysis showed that adjuvant chemotherapy (adjCTx) results in a significant improvement in overall survival (HR = 0.86; CI-95%: 0.75-0.97; p = 0.017) compared to the standard treatment of surgery ± radiatherapy alone. Combined treatment with regional hyperthermia and neoadjuvant chemotherapy (HTx+nadjCTx) also improves OS (HR = 0.45; CI-95%: 0.20-1.00; p = 0.049). Preoperative chemotherapy alone (nadjCTx) as well as perioperative chemotherapy (periopCTx) resulted both in non-statistically significant improvements in OS (HR = 0.61; CI-95%: 0.29-1.29; p = 0.195) and (HR = 0.48; CI-95%: 0.15-1.55; p = 0.218). Histology-tailored neoadjuvant chemotherapy (tNaCTx) also showed no effect on overall survival (HR = 1.08; CI-95%: 0.45-2.61; p = 0.868). The analysis of DFS, LRFI and DRFI disclosed a similar pattern between the different treatment regimens. **Conclusions:** The addition of cytotoxic chemotherapy in resectable high-risk soft tissue sarcomas provides a measurable benefit in overall survival. Shifting of systemic therapy to the neoadjuvant setting and combination with regional hyperthermia might be favored. Predictive clinical and molecular markers are needed to evaluate and limit potentional risks prospectively going forward. Research Sponsor: None.

11550 Poster Session (Board #438), Fri, 8:00 AM-11:00 AM

Phase Ib study of decitabine in combination with gemcitabine in treatment of advanced soft tissue and bone sarcomas. *First Author: Varun Monga, Holden Comprehensive Cancer Center, University of Iowa, Iowa City, IA*

Background: Sarcomas are a heterogeneous group of tumors and are associated with high rates of metastases leading to poor prognosis. Numerous epigenetic changes including hypermethylation have been identified in several sarcoma subtypes. Restoration of normal methylation patterns using DNA hypomethylating agent when combined with chemotherapy has shown to slow tumor growth in preclinical studies. Low continuous dosing of hypomethylating agent has epigenetic modulating effect with less toxicity. We conducted a Phase 1b study evaluating safety & tolerability and identifying the recommended phase 2 dose (RP2D) of subcutaneous (SQ) decitabine (DEC) given with fixed dose infusion gemcitabine (GEM) in patients with advanced soft tissue sarcomas (STS) and bone sarcomas. **Methods:** Eligible patients at least age 18 yrs with metastatic histologically confirmed STS or bone sarcoma after progression on one line or if refused adriamycin for STS were included. Prior GEM use was permitted. A modified 3+3 dose escalation design was used exploring two dose cohorts of DEC, 0.1 and 0.2 mg/kg SQ administered on a twice weekly schedule for three weeks and GEM given as 900 mg/m^2, IV over 90 min on days 1, 8 & 15 of a 28-day cycle. Treatment was continued until disease progression or unacceptable toxicity. Dose limiting toxicity (DLT) was defined as any drug related non-hematological grade 3 or 4 toxicity per CTCAE v4.0. Disease assessment was performed every 8 weeks using RECIST v1.1. **Results:** 31 patients (25 STS & 6 bone sarcomas) were enrolled of which 7 were non-evaluable. There were 12 evaluable patients in each dosing cohort. Of the total 744 adverse events (AE) 17.2% were grade 3/4 and most were neutropenia without neutropenic fever. 45.7% AEs were possibly (44.6%) or probably (1.1%) attributed to DEC use. The toxicities were not significantly different between DEC doses. No DLTs were observed. One patient died due to progressive disease. **Conclusions:** Combination of fixed dose infusion GEM with low dose subcutaneous DEC is moderately toxic. Most toxicities were hematological. While there were few responses, the RP2D of DEC selected was 0.1 mg/kg as it showed prolonged disease stabilization. Clinical trial information: NCT02959164. Research Sponsor: Holden Comprehensive Cancer Center.

	Decitabine	
Best response	**0.1 mg/kg N = 12**	**0.2 mg/kg N = 12**
Partial Response	2 (16.7%)	2 (16.7%)
Stable Disease	7 (58.3%)	3 (25%)
Progressive Disease	3 (25%)	7 (58.3%)

Partial responses were noted in leiomyosarcoma, chondrosarcoma, adenosarcoma and carcinosarcoma. A clinical benefit rate of 58% was noted. Eleven patients had previously received and progressed on GEM based therapy.

11552 Poster Session (Board #440), Fri, 8:00 AM-11:00 AM

A phase I trial of pomalidomide in combination with liposomal doxorubicin in patients with Kaposi sarcoma with or without other KSHV-associated diseases. *First Author: Ramya Ramaswami, HIV/AIDS Malignancy Branch, CCR, NCI, Bethesda, MD*

Background: Kaposi sarcoma herpesvirus (KSHV, also known as human herpesvirus 8 [HHV-8]), is the causative agent of Kaposi sarcoma (KS), a multicentric angioproliferative tumor, a form of multicentric Castleman disease (KSHV-MCD), and KSHV inflammatory cytokine syndrome (KICS). KS can be difficult to treat when it occurs with KSHV-MCD or KICS; resulting in high mortality rates. Liposomal doxorubicin (LD) is an FDA-approved treatment for KS. Pomalidomide, an oral immunomodulatory drug, is safe and has demonstrated activity in KS, but the activity of the combination (pomalidomide+LD) in KS alone or with KSHV-associated diseases is unknown. **Methods:** The primary objective was to evaluate safety and tolerability of pomalidomide+LD in two groups of patients with KS requiring systemic therapy: Group I (GI)- KS alone; Group II (GII)- KS with concurrent KSHV-MCD or KICS. Patients received LD at 20 mg/m^2 intravenously on day 1 of a 28-day cycle combined with pomalidomide once daily on days 1 to 21 at escalating dose levels (DL) (I - 2mg, II - 3mg, or III- 4mg) in a 3+3 design until plateau of response or other pre-specified criteria. Patients received 81mg of aspirin daily as thromboprophylaxis. KS responses were evaluated using the modified AIDS Clinical Trial Group criteria. **Results:** Thirty-four cisgender men, all with T1-stage KS [21 patients (62%) in GI and 13 patients (38%) in GII] were treated; 32 (94%) were HIV-infected and 22 (65%) had prior chemotherapy for KS (15/21 GI and 7/13 GII). There were no dose-limiting toxicities (DLTs) at DLIII for GI, and additional patients were treated at DLIII. In GII, grade 3 rash and pharyngeal edema were DLTs observed at 3mg of pomalidomide. Overall a median of 6 cycles were administered; the most common grade 3/4 toxicity was neutropenia. Among evaluable patients receiving >2 cycles,17/21 patients in GI had a response (all partial) (81% [95% confidence interval (CI) 58-95%]) and 5/10 patients in GII had a response (4 partial and 1 complete) (50% [95% CI 19-81%]). **Conclusions:** Pomalidomide+LD was well-tolerated and active in heavily pretreated patients with KS alone. In patients with KS and other KSHV-associated diseases, activity was noted but less well-tolerated. Clinical trial information: NCT02659930. Research Sponsor: U.S. National Institutes of Health, CRADA with Celgene.

11553 Poster Session (Board #441), Fri, 8:00 AM-11:00 AM

Apatinib for patients (pts) with advanced soft tissue sarcoma (STS) after chemotherapy: A prospective, open-label, single-arm, multicentered study. *First Author: Haiyan Hu, Affiliated Sixth People's Hospital, Shanghai Jiaotong University, Shanghai, China*

Background: The development of STS therapeutics has been challenging, especially patients who failed chemotherapy. Anti-angiogenesis inhibitors had shown activity in STS, Apatinib is a TKI targeting on VEGFR-2 which has shown activity in many solid tumors. **Methods:** A Phase II, open-label, Single-arm, multicentered study was conducted in previously treated pts with advanced STS in China. The patients received apatinib 500mg orally qd in a 28-day-cycle, until disease progression or unacceptable adverse events. Antitumor response assessment was performed every 8 weeks per RECIST V1.1. The primary endpoint was PFS rate in 6 months and secondary endpoint was ORR and OS. **Results:** As cut-off on Jan 20th 2019, a total of 53 patients were enrolled in 9 centers, 51 patients received at least 2 cycles of Apatinib, 1 patient is still in treatment. The main histological subtypes were alveolar soft part sarcoma(n = 11), synovial sarcoma(n = 6), leiomyosarcoma (n = 6), clear cell sarcoma(n = 6) and undifferentiated pleomorphic sarcoma(n = 5). Overall, 27 of 51 patients were progression free at six months and the 6-m PFS rate was 53.32% (95%CI 37.76%, 66.63%). Until final follow-up, the ORR was 18.75% (9/48) and DCR was 87.5% (42/48). Additionally, median PFS was 7.13 (95%CI 3.84, 9.23) months and median OS has reached up to 24.67 (9.30-NE) months. Adverse events (AEs) were detected among all pts, hypertension and proteinuria are the most common AEs, occurred in 84.91% and 73.57% pts respectively. Grade 3/4 related adverse events were detected in 86.79% of pts, Grade 3/4 hypertension was the most common grade3/4 AE (56.60%). **Conclusions:** Overall, the present study demonstrates that apatinib has a clinically meaningful anti-tumor activity in pretreated STS pts, showing durable responses and prolonged overall survival. Some of the pts had a long-time benefit from the treatment. Apatinib was safe and generally well tolerated. Further studies on specific STS subtypes would be meaningful. Clinical trial information: NCT03064243. Research Sponsor: Jiangsu Hengrui Pharmaceutical CO.,LTD.

11554 Poster Session (Board #442), Fri, 8:00 AM-11:00 AM

Which patients with pre-treated locally advanced or metastatic sarcoma benefit most from trabectedin treatment: First results of a retrospective study of the German Interdisciplinary Sarcoma Group (GISG-14 - ReTraSarc). *First Author: Daniel Pink, Helios Klinikum Bad Saarow-Sarcoma Center Berlin-Brandenburg and University Medicine Greifswald, Germany, Bad Saarow, Germany*

Background: Despite the growing amount of published data regarding the outcomes of sarcoma patients treated with trabectedin, still some questions remain unanswered. The aim of the ReTraSarc trial (NCT03284320) was to evaluate the efficacy and safety of trabectedin in a large German population. **Methods:** Patients treated between 2007-2018 were retrospectively analyzed. All patients had histologically confirmed soft tissue (STS; n = 478) or bone (BS; n = 31) sarcoma; either metastatic (n = 468) or locally advanced (n = 41) disease, and had received at least one cycle of trabectedin. Based on follow-up data (until October 2019), progression-free survival (PFS) and overall survival (OS) after initiation of trabectedin treatment were estimated according to the Kaplan-Meier method. **Results:** A total of 509 patents were analyzed. Patients had a mean age of 54 years for STS and 30 years for BS-patients, and 25.4% of them aged > 65 years. Overall, 71.4% of patients had a good performance status (ECOG 0/1), and 37.7% received two prior lines, 28.3% three and 34% received > 3 prior lines of systemic treatment. Patients received a median of 3 cycles (IQR: 2-6 cycles) of trabectedin. Trabectedin resulted in an objective response rate (ORR) of 10% with a 37.4% of disease control rate (DCR). The median PFS and OS were 2.5 months (IQR: 1.4-6.1 months) and 8.2 months (IQR: 3-21 months), respectively. Significantly more patients with liposarcoma (22.1%; 95% CI: 15.2-32.2) were free from progression at 12 months after treatment as compared with patients with leiomyosarcoma (8.5%; 95% CI: 4.8-14.9). More analyses of effectiveness and safety are in progress (e.g. stratified per sarcoma subtypes or therapeutic line) and will be presented. **Conclusions:** The results of this real-life study, with a large number of patients and long-term follow-up, allow us to better analyze PFS and OS in sarcoma patients treated with trabectedin, given in different treatment lines and after dose modifications and/or cycle delays. Additionally, the results of this study enable us to evaluate the real-life impact of rechallenge with trabectedin in a further therapy line. Clinical trial information: NCT03284320. Research Sponsor: PharmaMar.

11555 Poster Session (Board #443), Fri, 8:00 AM-11:00 AM

Efficacy and safety of hypofractionated preoperative radiotherapy in treatment of patient with primary locally advanced soft tissue sarcoma of limbs/trunk wall. *First Author: Hanna Kosela, Department of Soft Tissue/Bone Sarcoma and Melanoma; Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland*

Background: Soft tissue sarcomas (STS) are rare often malignant tumors. The primary treatment of most STS is radical resection with adjuvant radiotherapy. Our previous study showed that the use of preoperative hypofractionated radiotherapy is safe and efficient in the treatment of unselected group of patients with STS. Aim of this study was to assess the use of the treatment scheme in patients with primary STS treated in one institution. **Methods:** 311 patients (52% female) with primary locally advanced STS participated in this prospective trial conducted from 2010 till 2017. Median age was 55 years (range: 17-91). Median follow up is 57 months (95%CI 55-61). The most common subtypes were pleomorphic sarcoma, liposarcoma and synovial sarcoma. Median tumor size was 11cm. 258 patients (83%) had high grade tumors. The most common tumor localization were lower limbs (72%). 30% of patients received preoperative chemotherapy. For five consecutive days radiotherapy in 5 x 5Gy fraction was applied, with immediate (2-4 days) resection of the tumor. **Results:** In 260 patients (83.6%) clear surgical margins (R0) were obtained. 107 patients were dead at the time of the analysis.5-year overall survival is 63%. 156 (50%) had a recurrence of the disease. Local recurrence (LR) was found in 13.8% of the patients. Median time from surgery to LR was 14.7 months. In 56% of patients with LR another limb spearing radical surgery could be performed. Factors that had a significant adverse impact on LR were histological subtype (p = 0.017) and surgical margin status (p = 0.013). Factors that had a significant adverse impact on overall survival were tumor size (p < 0.0001), grade (p = 0.0047) and surgical margin status (p = 0.013). 96 patients (30.8%) had any kind of treatment toxicity, factor having negative impact on the toxicity was lower limb location of the tumor (p = 0.0012). 20 patients (6.4%) required surgery for treatment of the complications. 14.6% patients had prolonged healing of the wound (> 1 month), 8.3% had wound dehiscence, 1.4% required prolonged punctures of the lymph fluid, 2.3% had severe fibrosis leading to contracture of limb, 11% patients prolonged edema of the operated limb. 0.9% of patients had a fracture of the treated limb. **Conclusions:** In this group, with a big percentage of patients with large, high grade STS use of hypofractionated preoperative radiotherapy was associated with similar local control when compared to published studies. The early toxicity is tolerable, with a small amount of late complications. Research Sponsor: None.

11556 Poster Session (Board #444), Fri, 8:00 AM-11:00 AM

Activity of cabazitaxel in patients with metastatic or inoperable locally advanced dedifferentiated liposarcoma: European Organization for Research and Treatment of Cancer (EORTC) Phase II trial 1202. *First Author: Roberta Sanfilippo, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: The optimal treatment for patients with advanced dedifferentiated (DD) liposarcoma (LPS) remains uncertain. Single agents which are most effective include doxorubicin and ifosfamide but, as with soft tissue sarcomas (STS) in general, objective response rates (ORR) and progression free survival (PFS) are very modest. Cabazitaxel exerts its effect through inhibition of microtubular disassembly and has been shown to be relatively safe, effective and well-tolerated. EORTC 1202 assessed whether cabazitaxel demonstrated sufficient antitumor activity in patients with metastatic or inoperable locally advanced DD LPS to justify further investigation in a phase III setting. **Methods:** This was an international multi-center, open label single arm phase II trial. Eligible patients with metastatic or inoperable locally advanced DD LPS were treated with cabazitaxel 25mg/m^2 IV infusion over 1 hour every 21 days. Primary endpoint was PFS rate at 12 weeks assessed by local investigator per RECIST 1.1. Based on a Simon two-stage design, at least 4 out of 17 (Stage 1) and 11 out of 37 (Stage 2) eligible and evaluable patients who are progression-free at 12 weeks were needed. **Results:** Forty patients were registered by 10 institutions in 4 countries between March 2015 and March 2019, with 2 patients being ineligible. Among the 38 eligible patients who started treatment, 3 (7.5 %) were still on treatment at the time of analysis. The number of cycles ranged from 1 to 30, with a median of 5; 26 patients (65%) received at least 4 cycles of cabazitaxel. Among the first 17 (Stage 1) and 37 (Stage 2), 11 and 20 patients were progression-free at 12 weeks respectively, satisfying the study decision rules. The PFS rate at 12 weeks for all 38 eligible patients was 52.6% (conditional 1-sided 95 % CI 38.3 – 100). Two patients (5.3%) achieved a confirmed partial response (PR) and 23 stable disease (SD) (60.5%). Disease control (PR+SD) was achieved in 25 patients (65.8%). Median PFS was 7.4 months (95%CI 2.8-10.3). The most common cabazitaxel -related grade >3 adverse events in all 40 registered patients were neutropenia (60%), febrile neutropenia (25%), fatigue (12.5%), and anemia (10%). There were no cabazitaxel-related deaths. **Conclusions:** EORTC 1202 met its primary endpoint, with 20/37 pts (54%) being progression-free at 12 weeks. Results of this trial confirm activity of cabazitaxel in patients with metastatic or inoperable locally advanced DD LPS and warrant further exploration of the drug. Clinical trial information: NCT01913652. Research Sponsor: Sanofi Aventis, Other Foundation.

11557 Poster Session (Board #445), Fri, 8:00 AM-11:00 AM

A phase I study of TGF-β inhibitor, vactosertib in combination with imatinib in patients with advanced desmoid tumor (aggressive fibromatosis). *First Author: Hyo Song Kim, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea*

Background: Desmoid tumor (aggressive fibromatosis) is fibroproliferative neoplasm arising from deep connective tissues. TCGA pan-cancer analysis revealed high expression TGF-β responsive signature in desmoid tumor. This phase I study assessed the safety, tolerability, and pharmacokinetics of the TGF-β inhibitor, vactosertib in combination with imatinib for desmoid tumor. **Methods:** Patients with advanced desmoid tumors not treatable by surgery or radiotherapy were eligible. The primary objective is to assess the safety and recommended phase 2 dose (RP2D) of vactosertib given 5 days on and 2 days off in combination with imatinib (400 mg QD). Two dose levels of vactosertib were tested; cohort -1 (100 mg BID) and cohort 1(200 mg BID). Secondary objectives include pharmacokinetics, anti-tumor activity by response rate (RECIST v1.1), and biomarker analysis. **Results:** Seven patients (cohort -1, n = 4; cohort 1, n = 3) were enrolled and finished the safety evaluation. The most frequently reported treatment related adverse events were myalgia (57.1%), fatigue (42.8%), diarrhea (42.8%), anemia (28.5%) and stomatitis (28.5%) with mostly grade 1. No dose limiting toxicity was observed. Tumor response included 2 (28.5%) partial response (PR) and 2 stable disease (SD) in the cohort -1, and 3 SD in the cohort 1. The time to response were 5.5 and 8.2 months and all 7 cases are ongoing. Updated safety, pharmacokinetics, efficacy and biomarker data will be presented at the meeting. **Conclusions:** The combination of vactosertib plus imatinib was well tolerated and showed promising activity in desmoid tumor. RP2D of vactosertib was defined as 200 mg BID. Further efficacy will be explored in the phase 2 part of the study. Clinical trial information: NCT03802084. Research Sponsor: None.

11558 Poster Session (Board #446), Fri, 8:00 AM-11:00 AM

Prognostic role of % changes in longest tumor diameter (LTD) in localized high-risk soft tissue sarcoma (STS) treated with neoadjuvant chemotherapy in a randomized clinical trial. *First Author: Silvia Stacchiotti, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: We investigated the prognostic relevance of % change in LTD in patients (pts) with localized high-risk STS treated with neoadjuvant chemotherapy in a phase 3 randomized trial (NCT01710176), aimed at comparing 3 cycles of a neoadjuvant histology-tailored (HT) over 3 cycles of standard anthracycline + ifosfamide chemotherapy (S). **Methods:** Pts with localized high-risk STS of extremities or trunk wall, and a diagnosis of myxoid liposarcoma, leiomyosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumors, undifferentiated pleomorphic sarcoma were randomly assigned to receive 3 cycles of S or HT. Pts affected by myxofibrosarcoma, pleomorphic liposarcoma, pleomorphic rhabomyosarcoma unclassified spindle cell sarcoma were prospectively registered and treated by S. Change of LTD was assessed comparing baseline dimension with that measured after 3 cycles of S or HT, before surgery. Only pts treated with neodjuvant chemotherapy alone were selected for the analysis. We first investigated Overall Survival (OS) from surgery of the groups identified by "any % reduction", "no-change" or "increase" in LTD by Kaplan-Meier estimates and log-rank tests. Then we searched for cutoffs able to separate prognosis among pts with a LTD reduction applying the change-point method proposed by Contal - O'Quigley. **Results:** Of 325 pts who entered the study and evaluable for response, 181 received neoadjuvant chemotherapy alone (92 S and 89 HT group respectively) and were analyzed, while 144 received concurrent chemo-radiotherapy and were excluded. In the whole population, % changes in LTD were significantly associated (log rank p = 0.032) to OS. "Any % reduction in LTD (101/181pts) displayed a better prognosis compared to "no-change" (28/181 pts) or "any % increase" (52/181). The change-point analysis was applied to all, S and HT groups separately; a cutoff of = / > 18.75% decrease in LTD was the optimal predictor of outcome for the S group (p = 0.031), while no size cut-off could be identified for the HT group. **Conclusions:** In our study, % change in LTD of pts treated with neoadjuvant chemotherapy for localized high-risk STS correlated with OS. However, a % decrease in LTD cut-off able to predict the best outcome could be identified only for pts treated in the S group, while no differences in outcome were found by any % LTD change in the HT group. Interestingly, the LTD cut-off identified in the S group was lower than the one selected to define a response by RECIST (= / > 18.75% decrease in LTD vs = / > 30%). Clinical trial information: NCT01710176. Research Sponsor: None.

11559 Poster Session (Board #447), Fri, 8:00 AM-11:00 AM

Phase II study of eribulin and pembrolizumab in patients (pts) with metastatic soft tissue sarcomas (STS): Report of LMS cohort. *First Author: Michael Nathenson, Department of Medical Oncology; Dana-Farber Cancer Institute, Boston, MA*

Background: Responses to single agent PD-1/PD-L1 inhibitors in STS remain limited with occasional responses in undifferentiated pleomorphic sarcomas (UPS), liposarcomas (LPS), and other sarcomas, and rare responses in leiomyosarcoma (LMS). Since cytotoxics and/or targeted therapies such as CDK4/6 inhibitors may alter the tumor microenvironment (TME) and potentiate the effect of immunotherapy, combination approaches may be needed to potentiate STS immunotherapy. The mechanism by which eribulin controls LPS may involve TME modification, and therefore it is attractive to test in combination with pembrolizumab in STS subtypes. This report summarizes the results from the LMS cohort from this ongoing trial. **Methods:** Pts treated with at least one prior therapy received eribulin 1.4mg/m2 (day 1, 8) and pembrolizumab 200mg (day 1), every 21 days. Pts continued therapy until progressive disease, death, or unacceptable toxicity. Primary endpoint was progression-free survival (PFS) at 12 weeks, with 60% PFS at 12 weeks required to deem the combination promising. Tumor assessments (RECIST 1.1) were performed at screening and every 6 weeks thereafter. Secondary endpoints included overall survival (OS), objective response rate (ORR), and clinical benefit rate (CBR). **Results:** Nineteen pts with LMS were enrolled from May 2019 to Sept 2019. The median age was 62 (range 48-80). Eleven (58%) patients had uterine LMS. The median # of prior therapies was 4 (range 1-7). The median follow-up was 19.7 weeks. The PFS at 12 weeks was 42.1% (90% CI: 27.0%-65.5%), with median PFS of 11.1 weeks. Median OS was not reached during the follow-up period. There was 1 partial response, and 5 confirmed stable disease for ORR of 5.3% and CBR of 26.3%, after 12 weeks. The rate of grade 3 or higher toxicity was 68% overall, most commonly neutropenia, anemia, weight loss, diarrhea, elevations of lipase, and alkaline phosphatase. These side effects were reversible. The most common adverse events were fatigue, neutropenia, anorexia, AST increase, and nausea. **Conclusions:** Eribulin and pembrolizumab in LMS did not meet the predefined endpoint for efficacy. The LPS and "other STS subtype" cohorts of this trial are actively enrolling. Clinical trial information: NCT03899805. Research Sponsor: Eisai, Pharmaceutical/Biotech Company.

11560 Poster Session (Board #448), Fri, 8:00 AM-11:00 AM

Nationwide incidence of sarcomas and tumors of intermediate malignancy in the NETSARC network with central pathology review: Correlation with published clinical research. *First Author: Gonzague De Pinieux, Hopital Trousseau, Tours, France*

Background: Since 2010, presentation to a designated sarcoma tumor board and pathological review by an expert network are mandatory for sarcoma patients in France. NETSARC+ (merging the 3 initial RREPS, RESOS & NETSARC) collected prospectively all cases of reviewed sarcomas and tumors of intermediate malignancy (TIM) nationwide. We report on the incidence of subtypes according to WHO classification from 2013 to 2016. **Methods:** Sarcoma expert pathologists reviewed samples were all prospectively integrated in the database; the results using the latest WHO classification are presented for the years 2013 to 2016, including yearly variations. Correlation of the incidence of each histotype with dedicated published clinical trials was conducted. **Results:** 139 different histological subtypes are reported among the 25172 patients with sarcomas (n = 18710, 64%) or TIM (n = 6460, 36%), respectively n = 5838, n = 6153, n = 6654, and n = 6527 yearly from 2013 to 2016. Over these 4 years, the observed yearly incidence of sarcomas, TIM, and all was therefore 79.7, 24.9 and 95.1/10e6/year, above that previously reported. GIST, liposarcoma, leiomyosarcomas, undifferentiated sarcomas represented 13%, 13%, 11% and 11% of all sarcomas. Only GIST, as a single entity exceeded a yearly incidence above 10/million per year. There were respectively 30, 63 and 66 different histological subtypes of sarcomas or TIM (single entities or lumped together, e.g. MPNST, or vascular sarcomas...) with an incidence ranging from 10 to 1/10e6/year, 1-0.1/10e6 per year, or < 0.1/10e6/year respectively. The 2 later "incidence groups" included 21% of the patients. The incidence of 8 histotypes varied significantly over this 4 years. Patients with tumors with an incidence above 1/10e6 per year have significantly higher numbers of dedicated published phase III and phase II clinical trials (p < 10e-6). **Conclusions:** This nationwide registry of sarcoma patients with an histology reviewed by sarcoma experts shows that the incidence of sarcoma and TIM is higher than previously reported, may vary over years for some histotypes, and that tumors with an incidence < 10e6 have a much lower access to clinical trials. Research Sponsor: Institut National du Cancer.

11561 Poster Session (Board #449), Fri, 8:00 AM-11:00 AM

Multicenter, open-label phase II study of daily oral regorafenib for chemotherapy-refractory, metastatic and locally advanced angiosarcoma. *First Author: Mark Agulnik, Northwestern University, Feinberg School of Medicine, Chicago, IL*

Background: Angiosarcoma has a particularly poor prognosis with 5-year overall survival rates of approximately 30-40%. Treatment of locally advanced and metastatic angiosarcoma is inadequate. Data strongly suggest concurrent, potent inhibition of VEGFR and Tie2 represents an attractive therapeutic strategy in angiosarcoma. Regorafenib displays potent VEGFR and Tie2 receptor inhibition and also possesses activity against additional potential targets in angiosarcoma including PDGFRs, RAF, KIT and FGFR, amongst others. **Methods:** A multicenter phase II study of regorafenib in patients with locally advanced or metastatic angiosarcoma was conducted through the Midwest Sarcoma Trials Partnership. Adequate performance status, organ function, measurable disease (RECIST 1.1) and 1-4 prior therapies were required. Regorafenib 160 mg PO daily was given in 28-day cycles (21 days on, 7 days off) until disease progression (PD) or unacceptable toxicity. The primary endpoint was progression-free survival (PFS), assessed at 16 weeks. Secondary endpoints include overall response rate (ORR), clinical benefit rate (CBR), OS, and safety and tolerability. A Simon 2-stage design was used. **Results:** After final enrollment of the second stage, a total of 31 pts were enrolled at 6 sites, 23 are evaluable for response. Median age was 65 (range 30-91); 50% were female, 67.7% had metastatic disease. PFS at 4 months is 52.2% with a median PFS and OS of 3.55 and 11.4 months. 1 confirmed CR and 2 PR, 12 SD and 8 PD were observed. ORR and CBR are 14.29 and 65.2%, respectively. No uncommon grade 3-4 adverse events were observed. 6 pts were non-evaluable due to refusal of further therapy and 2 patients progressed prior to first evaluation. **Conclusions:** Regorafenib was well tolerated in this study of pretreated patients with angiosarcomas and met its primary endpoint with a median PFS $>$ 45% at 4 months. Treatment was feasible and did not reveal any previously unreported toxicities. Efficacy outcomes were complicated by early withdrawals of patients. RECIST responses were encouraging and regorafenib has a clinically meaningful 4-month PFS. Clinical trial information: NCT02048722. Research Sponsor: Bayer.

11562 Poster Session (Board #450), Fri, 8:00 AM-11:00 AM

A randomized phase II study of MLN0128 (M) versus pazopanib (P) in patients (pt) with advanced sarcoma (Alliance A091304). *First Author: Matthew Ingham, Columbia University Irving Medical Center, New York, NY*

Background: Soft tissue sarcoma (STS) is a heterogeneous malignancy of connective tissue. Although mTOR is implicated in STS pathogenesis, clinical activity from mTORC1 inhibitors is modest. M, a potent selective mTORC1/mTORC2 inhibitor, was more effective in STS preclinical models than inhibitors of mTORC1, IGF1R and mTORC1+IGF1R, owing to more complete suppression of PI3K/AKT/mTOR and abrogation of feedback AKT activation. P, an oral multikinase inhibitor, is approved for non-adipocytic STS and often used after progression (PD) on chemotherapy. In phase 1, the RP2D of M was 30 mg weekly. A091304 was to evaluate M as a novel targeted therapy for STS. **Methods:** In A091304, pts were randomized 1:1 to M 30 mg weekly or P 800 mg daily. Eligibility required Eastern Cooperative Oncology Group PS $\leq$ 1, progression on $\geq$ 1 prior chemotherapy and specific STS subtypes (cohort 1: UPS; 2: LMS; 3: MPNST, SS). Crossover to M was allowed after PD on P. 1° endpoint was progression-free survival (PFS). Assuming median PFS of P was 4.6 months (mo), 98 pts yielded 80% power to detect a hazard ratio of 0.66 favoring M [1-sided test, alpha = 0.15] and including 1 planned futility analysis. 2° endpoints were response rate, clinical benefit rate (CBR) at 4 mo and safety. After 4 of the first 12 pts randomized to P experienced $\geq$ grade (gr) 3 toxicity, the study was amended to begin at P 400 mg, allowing titration to 800 per investigator discretion. **Results:** After protocol amendment, 114 pt underwent randomization (M: 56, P: 58), and 111 initiated treatment. Median PFS was 2 mo for M and 2.1 mo for P (HR = 1.47; 1-sided 85% upper confidence boundary = 1.85), with 2 partial responses in each arm. CBR was 5.4% for M and 13.8% for P. Median OS was 10.7 mo for M and 13.9 mo for P (HR = 1.41; 95% CI 0.80-2.49). 26/43 pt with PD on P crossed over to M. Median PFS after crossover was 1.8 mo (95% CI 1.5-3.5). Gr 3 drug-related adverse events (AEs) occurred in 36% on M and 41% on P; gr 4 toxicity was rare. AEs were consistent with known effects of M and P. **Conclusions:** P at 400 mg daily (allowing escalation to 800 mg per investigator discretion) demonstrated a shorter PFS as compared prior randomized studies with P. Despite this, M failed to demonstrate superior clinical activity as compared to P at the interim analysis. Further work will examine activity within histology-specific cohorts and evaluate available tissue samples for evidence of pharmacodynamic activity. Support: U10CA180821, U10CA180882, U10CA180888, UG1CA233324 (SWOG); https://acknowledgments.alliancefound.org. Clinical trial information: NCT02601209. Research Sponsor: U.S. National Institutes of Health.

11564 Poster Session (Board #452), Fri, 8:00 AM-11:00 AM

Efficacy, safety, and immune priming effect of tazemetostat in patients with epithelioid sarcoma. *First Author: Mrinal M. Gounder, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Epithelioid sarcoma (ES) is a rare, aggressive soft tissue sarcoma characterized by loss of inhibitor of integrase 1 (INI1), allowing enhancer of zeste homologue 2 (EZH2) to repress cell differentiation and promote tumorigenesis. Tazemetostat (TAZ) is a selective inhibitor of EZH2 approved by the FDA for treatment of patients (pts) aged $\geq$16 years with metastatic or locally advanced ES ineligible for complete resection. **Methods:** This open-label, multicenter, multi-cohort phase 2 study (NCT02601950) evaluated safety and efficacy of TAZ in pts with INI1-negative tumors. ES pts were enrolled in Cohorts 5 and 6; pts in Cohort 6 underwent mandatory pre-dose (at screening) and post-dose biopsies (at Day 1 of cycle 2). Herein, we report the interim efficacy and safety data from Cohort 6. **Results:** As of July 31 2019, 44 pts were enrolled into Cohort 6 and treated with TAZ 800 mg BID. The objective response rate (ORR) was 11.4%; 4 pts (9.1%) had a partial response and 1 pt (2.3%) had a complete response (Table). Another 17 pts (38.6%) had stable disease (SD). 18 pts had progressive disease; 13 of these pts remained on study beyond progression. Progression-free survival (PFS) and overall survival (OS) at 56 weeks were 19.4% and 59.4%, respectively. In a pooled posthoc analysis of 106 ES pts from Cohorts 5 (n = 62), and 6, ORR was 13.2%. Grade 34 adverse events (AEs) were reported in 16 pts (36.4%), most commonly anemia (6.8%; n = 3) and tumor pain (6.8%; n = 3). 3 pts (6.8%) experienced grade 34 treatment-related AEs. One pt discontinued study drug and there were no treatment-emergent dose reductions or treatment-related deaths. These safety data from Cohort 6 are consistent with previously reported data from Cohort 5. 19 paired biopsies were included for translational endpoint analyses. Preliminary RNA seq and pathway analyses are currently ongoing and updated data, including additional biomarker data will be presented. **Conclusions:** Consistent with previously reported data from the completed Cohort 5, TAZ demonstrated clinically meaningful, durable, single agent activity in ES pts. Efficacy data from Cohort 6 continue to mature with 8 patients still on treatment. TAZ was well tolerated with a low incidence of treatment related AEs. Clinical trial information: NCT02601950. Research Sponsor: Epizyme, Inc.

	Cohort 6 n = 44	Cohort 5 n = 62	Cohorts 5 and 6, pooled N = 106
ORR, %	11.4	15	13.2
Disease control rate*, %	13.6	21	17.9
Median duration of response, months	Not evaluable	16.1	16.1
Median PFS, months	3.7	3.7	3.7
Median OS, months	16.6	19.0	18.0

*Percent of pts who achieved CR + PR of any duration or had SD lasting for $\geq$32 weeks.

11565 Poster Session (Board #453), Fri, 8:00 AM-11:00 AM

Cost-utility analysis of surveillance strategies for soft tissue sarcoma recurrence. *First Author: Bonny Chau, University of Washington, Seattle, WA*

Background: Soft tissue sarcomas (STS) are uncommon malignancies with significant biological and clinical variation. After primary curative therapy, patients enter a program of surveillance for recurrence with periodic chest x-rays (CXR) or computed tomography (CT). We compared costs and health outcomes of CXR and CT at a range of frequencies and durations of follow-up. **Methods:** We used a Markov model to simulate a cohort of 10,000 STS patients through their surveillance experience for lung metastasis after completion of definitive treatment for stage II or III primary disease. Health states in the model were no evidence of disease, recurrence, and death. We assessed the method of chest imaging, duration of follow-up, and interval (every 3 months or 6 months) of surveillance in the first 3 years. Cost effectiveness was assessed for each screening modality and screening frequency. Recurrence probabilities, utilities, treatment costs, and other parameters were from previously published data. Outcomes were costs, quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICER). **Results:** The initial evaluation comparing screening every 3 months for 3 years, every 6 months for years 4 and 5, and annually from years 6 to 10 resulted in 632,264 QALYs and $1,038,351,481 costs for CT, compared to 631,834 QALYs and $746,019,937 for CXR, resulting in an ICER of $679,322/QALY. In comparing screening intervals, less frequent screening intervals of every 6 months compared to every 3 months for the first three years using CT resulted in an ICER of $690,527/QALY and for CXR, the ICER was $271,423/QALY. In comparing screening duration between 6 years and 10 years of follow-up, strategies with longer follow-up resulted in slightly higher QALYs in each of the comparison scenarios, at a much higher cost. **Conclusions:** In our evaluation, more frequent screening the first 3 years and longer duration of surveillance resulted in higher QALYs in both screening modalities. However, in the comparisons the ICERs exceed common willingness to pay thresholds of $150,000/QALY gained; CXR is the more cost-effective imaging modality. Limitation of this model includes the simplification of disease progression and heterogeneity in STS. Research Sponsor: None.

TPS11567 Poster Session (Board #455), Fri, 8:00 AM-11:00 AM

A phase I/II clinical trial of the reversible LSD1 inhibitor, seclidemstat, in patients with relapsed/refractory Ewing sarcoma. *First Author: Damon R. Reed, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Ewing sarcoma (ES) is a rare, aggressive bone and soft tissue cancer that predominantly afflicts adolescents and young adults. Novel therapeutic agents are needed as there are no approved targeted treatments for this disease. ES is characterized by a chromosomal translocation resulting in an EWS/ETS fusion oncoprotein, a transcription factor that results in aberrant gene expression leading to ES progression. Lysine specific demethylase 1 (LSD1) associates with EWS/ETS oncoproteins to alter gene expression and contribute to disease progression. Directly inhibiting EWS/ETS is challenging and little progress has been made, though targeting LSD1 presents a viable therapeutic strategy for ES. Seclidemstat (SP-2577, Salarius Pharmaceuticals) is a first-in-class, orally bioavailable, small molecule with reversible and noncompetitive selective inhibition of LSD1 at low nanomolar concentrations (IC_{50}: 25-50 nM). Seclidemstat inhibits LSD1's scaffolding functions and enzymatic activity to help reverse aberrant gene expression. *In vitro* data show that treatment with seclidemstat, or seclidemstat analog, modulates EWS/ETS transcriptional activity, down-regulating oncogene expression and up-regulating tumor-suppressor gene expression. In *in vivo* xenograft studies (e.g., SK-N-MC, A673), mice treated with seclidemstat show significant tumor growth inhibition/regression vs the control vehicle group. **Methods:** This phase 1/2 clinical study of seclidemstat is being conducted in relapsed or refractory ES (NCT03600649). The trial is an open-label, non-randomized dose-escalation/dose-expansion study designed to determine the maximum tolerated dose through single-patient dose escalation followed by traditional 3+3 design. The primary objective is to assess seclidemstat's safety and tolerability while secondary objectives include pharmacokinetics, efficacy and exploratory pharmacodynamic markers. Patients must be $\geq$12 years old, have received at least 1 prior line of therapy including a prior camptothecin-based regimen, with a life expectancy $>$ 4 months. All patients receive seclidemstat twice-daily (BID) as oral tablets until unacceptable toxicity or disease progression. Patients are followed for survival until the end of study. The trial is currently recruiting across 8 locations in the United States. Upon identification of the recommended phase 2 dose, that cohort will be expanded to enroll a total of 20 patients. Clinical trial information: NCT03600649. Research Sponsor: Salarius Pharmaceuticals, Other Foundation, The Cancer Prevention and Research Institute of Texas (CPRIT).

TPS11568 Poster Session (Board #456), Fri, 8:00 AM-11:00 AM

LENVAGIST - A multicenter, comparative, placebo-controlled, double-blinded, phase II study of the efficacy of lenvatinib in patients with locally advanced or metastatic GIST after failure of imatinib and sunitinib. *First Author: Axel Le Cesne, Institut Gustave Roussy, Villejuif, France*

Background: GastroIntestinal Stromal Tumors (GIST) are paradigmatic models of cancers with a driver mutation of an oncogene, in which imatinib is recommended as adjuvant therapy or treatment of locally advanced and metastatic forms. After failure of imatinib (either progression or toxicity), sunitinib and regorafenib are indicated as 2nd and 3rd lines, respectively. Beyond approved drugs, tyrosine kinase inhibitors (TKI) can bring clinical benefit because some clones remain sensitive to TKI. Lenvatinib is a broad spectrum TKI targeting KIT, RET, PDGFRA, VEGFR 1-3 and FGFR 1-4, that is approved in the treatment of differentiated thyroid carcinoma and metastatic renal cell carcinoma and hepatocellular carcinoma. **Methods:** This prospective, randomized, placebo-controlled, double-blinded, multicenter trial evaluates the efficacy and safety of Lenvatinib in adult GIST patients (pts) who failed at least to previous imatinib and sunitinib. Seventy-four pts will be randomly allocated in a 1:1 ratio to receive either oral lenvatinib, at a daily dose of 24mg, or its matching placebo, continuously, until progression of disease (PD) or unacceptable toxicity. Randomization will be stratified according to the number of different previous anticancer drugs (2 or $>$ 2). The primary objective is to compare the Progression-free survival (PFS) between arms. The expected median PFS are 1.5 month in the control arm and 3.0 months in the experimental arm (HR = 0.5). Seventy one events will provide 90% power to show significant improvement in PFS, using a 2-sided log-rank test at a 10% level. Secondary endpoints include the overall survival, the objective response rate, the best overall response, the quality of life and the safety profile. Patients allocated in the placebo arm who experience PD (RECIST 1.1) may switch to active lenvatinib. Radiological endpoints will be evaluated using the RECIST 1.1. Translational objectives will be to identify blood and tumor parameters as predictive markers of lenvatinib efficacy. Recruitment has been activated in January 2020. Ten participating sites of the French Sarcoma Group will participate in the trial. Clinical trial information: NCT04193553. Research Sponsor: EISAI.

TPS11569 Poster Session (Board #457), Fri, 8:00 AM-11:00 AM

SPEARHEAD-1: A phase II trial of ADP-A2M4 SPEAR T cells in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma. *First Author: Dejka M. Araujo, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: ADP-A2M4 specific peptide enhanced affinity receptor (SPEAR) T-cells are genetically engineered to target MAGE-A4^{+} tumors in the context of HLA-A*02. MAGE-A4 has been described as having high expression in synovial sarcoma (SS) and myxoid/round cell liposarcoma (MRCLS) [1, 2]. This Phase 2 trial was initiated based on the favorable benefit:risk profile of ADP-A2M4 observed in a Phase 1 trial (NCT03132922) of ADP-A2M4 which demonstrated compelling clinical responses in patients with SS. **Methods:** This Phase 2, open-label trial (SPEARHEAD-1; NCT04044768) is designed to evaluate the efficacy, safety and tolerability of ADP-A2M4 in patients with advanced/metastatic SS or MRCLS who are HLA-A*02 positive and whose tumors express the MAGE-A4 protein. Enrolled patients are to undergo apheresis, and their isolated T-cells are then transduced with the MAGE-A4^{c1032} TCR, and expanded. Prior to ADP-A2M4 infusion, patients are to receive lymphodepleting chemotherapy consisting of fludarabine (30 mg/m^2/day x 4 days) and cyclophosphamide (600 mg/m^2/day x 3 days). Patients are to receive $1 - 10 \times 10^9$ transduced T-cells. An independent Data Safety Monitoring Board will review ongoing safety and benefit:risk during the interventional phase of the study. Disease will be assessed by independent review per RECIST v1.1 by CT/MRI at weeks 4, 8, 12, 16, 24, and every 2 months thereafter until confirmed disease progression. As of 24 Jan 2020, there were 17 clinical sites open in the US, one in Canada, and two in Spain. References: 1. Iura K, et al. Cancer-testis antigen expression in synovial sarcoma: NY-ESO-1, PRAME, MAGEA4, and MAGEA1. Human Pathology 2017; 61:130-139. 2. Iura K, et al. MAGEA4 expression in bone and soft tissue tumors: its utility as a target for immunotherapy and diagnostic marker combined with NY-ESO-1. Virchows Archiv 2017;471: 383–392. Clinical trial information: NCT04044768. Research Sponsor: Adaptimmune Therapeutics plc.

TPS11570 Poster Session (Board #458), Fri, 8:00 AM-11:00 AM

NCI protocol 10250: A phase II study of temozolomide and olaparib for the treatment of advanced uterine leiomyosarcoma. *First Author: Matthew Ingham, Columbia University Irving Medical Center, New York, NY*

Background: Soft tissue sarcoma (STS) is a heterogenous malignancy of mesenchymal origin and includes more than 50 biologically distinct subtypes. Leiomyosarcoma (LMS), a neoplasm of smooth muscle origin, represents up to 20% of STS. The uterus is the most common site of origin in women. Advanced uterine LMS (uLMS) is initially treated with gemcitabine + docetaxel or anthracycline-based chemotherapy but overall survival remains $<$ 24 mos. Besides recurrent alterations in RB1, TP53 and ATRX, insight into cancer biology of uLMS remains limited. Recently, whole exome and transcriptomic sequencing studies suggest uLMS harbors characteristic defects in the homologous recombination (HR) DNA repair pathway and thus features of BRCAness. HR-deficient cancers are unable to efficiently repair double-stranded DNA breaks and appear sensitive to treatment with poly ADP-ribose polymerase (PARP) inhibitors. In preclinical studies, the combination of temozolomide (T), an alkylating agent, and olaparib (O), a PARP inhibitor, was synergistic and markedly suppressed proliferation of uLMS models. A recent phase II study in small cell lung cancer defined the RP2D for T + O where the chief toxicity was myelosuppression. **Methods:** NCI Protocol #10250 is a single-arm, open-label, multi-center phase II clinical trial of T + O in patients with advanced uLMS. Eligible pts have ECOG PS $\leq$ 2, progression on $\geq$ 1 prior line of therapy and disease measurable by RECIST v1.1 and amenable to image-guided biopsy. Pts receive T 75 mg/m2 PO daily + O 200 mg PO BID on days 1-7 in 21-day cycles. The 1° endpoint is objective response rate (ORR). A one-stage binomial design is used to evaluate for an ORR $\leq$ 10% (null hypothesis) versus $\geq$ 35% (alternative hypothesis). The design calls for 22 patients. If 5/22 respond, the treatment is promising. This design yields 93% power and 1-sided type I error of 6%. 2° endpoints include progression free survival and safety. All pts undergo tumor biopsies pre-treatment and during cycle 2. Tissue is used for correlative analysis interrogating uLMS for features of BRCAness through (a) whole exome sequencing/RNAseq to evaluate for alterations in HR pathway component genes, (b) RAD51 foci formation by immunohistochemistry as a functional marker of HR pathway activity and (c) protein expression of Schlafen family member number 11 (SLFN11), an emerging biomarker for PARPi. Tumors are also evaluated for MGMT protein expression, a known determinant of sensitivity to T. The study opened to accrual 10/2019. Clinical trial information: NCT03880019. Research Sponsor: U.S. National Institutes of Health, Conquer Cancer Foundation of the American Society of Clinical Oncology.

TPS11571 Poster Session (Board #459), Fri, 8:00 AM-11:00 AM

Safety and activity of autologous T cells with enhanced NY-ESO-1–specific T-cell receptor (GSK3377794) in HLA-a*02$^+$ previously-treated and -untreated patients with advanced metastatic/unresectable synovial sarcoma: A master protocol study design (IGNYTE-ESO). *First Author: Sandra P. D'Angelo, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: T cells modified to target NY-ESO-1 have shown encouraging activity in HLA-A*02$^+$ patients with NY-ESO-1–positive synovial sarcoma. NY-ESO-1 is a cancer/testis antigen that is expressed across multiple tumor types and highly expressed in synovial sarcoma. NY-ESO-1 TCR T (GSK3377794) are autologous polyclonal T cells transduced by a self-inactivating lentiviral vector to express an affinity-enhanced TCR able to recognize NY-ESO-1 epitope in complex with HLA-A*02. Ongoing trials are evaluating GSK3377794 in multiple solid tumors and multiple myeloma. **Methods:** This study (NCT03967223) uses a Master Protocol design that allows investigation of GSK3377794 in multiple tumor types under the same protocol in separate substudies. The first two are single-arm substudies in patients with advanced metastatic or unresectable synovial sarcoma: treatment-naïve (1st line [1L], substudy 1; n = 10 planned) and progressing after anthracycline-based chemotherapy (2L+, substudy 2; n = 55 planned). Patients must be aged ≥10 years, have adequate organ function, ECOG performance status 0–1, measurable disease, and no central nervous system metastases. Excluded prior treatments include gene therapy with an integrating vector or NY-ESO-1–specific T cells, vaccine or targeting antibody, or allogeneic stem cell transplant. Patients will undergo leukapheresis and manufacture of GSK3377794; lymphodepletion then GSK3377794 infusion, followed by safety and disease assessments; and long-term follow-up for 15 years (under a separate protocol). The primary objective of substudy 2 is overall response rate per RECIST v1.1 by central independent review. Secondary objectives include time to response, duration of response, disease control rate, progression-free survival, overall survival, plus safety and tolerability. Exploratory objectives include assessment of the correlation of T-cell persistence with safety, clinical responses, and infused T-cell phenotype. Evaluation of quality of life and daily functioning of patients will also be assessed. Enrollment began in December 2019. These data are presented on behalf of the original authors with their permission. A similar presentation (P453) was presented at the SITC Annual Meeting, National Harbor, MD, USA, Nov 6–10, 2019. Funding: GlaxoSmithKline (208467) Clinical trial information: NCT03967223. Research Sponsor: GlaxoSmithKline.

TPS11572 Poster Session (Board #460), Fri, 8:00 AM-11:00 AM

The TNT protocol: A phase II study using talimogene laherparepvec (TVEC), nivolumab (N) and trabectedin (T) as first, second/third line therapy for advanced sarcoma, including desmoid tumor and chordoma. *First Author: Sant P. Chawla, Sarcoma Oncology Research Center, Santa Monica, CA*

Background: Talimogene laherparepvec (TVEC), an oncolytic HSV expressing huGMCSF, may be synergistic with trabectedin (T) and nivolumab (N) in treating advanced sarcoma. Objectives: (1) To evaluate the best overall response by RECIST v1.1, progression-free survival rate (PFS), and overall survival rate, (2) To determine the incidence of conversion of an unresectable tumor to a resectable one, and (3) To evaluate the incidence of adverse events related to the drug combination. **Methods:** This is an open label phase 2 study. A total of 40 patients will receive T (1.2 mg/m2 CIV over 24 hours q3 weeks), N (240 mg IV over 30 min q 2 weeks) and TVEC (intratumorally q 2 weeks according to tumor size). Eligible patients are those with histopathologically confirmed diagnosis of locally advanced, unresectable or metastatic sarcoma including desmoid tumor and chordoma, previously untreated or treated, with measurable disease by RECIST v1.1, and at least, one accessible tumor for intratumoral injection of TVEC. Currently, 31 of the 40 patients have been enrolled. Statistical Considerations: Continuous variables will be summarized by the sample size (n), mean, standard deviation, first and third quartiles, minimum and maximum. Categorical variables will be summarized by the n and percent in each category. Point estimates for efficacy endpoint incidences will be accompanied by a 2-sided 95% exact binomial CI. Time to event endpoints will be summarized descriptively using the KM method. Safety (incidence and severity of adverse events and significant laboratory abnormalities) will be performed on all patients (ITT population). Patient incidence of all treatment emergent AEs will be tabulated by system organ class and preferred term. Clinical trial information: 03886311. Research Sponsor: AmGen.

TPS11573 Poster Session (Board #461), Fri, 8:00 AM-11:00 AM

A phase Ib/III randomized, double-blind, placebo-controlled study of tazemetostat plus doxorubicin as frontline therapy for patients with advanced epithelioid sarcoma. *First Author: Shiraj Sen, Sarah Cannon Research Institute at HealthONE, Denver, CO*

Background: Epithelioid sarcoma (ES) is characterized by loss of inhibitor of integrase 1 (INI1), allowing enhancer of zeste homologue 2 (EZH2) to repress cell differentiation and promote tumorigenesis. Tazemetostat (TAZ) is an EZH2 inhibitor approved by the FDA as monotherapy for the treatment of patients (pts) aged ≥16 years with metastatic or locally advanced ES ineligible for complete resection. The most common (> 20%) adverse events include pain, fatigue, nausea, decreased appetite, vomiting, and constipation. TAZ demonstrated anticancer activity in ES pts who previously received doxorubicin (dox), a commonly used front line FDA approved therapy for soft tissue sarcomas (STS), including ES. Preclinical studies have demonstrated synergy between TAZ and dox. This phase 1b/3 study (NCT04204941) is assessing the safety and efficacy of TAZ + dox in pts with advanced ES. **Methods:** This study is enrolling treatment-naïve adult pts with histologically confirmed STS (phase 1b) or INI1-deficient ES pts (phase 3) with ECOG performance status of 0-2 and life expectancy of ≥3 months. The open-label phase 1b portion is currently enrolling up to 24 patients with STS. The primary objectives are to evaluate the safety and tolerability of TAZ + dox, and to identify the recommended phase 3 dose (RP3D). Using a standard 3 + 3 design, TAZ will be evaluated at 3 dose levels (400 mg, 600 mg, and 800 mg orally BID) with standard fixed dose of dox (75 mg/m^2 on day 1 of 21-day cycles for up to 6 cycles). After completion of dox, pts will continue to receive TAZ monotherapy until disease progression or intolerable toxicity. Up to 12 additional pts will be enrolled at the maximum tolerated dose for collection of additional safety and pharmacokinetic (PK) data. The double-blind phase 3 study will randomize (1:1) up to 140 pts to receive either TAZ (RP3D) + dox (75 mg/m^2) or placebo + dox. The adaptive study design will allow sample size re-estimation (at interim analysis) to up to 200 pts. Pts may continue TAZ or placebo monotherapy after completing 6 cycles of TAZ + dox. Tumor assessments will be performed at screening and every 6 weeks from the start of dosing. The primary objective of phase 3 will be to evaluate the progression-free survival (PFS) by independent review committee. Secondary objectives will include assessment of PFS by investigators, overall survival, safety, disease control rate, overall response rate, duration of response, time to subsequent anticancer therapy, PFS on next treatment, quality of life, and PK. Clinical trial information: NCT04204941. Research Sponsor: Epizyme, Inc.

12000 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Multisite randomized trial of integrated palliative and oncology care for patients with acute myeloid leukemia (AML). *First Author: Areej El-Jawahri, Massachusetts General Hospital, Boston, MA*

Background: Patients with AML receiving intensive chemotherapy experience substantial decline in their quality of life (QOL) and mood during their hospitalization for induction chemotherapy and often receive aggressive care at the end of life (EOL). We sought to examine the effect of integrated palliative and oncology care on QOL, mood, post-traumatic stress (PTSD) symptoms, and EOL outcomes in patients with AML. **Methods:** We conducted a multi-site randomized trial of integrated palliative and oncology care (n = 86) versus usual oncology care (n = 74) for patients with AML undergoing intensive chemotherapy. Patients assigned to the intervention were seen by palliative care clinicians at least twice per week during their hospitalization for induction chemotherapy and all subsequent hospitalizations. Patients completed the Functional Assessment of Cancer Therapy-Leukemia, the Hospital Anxiety and Depression Scale, and the PTSD Checklist to assess their QOL, mood, and PTSD symptoms at baseline, weeks 2, 4, 12, and 24. The primary endpoint was QOL at week-2. We used analysis of covariance and mixed linear effect models, controlling for baseline scores, to assess the effect of the intervention on patient-reported outcomes. **Results:** Between 1/2017 and 7/2019, we enrolled 160/235 (68.1%) of eligible patients. Compared to those receiving usual care, intervention patients reported better QOL (107.59 vs. 116.45, P = 0.039) and lower depression (7.20 vs. 5.68, P = 0.021), anxiety (5.94 vs. 4.53, P = 0.018), and PTSD symptoms (31.69 vs. 27.79, P = 0.009) at week 2. Intervention effects were sustained up to week 24 for QOL (B = 2.35, P = 0.048), depression (B = -0.42, P = 0.039), anxiety (B = -0.38, P = 0.042), and PTSD symptoms (B = -1.43, P = 0.002). Among deceased participants, those receiving the intervention were more likely to report discussing their EOL care preferences with their clinicians (75.0% vs. 40.0%, P = 0.009) and less likely to receive chemotherapy in the last 30 days of life (34.9% vs. 65.9%, P = 0.008). There was no difference in hospice utilization or hospitalization at the EOL. **Conclusions:** The integrated palliative and oncology care model for patients with AML receiving intensive chemotherapy led to substantial improvements in patients' QOL, psychological distress, and EOL care. Thus, palliative care should be considered a new standard of care for patients with AML. Clinical trial information: NCT02975869. Research Sponsor: Lymphoma and Leukemia Society.

12001 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A randomized trial of a palliative care intervention for patients on phase I studies. *First Author: Thomas J. Smith, Johns Hopkins University School of Medicine, Baltimore, MD*

Background: The purpose of this study was to test a Palliative Care Intervention for patients with solid tumors enrolled in phase I therapeutic trials. **Methods:** This randomized trial compared patients accrued to phase I Clinical Trials in groups of Usual Care compared to a Palliative Care Intervention (PCI) in two comprehensive cancer centers. The PCI included assessment of quality of life (QOL) and symptoms, an interdisciplinary meeting to discuss the care plan, including goals of care, and two nurse-delivered teaching sessions. Subjects (n=479) were followed for 24 weeks, with 12 weeks as the primary outcome point. **Results:** Outcomes revealed that relative to Usual Care, PCI subjects showed less Psychological Distress (1.9 in Intervention and 1.2 in Control pts, p=0.03) and a trend toward improved QOL (3.7 versus 1.6, p=0.07), with differences between sites. We observed high rates of symptom-management admissions (41.3%) and low rates of Advance Directive completion (39%), and use of supportive care services including hospice (30.7%, for only1.2 months duration), despite a median survival for all patients in both groups of 10.1 months from initiating a phase 1 study until death. Patient satisfaction with oncology care was already high at baseline, and we did not see clinically significant changes in those scores by week 12. **Conclusions:** Palliative care interventions can improve QOL outcomes and distress for patients participating in phase 1 trials. Greater integration of PC is needed to provide quality care to these patients and to support transitions from treatment to supportive care, especially at the end of life. Clinical trial information: NCT01828775. Research Sponsor: U.S. National Institutes of Health.

12002 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Effect of integrating machine learning mortality estimates with behavioral nudges to increase serious illness conversions among patients with cancer: A stepped-wedge cluster randomized trial. *First Author: Chris Manz, University of Pennsylvania, Philadelphia, PA*

Background: Most patients with cancer die without a documented serious illness conversation (SIC) about prognosis and goals. Interventions that increase SICs between oncology clinicians and patients may improve goal-concordant care and end-of-life outcomes. **Methods:** In this stepped-wedge cluster randomized trial (NCT03984773), we tested the effect of an intervention delivering machine learning-based mortality estimates with behavioral nudges to oncologists to increase SICs among patients with cancer. The clinician-focused intervention consisted of 1) weekly emails providing individual SIC performance feedback (number of SICs in the past month) and peer comparisons; 2) a list of patients scheduled for the next week with a ≥10% predicted risk of 6 month mortality by a validated machine learning prognostic algorithm, and 3) automated opt-out text prompts on the patient's appointment day to consider an SIC. Eight medical oncology clinics were randomized to receive the intervention in a stepped-wedge fashion every four weeks for a total of 16 weeks. Medical oncology clinicians were included if they were trained to use the SIC Guide (Ariadne Labs, Boston MA). Patients were included if they had an outpatient encounter with an eligible clinician between June 17 and November 1, 2019. The primary outcome was the percent of patient encounters with a documented SIC. Intention to treat analyses adjusted for clinic and wedge fixed effects and clustered at the oncologist level. **Results:** The sample consisted of 78 clinicians and 14,607 patients. The mean age of patients was 61.7 years, 55.7% were female, 70.4% were white, and 19.6% were black. The percent of patient encounters with an SIC was 1.2% (106/8536) during the pre-intervention period and 4.0% (401/10,152) during the intervention period. In intention to treat adjusted analyses, the intervention led to a significant increase in SICs (adjusted odds ratio, 3.7; 95% CI, 2.5 to 5.4, *P* value < 0.0001). **Conclusions:** An intervention consisting of machine learning mortality estimates and behavioral nudges to oncology clinicians increased SICs by three-fold over 16 weeks, a significant difference.This is one of the first studies evaluating a machine learning-based behavioral intervention to improve serious illness communication in oncology. Secondary analyses (completed April 2020) will clarify whether this intervention leads to a sustained increase in SIC rates and improves goal-concordant care and end-of-life outcomes. Clinical trial information: NCT03984773. Research Sponsor: Penn Center for Precision Medicine Accelerator Grant.

12003 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

ACUFOCIN: Randomized clinical trial of ACUpuncture plus standard care versus standard care alone FOr Chemotherapy Induced peripheral Neuropathy (CIPN). *First Author: Andrew M. Wardley, The Christie NHS Foundation Trust, Manchester Academic Health Science Centre & Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology Medicine & Health, University of Manchester, Manchester, United Kingdom*

Background: CIPN is a dose limiting toxicity, and a major clinical challenge. This study aims to explore the use of acupuncture with standard care (Acu +SC) against SC alone, to reduce symptoms of CIPN. **Methods:** A phase II, randomised, parallel group design was used to investigate the effectiveness of a 10 week course of acupuncture to manage CIPN. Patients experiencing CIPN ≥ Grade II (CTCAE v4.03), recording a 'Most Troublesome' CIPN symptom score of ≥ 3 using the "Measure Yourself Medical Outcome Profile" (MYMOP 2), were randomised (1:1) to either Acu+SC or SC alone. The primary end-point was a ≥ 2 point improvement in MYMOP2 score at week 10 (logistic regression adjusted for stratification factors and baseline MYMOP2 score). The necessary sample size was 100 patients;120 were randomised to allow for attrition (90% power; 10% one-sided alpha), for a hypothesised improvement in success proportions from 30% to 55%. **Results:** 120 patients were randomised to ACUFOCIN; diagnosis: breast 61 (51%), multiple myeloma 9 (8%), GI 48 (40%), gynaecological 2 (2%). MYMOP2 score for most troubling CIPN symptom at baseline: 3-4 33 (28%), 5-6 87 (73%). CTCAE CIPN at baseline; grade II 103 (86%), grade III 17 (14%). Baseline characteristics were balanced between arms. Primary outcome data were available for 108 participants with 36/54 (67%) successes in the Acu+SC arm compared to 18/55 (33%) in the SC arm. Adjusted success odds ratio was 4.3 (95% CI 1.9-9.6; p < 0.001; Acu+SC vs SC). Additionally, 27/53 (51%) participants achieved a CIPN success (grade ≤ I) in the Acu+SC arm compared to 4/56 (7%) in the SC arm with adjusted odds ratio 13.1 (95% CI 4.1-41.7; p < 0.001; Acu+SC vs SC). Significant reduction in week 10 pain score; mean difference (SC+Acu – SC alone) -1.45 with 95% CI (-2.25, -0.65) after adjustment for week 1 pain, breast cancer diagnosis and treatment complete status. (note pain on a 0-10 scale). Significant increase in the EORTC QLQ-C30 summary score; mean difference (SC+Acu – SC alone) 9.51 with 95% CI (5.01, 14.02) after adjustment for the baseline score, breast cancer diagnosis and treatment complete status. (note summary score on a 0-100 scale). Significant effects seen at week 10 are also present at week 6. The week 6 effect estimates are consistently less than the week 10 effects (but not usually statistically significantly so). **Conclusions:** In this patient cohort, a 10 week course of acupuncture significantly improved symptoms of CIPN. These results support further investigation within a phase III trial. Clinical trial information: NCT02275403. Research Sponsor: National Institute for Health Research.

12004 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Effects of electroacupuncture and auricular acupuncture for chronic pain in cancer survivors: The PEACE randomized controlled trial. *First Author: Jun J. Mao, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: The national opioid crisis has created new challenges in oncology pain management and highlighted an urgent need for non-pharmacological treatments. We evaluated the comparative effectiveness of electro-acupuncture (EA) and auricular acupuncture (AA) versus usual care (UC) for chronic musculoskeletal pain in cancer survivors. **Methods:** We conducted a randomized controlled trial of cancer survivors experiencing moderate-severe musculoskeletal pain for at least 3 months. EA used a semi-individualized protocol involving electrical stimulation of needles placed in the body. AA used the standardized Battlefield Acupuncture protocol involving up to 10 needles placed in the ears. EA and AA groups received 10 weekly treatments, whereas participants in the UC group received standard care prescribed by their providers. The primary endpoint was average pain severity change measured by the Brief Pain Inventory at week 12 compared to baseline. Functional interference and quality of life were secondary outcomes. We analyzed longitudinal mixed-effects models based on intent-to-treat principles. **Results:** Among 360 participants, mean age (SD) was 62.1 (12.7) years, 251 (69.7%) were women, and 88 (24.4%) were non-white. Compared from baseline to week 12, EA significantly reduced pain severity by 1.9 points (95% Confidence Interval 1.5-2.3, $p < 0.001$), and AA significantly reduced pain severity by 1.6 points (1.1-2.0, $p < 0.001$). AA was non-inferior to EA at reducing pain severity ($p = 0.04$). Both EA and AA also significantly improved functional interference (both $p < 0.001$), physical health (both $p < 0.001$), and mental health ($p = 0.003$, $p < 0.001$) compared to UC. Adverse events (AEs) were mild in both groups; however, 16 (11.2%) in AA stopped treatment due to AEs (mostly ear discomfort) as compared to 1 in EA (0.7%), $p = 0.001$. **Conclusions:** Among cancer survivors with chronic musculoskeletal pain, both EA and AA effectively reduced pain and improved quality of life. AA was non-inferior to EA at reducing pain but associated with higher discontinuation rates. These results will guide implementation of acupuncture in oncology care to address the unmet pain management needs of cancer survivors in the era of the opioid epidemic. Clinical trial information: NCT02979574. Research Sponsor: Department of Defense, U.S. National Institutes of Health.

12005 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Effects of YOCAS yoga, cognitive behavioral therapy, and survivorship health education on insomnia: A URCC NCORP Research Base Phase III RCT in 740 cancer survivors. *First Author: Karen Michelle Mustian, University of Rochester Medical Center, Rochester, NY*

Background: Insomnia, a prevalent and troublesome side effect experienced by cancer survivors, significantly impairs recovery and survival. We conducted a nationwide, multicenter, phase III, blinded, randomized controlled trial testing whether 1) yoga is superior to survivorship health education (SHE) and 2) yoga is non-inferior to cognitive behavioral therapy for insomnia (CBT-I) for treating insomnia in survivors. **Methods:** The trial was conducted via the University of Rochester Cancer Center NCI Community Oncology Research Program (URCC NCORP) Research Base. Participants were cancer survivors between 2-60 months post adjuvant therapy, with insomnia, no metastatic disease, and no yoga participation during the previous 3 months. Survivors were randomized into 1) YOCAS yoga (2x/wk; 75 min/sess for 4 wks with pranayama, asana, and dhyana, N = 251), 2) CBT-I (1x/wk, 90 min/sess for 8 wks with sleep hygiene, stimulus control, sleep restriction, and cognitive therapy, N = 238), or 3) SHE (2x/wk; 75 min/sess for 4 wks with ASCO-recommended survivorship education, N = 251). Insomnia was assessed pre- and post-intervention via the Insomnia Severity Index. **Results:** 740 eligible cancer survivors were enrolled (93% female, mean age = 56 + 11, 75% breast cancer). ANCOVAs with baseline values as covariates revealed YOCAS is significantly better than SHE for treating insomnia at post-intervention (CS = change score; CS mean diff = -1.43, SE = 0.42, $p < 0.01$). Yoga participants demonstrated greater improvements in insomnia from pre- to post-intervention (CS = -3.61, SE = 0.30) compared to SHE participants (CS = -2.19, SE = 0.33, all $p < 0.01$). Intent-to-treat analyses of non-inferiority (non-inferiority margin set at 1.15 a priori) showed YOCAS is inferior to CBT-I (CS mean diff = 3.52, CI = 2.55 - 4.50, $p < 0.01$). However, analyses of non-inferiority using the optimal treatment effect in fully compliant survivors were inconclusive regarding whether YOCAS is non-inferior to CBT-I for treating insomnia (CS mean diff = 2.20, CI = 0.42 - 3.98, $p = 0.09$). Significantly more survivors withdrew from CBT-I and SHE due, in part, to disliking the interventions compared to YOCAS (30%, 25%, and 16%, respectively, $p < 0.01$). **Conclusions:** YOCAS yoga is better than SHE and results are inconclusive as to whether yoga is non-inferior to CBT-I for treating insomnia among survivors. Clinicians should consider prescribing YOCAS and CBT-I for survivors reporting insomnia. Funding: NCI UG1CA189961, R01CA181064, T32CA102618. Clinical trial information: NCT02613364. Research Sponsor: U.S. National Institutes of Health.

12006 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Neuroleptic rotation for refractory agitation in cancer patients with delirium in the acute palliative care unit: A double-blind randomized clinical trial. *First Author: David Hui, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Terminal agitation commonly occurs in the last days of life and is highly distressing. The role of neuroleptics is controversial and few studies have examined agitation as a primary outcome. We assessed the effect of 3 neuroleptic strategies on refractory agitation in cancer patients with terminal delirium. **Methods:** In this single-center, double-blind, double-dummy parallel group randomized trial, patients admitted to a palliative and supportive care unit with refractory agitation despite low dose haloperidol were randomized in a 1:1:1 ratio to (1) haloperidol dose escalation, (2) neuroleptic rotation to chlorpromazine, or (3) combined haloperidol and chlorpromazine. Intravenous medications at equivalent doses were scheduled every 4 h and every 1 h as needed until discharge. The primary outcome was change in Richmond Agitation Sedation Scale (RASS) from time 0 to 24 hours. With 15 patients per group and 13 measurements over time, we had 90% power to detect an effect size of 0.2 with alpha=2.5%. One way ANOVA was used to examine within group differences. We also compared among groups with the Wilcoxon rank sum test. **Results:** 68 patients were enrolled and 45 received the blinded study interventions. The median survival was 73 h (95% CI 49, 106 h). RASS decreased significantly within 30 minutes and remained low at 24 hours in the dose escalation group (mean RASS change between 0 and 24 h [95% CI]: -3.6 [-5, -2.2]) v. rotation group (-3.3 [-4.4, -2.2]) v. combination group (-3 [-4.6, -1.4]), with no difference among groups (P=0.71). A majority of patients were perceived to be more comfortable after treatment by blinded caregivers (escalation v. rotation v. combination: 62% v. 71% v. 60%; P=0.83) and bedside nurses (64% v. 75% v. 64%; P=0.82); however, the rotation group had significantly fewer breakthrough restlessness (escalation v. rotation v. combination: 73% v. 19% v. 50%; P=0.009), required fewer upward dose titration (escalation v. rotation v. combination: 27% v. 6% v. 50%; P=0.03) and required less rescue neuroleptics in the first 24 hours (haloperidol equivalent: 4 mg vs. 2 mg vs. 6 mg, P=0.09, trend only). Hypotension was more frequently observed with chlorpromazine. Overall survival did not differ (>0.99). **Conclusions:** Preliminary data from this study supported that all 3 strategies of neuroleptics reduced agitation and improved comfort in patients with terminal delirium; however, neuroleptic rotation provided better agitation control and confirmatory studies are needed. Clinical trial information: NCT03021486. Research Sponsor: U.S. National Institutes of Health.

12007 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

A phase III randomized, double-blind placebo controlled study of armodafinil (Nuvigil) to reduce cancer-related fatigue in patients with high-grade glioma (Alliance A221101). *First Author: Alyx B. Porter, Mayo Clinic, Phoenix, AZ*

Background: Up to 96% of patients with high grade glioma (HGG) report moderate to severe fatigue. Armodafinil, the R-enantiomer of modafinil, is a psychostimulant with low potential for abuse that has shown potential for improving severe fatigue in HGG patients. **Methods:** In this phase III double blinded placebo-controlled study, adults with HGG and moderate to severe fatigue, > 4 weeks after completing radiotherapy, were randomized to receive armodafinil daily (150 mg or 250 mg) or placebo for a total of 8 weeks. The primary outcome was efficacy in treating severe fatigue. Secondary outcomes included evaluation of tolerability, neurocognitive function, and quality of life. Patients were evaluated at baseline, 4 and 8 weeks. **Results:** A total of 328 patients were enrolled between 6/3/13-3/1/19. There were 103 (150 mg arm), 97 (250 mg arm) and 97 (placebo arm) evaluable patients with primary endpoint data available. The median age was 60 years (20-85) with a median Brief Fatigue Inventory (BFI) *worst* fatigue score of 8 (6-10). 60.3% were male, 80.5% received concomitant chemotherapy, and 39.7% were on corticosteroids. The global fatigue score at end of weeks 4 and 8 were lower than at baseline ($p<0.0001$) and in the 250 mg arm than placebo ($p=0.0356$) and was higher for corticosteroid users than non-users ($p=0.0002$). There was no statistically significant difference for clinically meaningful improvement in BFI *usual* fatigue score from baseline to end of week 8 between the three arms ($p=0.9601$). Patients reported an improvement in concentration at week 4 from baseline on the 150 mg arm($P=0.0311$). There was no statistically significant difference on neurocognitive tests from baseline to end of week 4 ($p>0.05$) or week 8 ($p>0.05$) between arms. More patients reported insomnia on the 250 mg arm ($p=0.0083$). **Conclusions:** There is no meaningful benefit of the use of armodafinil to reduce moderate to severe fatigue in patients with HGG. In certain cases there may be benefit of armodafinil 150 mg to aid concentration without the risk of insomnia.Support: UG1CA189823;U10CA180868 (NRG). Clinical trial information: NCT01781468. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

12008 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Results of crossover phase II component of randomized placebo-controlled trial evaluating oral THC/cannabis extract for refractory chemotherapy-induced nausea and vomiting (CINV). *First Author: Peter S. Grimison, Chris O'Brien Lifehouse, Sydney, Australia*

Background: The aim of this multi-centre, randomised, double-blinded, placebo-controlled, phase 2/3 trial is to determine efficacy of addition of oral cannabis in adults with any malignancy of any stage, experiencing CINV during moderate-highly emetogenic intravenous chemotherapy, despite guideline-consistent anti-emetic prophylaxis, requiring ≥ 2 chemotherapy cycles. Here we report the crossover phase 2 component results. **Methods:** Treatment consisted of 1 cycle of oral THC 2.5mg/CBD 2.5mg (TN-TC11M) capsules *tds* days -1 to 5 and 1 cycle matching placebo in a crossover design, then blinded patient preference for a 3rd cycle. Primary end-point is difference in proportion of patients with 'complete response' (no emesis & no use of rescue medications) during 0-120 hours from chemotherapy between cycles. 80 patients provides 80% power with 2p of 0.1 to detect a 20% difference. **Results:** 81 patients recruited (2016-9). 72 completing 2 cycles are included in efficacy analyses. 78 not withdrawing consent are included in safety analyses. Median age was 55 years (range 29-80), 78% were female, 42% report historic cannabis use, 55% were treated with curative intent. Most common regimens were AC (26%), FOLFOX (17%). All received steroids & 5-HT3 antagonist, 79% received NK-1 antagonist, 4% received olanzapine. Efficacy is shown in table. 83% preferred cannabis to placebo. Most common bothersome cannabinoid-related adverse events (cannabis, placebo) were sedation (19%,4%), dizziness (10%,1%), disorientation (3%,0%). No SAEs were attributed to THC/CBD. **Conclusions:** Addition of oral THC/CBD to standard anti-emetics was associated with less nausea & vomiting but additional side effects. Most preferred THC/CBD to placebo. Based on these positive results, the definitive parallel phase 3 trial component continues (additional n=170). Acknowledgements: Trial participants, investigators, research staff. Funding from NSW Government Dept of Health. Clinical trial information: ACTRN12616001036404. Research Sponsor: NSW Health.

ENDPOINTS	THC/CBD* %	PLACEBO* %	Difference % (90% CI)	p-value
Complete response	25	14	11 (3,19)	0.04
No emesis	69	57	12 (2,23)	0.05
No significant nausea**	21	10	11 (3,19)	0.03
No use of rescue medications	28	15	13 (3,22)	0.03

*n=72 (crossover design) ** <2 on 10-point rating scale

12009 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

A geriatric assessment (GA) intervention to reduce treatment toxicity in older patients with advanced cancer: A University of Rochester Cancer Center NCI community oncology research program cluster randomized clinical trial (CRCT). *First Author: Supriya Gupta Mohile, University of Rochester James Wilmot Cancer Institute, Rochester, NY*

Background: GA evaluates aging-related domains (e.g., function) known to be associated with cancer treatment toxicity. In this CRCT, we evaluated if providing a GA summary with management recommendations to oncologists can reduce toxicity in older patients (pts) with advanced cancer receiving chemotherapy and/or other agents with a high reported prevalence of grade 3-5 toxicity. **Methods:** Pts aged > 70 with incurable solid tumors or lymphoma and > 1 impaired GA domain starting a new treatment regimen were enrolled. Community oncology practices were randomized to intervention (oncologists received GA summary/recommendations for impairments) or usual care (none given). The primary outcome was proportion of pts who experienced any grade 3-5 toxicity (CTCAE v.4) within 3 months. Practice staff prospectively captured toxicities; blinded oncology clinicians reviewed medical records to verify. Secondary outcomes included 6 month overall survival (OS) and treatment intensity (standard vs reduced). Outcomes were analyzed using generalized linear mixed/Cox models with Arm as a fixed effect, controlling for practice. **Results:** From 2013-19, 718 pts were enrolled from 41 practices. Age (mean 77 yrs), sex (43% women), number of impaired GA domains (median 4/8), and treatment type (chemotherapy 88%) were not different by Arm. More pts in intervention were Black (12% vs 3%, p<0.01), had GI cancer (38% vs 31%, p<0.01), and had prior chemotherapy (31% vs 23%, p=0.02). Pts in intervention experienced a lower proportion of grade 3-5 toxicity (175/349; 50%) than pts in usual care (262/369; 71%). The relative risk (RR: intervention vs usual care) of grade 3-5 toxicity was 0.74 (95% CI: 0.63-0.87; p=0.0002); the difference was mostly driven by non-heme toxicities (RR 0.73; 95% CI: 0.53-1.0, p<0.05). OS was not significantly different (71% vs 74%, p=0.3). More pts in intervention received reduced intensity treatment at cycle 1 (49% vs 35%, RR 0.81, p=0.01). Dose modifications due to toxicity were lower in intervention (42% vs 58%, p<0.0001), but results were not significant after controlling for practice (RR 0.85; 95% CI: 0.67-1.08, p=0.2). **Conclusions:** Providing GA information to oncologists reduces the proportion of older pts who experience grade 3-5 toxicity from high-risk palliative cancer treatment, without compromising OS. Reduced treatment intensity at cycle 1 may explain these results. Funding: R01CA177592, U01CA233167, UG1CA189961. Clinical trial information: NCT02054741. Research Sponsor: U.S. National Institutes of Health.

12010 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Geriatric assessment-driven intervention (GAIN) on chemotherapy toxicity in older adults with cancer: A randomized controlled trial. *First Author: Daneng Li, City of Hope National Medical Center, Duarte, CA*

Background: Geriatric assessment (GA) can predict chemotherapy (chemo) toxicity in older adults (age ≥65) with cancer. However, evidence regarding the effect of GA-driven intervention (GAIN) on the incidence of chemo toxicity has been limited. Therefore, we conducted a randomized controlled trial evaluating the impact of GAIN vs. standard of care (SOC) on chemo toxicity in older adults with cancer. **Methods:** Patients (pts) age ≥65, diagnosed with a solid malignancy, and starting a new chemo regimen at City of Hope were eligible (NCT02517034). In a 2:1 ratio, 600 pts were randomly assigned to either GAIN (n = 398) or SOC (n = 202) arms. All pts completed a baseline GA prior to chemo. In the GAIN arm, a multidisciplinary team led by a geriatric oncologist, nurse practitioner, social worker, physical/occupation therapist, nutritionist, and pharmacist, reviewed GA results and implemented interventions based on predefined triggers built into the GA's various domains. In the SOC arm, GA results were sent to treating oncologists to use at their discretion. Pts were followed until either end of chemo or 6 months after start of chemo, whichever occurred first. The primary endpoint was incidence of grade 3-5 chemo-related toxicity (NCI CTCAE v.4.0). Secondary endpoints included advance directive (AD) completion, emergency room (ER) visits, hospitalizations, and average length of stay (ALOS). Chi-square and Fisher's exact tests were used to compare the categorical outcomes, and Kruskal-Wallis test was used to compare the ALOS between arms. **Results:** Pt characteristics were balanced between arms. Median age was 71 (range 65-91). Cancer types included: 33% gastrointestinal, 23% breast, 16% lung, 15% genitourinary, and 13% other. Most (71%) had stage IV disease. The incidence of grade 3-5 chemo-related toxicity was 50.5% (95% CI: 45.6-55.4%) in the GAIN arm and 60.4% (95% CI: 53.7-67.1%) in the SOC arm (p = 0.02). Compared to SOC, the GAIN arm had a reduction of 9.9% (95% CI: 1.6-18.2%) in chemo-related toxicity. At the end of study, AD completion increased 24.1% in the GAIN arm vs. 10.4% in the SOC arm (p < 0.001). No significant differences in ER visits (27.4% vs. 30.7%), hospitalizations (22.1% vs. 19.3%), or ALOS (median 4.8 vs. 5.0 days) were observed between the GAIN and SOC arms, respectively. **Conclusions:** Integration of multidisciplinary GA-driven interventions reduced grade 3-5 chemo-related toxicity and improved AD completion in older adults with cancer. GA-driven interventions should be included as a part of cancer care for all older adults. Clinical trial information: NCT02517034. Research Sponsor: UniHealth Foundation, City of Hope's Center for Cancer and Aging.

12011 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Integrated geriatric assessment and treatment (INTEGERATE) in older people with cancer planned for systemic anticancer therapy. *First Author: Wee-Kheng Soo, Monash University Eastern Health Clinical School, Box Hill, Australia*

Background: Older people experience significant adverse effects of cancer and anti-cancer therapy due to age-related vulnerabilities, including medical, functional, cognitive, nutritional and psychosocial issues. Comprehensive geriatric assessment and management (CGAM) provides a powerful framework to assess an older person's health status and offers a coordinated, person-centered approach to care. Despite its effectiveness, the uptake of CGAM in oncology has been limited due to a lack of randomized evidence in this setting. This study evaluated the effectiveness of CGAM in older people with cancer. **Methods:** INTEGERATE is a prospective, randomized, parallel group, open-label study in patients aged >70 years with cancer planned for chemotherapy, targeted therapy or immunotherapy. Patients were randomly assigned (1:1) to receive either geriatrician-led CGAM integrated with usual care (integrated oncogeriatric care) or usual care alone, using minimization to balance treatment intent, cancer type, age, sex and performance status. Health-related quality of life (HRQOL) was assessed using the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-ELD14 at 0, 12, 18 and 24 weeks. The primary outcome was HRQOL measured by the validated Elderly Functional Index (ELFI) score. Major secondary outcomes included function, mood, nutrition, health utility, treatment delivery, healthcare utilization and survival. **Results:** Of the 154 patients who underwent randomization, 13 died by week 12 and 130 (92.2% of the remaining patients) completed at least two primary outcome assessments. For the primary outcome, patients in the intervention group had significantly better ELFI score than the usual care group across all followup timepoints, with a maximal difference at week 18 (estimated marginal mean ELFI score 72.0 vs 58.7, p= 0.001). In addition, significant differences favoring the intervention group over the usual care group were seen in HRQOL (domains: physical, role and social functioning; mobility, burden of illness and future worries), unplanned hospital admissions (-1.2 admissions per person-years, p< 0.001) and early treatment discontinuation (32.9% vs 53.2%, p = 0.01). **Conclusions:** Integrated oncogeriatric care led to improvements in HRQOL, unplanned hospital admissions and treatment discontinuation in older people receiving systemic anti-cancer therapy. Older people (>70 years) planned for anti-cancer therapy should receive CGAM to optimize their clinical care and health outcomes. Clinical trial information: ACTRN12614000399695. Research Sponsor: National Health and Medical Research Council.

12012 Clinical Science Symposium, Fri, 8:00 AM-9:30 AM

Randomized trial of a perioperative geriatric intervention for older adults with cancer. *First Author: Carolyn L. Qian, Massachusetts General Hospital, Boston, MA*

Background: Older adults with gastrointestinal (GI) cancers undergoing surgery often experience poor outcomes, such as prolonged postoperative (post-op) length of stay (LOS), intensive care unit (ICU) use, and readmissions. Involvement of geriatricians in the care of older adults with cancer can improve outcomes. We conducted a randomized trial of a perioperative geriatric intervention in older adults with GI cancers undergoing surgery. **Methods:** We randomly assigned patients age ≥65 with GI cancers planning to undergo surgical resection to receive a perioperative geriatric intervention or usual care. Intervention patients met with a geriatrician preoperatively in the outpatient setting and post-op as an inpatient consultant. The geriatrician conducted a geriatric assessment and made recommendations to the surgical/oncology teams. The primary end point was post-op LOS. Secondary end points included post-op ICU use, readmission risk, and patient-reported symptom burden (Edmonton Symptom Assessment System [ESAS]) and depression symptoms (Geriatric Depression Scale). We conducted both intention-to-treat (ITT) and per protocol (PP) analyses. **Results:** From 9/13/16-4/30/19, we randomized 160 patients (72.4% enrollment rate; median age = 72 [65-92]). The ITT analyses included 137/160 patients who underwent surgery (usual care = 68/78, intervention = 69/82). The PP analyses included the 68 usual care patients and the 30/69 intervention patients who received both pre- and post-op intervention components. In ITT analyses, we found no significant differences between intervention and usual care in post-op LOS (7.2 v 8.2 days, P = .37), ICU use (23.3% v 32.4%, p = .23), and readmission rates within 90 days of surgery (21.7% v 25.0%, p = .65). Intervention patients reported lower depression symptoms (B = -1.39, P < .01) at post-op day 5 and fewer moderate/severe ESAS symptoms at post-op day 60 (B = -1.09, P = .02). In PP analyses, intervention patients had significantly shorter post-op LOS (5.9 v 8.2 days, P = .02) and lower rates of post-op ICU use (13.3% v 32.4%, p < .05), but readmission rates were not significantly different (16.7% v 25.0%, p = .36). **Conclusions:** Although this perioperative geriatric intervention did not have a significant impact on the primary end point in ITT analysis, we found encouraging results in several secondary outcomes and for the subgroup of patients who received the planned intervention. Future studies of this perioperative geriatric intervention should include efforts, such as telehealth visits, to ensure the intervention is delivered as planned. Clinical trial information: NCT02810652. Research Sponsor: NCCN Foundation Young Investigator Award.

12013 Poster Discussion Session; Displayed in Poster Session (Board #301), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Effect of early integration of specialized palliative care into standard oncologic treatment on the quality of life of patients with advanced head and neck cancers: A phase III randomized controlled trial. *First Author: Pankaj Singhai, Tata Memorial Centre, Mumbai, India*

Background: Early palliative care is an important aspect of palliative treatment but has never been evaluated in head and neck cancer. Hence we performed this study. **Methods:** This was an open-label phase 3 randomised study which enrolled adult patients with squamous cell carcinoma of the head and neck region which warranted palliative systemic therapy. They were 1:1 allocated to either systemic therapy with (EPC arm) or without the addition of early palliative care service (STD arm). Patients were administered the Edmonton Symptom Assessment Scale (ESAS-r) and FACIT HN questionnaire at baseline and 4 weekly thereafter for 12 weeks. The primary endpoint was change in the quality of life (QOL) measured using FACIT HN 12 weeks after randomization. The secondary endpoints were changed in symptom burden at 12 weeks in ESAS-r and overall survival. A repeated-measures analysis of covariance (ANCOVA) was performed to examine the effects of arm and stratum on change in QOL (or symptom score), after controlling for baseline score. **Results:** Ninety patients were randomised in each arm between 1st June 2016 to 14th August 2017. The compliance with the questionnaires was 100% at baseline. In EPC arm the 70 patients were alive at 3 months and 67 (95.7%) completed the FACIT HN and 64 (91.4%) completed ESAS-r questionnaires. While in the STD arm out of 69 alive the corresponding figures were 61(88.4%) and 59 (85.5%) respectively. There was no statistical difference in change in QOL scores and ΔESAS-r at 12 weeks between the 2 arms (Table). The median overall survival was similar between the 2 arms. (Hazard ratio for death-1.006 (95%CI 0.7347-1.346)). **Conclusion:** In this phase 3 study, integration of early palliative care in head and neck cancer patients did not result in improvement in the quality of life scores, symptom scores or overall survival. Clinical trial information: CTRI/2016/03/006693. Research Sponsor: Tata Memorial Center Research Administration Council.

Δ Scores	Early Palliative Care arm	Standard arm	P-value
FACT HN	-4.4876 (-19.5 to 12)	-1.2514 (-11.5 to 13.5)	0.9357
FACT TOI	-2.8607 (-14 to 9)	-.1803 (-12.5 to 10.5)	0.9516
FACT G	-3.8905 (-15.6667 to 9.3333)	-1.5464 (-10 to 11)	0.8392
Pain	-0.6875 (-3 to 1)	-0.8305 (-3 to 1)	0.3079
Fatigue	0.6875 (-2 to 3)	0.322 (-2 to 3)	0.7975
Drowsiness	0.125 (-2 to 3)	1.1525 (0 to 2)	0.1985
Nausea	0.9063 (0 to 2)	0.6271 (0 to 2)	0.2954
Loss of appetite	0.2656 (-1 to 2)	-.0678 (-2 to 2)	0.3813
Depression	1.0313 (-0.75 to 4)	0.0339 (-1 to 2)	0.4678

Table depicting the mean delta (Δ) scores with the interquartile range at 12 weeks.

12014 Poster Discussion Session; Displayed in Poster Session (Board #302), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Randomized trial of a symptom monitoring intervention for hospitalized patients with advanced cancer (NCT03396510). *First Author: Ryan David Nipp, Massachusetts General Hospital Cancer Center, Boston, MA*

Background: Hospitalized patients with advanced cancer experience a high symptom burden, which is associated with poor clinical outcomes and increased health care use. Symptom monitoring interventions are increasingly becoming standard of care in oncology, but studies of these interventions in the hospital setting are lacking. We evaluated the impact of a symptom monitoring intervention in hospitalized patients with advanced cancer. **Methods:** We randomly assigned hospitalized patients with advanced cancer who were admitted to the oncology service to a symptom monitoring intervention or usual care. Patients in both arms reported their symptoms (Edmonton Symptom Assessment System [ESAS] and Patient Health Questionnaire 4 [PHQ4], higher scores on both indicate greater symptom severity) daily via tablet computers. Patients assigned to the intervention had their symptom reports presented graphically with alerts for moderate/severe symptoms during daily oncology rounds. The primary endpoint was the proportion of days with improved symptoms for those who completed two or more days of symptoms. Secondary endpoints included hospital length of stay (LOS) and readmission rates. **Results:** From 2/2018-10/2019, we randomized 390 patients (76.2% enrollment rate); 320 completed two or more days of symptoms (median age=65.6 [range 18.8-93.2]; 43.8% female). The most common cancers were gastrointestinal (36.9%), lung (18.8%), and genitourinary (12.2%). Nearly half of patients (48.5%) had one or more comorbid conditions in addition to cancer. We found no significant differences between intervention and usual care regarding the proportion of days with improved ESAS total (B=-0.05, P=.17), ESAS physical (B=-0.02, P=.52), PHQ4 anxiety (B=-0.03, P=.33), and PHQ4 depression (B=-0.02, P=.44) symptoms. Intervention patients also did not differ from usual care with respect to secondary endpoints of hospital LOS (7.50 v 7.59 days, P=.88) and readmission rates within 30 days of discharge (32.5% v 25.6%, P=.18). **Conclusions:** For hospitalized patients with advanced cancer, this symptom monitoring intervention did not have a significant impact on their symptom burden and health care use. These findings do not support the routine integration of this type of symptom monitoring intervention for hospitalized patients with advanced cancer. The positive outcomes seen in previous studies of symptom monitoring interventions may not be reproduced in other patient populations and care settings. Support: UG1CA189823; Clinical trial information: NCT03396510. Research Sponsor: U.S. National Institutes of Health.

12015 Poster Discussion Session; Displayed in Poster Session (Board #303), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Impact of augmented intelligence (AI) on utilization of palliative care (PC) services in oncology. *First Author: Ajeet Gajra, Cardinal Health, Dublin, OH*

Background: Timely integration of palliative care in the management of patients with advanced cancer is a quality benchmark in oncology. However, PC is often underutilized as evidenced by delays in identification of appropriate patients, in referrals to a PC service, and in enrollment to hospice. Jvion has developed a prescriptive analytics solution, the Machine, which combines AI algorithms with machine learning techniques and applies them to clinical and exogenous datasets to identify patients with a propensity for poor outcomes. The Machine was applied to risk for patients' mortality within next 30 days, and recommended patient-specific, dynamic, and actionable insights. Use of the Machine requires no additional documentation within the electronic health record (EHR) and the insights generated can be integrated back in to any EHR to help inform the care plan. Herein, we report the results of a study evaluating the impact of AI-driven insights on PC utilization at a large community oncology practice. **Methods:** All patients were scored weekly using the Machine PC vector. The Machine risk stratified the patients and generated recommendations for the provider to consider as they developed a care plan. Patients identified as "at risk" by the Machine were assessed for a supportive care visit (PC referral) and then were referred as deemed clinically appropriate. The average monthly rates of PC consults and hospice referrals were calculated 5 months prior to and for 17 months after the launch of the Machine in the practice. **Results:** The oncology practice has 21 providers managing an average of 4329 unique patients per month (PPM). The mean rate of PC consults increased from 17.3 to 29.1 per 1000 PPM pre and post Machine deployment respectively (+168%). The mean monthly rate of hospice referrals increased by 8-fold from 0.2 to 1.6 per 1000 PPM pre and post deployment respectively. Eliminating the first 6 months of Machine deployment to account for user learning curve, the mean rates of monthly PC consults nearly doubled over baseline to 33.0, and hospice referrals rose 12-fold to 2.4 per 1000 patients in months 7-17 post Machine deployment. **Conclusions:** This oncology practice found deployment of this novel AI solution to be feasible and effective at generating actionable insights. These AI driven insights could be incorporated into workflow and improved the decision-making for whether and when a patient should be referred to PC and/or hospice services for end of life care. Further study is needed to confirm the value of AI for management of cancer patients at end of life. Research Sponsor: Jvion and Cardinal Health.

12016 Poster Discussion Session; Displayed in Poster Session (Board #304), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Risk of cardiovascular disease in women with and without a history of breast cancer: The Pathways Heart Study. *First Author: Heather Greenlee, Fred Hutchinson Cancer Research Center, Seattle, WA*

Background: Breast cancer (BC) survivors are at increased risk of cardiovascular disease (CVD) following diagnosis, as compared to women without BC. To provide a population-based estimate of CVD risk in BC survivors, we compared risk of CVD events in women with and without BC history enrolled in the Kaiser Permanente Northern California (KPNC) integrated health system. **Methods:** Data were extracted from KPNC electronic health records. All invasive BC cases diagnosed between 2005-2013 were identified and matched 1:5 with non-BC controls on birth year, race/ethnicity and KPNC membership at date of BC diagnosis. Cox regression models were used to assess differences in the hazard of four major CVD events (ischemic heart disease (IHD), heart failure (HF), cardiomyopathy, and stroke). Models were adjusted for factors known to influence risk of breast cancer or CVD.Other CVD events included arrhythmia, cardiac arrest, carotid disease, myocarditis/pericarditis, transient ischemic attack, valvular disease, and venous thromboembolism (VTE). We additionally examined subgroups of cases who received chemotherapy, radiation, and endocrine therapy, and their controls. **Results:** A total of 14,942 women with a new diagnosis of invasive BC were identified and matched to 74,702 women without BC history. On average, women were 62.0 years, 28.3 kg/m^{2}BMI, 64.9% non-Hispanic white. Among all cases and controls, there were no significant differences in hazard of developing IHD, cardiomyopathy, and stroke; there was a borderline difference in HF (HR: 1.08, 95% CI: 0.99, 1.19). Cases were more likely to have a cardiac arrest (HR: 1.39, 95% CI: 1.09, 1.78) and develop VTE (HR: 1.97, 95% CI: 1.74, 2.23). Women treated with chemotherapy were more likely than controls to develop HF (HR: 1.44, 95% CI: 1.21, 1.72), cardiomyopathy (HR: 2.01, 95% CI: 1.02, 3.98), and VTE (HR: 3.15, 95% CI: 2.62, 3.79). Women who received radiation therapy were more likely to develop carotid disease (HR: 5.49, 95% CI: 1.22, 24.66) and VTE (HR: 1.65, 95% CI: 1.35, 2.03) than controls. Women who received endocrine therapy were more likely to experience a cardiac arrest (HR: 1.49, 95% CI: 1.07, 2.09) and develop VTE (HR: 1.70, 95% CI: 1.42, 2.03) than controls. **Conclusions:** Women with BC were at increased risk of heart failure, cardiomyopathy, cardiac arrest, VTE and carotid disease. These risks varied by cancer treatment, with higher risk in those who received chemotherapy. Future studies should explore the effects of chemotherapy class and radiation dose exposure on diverse CVD endpoints in BC survivors. Research Sponsor: U.S. National Institutes of Health.

12017 Poster Discussion Session; Displayed in Poster Session (Board #305), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Onset of cardiovascular disease risk factors in women with and without a history of breast cancer: The Pathways Heart Study. *First Author: Marilyn L. Kwan, Kaiser Permanente, Oakland, CA*

Background: Women with a history of breast cancer (BC) are at increased long-term risk of dying from cardiovascular disease (CVD). However, the onset of CVD risk factors in women with BC has not been well-described. We compared risk of incident CVD risk factors in women with and without BC enrolled in the Kaiser Permanente Northern California (KPNC) integrated health system. **Methods:** Data were extracted from KPNC electronic health records. All invasive BC cases diagnosed between 2005-2013 were identified and matched 1:5 with controls on birth year, race/ethnicity and KPNC membership at the date of BC diagnosis. Cox regression models assessed the hazard of incident hypertension (based on diagnosis codes and filled prescriptions), dyslipidemia (based on diagnosis codes, filled prescriptions, and lab values), and diabetes (KPNC Diabetes Registry). Models were adjusted for baseline BMI, menopausal status, smoking status, neighborhood median household income, education, prevalent CVD conditions, and other baseline CVD risk factors. Subgroups of women who received chemotherapy, radiation therapy, and endocrine therapy were compared with controls. **Results:** A total of 14,942 women with a new diagnosis of invasive BC were identified and matched to 74,702 controls. On average, women were 62.0 years, 28.3 kg/m^{2}BMI, 64.9% non-Hispanic white. Overall, cases were more likely to develop hypertension (HR: 1.18, 95% CI: 1.13, 1.24) and diabetes (HR: 1.23, 95% CI: 1.16, 1.31). Across the board, receipt of any of the three therapies (chemotherapy, radiation therapy and endocrine therapy) was associated with increased risk of hypertension and diabetes, compared to controls. Risk-factor specific hazard ratios for receipt of chemotherapy were (HR 1.18, 95% CI: 1.10, 1.27) and (HR 1.38, 95% CI: 1.26, 1.51), for hypertension and diabetes, respectively. For receipt of radiation therapy, risk-factor specific hazard ratios were (HR: 1.17, 95% CI: 1.09, 1.26) and (HR: 1.15, 95% CI: 1.04, 1.27), for hypertension and diabetes, respectively. Risk-factor specific hazard ratios for receipt of endocrine therapy were (HR: 1.22, 95% CI: 1.14, 1.30) and (HR: 1.16, 95% CI: 1.06, 1.27), for hypertension and diabetes, respectively. **Conclusions:** The risk of developing hypertension and diabetes is increased in women with BC who received chemotherapy, radiation therapy, and/or endocrine therapy. Future studies should examine the roles of CVD risk factor diagnosis and management on cardiometabolic risk in women with a BC history. Research Sponsor: U.S. National Institutes of Health.

12018 Poster Discussion Session; Displayed in Poster Session (Board #306), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Effect of a tailored exercise intervention during or after chemotherapy on cardiovascular morbidity in cancer patients. *First Author: Gabriela G.F. Giovanna Femma van der Schoot, Department of Medical Oncology, University Medical Center Groningen, Groningen, Netherlands*

Background: Cancer treatment outcome may be impaired due to treatment-related adverse effects like decreased cardiorespiratory fitness. Evidence on exercise during or after chemotherapy shows positive effects on cardiorespiratory fitness, fatigue and quality of life (QoL) in cancer patients. However, optimal timing of starting exercise is unknown. This study aimed to investigate if an exercise intervention that starts during chemotherapy (early group) is superior to a program starting after completion of chemotherapy (late group) to reduce cardiovascular morbidity. **Methods:** In this multicenter randomized controlled trial, 266 patients (testicular-, (n = 95), breast-, (n = 139), and colon cancer (n = 30) or non-Hodgkin lymphoma (NHL) (n = 2)), treated with curative chemotherapy were randomized to a 24 week aerobic and resistance exercise intervention starting either early, i.e. during chemotherapy (n = 131) or late, i.e. at completion of chemotherapy (n = 135) (NCT01642680). Effect on VO_2 peak was evaluated with intention-to-treat linear mixed-effect models, adjusted for baseline values (T0) and diagnosis at post-chemotherapy (T1), post-exercise intervention (T2) and 1-year post-exercise intervention (T3, i.e., primary endpoint). Here we report T0, T1 and T2 data. Secondary endpoints were QoL (EORTC-QLQ-C30) and fatigue (MFI-20), with higher scores indicating more fatigue. **Results:** Median age was 33 yrs for testicular-, 52 yrs for breast- and 64 yrs for colon cancer and NHL patients. Patients in the early group declined significantly less in VO_2 peak and QoL at T1 compared to the late group (adjusted between-group differences were 3.2 ml/min/kg (95% confidence interval CI 2.3 to 4.1, $P < 0.0001$) and 5.8 (95% CI 0.6 to 10.9, P = 0.028). Patients in the early group experienced reduced general and physical fatigue at T1 (adjusted between-group differences were -2.0 (95% CI -3.3 to -0.8, P = 0.002) and -2.9 (95% CI -4.3 to -1.5, $P < 0.0001$). At T2, VO_2 peak, QoL, general and physical fatigue were comparable and regained baseline levels (adjusted between-group differences - 0.08 ml/min/kg (P = 0.9), -1.4 (P = 0.7), 0.7 (P = 0.3) and 0.2 (P = 0.7), respectively. **Conclusions:** A supervised exercise program for patients with testicular-, breast- and colon cancer that is initiated at start of curative chemotherapy effectively reduces a decline in VO_2 peak and QoL and reduces fatigue. After completion of the exercise intervention, initiated both during and after chemotherapy, patients regained their baseline VO_2 peak, levels of fatigue and QoL. Clinical trial information: NCT01642680. Research Sponsor: Dutch Cancer Society. Grant: DCS 2011-5265.

12019 Poster Discussion Session; Displayed in Poster Session (Board #307), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Predictive model of aromatase inhibitor non-adherence using patient-reported outcomes in women with breast cancer (SWOG S1105). *First Author: Dawn L. Hershman, Columbia University Medical Center, New York, NY*

Background: Non-adherence to aromatase inhibitors (AIs) for breast cancer is common and increases risk of recurrence. Few prospective studies have systematically evaluated factors associated with non-adherence. We analyzed baseline sociodemographic, prescription, and patient reported outcome (PRO) symptoms and quality-of-life to identify factors associated with non-adherence prospectively over 3-years. **Methods:** Patients enrolled in SWOG S1105 were required to have been on an AI for ≥30 days. Patients were assessed for non-adherence to AIs every 3 months for 36 months, with non-adherence defined as urine AI metabolite assay results satisfying any of the following: < 10 ng/mL, undetectable, specimen submitted outside of the ± 21 day follow-up appointment window, or no submitted specimen. At baseline patients were asked about insurance, pill number dispensed and medication cost, and they completed PROs focused on pain and endocrine symptoms (BPI (Brief Pain Inventory), FACT-ES (Endocrine Symptoms)), as well as their beliefs about medications (TSQM (Treatment Satisfaction Questionnaire for Medicine) and BMQ (Brief Medication Questionnaire)). PRO scales were split at the median creating high vs low binary predictors. We determined the association of baseline factors and non-adherence at 36 months. We also evaluated an adverse risk model for AI non-adherence by summing the number of statistically significant adverse factors associated with non-adherence. Logistic regression was used. **Results:** In total, 724 patients were registered from 40 institutions between May, 2012 and September, 2013. The median age was 60.9 years, and 64.5% were on AI < 12 months prior to registration. Overall, 35.9% were non-adherent at 36 months. Younger patients (< 65 years) were less adherent (39% vs. 29% non-adherence, OR = 1.51, p = 0.02). Baseline scores on the BPI, FACT-ES, BMQ and TSQM were each statistically significantly associated with AI adherence. Non-adherence was significantly higher among patients scoring poorly on all 4 PRO instruments (65%) compared to those scoring poorly 0 or 1 PRO instruments (27%; OR, 4.68 [2.84-7.73], p < .0001). For each increase in the number of adverse risk PRO scores, the risk of non-adherence increased by 45% (OR = 1.45, p < .0001). Similar results were found when age was included in the score. **Conclusions:** Presence of multiple baseline risk factors identified through PRO instruments increases non-adherence to AI's 4-fold. Use of PROs can identify patients for targeted interventions to improve adherence. Research Sponsor: U.S. National Institutes of Health, Conquer Cancer Foundation of the American Society of Clinical Oncology.

12020 Poster Discussion Session; Displayed in Poster Session (Board #308), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Impact of baseline symptom burden as assessed by patient-reported outcomes (PROs) on overall survival (OS) of patients with metastatic cancer. *First Author: Atul Batra, Tom Baker Cancer Center, Calgary, AB, Canada*

Background: Patients with metastatic cancer experience variable symptom burden, but serial symptom assessments using PROs may be challenging to implement in routine clinical practices. We aimed to determine if a single measurement of symptom burden at the time of metastatic diagnosis is associated with survival. **Methods:** We examined prospectively collected baseline PROs of patients newly diagnosed with metastatic breast, lung, colorectal, or prostate cancer using the revised Edmonton Symptom Assessment System (ESASr) questionnaire from a large province (Alberta, Canada) between 2016 and 2019. The ESASr was categorized into physical (PH), psychosocial (PS), and total symptom (TS) domains whereby scores were classified as mild (0-3), moderate (4-6), or severe (7-10). Multivariable Cox proportional hazards models were constructed to evaluate the effect of baseline symptom scores on OS. **Results:** We identified 1,315 patients, of whom 57% were men and median age was 66 (IQR, 27-93) years. There were 180, 601, 240, and 294 patients with breast, lung, colorectal, and prostate cancer, respectively. Approximately one-quarter of all patients reported moderate to severe PH, PS, and TS scores, with lung cancer patients experiencing the highest symptom intensity across all domains ($P<0.0001$). While age did not affect symptom scores, women were more likely to report severe PH, PS, and TS scores as compared to men ($P=0.02$, 0.002, and 0.007, respectively). On multivariable Cox regression analysis, older age (HR 1.02, 95% CI, 1.02-1.03, $P<0.0001$) and female sex (HR 1.67, 95% CI, 1.39-1.99, $P<0.0001$) were predictive of worse OS as were severe baseline PH and TS scores (see Table) . However, baseline PS scores were not related to OS. **Conclusions:** A single assessment of baseline symptom burden using the ESASr in patients with metastatic cancer has significant prognostic value. This may represent a feasible first step toward routine collection of PROs in real-world settings where serial symptom measurements can be challenging to implement. Research Sponsor: None.

OS by symptom burden.

Group (n)	Median OS, in months (95% CI)	HR (95% CI)	*P* value
PH			
Mild (885)	33.5 (30.2-36.4)	-	-
Moderate (368)	12.2 (10.1-15.1)	1.68 (1.32-2.13)	<0.0001
Severe (62)	10.8 (4.9-17.7)	1.89 (1.26-2.83)	0.002
PS			
Mild (946)	29.1 (25.5-33.3)	-	-
Moderate (243)	16.1 (12.4-20.8)	1.15 (0.94-1.41)	0.17
Severe (117)	10.7 (8.1-16.9)	1.13 (0.85-1.52)	0.39
TS			
Mild (924)	32.5 (28.6-35.1)	-	-
Moderate (350)	12.2 (10.1-15.1)	1.27 (0.96-1.68)	0.09
Severe (41)	7.9 (3.5-16.9)	1.71 (1.01-2.91)	0.04

12021 Poster Discussion Session; Displayed in Poster Session (Board #309), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Integrating PROs with prognostic value into oncologic care: High ESAS global distress score associated with lower overall survival in advanced cancer patients. *First Author: Ishwaria Mohan Subbiah, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Despite compelling data supporting their use, patient reported outcomes (PROs) are not widely integrated into routine cancer care. In our Palliative Care (PC) practice, all patients complete the Edmonton Symptom Assessment Scale (ESAS), a simple, validated 10-item PRO tool which uses a 0 to 10 rating of 10 common symptoms (pain, fatigue, nausea, drowsiness, appetite, sleep, dyspnea, well-being, anxiety & depression). Our team has previously validated the Global Distress Score (GDS), a sum of 9 physical + psychosocial ESAS items. Here, we studied the implementation of the GDS as a streamlined way to capture the overall symptom burden while providing prognostic value. **Methods:** We queried a PC database for patients w metastatic cancer at time of 1st PC visit. GDS was calculated & grouped into 3 cohorts based on previous work & clinical experience: high (GDS of 35+), Moderate (16-34) or Low (0-15). Overall Survival was defined as time from 1st PC visit date to death. Regression analysis, ANOVA and t-tests were conducted. **Results:** 333 patients met the inclusion criteria: median age 62.4y (range 20.5-88.4y), 25 AYA (15-39y), 169 mid age (35-64y), 140 seniors (65y+); 190 female 143 male; median prior therapies 2 (range 0-11), 227 patients were in 2nd line + above therapy. Median ECOG PS 2; 124 patients w ECOG PS 3 & 33 w ECOG PS 4. 262 patients had died at time of analysis. Lower OS was associated w higher GDS (r 0.21, $P < 0.001$). OS in Low, Mod, High GDS cohorts was 13.1m, 7.9m, & 3.7m, respectively ($p < 0.001$). There were no sig OS difference between 3 age cohorts (AYA 5.2m, mid age 6m, seniors 5.4m, p0.56). **Conclusions:** Higher GDS score was associated with a clinically significant decrease in overall survival highlighting the potential of the ESAS as a PRO tool in prognostication and clinical decision making for patients with advanced cancers with a high symptom burden. In the realm of increasingly complex PRO instruments, the ESAS represents a simple, well-validated tool which, in our studies and 25 years of clinical experience, takes the patient less than a minute to complete, with subscores such as the GDS which carry a highly prognostic utility for patients with advanced cancers. Research Sponsor: None.

12022 Poster Discussion Session; Displayed in Poster Session (Board #310), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Temporal trends in opioid prescribing patterns among oncologists in the Medicare population. *First Author: Vikram Jairam, Department of Therapeutic Radiology, Yale School of Medicine, New Haven, CT*

Background: In the wake of the United States (U.S.) opioid epidemic, there have been significant governmental and societal efforts to curb opioid prescribing. However, it is unknown whether these efforts have affected prescribing among oncologists, whose patient population often requires narcotics for symptom management. We investigated temporal patterns in opioid prescribing for Medicare patients among oncologists. **Methods:** We queried the Centers for Medicare and Medicaid Services Part D prescriber dataset to identify independently practicing physicians between January 1, 2013 and December 31, 2017. We used population-averaged multivariable negative binomial regression to estimate the association between time and per-provider opioid prescribing rate, defined as number of opioid claims (original prescriptions and refills) per 100 patients, among oncologists and non-oncologists on both a national and statewide level. All models were adjusted for provider characteristics and annual total patient count per provider. **Results:** The final study sample included 20,513 oncologists and 711,636 non-oncologists. From 2013 to 2017, the national opioid prescribing rate declined by 19.3% (68.8 to 55.5 opioid prescriptions per 100 patients; $P< 0.001$) among oncologists and 20.4% (50.7 to 40.3 prescriptions per 100 patients; $P< 0.001$) among non-oncologists. During this timeframe, 40 U.S. states experienced a significant ($P< 0.05$) decrease in opioid prescribing among oncologists, most notably in Vermont (-43.2%), Idaho (-34.5%), and Maine (-32.8%). In comparison, all 50 states exhibited a significant decline ($P< 0.05$) in opioid prescribing among non-oncologists. In 5 states, opioid prescribing decreased more among oncologists than non-oncologists, including Oklahoma (-24.6% vs. -7.1%), Idaho (-34.5% vs. -17.8%), Utah (-31.7% vs. -18.7%), Texas (-19.9% vs. -14.7%), and New York (-24.0% vs. -19.7%) (all $P< 0.05$). **Conclusions:** Between 2013 and 2017, the opioid prescribing rate decreased by approximately 20% nationwide among both oncologists and non-oncologists. These findings raise concerns about whether opioid prescribing legislation and guidelines intended for the non-cancer population are being applied inappropriately to patients with cancer and survivors. Research Sponsor: None.

12023 Poster Discussion Session; Displayed in Poster Session (Board #311), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Prevalence and temporal trends of prescription drug use in cancer survivors: A population study, 2001 to 2016. *First Author: Elisa Liu, NYU School of Medicine, New York, NY*

Background: The burden of prescription drug use is higher in cancer survivors than the general population. We examined the prevalence and temporal trends of prescription drug use among cancer survivors, with an emphasis on central nervous system (CNS) active medications used to manage long-term cancer sequelae. **Methods:** Adult respondents with (n=3207) and without (n=40,440) a prior cancer diagnosis from 8 cycles (2001-2016) of the National Health and Nutritional Examinational Survey (NHANES) were evaluated for prescription drug usage. Cross-sectional analyses and temporal trends across cycles were evaluated and weighted to represent the US adult population. **Results:** Cancer survivors report higher rates of prescription drug usage (85.1% vs 54.3%, p<0.001, and 75.8%, p<0.001) and polypharmacy (27.8% vs 10.7%, p<0.001, and 22.7%, p<0.001) than both unadjusted and age-adjusted controls. Younger survivors report greater usage of CNS (36.8% vs 13.1%, p<0.001), psychotherapeutic (18.4% vs 7.7%, p<0.001), hormonal agents (19.1% vs 10.1%, p=0.003), and gastrointestinal (10.7% vs 4.7%, p=0.02) than controls, while differences are attenuated in older cohorts. Among broad drug categories, the usage of cardiovascular (p-trend<0.001), metabolic (p-trend<0.001), and immunologic agents (p-trend=0.01) has increased. Among CNS active subclasses, the usage of anticonvulsants (p-trend<0.001), anxiolytics (p-trend =0.02), narcotics (p-trend=0.02) and GABA analogs (p-trend<0.001) has increased. When comparing respondents with and without a history of cancer, the increased usage of anti-depressant prescription medications (18.3% vs 1.5% p<0.001), including SSRIs (11.2% vs 1.0%, p<0.001), SSNRIs (3.5% vs 0.3%, p<0.001), tricyclics (2.8% vs 0.1%, p<0.001), among cancer survivors was disproportionate compared to the increased proportion of positive depression screens (9.2% vs 7.0%, p=0.006). **Conclusions:** Cancer survivors report higher prescription drug use for both chronic conditions and late effects of cancer. The usage of CNS active medications, many of which are used on and off label for their pain management properties, has increased. The higher rates of pharmaceutical use may result in unanticipated long-term toxicities and financial burdens. Research Sponsor: None.

12024 Poster Discussion Session; Displayed in Poster Session (Board #312), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

FDA analysis of ECOG performance status and safety outcomes. *First Author: Harpreet Singh, U.S. Food and Drug Administration, Silver Spring, MD*

Background: Patients with poor performance status are often excluded from clinical trials. The FDA has published several guidances on modernizing oncology clinical trial eligibility criteria to more accurately reflect the patient population. Many patients receiving novel oncology therapeutics are heavily pretreated, and often have comorbidities, organ dysfunction, and frailty syndromes. Little is known about the safety of novel therapeutics in patients with poor performance status. **Methods:** Data from six randomized trials (n=4465) leading to registration for several solid tumor and malignant hematologic cancers, including multiple therapeutic mechanisms of action, such as EGFR TKI's, immune checkpoint inhibitors (ICI), and chemotherapy, were pooled. Cumulative incidence of Grade 3-5 adverse events and serious adverse events at Days 30, 90, and 180 were evaluated based on ECOG 0-2. Rates of treatment discontinuation by ECOG was also examined. **Results:** Cumulative incidence of toxicity events at days 30, 90, and 180 are shown in Table. Patient dropout rates due to death were 3.9%, 6.7%, and 10.9%; dropout rates due to disease progression were 66.5%, 66.6% and 56.9%; and dropout rates due to reasons other than progression or death were 29.7%, 26.7% and 32.1% for ECOG PS 0, 1 and 2, respectively. **Conclusions:** This FDA exploratory analysis of safety outcomes in registration trials based on ECOG suggests increasing rates of adverse events and rates of treatment discontinuation due to death with worsening performance status. Discontinuation rates due to disease progression and other reasons did not appear to be worse for ECOG 2 compared to 0-1. These findings were consistent across therapies (targeted therapy, ICI, chemotherapy). All trials in the analysis led to FDA approval, thus inclusion of patients with ECOG 2 did not adversely affect the trial outcome for this set of FDA approved agents. ECOG performance status eligibility criteria should be evaluated and modified on a frequent basis during drug development. Additional analysis of trials which enroll patients with ECOG 2 is needed. Research Sponsor: None.

Cumulative incidence of AEs at days 30, 90, and 180.

	ECOG 0 (n= 1260)	ECOG 1 (n= 2402)	ECOG 2-3 (n=803)
Serious Adverse Events			
Day 30	14.6%	19.3%	29.1%
Day 90	24.9%	33.8%	44.3%
Day 180	30.2%	40.4%	50.6%
Grade 3-5 Adverse Events			
Day 30	32.3%	36.5%	47.8%
Day 90	49.5%	55.5%	63.1%
Day 180	56.2%	63.1%	68.1%

12025 Poster Session (Board #313), Fri, 8:00 AM-11:00 AM

Aggressive care at end-of-life in the Veteran's Health Administration versus fee-for-service Medicare among patients with advanced lung cancer. *First Author: Carolyn J Presley, The Ohio State University, Columbus, OH*

Background: The Veteran's Health Administration (VHA) allows simultaneous receipt of cancer treatment and hospice care, termed concurrent care, while fee-for-service Medicare does not. Although many physicians who care for patients in the VHA also care for private sector patients, it is unclear whether there is a "spillover" relation between end of life (EOL) care in the VHA and Medicare systems at the regional level. We examined temporal trends, as well as regional-level associations between Medicare and VHA EOL practice for patients with advanced lung cancer. **Methods:** We conducted a retrospective study on VHA and SEER-Medicare (SM) decedents from 2006-2012 with stage IV non-small cell lung cancer (NSCLC) who received any lung cancer care. Aggressive care (AC) at EOL was defined as any of the following within 30 days of death– intensive care unit (ICU) admission, no-hospice care, cardiopulmonary resuscitation(CPR), mechanical ventilation (MV), > 1 inpatient admission and receipt of chemotherapy. Descriptive statistics were used to compare outcomes. We also analyzed the association between Medicare hospital referral region (HRR) hospice admissions, Medicare HRR EOL spending, and VHA AC use adjusted for patient's characteristics using a random intercept mixed effect logistic regression model after matching VHA facilities with Medicare facilities in a particular HRR. **Results:** AC use significantly decreased during the study period, from 46% to 31% among 18,371 Veterans and from 42% to 38% among 25,283 in the SM cohort, (t-test $P < .05$). Hospice use significantly increased within both cohorts ($p < .001$). The receipt of chemotherapy at EOL was similar for both cohorts throughout the study period. Veterans who received care in regions with higher hospice admissions among Medicare beneficiaries were significantly less likely to receive AC at EOL (adjusted Odds Ratio (aOR): 0.13 95%CI: 0.08-0.23, $P < .001$) than veterans in regions with lower Medicare hospice use. Medicare HRR spending at the EOL was not associated with receipt of AC among Medicare beneficiaries (aOR): 1.004 95%CI: 1.00-1.009, P = 0.07). **Conclusions:** Perhaps due to availability of concurrent care, VHA patients received less aggressive care at EOL as compared to SM patients. At the regional level, greater hospice use among Medicare beneficiaries was significantly associated with reduced AC within the VHA. Research Sponsor: REDCap project and The Ohio State University Center for Clinical and Translational Science grant support(National Center for Advancing Translational Sciences, Grant UL1TR002733),Carolyn Presley is a Paul Calabresi Scholar supported by the OSU K12 Training, Other Foundation.

12026 Poster Session (Board #314), Fri, 8:00 AM-11:00 AM

Impact of palliative care on end-of-life outcomes in hematologic malignancies. *First Author: Ari Pelcovits, Brown University, Providence, RI*

Background: Patients (pts) with hematologic malignancies (HMs) receive more aggressive end-of-life (EOL) care and often die in the hospital. The impact of palliative care (PC) on EOL quality outcomes in HMs has not been well described. In 2017 we embedded a PC specialist within our inpatient malignant hematology team to facilitate the use of early PC. We sought to determine if this practice was accompanied by a shift in EOL outcomes. **Methods:** We conducted a retrospective review of pts diagnosed with acute myeloid leukemia (AML) at our institution in the 2 years before (Cohort A) and after (Cohort B) implementation of embedded PC. We identified pts who received PC and if it was early (during initial inpatient stay) or late (sometime after). We then examined EOL quality outcomes: hospitalizations and intensive care (ICU) admissions in the last 30 days of life, chemotherapy use in the last 14 days of life, and use of hospice and death out of hospital (DOH), using Fisher's exact test to compare proportions. **Results:** Among 139 AML pts, 46 in Cohort A, 93 in Cohort B, we identified 34 and 47 decedents in each cohort respectively. The use of PC was significantly higher in Cohort B (75% vs 43%, $P= 0.0006$), with a significant increase in early PC (52% vs 11%, $P < 0.0001$). There was no significant improvement in EOL quality outcomes between Cohort A and B, or uniquely among pts receiving early PC ($P > 0.05$); however, PC use in general across all cohorts was associated with significant increase in hospice use and fewer ICU admissions (P =0.016 and 0.0043, respectively). Among pts not receiving PC, a numerical improvement was noted in EOL metrics between Cohorts A and B ($P > 0.05$; see table). **Conclusions:** PC for pts with AML was associated with significantly better EOL quality outcomes. We also observed improvement in EOL metrics over time among pts not receiving PC, which may indicate a culture shift with the embedded PC service, whose benefit extended to pts not directly receiving PC. Embedding a PC specialist and early PC in AML, however, was not significantly associated directly with EOL care improvements. The value of these interventions in HMs may be better measured using patient-reported outcomes and quality of life measures rather than strict EOL outcomes. Further research should consider potential differential role of PC among pts with HM undergoing aggressive/curative, or non-intense/palliative therapy. Research Sponsor: None.

	Overall				No PC	
	Cohort A	Cohort B	PC	No PC	Cohort A	Cohort B
Hospice Use	59%	63%	72%	43%	31%	58%
DOH	55%	56%	65%	39%	29%	55%
Hospitalization	81%	85%	84%	83%	94%	69%
ICU Admission	32%	26%	17%	48%	59%	33%
Chemotherapy	32%	24%	25%	31%	35%	25%

12027 Poster Session (Board #315), Fri, 8:00 AM-11:00 AM

The adoption of immune checkpoint inhibitors and patterns of care at the end of life. *First Author: Fauzia Riaz, Stanford School of Medicine, Stanford, CA*

Background: As immune checkpoint inhibitors (ICIs) have transformed the care of patients with cancer, it is unclear whether treatment at end of life (EOL) has changed. Because aggressive therapy at EOL is associated with increased costs and patient distress, we explored the association between the FDA approvals of ICIs and treatment patterns at EOL. **Methods:** We conducted a retrospective, observational study using patient-level data from the Flatiron health EHR-derived de-identified database. Patients had advanced melanoma, non-small cell lung cancer (NSCLC) (cancer types with an ICI indication) or microsatellite stable (MSS) colon cancer (a cancer type without an ICI indication) and died between 2013 and 2017. We calculated annual proportions of decedents who received systemic cancer therapy in the final 30 days of life and used logistic regression to model the association between the post-ICI Federal Drug Administration (FDA) approval time period and use of systemic therapy at EOL, adjusting for patient characteristics. We also assessed the use of chemotherapy or targeted/biologic therapies at EOL, before and after FDA approval of ICIs using Pearson Chi Square test. **Results:** There was an increase in use of EOL systemic cancer therapy in the post-ICI approval period for both melanoma (33.9% to 43.2%, p-value < 0.001) and NSCLC (37.4% to 40.3%, p-value < 0.001). In contrast, the control group of decedents with MSS colon cancer demonstrated no significant increase in use of systemic therapy at EOL. After controlling for patient characteristics, there was a significantly higher odds of receiving systemic treatment at EOL in the post-ICI time period compared to the pre-ICI time period in melanoma (OR 1.42, 95% CI 1.09-1.86, p-value < 0.001) and NSCLC (OR 1.13, 95% CI 1.06-1.20, p value < 0.001), with no significant difference in receipt of systemic therapy in patients with MSS colon cancer. After FDA approval of ICIs, patients with NSCLC and melanoma had a decrease in the use of chemotherapy, with a concomitant increase in use of ICIs at EOL. Decedents with MSS colon cancer did not have a statistically significant change in use of chemotherapy or targeted/biologic therapies during the study period. **Conclusions:** The adoption of ICIs was associated with a substantive increase in the use of systemic therapy at EOL in melanoma, and a smaller yet significant increase in NSCLC. Research Sponsor: U.S. National Institutes of Health.

12028 Poster Session (Board #316), Fri, 8:00 AM-11:00 AM

Impact of performance status on response and survival among patients receiving checkpoint inhibitors for advanced solid tumors. *First Author: Mridula Krishnan, University of Nebraska Medical Center, Omaha, NE*

Background: Clinical trials leading to the approval of immune checkpoint inhibition (ICI) have almost exclusively been performed in patients with good performance status (ECOG PS of 0-1). However, ICI remains an attractive option for patients with advanced tumors and poor performance status, considering their overall tolerability. While use of ICI in patients with poor PS (ECOG PS of 2 or greater) has been rapidly adopted, whether these patients derive the same benefits as expected in the studied populations is largely unknown. We therefore performed an institutional retrospective analysis of all patients treated with palliative single agent anti-PD1 or anti-PDL1 to determine response and survival for those with poor performance status. **Methods:** We retrospectively identified patients with advanced solid tumor malignancies who were treated with ICI monotherapy with palliative intent at our institution between 2015-2019. The primary objective was to compare overall survival (OS) for patients with good PS (ECOG PS 0-1) with those with poor PS (ECOG PS 2 or 3-4). The log-rank test compared the survival among patients with different ECOG PS. In addition, we used a proportional hazards model to assess association between ECOG PS and the OS with adjustment for age, gender, and smoking status. A secondary objective was to compare overall response rates (ORR) of the three ECOG PS groups which were evaluated with a binary rate model. **Results:** We identified 266 patients treated with ICI, 87 with NSCLC, 34 with melanoma, 33 with RCC, 24 with bladder cancer, 22 with head/neck cancer, and the rest with other histologies. 187 (70%) were ECOG PS 0-1, 62 (23%) were ECOG PS 2, and 17 (7%) were ECOG PS 3-4. 89 of these patients (33%) were still alive at time of last follow-up. Across all tumor types, patients with ECOG PS 0-1 had superior survival compared to ECOG PS 2 (median survival 12.4 months vs 4.6 months, HR 0.41, $p < 0.001$). Median survival for ECOG PS 3-4 was lower at 2.3 months. The ORR for ECOG PS 0-1 (23%) was significantly higher to that of ECOG PS 2 (6%, $p = 0.02$). ORR for ECOG PS 3-4 was 12%. **Conclusions:** Despite the appeal of ICI for patients with advanced malignancy and poor performance status, outcomes were poor. Survival and objective response rates for patients with ECOG PS 2 and higher were significantly worse than those with ECOG PS 0-1. ICI treatment comes with cost, including potentially forgoing early hospice referral or optimal support at the end of life. Prospective trials defining the activity and role of ICI in poor PS are urgently needed. Research Sponsor: None.

12029 Poster Session (Board #317), Fri, 8:00 AM-11:00 AM

Prospective study comparing self-administered geriatric assessment to provider's routine clinical assessment of older patients with metastatic breast cancer treated at community oncology practices. *First Author: Rino S. Seedor, Fox Chase Cancer Center, Philadelphia, PA*

Background: Geriatric Assessment (GA) is recommended for evaluating an older cancer patient's (pt) fitness for treatment. We conducted a prospective study evaluating the current gaps that exist in the assessment of older pts with metastatic breast cancer (MBC) in community practices (CP). **Methods:** Self-administered validated GA was compared to provider assessment (PA) of MBC pts $\geq$ 65-years-old treated at CP in the US. Providers were blinded to the GA results until their evaluation was completed. Differences in PA vs GA detected abnormalities were assessed using McNemar's test. The effect of patient/provider factors on the rate of abnormalities not identified was assessed using regression models, clustering by provider and adjusting for the number of prior pts seen. **Results:** 100 pts were enrolled across 9 CP (median age 73.9, (65-90)). GA detected a total of 356 abnormalities in 96/100 (96%) pts, of which 223 required immediate interventions. African American and widowed/single pts were more likely to have abnormalities identified by GA. On average PA did not identify abnormalities detected by validated GA in 2 of 8 domains. 73% of functional status, 86% of social support, 44% of nutritional, and 96% of cognitive abnormalities detected by GA were not identified by PA (all $P < 0.0001$). Providers with more years of clinical experience were more likely to identify abnormalities (compared to < 5 years (y) in practice: 5-10 y in practice, $p = 0.149$; 11-15 y in practice, $p = 0.028$; > 15 y in practice, $p = 0.017$). GA had the most significant impact on pts with decreased ECOG PS ($p = 0.045$). Pts found to have an abnormal Timed Up and Go (TUG) test were more likely to have additional abnormalities in other domains (mean 4.3 vs 2.1, Wilcoxon $p < 0.001$), and more abnormalities not identified by the PA ($p < 0.001$). Providers were "surprised" by GA results in 33% of cases, mainly with cognitive or social support findings, and reported plans for management change for 40% of pts based on GA findings. **Conclusions:** Including a GA in the care of older pts with MBC in CP is beneficial as validated GA has a high detection rate of abnormalities not detected by PA. Research Sponsor: NCCN and Pfizer Independent Grants for Learning & Change Metastatic Breast Cancer.

12030 Poster Session (Board #318), Fri, 8:00 AM-11:00 AM

Development and validation of an early death risk score for older patients treated with chemotherapy for cancer. *First Author: Jaime Feliu Batlle, Medical Oncology Department, Hospital Universitario La Paz, Madrid, Spain*

Background: Determining life expectancy in older patients is needed to select the best treatment strategy. We aimed to develop and validate a score to predict early death risk (< 6 months) in elderly patients with cancer that are planned to initiate chemotherapy treatment. **Methods:** Patients over 70 years starting new chemotherapy regimens were prospectively included in a multicenter study. A pre-chemotherapy assessment that included sociodemographics, tumor/treatment variables, and geriatric assessment variables, was performed. Association between these factors and early death was examined by using multivariate logistic regression. Score points were assigned to each risk factor based on their b coefficient. We validated the risk score with an external validation cohort of 206 patients. **Results:** Three hundred forty two patients were included in the training cohort. The independent predictors for early death were metastasic cancers (odds ratio [OR] 4.8, 95% confidence interval [CI], [2.4-9.6]), ECOG performance status (OR 2.3, 95% CI:1.084-5.232), ADL (OR 1.7, 95% CI:1.08-3.5), serum albumin levels (3.3, 95% CI: 1.6-6.6), BMI (OR 2.4, 95% CI:1,2-4.8), serum GGT levels (OR 1.5, 95% CI:1.05-1.8) and hemoglobin levels (OR 2.3, 95% CI:1.2-4.6). With these results, a score was to stratify patients regarding their risk of early death: low (0 to 2 points; 5%), intermediate (3 to 5 points; 19%) or high (6 to 14 points; 50%) ($p < 0.001$). The area under the curve of the receiver-operating characteristic (ROC) curve was 0.79 for the training cohort (95% CI, 0.74 to 0.85), and 0.70 (95% CI: 0.60-0.80) for the validation cohort (difference between cohorts not statistically different). **Conclusions:** We developed a highly accurate tool that uses basic clinical and analytical information to predict the probability of early death in elderly patients with cancer that are planned to initiate chemotherapy treatment. This tool can help physicians in decision making for this population of patients. Research Sponsor: None.

12031 Poster Session (Board #319), Fri, 8:00 AM-11:00 AM

Is there a benefit of immune checkpoint inhibitors for patients over 75 years of age with advanced cancer in first and second line setting: A meta-analysis. *First Author: Thierry Landre, UCOG-HUPSSD-APHP, Paris, France*

Background: The impact of aging on Immune Checkpoint Inhibitors (ICIs) effectiveness is controversial. Currently, data from clinical studies do not show any difference between patients over 65 years and those under 65 years. We propose to compare the clinical benefit of ICIs in those over 75 and in those under 75. **Methods:** We performed a meta-analysis of published randomized control trials (RCTs) concerning ICIs versus standard therapy in patients with advanced solid tumours. Overall Survival (OS) among the older ($\geq$75 years) was compared with that of younger patients (< 75 years) in first and second line setting. Hazard ratios (HRs) with their 95% confidence interval (CI) were collected from the studies and pooled. **Results:** Fifteen phase III studies evaluating anti-PD-1 (nivolumab or pembrolizumab), anti-PD-L1 (atezolizumab or avelumab) or anti-CTLA-4 (ipilimumab) were included. Patients were enrolled for Non-Small-Cell-Lung-Cancer, Renal-Cell-Carcinoma, Melanoma, Head-and-Neck-Squamous-Cell-Carcinoma or Gastric-Cancer. Eight studies assessed treatment in first line setting and seven in second line. The median age was 64 years, with 906 patients over 75 years of age and 5233 younger. In first line setting, HRs for death were 0.78 (95% CI: 0.61-0.99) in patients $\geq$75 years versus 0.84 (95% CI: 0.71-1.00) in younger. In second line setting, HRs for death were 1.02 (95% CI: 0.77-1.36) in patients $\geq$75 years versus 0.68 (95% CI: 0.61-0.75) in younger with a statistically significant difference observed between subgroups (p interaction = 0.009). **Conclusions:** ICIs appears to be effective in patients over 75 years of age. However, the survival benefit comes mainly from the first line of treatment. This result encourages the use of ICIs early in the therapeutic management of patients over 75 years of age. Research Sponsor: None.

12032 Poster Session (Board #320), Fri, 8:00 AM-11:00 AM

Omission of adjuvant chemotherapy in elderly patients with early stage breast cancer. *First Author: Sung Jun Ma, Department of Radiation Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: Breast cancer incidence in elderly population over 70 years is anticipated to grow up to 35% by 2030. However, this elderly population is under-represented in the TAILORx (Trial Assigning Individualized Options for Treatment) with less than 5% of the entire study cohort. As the omission of radiation therapy among the elderly with favorable prognosis is a reasonable alternative option, omission of chemotherapy has not been prospectively investigated. To address this knowledge gap, we conducted an observational cohort study to evaluate the omission of chemotherapy in elderly patients with early breast cancer. **Methods:** The National Cancer Database (NCDB) was queried for patients above the age of 70 diagnosed with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, pT1-2N0 breast cancer who underwent hormone therapy with or without chemotherapy (2010-2015). Kaplan-Meier method and Cox multivariable analysis (MVA) were performed for survival analysis. Propensity score matching in a 1:1 ratio without any replacement was used to address selection bias. Sensitivity analysis was performed on a subgroup of those with a high 21-gene recurrence score (RS) $>$ 25. **Results:** A total of 12004 patients were identified, including 10802 and 1202 patients with and without adjuvant chemotherapy, respectively. The median follow up was 38.2 months (IQR 22.5-57.2). On univariate analysis, chemotherapy was not associated with improved overall survival (HR 0.96, p = 0.71), ineligible for inclusion in the final MVA model. On interaction analysis, the use of chemotherapy had no interaction with RS (p = 0.46), age (p = 0.08), tumor size (p = 0.23), tumor grade (p = 0.42), and comorbidity score (p = 0.22). On 1030 and 689 matched pairs for all RS and RS $>$ 25, respectively, there was no association of overall survival with chemotherapy (all RS: HR 0.76, p = 0.08; RS $>$ 25: HR 0.74, p = 0.10). **Conclusions:** For elderly patients with early stage breast cancer, the addition of adjuvant chemotherapy may not be associated with improved survival even in the setting of high RS $>$ 25. Given the toxicity profile of systemic therapy, shared decision making between clinicians and elderly patients is needed to individualize treatment options. Research Sponsor: None.

12034 Poster Session (Board #322), Fri, 8:00 AM-11:00 AM

Factors associated with referral for perioperative geriatric comanagement (GERI-CO) program in 12,398 older adults with cancer. *First Author: Armin Shahrokni, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: At ASCO 2019, we showed that the Memorial Sloan Kettering (MSK) Geriatric Co-management (GERI-CO) program was associated with improvement in 90-day postoperative mortality rate. Now, we present factors associated with the use of such program. **Methods:** At MSK, patients aged 75+ can be referred for perioperative GERI-CO. We retrospectively reviewed the available data of patients aged 75+ who underwent surgery within two months of their initial visit with the surgeon (2011 to 2019). Patients that were referred for GERI-CO were compared with those who were not: sociodemographic, frailty, comorbid conditions, and surgery characteristics. Frailty level was determined using the MSK Frailty Index (score ranges from 0-11, higher scores suggest more frailty). Multivariable regression analysis was used to assess factors associated with the use of the GERI-CO Program. **Results:** In total 12,398 patients (4422, 35.7% GERI-CO) were included. Average time from surgical consult to geriatric visit was 9 days. Patients in the GERI-CO program were older (80.7 vs. 79.6), less likely to be non-Hispanic White (87% vs. 91%), have English as primary language (84% vs. 89%), and be fit (12% vs. 17% with MSK-FI 0). They were more likely to have stroke history (5% vs. 4%), have diabetes (DM) (25% vs.20%), hypertension (78% vs. 71%), and peripheral vascular disease (14% vs. 12%), but less likely to have cardiac disease (22% vs. 26%), myocardial infarction (MI) (7% vs. 10%), pulmonary disease (13% vs. 16%). Patients referred for GERI-CO were more likely to undergo 3+ hours surgeries (25% vs. 8%), with 100+ cc intraoperative blood loss (41% vs. 22%), and hospital length of stay (LOS) of 3+ days (42% vs. 19%). In multivariable analysis, being frail (OR = 1.3 and 1.6 for MSK-FI 1-2 and 3+), longer surgery (OR = 2.6 and 3.6 for operation time 1.5-3 and 3+ hours), longer LOS (OR = 1.3 and 1.5 for LOS 1-2 and 3+ days), older age (OR = 1.06), having DM (OR = 1.15) were associated with higher likelihood of GERI-CO while having history of cardiac disease (OR = 0.55), MI (OR = 0.84), pulmonary disease (OR = 0.69) were associated with less likelihood of referral for GERI-CO. **Conclusions:** Our result shows the unique characteristics of patients managed in the GERI-CO program. This has implications for both implementation of GERI-CO program in other institutions and assessing outcomes of these patients. Research Sponsor: U.S. National Institutes of Health.

12035 Poster Session (Board #323), Fri, 8:00 AM-11:00 AM

Abbreviated geriatric assessment (GA) in new oncology patients and its association with early death. *First Author: Michael Maranzano, University of Chicago Medical Center, Chicago, IL*

Background: The ASCO 2018 Geriatric Oncology Guidelines support the broad application of GA to risk-stratify patients age ≥65 undergoing cancer-directed therapy. Despite this, GA has not been widely adopted due largely to perceived time and resource constraints. We administered an abbreviated GA by medical assistants (MAs) in an outpatient oncology clinic to explore its feasibility and correlation with adverse events. **Methods:** This is a single-institution, retrospective study of adults establishing oncology care at an academic medical center from 11/2016-4/2017. MAs completed an abbreviated GA of well-validated tests. Cognitive function was screened by the Mini-Cog (score $<$ 4) and physical function by the Five Times Sit-to-Stand Test (FTSST ≥ 15 seconds). Patient-reported Outcomes (PRO) screened for malnutrition by the Malnutrition Screening Test (MST ≥ 2), for vulnerability by Vulnerable Elders Survey (VES-13 ≥ 3) and for depression by Patient Health Questionnaire-4 (PHQ-4 $>$ 2). The first result within 3 months of the initial visit was used for analysis. ED visits, inpatient admissions and early death, defined as within the first 6 months from the initial visit, were collected from the electronic medical record. GA results and baseline characteristics were modeled for these events using univariate logistic regression. Multivariable regression was performed when univariate regression revealed at least 2 factors with p$<$ 0.1. **Results:** New patients 65+ years (n=304, median age 72) established care in our practice during this six-month period. Nearly all patients (n=285, 94%) completed at least one GA test. Fewer patients completed the Mini-Cog and FTSST (60% completed) compared to the PRO screenings (83-90% completed). Those with any positive GA screening test were nearly 3 times as likely to die within 6 months of their initial outpatient visit compared with those with no deficits (OR 2.95, 95% CI 1.11-9.30). Those with FTSST ≥ 15 sec or unable to complete were more likely to have an ED visit within 6 months (OR 2.40, 95%CI 1.04-5.46).No other individual screening test had a statistically significant association with adverse events. **Conclusions:** An abbreviated version of GA completed by MAs can be incorporated into new oncology patient visits for all older adults, and those with any abnormalities on screening tests had a higher likelihood of early death. Research Sponsor: None.

Adverse events by abbreviated GA.

	At Least 1 Positive Screening Test n = 143	All Negative Screening Tests n = 131
Death	15 (11%)	5 (4%)*
ED Visit	33 (23%)	28 (21%)
Admission	53 (37%)	52 (40%)

*p $<$ 0.05

12036 Poster Session (Board #324), Fri, 8:00 AM-11:00 AM

Association of geriatric comanagement with reduction in adverse surgical outcomes among patients 75 or older with cancer with prolonged hospital stay. *First Author: Armin Shahrokni, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Patients with prolonged hospital stay following surgery are at higher risk of readmission, emergency room visits, and mortality. In our study, we assessed the relationship between Geriatric Comanagement (GERI-CO) and adverse outcomes among these patients. **Methods:** In a retrospective study, patients aged 75+ with cancer who had hospital length of stay longer than 75% of cohort (8 days or longer) postoperatively at Memorial Sloan Kettering Cancer Center from 2011-18 were studied. GERI-CO status was obtained from medical records. Differences in sociodemographic, frailty, surgery, and comorbid conditions between GERI-CO and non-GERI-CO patients were assessed. Frailty was assessed by Memorial Sloan Kettering Frailty Index, score 0 to 11, higher score reflective of more frailty. Composite adverse outcome is a composite score of 30-day readmission, or emergency room visit, or 90 day mortality. Multivariable regression analysis was used to assess the relationship between GERI-CO and postoperative adverse outcome. **Results:** In total 1118 patients (634, 56.7% in the GERI-CO) were included. Patients in GERI-CO were older (80.8 vs. 79.9), more likely to undergo 3+ hours of surgery (66% vs. 43%), have 100+ cc intraoperative blood loss (78% vs. 72%), and have liver disease (16% vs. 10%), but were less likely to have kidney disease (19% vs. 25%), cardiac disease (28% vs. 35%), myocardial infarction (8% vs. 12%), pulmonary disease (15% vs. 20%), ASA-PS 4+ (11% vs. 21%) compared to non-GERI-CO patients. Gender, Frailty and the rest of comorbid conditions, and average length of stay (15 days) did not differ between groups. GERI-CO patients were less likely to have 30-day hospital admission (11% vs. 18%), emergency room visit (14% vs. 22%), or 90 day mortality (6% vs. 15%), and composite adverse outcome (20% vs. 37%) compared to non-GERI-CO patients. In the multivariable analysis, after adjustment for age, frailty, ASA-PS, operation time, intraoperative blood loss, kidney, cardiac and pulmonary disease, patients in GERI-CO were less likely to have composite adverse outcome (OR = 0.57, p = 0.002). **Conclusions:** GERI-CO program for patients with prolonged length of stay following surgery is associated with reduced 30-day hospital readmission, emergency room use, and 90-day mortality. Research Sponsor: U.S. National Institutes of Health.

12037 Poster Session (Board #325), Fri, 8:00 AM-11:00 AM

Treatment patterns and outcomes by age in metastatic melanoma: A study of the National Cancer Database. *First Author: Justin Moyers, Loma Linda University Medical Center, Loma Linda, CA*

Background: Metastatic melanoma carries poor prognosis and traditional chemotherapy has limited efficacy. Immune checkpoint inhibitors (ICI) have drastically improved disease outcomes since first approved in 2011. Elderly patients were underrepresented in landmark early trials of ICI leading to limited clinical trial data on efficacy and treatment patterns in this population. We aimed to examine the real-world IO outcomes and demographics of elderly patients in the National Cancer Database. **Methods:** We queried the database for patients with stage IV melanoma diagnosed between 2011-2015 with survival data available. Patients were divided into receipt of immunotherapy (IO) or no receipt of IO; those without documentation were excluded. Cases were separated into 3 cohorts of age at diagnosis (60 years-old or younger, 61-74 years-old, and 75 years-old and greater). Descriptive variables were compared by Chi-squared analysis and survival analyses were performed by Kaplan-Meier method and log-rank test. **Results:** 11,265 cases met inclusion criteria: 4,117 aged 60 or less, 3,940 aged 61-74, and 3,208 aged 75 or older. Those receiving immuno-oncologic agents (IO) in all age groups showed a longer median OS (mOS) than those who did not receive IO (mOS overall 17.28 v 7.49; $p<0.01$). Survival was longer in all age cohorts when IO was received compared to not received; ages less than 60 (mOS 20.3 v 9.2m; $p<0.01$), ages 61-74 (mOS 15.5 v 7.8m; $p<0.01$), and ages 75 or greater (mOS 14.4 v 5.8m; $p<0.01$). A greater percentage of patients received IO in younger than older cohorts, 20.1% in $\geq$ 75, 37.6% in 61-74, and 42.3% in $\leq$ 60; $p<0.01$. Additional descriptive variables shown in the table were compared between the cohorts include care at academic or integrated cancer network, uninsured, Charlson-Deyo Comorbidity Index (CDCI) of 2 or greater, and documented inclusion of palliative care treatment. **Conclusions:** Substantial survival benefit is realized with IO in all age cohorts although elderly cohorts did not receive IO as often as younger cohort. Elderly patients experienced lower rates of care at academic/network cancer programs, lower uninsured rate, and higher CDCI. Research Sponsor: None.

Variable	Age Category ≤60 years	61-74 years	≥ 75 years	p-value
Patients (n)	4117	3940	3208	
Received Immunotherapy (%)	42.3	37.6	20.1	<0.01
Treated in Academic or Network Cancer Programs (%)	59.0	55.9	48.9	<0.01
Uninsured (%)	8.7	3.0	0.5	<0.01
CDCI of 2 or greater (%)	4.2	8.3	10.5	<0.01
Palliative care included in treatment (%)	4.2	3.2	4.2	0.14

12038 Poster Session (Board #326), Fri, 8:00 AM-11:00 AM

Metastasis free survival in older men with nonmetastatic castration-resistant prostate cancer treated with androgen receptor inhibitors: An FDA-pooled analysis. *First Author: Harpreet Singh, U.S. Food and Drug Administration, Silver Spring, MD*

Background: The FDA has approved three androgen receptor (AR) inhibitors for nonmetastatic castration-resistant prostate cancer (nmCRPC) based on improvements in metastasis-free survival (MFS). MFS is an earlier endpoint, defined as the time from randomization to either imaging-detectable distant disease or death. This pooled analysis examines MFS, time to initiation of cytotoxic chemotherapy (TTCyto), and safety outcomes in men over 80 treated with AR inhibitors. **Methods:** Data was pooled from three randomized controlled studies (n=4117) of AR inhibitors for nmCRPC. The treatment effect of AR inhibitors on MFS and TTCyto across age groups was evaluated using Kaplan-Meier estimates and a Cox proportional hazards regression model. Hazard Ratios for MFS and TTCyto were adjusted for baseline ECOG, total Gleason score, PSA doubling time, and prior bone-targeting therapy. **Results:** For patients age 80 years or older (n=675) who were treated with AR inhibitors, the hazard ratio was 0.38 (95% CI 0.29, 0.49) with an estimated median MFS of 40 months (95% CI 36, 41) versus 22 months (95% CI 18, 29) for those treated with placebo (n=348). For patients <80 (n=2019) treated with AR inhibitors, the HR was 0.31 (95% CI 0.27, 0.36) with an estimated median MFS of 41 months (95% CI 36, NR) versus 16 months (95% CI 15, 18) for those treated with placebo (n=1075). Patients over 80 also derived similar improvements in time to initiation of cytotoxic chemotherapy (HR 0.43 95% CI 0.23, 0.82), compared to their younger counterparts (HR 0.41 95% CI 0.33, 0.50). See Table for selected safety outcomes. **Conclusions:** In an exploratory subgroup analysis, older men (≥80) with nmCRPC derived similar benefit in MFS and time to initiation of cytotoxic chemotherapy with AR inhibitors compared with younger patients. Men age 80 and above experienced higher rates of Grade 3-4 adverse events, serious adverse events, falls, and fractures. This trend towards increased toxicity was observed regardless of treatment arm. Analysis of patient reported outcomes is ongoing. Research Sponsor: None.

Toxicity and selected adverse events of AR inhibitors by age.

	Androgen Receptor Inhibitors		Placebo	
	Age < 80 (n=2015)	Age ≥ 80 (n=672)	Age < 80 (n= 1073)	Age ≥ 80 (n=344)
Grade 1-2	1123 (55.7)	323 (48.1)	608 (56.7)	177 (51.5)
Grade 3-4	603 (29.9)	249 (37.1)	244 (22.7)	106 (30.8)
Serious Adverse Events	461 (22.9)	206 (30.7)	190 (17.7)	99 (28.8)
Falls	166 (8.2)	101 (15)	51 (4.8)	27 (7.8)
Fractures	157 (7.8)	70 (10.4)	41 (3.8)	35 (10.2)

12039 Poster Session (Board #327), Fri, 8:00 AM-11:00 AM

Hospitalizations following cancer diagnosis: National values for frequency, duration, and charges. *First Author: Michael T. Halpern, National Cancer Institute at the National Institutes of Health, Bethesda, MD*

Background: US medical care costs for cancer are projected to be $158 billion in 2020. Hospitalization is a substantial component of these costs; however, little is known about national patterns of hospitalization among individuals with cancer. This study used Medicare data to determine national rates and charges for hospitalizations among older cancer patients. **Methods:** We used data from 100% of individuals diagnosed with cancer in SEER-Medicare in the most recent 5 years available, 2011-2015. Analyses determined proportion of patients hospitalized, number/duration of hospitalizations, and charges by patient clinical and sociodemographic characteristics within 12 months of diagnosis. **Results:** Among 307,944 unique patients, 65% were hospitalized in the first year following diagnosis. Rates ranged from 34% for patients with in situ disease to 82%-84% for patients with advanced disease; 31% had 2 or more hospitalizations. Hospitalization rates were lowest among skin melanoma (25%) and breast (42%) cancer patients, highest for brain/nervous system (97%) and ovarian (96%) cancer patients. Hospitalized patients had a mean of 2.1 hospitalizations; mean days per hospitalization within 12 months was 8.8 (median 4). Duration of hospitalization varied little by stage at diagnosis. Mean days per hospitalization was shortest for thyroid and prostate cancer patients (5.7 & 6.0 days), longest for colorectal cancer and leukemia patients (10.6 & 11.3 days). DRGs varied substantially by cancer type; DRG for chemotherapy administration was more frequent among hospitalizations for patients with hematologic malignancies or distant stage disease. Mean Medicare charge (2016 $) per hospitalization was $67,368 (median $41,973), and was lowest for breast cancer patients ($48,021), highest for leukemia patients ($91,799). Patient charges per hospitalization averaged $1107 (median $1317) and showed little variation by cancer type or stage. **Conclusions:** Most older individuals experience at least one hospitalization within 12 months of cancer diagnosis. Frequency, duration, and charges of hospitalizations vary by cancer type and stage. This nationally representative information will aid in projecting cancer care costs and potential economic impacts of new therapies and treatment program. Research Sponsor: None.

12040 Poster Session (Board #328), Fri, 8:00 AM-11:00 AM

Communication about comorbidities among 527 older patients with advanced cancer and their oncologists and caregivers: A multisite cluster-randomized controlled trial. *First Author: Amber Kleckner, University of Rochester Medical Center, Rochester, NY*

Background: Older patients with advanced cancer often have comorbidities that increase the risk of toxicity from neoplastic therapy but are not always considered in treatment planning. We assessed the utility of a geriatric assessment (GA) intervention to increase the number and quality of discussions about comorbidities among oncologists, older patients, and caregivers. **Methods:** This multi-site trial enrolled patients who were ≥70 years, had advanced solid tumors or lymphoma, had ≥1 GA impairment, and who were considering or receiving cancer treatment. All patients received the GA and completed an Older Americans Resources and Services Comorbidity survey, which evaluated 15 conditions and interference with activities (clinical impairment = ≥3 comorbidities or ≥1 highly interfering). Oncology practices were randomized to intervention (GA with a summary with management recommendations provided to oncologists) or usual care (GA only). The clinic visit after GA was audio-recorded, transcribed, and coded for GA topics including comorbidity. Generalized linear mixed models adjusting for site (random effect) were used to assess the effect of the intervention. **Results:** Patients (n=527 evaluable, 76.6±5.2 years, 49% female) and oncologists (n=131, 63 in intervention) were enrolled from 31 sites. In total, 94.5% of patients had ≥1 comorbidity with an average of 3.2±1.9; 64% were clinically impaired by comorbidity (p=0.76 between arms). The intervention arm had twice the number of conversations about comorbidities (1.02 vs. 0.52 conversations per patient, difference 0.50, 95% CI 0.18-0.81, p=0.004) and conversations were more likely to be initiated by the oncologist ($p<0.001$, Table). Moreover, among patients who had conversations about comorbidities, more patients in the intervention arm had discussions specifically addressing comorbidities (e.g., cancer treatment modification, communication with the primary care physician; 24.3% vs. 7.5%, p=0.003). **Conclusions:** Providing oncologists with a GA summary and recommendations encouraged them to engage in more discussions about their patients' comorbidities with the goal of addressing interactions between comorbidities, cancer, and its treatments. Funds: PCORI CD4634, NCI UG1CA189961 Clinical trial information: NCT02107443. Research Sponsor: U.S. National Institutes of Health, Patient-Centered Outcomes Research Institute.

No. of comorbidity-related discussions during a clinic visit (unadjusted).

Conversation initiator	Usual care (n=14 sites 243 patients)	Intervention (n=17 sites 284 patients)
Oncologist	71	243
Patient	45	42
Caregiver	6	17
Other	4	3
Total	126	305

12041 Poster Session (Board #329), Fri, 8:00 AM-11:00 AM

Gait speed and recommended treatment intensity among older adults with blood cancers. *First Author: Andrew Hantel, Dana-Farber Cancer Institute, Boston, MA*

Background: Gait speed identifies frailty and predicts survival among older adults with hematologic malignancies (Liu, *Blood*, 2019). It is not known if gait speed correlates with the intensity of oncologists' recommended treatment in this population. **Methods:** From 2/2015-11/2019, patients ≥75 years presenting for an initial hematologic malignancy consultation at the Dana-Farber Cancer Institute were approached for a screening frailty assessment including a 4-meter gait speed test, reported as <0.4, 0.4-0.6, 0.6-0.8, or >0.8 meters/second (m/s). Faster gait speed is associated with less frailty and predicts better survival. Gait speed was not reported to the oncologist. Treatment recommendations were categorized into standard, reduced, or no therapy based on NCCN guidelines, as applicable. Gait/treatment intensity "mismatches" were characterized as patients with lowest quartile gait speed recommended standard intensity and highest quartile not recommended standard intensity. Multivariable regression was performed to assess if gait speed predicted treatment intensity (controlling for age, sex, ECOG performance status [PS], and disease type). **Results:** Of 786 patients enrolled, 408 required active treatment where NCCN guidelines vary by fitness. Mismatches were seen in 26.7% of patients (Table: column percentages with 95% CI, mismatches starred): 10 (21.3%) with lowest quartile gait speed recommended standard intensity and 99 (55.0%) with highest quartile recommended reduced or no therapy. In multivariable analysis, PS was predictive of no therapy as compared to standard intensity (all $p<0.02$) and age was predictive of reduced as compared to standard intensity ($p<0.01$); gait speed was not reliably predictive in either case. **Conclusions:** In this large cohort of older adults with hematologic malignancies, gait/treatment intensity mismatches occurred in over one-quarter of patients. Oncologists' recommendations were predicted by age and PS but not gait speed. Given that gait speed is a strong predictor of survival in this population, oncologists should integrate it to minimize over- and under-treatment when making treatment recommendations. Research Sponsor: None.

		Gait Speed (m/s)			
		<0.4 (N=47)	0.4-0.6 (N=52)	0.6-0.8 (N=129)	>0.8 (N=180)
Recommended Treatment Intensity	No Therapy	10	7	13	4*
		21.3%	13.5%	10.1%	2.2%
		[11.8,35.3]	[6.5,25.7]	[5.9,16.6]	[8.3,5.8]
	Reduced Intensity	27	35	67	95*
		57.5%	67.3%	51.9%	52.8%
		[43.0,70.7]	[53.5,78.7]	[43.3,60.5]	[45.5,60.0]
	Standard Intensity	10*	10	49	81
		21.3%	19.2%	38.0%	45.0%
		[11.8,35.3]	[10.6,32.3]	[30.0,46.68]	[37.9,52.4]

12044 Poster Session (Board #332), Fri, 8:00 AM-11:00 AM

Investigating the disparate enrollment of older adults on phase I clinical trials: Evolving participation patterns of patients 65 years and older w advanced cancer on phase I trials. *First Author: Ishwaria Mohan Subbiah, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: While safety and dose-finding remain the primary objective of Phase 1 trials, the potential for clinical benefit has taken a greater meaning in the last decade with the novel therapies. With data from phase I trials being submitted for regulatory approval, the finer details of these studies are under even more scrutiny: in particular, do the trial participants reflect the general patient population for whom the drug may be indicated? To that end, we investigated age-based enrollment on phase I clinical trials over time. **Methods:** We queried a prospectively maintained database at a major phase I trials center to identify eligible patients and demographic + clinical variables including phase I trial characteristics, age at date of enrollment into 3 age-based cohorts: AYA ages 15-39y, mid-age 40-64y, older adults aged 65y+. We calculated descriptive statistics, and explored correlations (Pearson/Spearman) and associations (linear regression) between age and independent variables. **Results:** Over a 3-year period (1/1/17 to 12/31/19), we identified 6267 pts enrolled on 338 phase I trials. Median overall age 58.4y (range 15.5-95.1y). 729 (12%, median age 34.8y) were AYA, 3652 (58%, median age 55.4y) mid-age and 1886 (30%, median 70y) older adults, of whom 870 pts were aged 70-79y and 76 pts aged 80y+ (18 being >85y). There was no association b/w senior participation and year of enrollment (2017 31%, 2018 29%, 2019 30%, b/w age and type of therapy (i.e. targeted vs immunotherapy, etc.) or b/w age and # of drugs given on trial (single agent vs combo) (all $p > 0.05$). **Conclusions:** Older adults remain underrepresented on phase I trials esp. when compared to incidence of cancer in that age group (30% enrollment vs 60% incidence), a discordance more staggering in the oldest old pts (85y+; only 18 pts enrolled over 3 yrs when compared to 140,690 pts 85y+ w a new cancer dx in just 2019). Once enrolled, older adults received similar types of phase I therapies with comparable number of drugs as compared to middle age patients, i.e. older adults were just as likely to get immunotherapy or targeted therapy as well mono- vs combo therapy as mid-age pts. Research Sponsor: None.

Types of Therapy	Older adult	%	Midage	%
Immunotherapy agent(s)	**662**	**35%**	**1292**	**35%**
Single Agent IO	286	43%	585	45%
Combo IO	376	57%	707	55%
Chemotherapy	**49**	**3%**	**79**	**2%**
Single Agent	47	96%	77	97%
Combo	2	4%	2	3%
Targeted	**801**	**42%**	**1566**	**43%**
Single Agent	633	79%	1260	80%
Combo	168	21%	306	20%
Immuno+Targeted	**259**	**14%**	**463**	**13%**
Targeted+Chemo	**85**	**5%**	**171**	**5%**
Other (biologics, combo)	**30**	**2%**	**81**	**2%**

12045 Poster Session (Board #333), Fri, 8:00 AM-11:00 AM

Association of geriatric conditions with survival and health care use in older adults with colon cancer living in long-term care facilities. *First Author: Daniel E Lage, Harvard Medical School, Boston, MA*

Background: Older adults with colon cancer residing in nursing homes are at risk for experiencing geriatric conditions such as cognitive decline, limitations in activities of daily living (ADLs), needing pain medications, and incontinence, due to cancer and its treatment. We sought to investigate these factors pre- and post-diagnosis and explored their relationship with health care use and survival. **Methods:** We identified 483 patients age 65+ with colon cancer from 2011-2015 in SEER-Medicare with linked quarterly nursing home assessments from the Minimum Data Set both pre- and post-cancer diagnosis. We determined the number of geriatric conditions (cognitive functioning, limitation in any ADL, pain medication use, bowel/urinary incontinence) at the pre- and post-cancer diagnosis assessment. We created four groups based on changes in these factors from pre- to post- assessment: improved (n = 105), worsened (n = 25), remained limited (n = 240), never limited (n = 113). Regression models estimated how changes from pre- to post-cancer diagnosis were associated with number of emergency department (ED) visits, hospitalizations, and survival, adjusted for age, sex, race/ethnicity, insurance status, cancer stage, number of pre-cancer comorbidities, urban/rural status, and time from diagnosis. **Results:** Overall, 55.3% of patients were age > 80 at diagnosis, with 64.8% female; 73.3% non-Hispanic white; and 9.9% Stage IV. Pre- versus post-diagnosis, 20.7% vs. 34.8% of patients were limited in cognitive functioning, and 75.4% vs. 77.8% were limited in ADLs. About a third of patients required pain medication, and about half of patients had urinary incontinence, which did not change pre- and post-diagnosis. Patients who remained limited had higher rates of ED visits (Risk ratio [RR] 1.05, $p < .01$) compared to those never limited. Those who worsened had higher rate of hospitalization (RR 1.44, $p < .01$) and ED visits (RR 1.63, $p < .01$). 12-month and 5-year survival was 46.7% and 6.1%, respectively. Factors associated with worse survival in a multivariable model included: remaining limited at both assessments (OR 1.52, $p < .01$), worsening from prior (OR 2.00, $p = .01$), as well as older age and higher cancer stage. **Conclusions:** Older adults with colon cancer residing in nursing homes have high prevalence of geriatric conditions and differential health care use and survival based on the presence of geriatric conditions, highlighting the need to consider geriatric conditions when providing cancer care to this population. Research Sponsor: American Cancer Society.

12046 Poster Session (Board #334), Fri, 8:00 AM-11:00 AM

Use of self-rated health to identify frailty and predict mortality in older adults with cancer. Results from the care study. *First Author: Mustafa Al Obaidi, University of Alabama at Birmingham, Birmingham, AL*

Background: Poor self-rated health (SRH) is a known predictor of mortality in the general adult population, but little is known about its use in older adults with cancer. The purpose of this study was to examine the association and ability of SRH to identify frail older adults and assess its ability to predict mortality in older adults with cancer. **Methods:** Using participants from the Cancer & Aging Resilience Evaluation (CARE) Registry who had undergone a geriatric assessment, we examined SRH using a single-item from the Patient-Reported Outcomes Measurement Information System (PROMIS) global health scale. SRH scores were dichotomized into Poor (poor and fair) and Good (good, very good, and excellent). Multivariable logistic regression analyses were used to examine associations between SRH and frailty (based on frailty index) and specific geriatric impairments adjusting for age, sex, comorbidity, cancer type and stage. Finally, the impact of SRH on all-cause mortality was assessed with a multivariable cox regression model. **Results:** A total of 708 participants with malignancy were included, median age was 68y, 41.5% male, and 74.6% White. Colorectal cancer was the most common cancer (27.1%) and 48.2% of the participants had Stage IV disease. Poor SRH was reported by 42% of participants and was associated with significantly higher odds of frailty (adjusted Odds Ratio [aOR] = 21.8; 95%CI 13.7-34.8). Similarly, poor SRH was independently associated with higher odds of impairments in Activities of Daily Living (ADL) (aOR = 5.6, 95%CI, 3.6-8.9), independent ADL (aOR = 8.4, 95%CI, 5.8-12.4), cognition (aOR = 4.6, 95%CI 2.3-9.3), malnutrition (aOR = 4.5, 95%CI 3.2-6.4), falls (aOR = 3.6, 95%CI 2.4-5.4), anxiety (aOR = 4.6, 95%CI 2.9-7.3), and depression (aOR = 5.4, 95%CI 3.0-9.7). The SRH demonstrated high sensitivity (84.3%) and specificity (78.4%) for identifying frailty, with a positive predictive value of 67% and negative predictive value of 90.6%. The 1y survival rate in those with Poor SRH was significantly worse (64.7% *vs* 84.3%, log rank p value < 0.001). In a multivariate cox regression analysis, poor SRH remained an independent predictor of worse survival (adjusted Hazard Ratio 2.29 [1.6-3.2], $p< 0.01$) after adjusting for age, sex, race, cancer type, stage, comorbidity, and planned treatment. **Conclusions:** Poor SRH is highly associated with frailty and could be a simple tool to identify frail older patients with cancer at risk for adverse events and increased mortality. Research Sponsor: U.S. National Institutes of Health.

12047 Poster Session (Board #335), Fri, 8:00 AM-11:00 AM

Geriatric assessment (GA) predictors of 1y mortality in older adults with gastrointestinal (GI) malignancies: Results from the CARE study. *First Author: Grant Richard Williams, University of Alabama Birmingham, Birmingham, AL*

Background: Chronologic age is an imperfect predictor of morbidity and mortality in older patients with newly-diagnosed GI malignancies. Identifying patients with GI malignancies that are at increased risk of mortality within the 1st year remains challenging given no prior studies have focused on this population, yet is critical to developing personalized treatment plans. To fill this gap, we examined predictors of 1y mortality using variables from a patient-reported GA in a prospective cohort of older adults with GI malignancies. **Methods:** Cancer and Aging Resilience Evaluation (CARE) is a prospective registry of older adults (≥60y) with cancer seen at UAB (J Geri Onc 2019; PMID 31005648). Patients with GI malignancies with GA completed within the timeframe of 3 mo. before and up to 6 mo. after diagnosis were included. Vital status (up to 12/7/2019) was ascertained by linking participants to LexisNexis. Multivariable Cox regression analysis was used to estimate associations between GA variables and 1y mortality, adjusting for age at cancer diagnosis, race, cancer stage (IV *vs.* I-III), cancer group (high risk: pancreatic, hepatobiliary, esophageal *vs.* low risk: colorectal, GIST, neuroendocrine, etc.), and planned chemotherapy (yes/no). **Results:** A total of 356 participants met eligibility criteria. Mean age at enrollment was 70y; 56.4% were females; 25% black; 47.1% had high-risk cancers. In unadjusted analysis, high-risk cancers, cancer stage, malnutrition, impaired performance status, limitations in social activities, impaired instrumental activities of daily living (IADL), physical health, mental health, anxiety, and ≥3 comorbidities were associated with higher 1y mortality. Our base model (demographic and clinical variables) demonstrated good discrimination (c statistic 0.758), but was improved with the addition of all significant GA variables (c-statistic 0.810). Fatigue and malnutrition were identified as the strongest predictors among the GA variables, and a model adding those to the base model retained high discrimination (c-statistic 0.804). The estimated 1yr survival was 53.1% for those with both fatigue and malnutrition compared to 88.1% in those with neither. **Conclusions:** Among older adults with GI malignancies, malnutrition and fatigue were the strongest GA predictors of 1yr mortality after adjusting for age and clinical factors. These findings provide evidence for developing targeted interventions in older patients with newly-diagnosed GI malignancies to reduce 1y mortality. Research Sponsor: U.S. National Institutes of Health.

12048 Poster Session (Board #336), Fri, 8:00 AM-11:00 AM

Association between chronological age and geriatric assessment (GA) to identify deficits in elderly adults with cancer: Findings from the Care Registry. *First Author: Grant Richard Williams, University of Alabama Birmingham, Birmingham, AL*

Background: Although ASCO and NCCN guidelines recommend that adults with cancer diagnosed at age ≥65y undergo a GA, the association between chronologic age and GA identified deficits remains understudied, and thus, the appropriate age cut-off for employing GA in clinical settings remains unknown. We addressed this gap by examining the association between chronologic age and GA deficits in older adults with cancer. **Methods:** The Cancer and Aging Resilience Evaluation (CARE) is an ongoing prospective registry of older adults (≥60y) with cancer at a single site. Eligible patients underwent a patient-reported GA adapted from the Cancer and Aging Research Group. The association between age categories (10y increments) and presence of GA deficits was tested using chi-squared tests of trend. Linear association between age and GA deficits was examined using Pearson correlation. **Results:** The median age at enrollment was 70y (60-96) for 08 participants; 58% were male. Most common cancer types were colorectal (27%), pancreatic (17%), and hepatobiliary (12%). No significant correlation was found between chronologic age and the number of GA deficits (r = 0.03). There was no association between the youngest (60-70y) vs. the oldest age groups (≥80y) with respect to the prevalence of GA deficits: frailty (33% *vs.* 33%, *p*= 0.97); impairment of activities of daily living (ADL) (20% *vs.* 16%, *p*= 0.7);impairment of instrumental ADL (50% vs 60%, *p*= 0.3); malnutrition (42% *vs.* 33%, *p* =0.4), cognitive impairment (8% *vs.* 6%, *p*= 0.6), falls (19% *vs.* 30%, *p* 0.1), anxiety (19% *vs.* 11%, *p*= 0.1) and depression (13.4% *vs.* 13.7%, *p*= 0.2) (Table). Prevalence of 3+ comorbidities was higher in the older patients (45% *vs.* 59%, *p*= 0.03). **Conclusions:** In our cohort of older adults with mostly gastrointestinal malignancies, age was not associated with GA identified deficits and the prevalence of most impairments was similar across age-groups. The use of chronologic age alone to identify which patients may benefit from GA is problematic, and adults 60yrs and above, or perhaps even younger, may derive benefits from a GA. Research Sponsor: U.S. National Institutes of Health.

	Age 60-70	Age 70-79	Age ≥80	*p* value
No. of patients	**422**	**223**	**63**	
Frail	140 (33%)	76 (34%)	21 (33%)	0.97
Comorbidity > = 3	180 (45%)	114 (54%)	34 (59%)	**0.03**
Any IADL impairment	210 (50%)	112 (50%)	38 (60%)	0.29
Any ADL impairment	85 (20%)	44 (20%)	10 (16%)	0.73
Malnutrition	178 (42%)	90 (40%)	21 (33%)	0.41
Falls > = 1	81 (19%)	45 (20%)	19 (30%)	0.13
Cognitive Impairment	33 (8%)	13 (6%)	4 (6%)	0.63
Anxiety	81 (19%)	30 (13%)	7 (11%)	0.08
Depression	54 (13%)	19 (9%)	8 (13%)	0.25

12049 Poster Session (Board #337), Fri, 8:00 AM-11:00 AM

An international cohort study investigating the impact of age on clinical outcome in patients with hepatocellular carcinoma treated with sorafenib. *First Author: Rohini Sharma, Imperial College London, London, United Kingdom*

Background: There is no consensus on the effect of sorafenib dosing on efficacy and toxicity in elderly patients with hepatocellular carcinoma (HCC). Older patients are often empirically started on low dose therapy with the aim to avoid toxicities whilst maximising clinical efficacy. We aimed to verify whether age impacts on overall survival (OS) of patients with HCC, and whether a reduced starting dose of sorafenib impacts on OS or rates of toxicity experienced by the elderly. **Methods:** In this international, multicentre cohort study, patients with a confirmed diagnosis of advanced-stage HCC receiving sorafenib were recruited from seven specialist centres. Demographic and clinical data including development and grade of sorafenib toxicity and sorafenib starting dose were collected prospectively. Survival time (months) was recorded prospectively. Outcomes for those < or > 75 years were determined **Results:** A total of 5598 patients were recruited; 792 (14.1%) were over the age of 75. The elderly were more likely to have larger tumours (> 7cm)(39 vs 33%, p = 0.07) with Child-Pugh A liver function(67 vs 57.7%) and less portal vein thrombosis compared to those < 75years(22.1 vs 29.4)(p < 0.001). They were more likely to be commenced on lower starting dose of sorafenib i.e 400mg/200mg (38.7 vs 37.2%, P < 0.01). In terms of OS, there was no difference in the median OS of those >75 years and patients < 75 (7.3months vs 7.2months; HR 0.98 (95% CI 0.90–1.06), p = 0.63). There was no relationship between starting dose of sorafenib, 800mg vs 400mg/200mg, and OS between those < or > 75years. The elderly experienced a similar incidence of grade 2-4 sorafenib-related toxicity compared to < 75years(74.3 vs 61.7%, p = 0.051)(except for anorexia (14.0 vs 7.2%, p < 0.01) and rash (3.1 vs 6.3%, p < 0.05), irrespective of the dose prescribed. The elderly were more likely to discontinue sorafenib due to toxicity (27.0 vs 21.6%, p < 0.01). This did not vary between different starting doses of sorafenib. The mean duration of treatment was similar between those < and > 75 and, again, the starting dose of sorafenib did not affect treatment duration in the elderly. **Conclusions:** The median OS in the elderly is the same for that of patients under 75 years and is independent of the dose of sorafenib prescribed. Therefore, sorafenib should be offered to elderly patients and they should not be excluded from therapy Research Sponsor: None.

12050 Poster Session (Board #338), Fri, 8:00 AM-11:00 AM

External validation of two predictive scores of chemotherapy toxicities among older patients with solid cancer, from ELCAPA prospective cohort. *First Author: Maxime Frelaut, Institut Curie, Paris, France*

Background: Severe chemotherapy toxicities are frequent among older patients, and may have a major impact on mortality, comorbidities, and quality of life. Two scores were developed to predict severe toxicities: Chemotherapy Risk Assessment Scale for High-age patients (CRASH) score, and Cancer and Aging Research Group Study (CARG) score. The main objective of the present study was to evaluate the predictive value of both scores on an external cohort. Secondary objective was to identify individual predictive factors of severe chemotherapy toxicities. **Methods:** The Elderly Cancer Patients (ELCAPA) survey consists in a prospective cohort including patients aged 70 years or older referred for a geriatric assessment (GA) before anticancer treatment, such as chemotherapy for solid cancer. CARG and CRASH score were retrospectively collected. Main endpoint was grade 3/4/5 toxicities for CARG-score, hematologic grade 4/5 and non-hematologic grade 3/4/5 toxicities for CRASH-score. Calibration and discrimination (Area Under ROC Curve, AUC) were evaluated. **Results:** From July 2010 to March 2017, 248 patients were included. Among them, 150 (61%) experienced severe toxicity as defined in CARG study, and 126 (51%) as defined in CRASH study. There was no increased risk of toxicity in intermediate and high risk groups of CARG-score compared to low risk group (OR = 0.3, $IC_{95\%}$ [0.1 – 1.4], *p*= 0.1; and OR = 0.4, $IC_{95\%}$[0.1 – 1.7], *p*= 0.2 respectively, AUC-ROC = 0.55). Similarly, there was no more risk of severe toxicities in intermediate low, intermediate high, and high risk groups compared to low risk groups of CRASH combined score (respectively OR = 1, $IC_{95\%}$ [0.3 – 3.6], *p*= 0.99; OR = 1, $IC_{95\%}$ [0.3 – 3.4], *p*= 0.9; OR = 1.5, $IC_{95\%}$ [0.3 – 8.1], *p*= 0.67; AUC-ROC = 0.52). A multivariate predictive model including cancer type, performance status (PS 0 *vs.* PS 1-2), number of severe comorbidities (Cumulative Illness Rating Scale for Geriatrics, CIRS-G, ≥1 grade 3 or 4 comorbidity), body mass index (BMI > 25 kg/m² protective *vs.* normal BMI), and Chemotox score (1 *vs.* 0) had an AUC of 0.78. **Conclusions:** Neither CARG nor CRASH score was predictive of severe chemotherapy toxicities in the ELCAPA cohort. There is a need to identify new predictors of chemotherapy toxicity in older patients with solid cancers. Research Sponsor: INCA (Institut national du Cancer), Canceropôle Ile de France and Gérontopôle Ile de France.

12051 Poster Session (Board #339), Fri, 8:00 AM-11:00 AM

Regaining a satisfactory quality of life and predicting functional decline after major cancer surgery in older adults: The Geriatric Oncology Surgical Assessment and Functional rEcovery after Surgery (GOSAFE) study. *First Author: Isacco Montroni, Degli Infermi Hospital, Faenza, Italy, Faenza, Italy*

Background: Older cancer patients value quality of life (QoL) and functional outcomes as much as survival but surgical studies lack specific data. The international, multicenter GOSAFE study (ClinicalTrials.gov NCT03299270) aims to evaluate patients' QoL and functional recovery (FR) after cancer surgery and to assess predictors of FR **Methods:** GOSAFE prospectively collected functional and clinical data before and after major elective cancer surgery on senior adults (≥70 years). Surgical outcomes were recorded (30, 90, and 180 days post-operatively) with QoL (EQ-5D-3L) and FR (Activities of Daily Living (ADL), Timed Up and Go (TUG) and MiniCog), 26 centers enrolled patients from February 2017 to April 2019. **Results:** 942 patients underwent a major cancer resection. Median age was 78 (range 70-95); 52.2% males, ASA III-IV 49%. 934 (99%) lived at home, 51% lived alone, and 87% were able to go out. Patients dependent (ADL $<$ 5) were 8%. Frailty was detected by means of G8 ≤14 in 68.8% and fTRST ≥2 in 37% of patients. Major comorbidities (CCI $>$ 6) were reported in 36% and 21% had cognitive impairment according to MiniCog (2.2% self-reported). 25% had $>$ 3 kg weight loss, 27% were hospitalized in the last 90 days, 54% had ≥3 medications (6% none). Postoperative overall morbidity was 39.1% (30 day) and 22.5% (90 day), but Clavien-Dindo III-IV complications were only 13.4% and 6.9% respectively. 30/90/180-day mortality was 3.6/6/8.9% (10/30/33% in patients with severe functional disability). At 3 months after surgery, QoL was stable/improved (mean EQ-5D index 0.78 was equivalent before vs. after surgery, while the EQ-5D VAS score $>$ 60 raised from 74.3% at baseline to 80.2%, $p < 0.01$). 76.6% experienced postoperative FR/stability. Logistic regression analysis showed that ASA 3-4, CCI≥7 and CD III-IV complications are significantly associated with functional decline while a G8 $>$ 14 has a positive association with functional recovery. Age is not associated with functional outcomes. **Conclusions:** The largest prospective study on older patients undergoing structured frailty assessment before and after major elective cancer surgery has shown that QoL remains stable/improves after cancer surgery. The majority of patients return to independence and G8 can predict functional recovery. Older patients with multiple comorbidities, high ASA score or postoperative severe complications are likely to functionally deteriorate after oncologic surgery Clinical trial information: NCT03299270. Research Sponsor: None.

12052 Poster Session (Board #340), Fri, 8:00 AM-11:00 AM

Living life post cancer treatment (LLPCT): An assessment of a 12-week multidimensional wellness intervention to improve quality of life and physical activity in cancer survivors. *First Author: Christopher C. Marino, University of Pittsburgh Medical Center, Pittsburgh, PA*

Background: Cancer survivors face unique health challenges with implications on health-related quality of life (HRQoL) and physical, social, and emotional well-being. With advancements in cancer treatment and aging populations, the prevalence of cancer survivors is expected to grow prompting the need for improved survivorship care delivery and comprehensive rehabilitative services. Living Life Post Cancer Treatment (LLPCT) is a community-based 12-week program that provides multidimensional support to patients of any cancer diagnosis transitioning from active treatment to post-treatment life. This single-arm intervention study aims to assess the program's impact on HRQoL and physical activity in cancer survivors. **Methods:** A total of 125 participants within 2 years of treatment completion were enrolled in a 12-week program comprised of 9 sessions of engaging workshops, personalized exercise training, and nutrition and psychosocial counseling with an interprofessional team of oncology providers, social workers, exercise trainers, and dietitians. The program consisted of 8 consecutive weekly sessions followed by a 1-month follow-up session at week 12. Ninety-six (77%) participants completed the eighth or ninth session of the program and were included in the analysis. A series of questionnaires were administered at baseline and weeks 8 and 12. Primary outcomes assessed were HRQoL using the Functional Assessment of Cancer Therapy-General (FACT-G) questionnaire and physical activity using average daily steps by pedometer and 2-minute step test performance. **Results:** Among the 96 participants (mean age 60.4 ± 11.7) who completed the program, the majority were female, white, and married. Post-intervention median FACT-G scores significantly increased from baseline at weeks 8 (+8.8, $p = 0.002$) and 12 (+7.3, $p < 0.001$). Average daily steps by pedometer increased by 1063 ($p = 0.003$) and 1233 ($p = 0.015$) and 2-minute step test performance increased by 18 ($p < 0.001$) and 21 ($p < 0.001$) steps at weeks 8 and 12, respectively. Participants reported high levels of satisfaction and improved self-efficacy to incorporate lifestyle modifications. **Conclusions:** These findings suggest that this 12-week intervention improves HRQoL and step-based physical activity levels in cancer survivors and could serve as a multidimensional model for post-treatment support. Further research is needed to determine if these benefits are sustained long-term. Research Sponsor: Our Clubhouse is a community-based non-profit organization funded primarily by individual contributions and partnerships with regional healthcare systems, specifically University of Pittsburgh Medical Center, Allegheny Health Network, and Excela Health.

12053 Poster Session (Board #341), Fri, 8:00 AM-11:00 AM

The impact of weight loss on physical function in overweight or obese breast cancer survivors. *First Author: Jennifer Y. Sheng, Johns Hopkins Hospital, Baltimore, MD*

Background: In the prospective POWER-remote trial, 51% and 12% of overweight/obese breast cancer survivors randomized to either a remotely delivered behavioral intervention or self-directed approach, respectively, lost ≥5% of baseline weight. We collected patient-reported outcomes (PROs) to examine the impact of >5% weight loss on symptoms, physical function (PF), and wellbeing. We hypothesized *a priori* that, regardless of study arm, those with ≥5% weight loss would have improved PF at 6 months v. those who did not. **Methods:** Women with stage 0-III breast cancer, who completed local therapy and chemotherapy, with a BMI ≥25 kg/m^2 were randomized to the 12-month intervention or self-directed weight loss. POWER-remote consists of telephone coaching and online tracking of diet, activity and weight. Women in the self-directed arm received a lifestyle booklet. All women completed PROs at baseline, 6 and 12 months: PROMIS PF, pain, fatigue, anxiety, depression, sleep; FACT-endocrine symptoms; MOS-sexual function. PROs were summarized descriptively and changes within and between groups were tested with multivariable mixed effects models, adjusted for age and baseline weight. **Results:** From 2013-2015, 96 women enrolled; 83 were evaluable at 6 months. At 6 months, PF scores improved in those with ≥5% weight loss v. not. While endocrine symptoms, fatigue, and anxiety improved in the group who lost ≥5%, differences between groups were not statistically significant. There was no significant change in sexual function, depression, or sleep within or between groups. Similar findings were seen across domains at 12 months, except pain improved in the group losing ≥5%. **Conclusions:** For overweight/obese breast cancer survivors, PF and other PROs improved among patients who lost ≥5%. These results support the patient-centered benefits of weight loss in this population. Clinical trial information: NCT01871116. Research Sponsor: U.S. National Institutes of Health, Other Foundation, Other Government Agency.

Changes (Δ) in PROs at 6 months from baseline (BL) by weight loss (WL).

	6 month follow up		
	≥5% WL n=28	<5% WL n=55	P, between groups
Physical function			
BL, Mean (SD)	49.3 (6.6)	49.8 (8.1)	.02
Δ from BL, Mean (SD)	4.4 (5.4)	.3 (8.2)	
P, within group	.009	.99	
Endocrine symptoms			
BL, Mean (SD)	42.4 (8.9)	39.4 (11.2)	.43
Δ from BL, Mean (SD)	2.9 (5.3)	.7 (9.3)	
P, within group	.02	.47	
Fatigue			
BL, Mean (SD)	48.7 (7.7)	51.4 (7.8)	.28
Δ from BL, Mean (SD)	-3 (5.2)	-.4 (7.9)	
P, within group	.09	.91	
Anxiety			
BL, Mean (SD)	48.9 (7.9)	49.2 (8.6)	.16
Δ from BL, Mean (SD)	-2.3 (6.5)	-.2 (8)	
P, within group	.05	.72	

12054 Poster Session (Board #342), Fri, 8:00 AM-11:00 AM

Moving toward precision: Understanding the heterogeneity of obesity. *First Author: Kin Wai (Tony) Hung, Olive View UCLA Medical Center, Sylmar, CA*

Background: Obesity is a global health epidemic and has been linked to detrimental impact on cancer incidence, recurrence, and mortality. Growing evidence have recognized the complex biopsychosocial relationship including microbial phenotypes that undermines the carcinogenic potential and heterogeneity of obesity. A precision understanding on obesity while at its infancy is necessary to accelerate reduction of its impact on cancer outcomes. **Methods:** With our aim to better understand the biopsychosocial relationship on obesity, we conducted a cross sectional study in healthy and obese individuals. Univariate and multivariate logistic regression models were used to examine obesity and its association with sociodemographic (age, gender, ethnicity, education, income, and marital status), clinical (waist to hip ratio), dietary-behavioral (daily calorie, fat, carbohydrate, protein consumption, and preference on cultural diet), and biological factors (gut microbiome). Parameters were controlled and corrected for multiple hypothesis testing. Gut microbial data using 16S rRNA sequencing were analyzed for alpha diversity, beta diversity, and association of taxa abundance. **Results:** Among 171 participants between July 2013 and August 2018, individuals were found to have a higher BMI if they were Hispanic [Adjusted Odds Ratio (AOR) 3.36, 95% CI 1.27-8.90], had an obese waist to hip ratio (AOR 8.51, 95% CI 3.45-21.02), and consumed an American diet (AOR 4.82, 95% CI 1.74-13.34). Multivariate permutation analysis controlling for BMI, sociodemographic, clinical, and dietary parameters found that Hispanic have a significantly different microbiome profile than non-Hispanic ($p = 0.042$). While microbial species richness (Chao1) were similar ($p = 0.22$), Hispanic had a lower microbial species evenness (Shannon) compared to non-Hispanic ($p = 0.029$). Differential expression of microbial species revealed a positive correlation of Firmicutes:Bacteroidetes ratio in individuals with higher BMI and consumed an American diet whereas a negative correlation to Hispanic ethnicity. **Conclusions:** Obesity association to Hispanic ethnicity uniquely expressed through microbial signature despite sociodemographic, clinical, and dietary differences. Microbial characterization as an emerging predictive marker for oncology therapeutics may also serve as selection biomarker in onco-obesity practices and clinical trials. Addressing ethnic disparities guided by microbial phenotypes may unlock novel understanding of obesity heterogeneity and transform its impact on cancer care. Research Sponsor: NIH/NIDDKK23 DK106528 (PI: Gupta), NIH/NCATS UL1TR001881 (CURE/CTSI funds to Gupta: PI), NIH/NIDDK DK 041301 (CURE/CTSI funds to Gupta: PI).

12055 Poster Session (Board #343), Fri, 8:00 AM-11:00 AM

Randomized clinical trial on the effect of a supervised exercise program on quality of life, fatigue, and fitness following esophageal cancer treatment (PERFECT study). *First Author: Anne Maria May, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands*

Background: Patients with potentially curable esophageal cancer are often treated with chemoradiotherapy followed by surgery. This treatment might have a negative impact on physical fitness, fatigue and quality of life (QoL). In patients with other types of cancer, evidence suggests that physical exercise reduces treatment related side effects. We investigated whether a supervised exercise program also beneficially affects QoL, fatigue and cardiorespiratory fitness (CRF) in patients after treatment for esophageal cancer. **Methods:** The multicenter PERFECT study randomly assigned patients in the first year after esophagectomy to an exercise intervention (EX) or usual care (UC) group. EX patients participated in a 12-week moderate to high intensity aerobic and resistance exercise program supervised by a physiotherapist. UC patients were advised to maintain their physical activity levels. Attendance and compliance with the exercise intervention protocol were retrieved from exercise logs. QoL (primary outcome, EORTC-QLQ-30, range 0-100), fatigue (MFI-20, range 4-20) and CRF (cardiopulmonary exercise testing) were assessed at baseline and after 12 weeks (post-intervention). The outcomes were analyzed as between-group differences using either linear mixed effects models or ANCOVA adjusted for baseline and stratification factors (i.e. sex, time since surgery, center), according to the intention-to-treat principle. **Results:** A total of 120 patients (age 64±8) were included and randomized to EX (n = 61) or UC (n = 59). Patients in the EX group participated in 96% (IQR:92-100%) of the supervised exercise sessions and compliance with all parts of the exercise program was high (> 90%). Post-intervention, global QoL was not statistically different between groups, but significant ($p < 0.05$) beneficial EX effects were found for QoL-Summary scores (between-group difference 3.5, 95% CI 0.2;6.8) and QoL-role functioning (9.4, 1.3;17.5). Physical fatigue wat non-significantly lower in the EX group (-1.2; -2.6;0.1, p = 0.08). CRF was significantly higher (VO_{2peak} (1.8 mL/min/kg, 0.6;3.0) following the EX intervention. **Conclusions:** Patients were well capable to complete an intensive supervised exercise program after esophageal cancer treatment, which led to small but significant improvements in several aspects of QoL and cardiorespiratory fitness. Our results suggest that supervised exercise is a beneficial addition to routine care of patients with esophageal cancer. Clinical trial information: NTR5045. Research Sponsor: World Cancer Research Fund The Netherlands (WCRF NL, project number 2013/997).

12056 Poster Session (Board #344), Fri, 8:00 AM-11:00 AM

Effect of evidence-based nutrition educational intervention on adherence to dietary guidelines (ADG) and weight management among early-stage breast cancer (EBC) patients (pts): A prospective trial. *First Author: Ilaria Trestini, Department of Oncology, University of Verona Hospital Trust, Verona, Italy*

Background: Excess adiposity is linked to an increased risk of worse outcome among EBC pts. Pts undergoing EBC treatment are susceptible to change in nutrition status. However, implementation and assessment of the adherence to lifestyle interventions have been limited. This prospective trial aimed to evaluate the impact of an evidence-based nutrition intervention, according to the ADG, in terms of body composition changes in EBC pts. **Methods:** Entry criteria: EBC pts candidate to neoadjuvant/adjuvant therapy. At study entry, pts received a nutrition evidence-based tailored intervention. Dietary and anthropometric assessments were evaluated at baseline and after 12-months nutritional intervention. Waist circumference (WC) was assessed as a surrogate measure of fat distribution. ADG was estimated by Med-Diet 14-item questionnaire. Health-Related Quality of Life was analysed with EORTC QLQ-C30. Descriptive statistics was adopted. Associations between variables and groups according to nutritional variables were analysed (Chi-square test). **Results:** From February 2016 to December 2019, 243 pts were enrolled (median age 49 years): 27.6%/48.6% neoadjuvant/adjuvant treatment. At baseline, 38.3% of pts were overweight and 23.9% were obese. Notably, tumor size was significantly correlated with WC in the whole population (p = 0.003). Moreover, pts with central obesity were more likely to present HER2-negative tumors (57.4% vs. 42.5%, p = 0.03). Most pts reported relevant nutrition impact symptoms and symptoms affected QoL. Particularly, dyspepsia and constipation were more prevalent in overweight and obese pts ($p < 0.0001$ and p = 0.009, respectively), as well as in pts who gained ≥5% of weight (p = 0.04 and p = 0.02, respectively). At baseline, there was low ADG. After the 12-months intervention, ADG significantly increased (median Med-Diet score: 6 vs.12, $p < 0.0001$). A high ADG (defines as a Med-Diet score ≥10) significantly correlated with: 1) loss of weight ≥5% from the baseline weight (p = 0.003); 2) change in terms of BMI; 3) prevalence of central obesity. **Conclusions:** A tailored evidence-based nutritional intervention for EBC pts represents a tool to improve their ADG, weight management and, thus, to potentially influence the disease outcome. Research Sponsor: None.

Variables	At baseline	After 12-months	p-value
BMI			p = 0.003
underweight	5 (3.3)	0 (0)	
normal weight	73 (48.0)	126 (82.9)	
overweight	60 (39.5)	21 (13.8)	
obese	14 (9.2)	5 (3.3)	
WC			p = 0.01
central obesity	58 (38.2)	11 (7.2)	

12057 Poster Session (Board #345), Fri, 8:00 AM-11:00 AM

The impact of high intensity interval training on functional performance, body composition and quality of life in a diverse group of cancer survivors. *First Author: Jennifer Lynn Beebe-Dimmer, Wayne State University School of Medicine, Karmanos Cancer Institute, Detroit, MI*

Background: Given the well-documented benefits of regular exercise to cancer survivors, in 2012, an expert panel assembled by the American Cancer Society recommended that patients engage in at least 150 minutes per week of moderate-to-vigorous physical activity. However, few patients meet this goal. We have also observed racial differences in reported participation in regular exercise among cancer survivors living in Metropolitan Detroit, Michigan. **Methods:** The CAPABLE study is a 12- week pilot exercise intervention that introduces cancer survivors to the sport of CrossFit. We evaluated the impact of this unique, high-intensity interval training method on functional performance, cardiovascular endurance, body composition and health-related quality of life (HRQOL) as measured by the Functional Assessment of Cancer Therapy (FACT) instrument. All measures were summarized at baseline and program exit. Paired signed rank tests were used to assess change in each of these measures over time. **Results:** Of the 48 participants enrolled in the pilot, 37 (77%) were considered adherent to the program (attending at least 75% of sessions over the 12-week period). The mean age of participants was 58.5 years, 73% identified as African American and the majority of participants were breast cancer survivors (N = 20). The mean body mass index (BMI) at baseline was 32.8 kg/m^2 decreasing to a mean of 31.7 kg/m^2 at exit (BMI change -1.1, $p < 0.001$). Similar changes were observed in % body fat measured by bioelectrical impedance. There were significant improvements in all measures of functional performance over 12-weeks (all $p < 0.001$). We observed significant and meaningful improvements in reported HRQOL measured by the FACT survey, overall (FACTG total change +9.5 ($p < 0.001$)) and in each one of the individual domains (physical, social, emotional, and functional well-being). **Conclusions:** We observed significant improvements in performance, body composition and quality of life among cancer survivors introduced to a high-intensity interval training program. Understanding and eliminating barriers to programs like these are critical to improving outcomes and reducing cancer health disparities. Clinical trial information: NCT03750981. Research Sponsor: Karmanos Cancer Institute.

12058 Poster Session (Board #346), Fri, 8:00 AM-11:00 AM

The impact of tobacco retail density on overall survival (OS) in lung cancer survivors. *First Author: Lawson Eng, Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Continued smoking after a cancer diagnosis is associated with poorer outcomes. We previously identified that tobacco retail outlet density is negatively associated with cessation in lung cancer survivors (ASCO 2019). However, the impact of tobacco retail density on survival has not been evaluated. We evaluated the impact of tobacco retail density on OS in lung cancer patients (pts). **Methods:** Lung cancer pts diagnosed from 2009-2012 were recruited at diagnosis and completed a baseline questionnaire on their sociodemographics, ECOG and smoking history. Clinicopathologic data including stage, histology and OS data were collected. Validated tobacco retail location data obtained from Ministry of Health and pt home addresses were geocoded using ArcGIS 10.6.1, which calculated tobacco outlet density within 250 meters (m) and 500m from pts. Multivariable Cox proportional hazard models evaluated the impact of tobacco outlet density on OS adjusted for significant clinicodemographic covariates. **Results:** Among 1411 pts, median age 66, 53% female, 8% small cell/56% adenocarcinoma/17% squamous/19% other, 28% stage 1/9% stage 2/20% stage 3/35% stage 4, 38% were current smokers at diagnosis and 40% were ex-smokers; median OS was 24 months. On average, there was one vendor (range 0-23) within 250m and four vendors (range 0-44) within 500m from pts; 33% and 60% of pts lived within 250m and 500m from at least one vendor respectively. The final baseline multivariable model consisted of age, gender, stage, smoking status, ECOG and neighbourhood marginalization index ($P< 0.05$). Among all pts, not living within 250m to an outlet improved OS (aHR 0.84 [0.72-0.97] P= 0.02). Living near more outlets within 250 m (aHR 1.03 per outlet [1.00-1.05] P= 0.03) or 500 m (aHR 1.01 per outlet [1.00-1.02] P= 0.04) worsened OS. Subgroup analysis based on smoking status at diagnosis, identified that among current smokers, not living within 250m to an outlet improved OS (aHR 0.76 [0.60-0.97] P= 0.03), and among ex-smokers, living near more outlets within 500 m worsened OS (aHR 1.02 per outlet [0.99-1.03] P= 0.07); other associations showed similar directionality. Among 135 current smokers at diagnosis with follow-up smoking status, not living within 250m to an outlet continued to show a trend towards improved OS (aHR 0.57 [0.31-1.03] P= 0.06), after also adjusting for follow-up smoking status. **Conclusions:** Living near a greater density of tobacco outlets is associated with poorer OS among lung cancer pts. Reducing the density of tobacco outlets may be a strategy that can help improve lung cancer pt outcomes. Research Sponsor: Cancer Care Ontario - ON-PROST.

12059 Poster Session (Board #347), Fri, 8:00 AM-11:00 AM

Panel-based methodology for assessing the impact of public policies on cancer patients and survivors. *First Author: Amy Farner, American Cancer Society Cancer Action Network, Washington, DC*

Background: Cancer interventions are subject to a range of regulations, but data from large, nationally representative surveys are not always available in time to inform the policy process and do not always address issues specific to cancer patients and survivors. Understanding their experiences is critical to achieving policy solutions to issues such as access to effective pain relief, reducing unexpected medical bills, and reducing the impact of high prescription drug costs on treatment for lower income cancer patients. This research intended to better understand patient experiences and opinions in a statistically valid manner specifically targeted to the policy process. **Methods:** 3057 panelists were identified from ACS contacts, health systems, and social media advertising through ACS/ACS CAN pages and paid Facebook ads, to participate in a series of surveys across a year. The panel included diverse survivors across age, gender, race, ethnicity, economic status, and cancer type. Online surveys deployed semi-monthly on cancer survivorship topics impacted by current policy, including access to/affordability of care, pain treatment, and prescription drug costs. Responses were analyzed for the entire population and across subgroups of cancer survivors. **Results:** Each survey achieved a response rate between 35% and 50% of all panel members, resulting in a margin of error +/- 3% and 95% confidence level. Insights from cancer patient and survivor experiences helped support public policies through findings such as (but not limited to): 41% of those prescribed opioids had trouble getting their medicine, creating difficulty participating in work, family, or social events; extra trips to the doctor or pharmacy; negative impact on treatment, and trips to the Emergency Room due to uncontrolled pain; 24% received a surprise medical bill, increasing their anxiety, reducing likelihood to see a specialist, and reducing likelihood to seek emergency care during a serious health issue; and 31% of those with household income less than $30,000 report trouble affording prescription drugs and 17% have delayed or not filled a prescription due to cost. Findings supported the policy process by helping craft policy positions aligned with cancer patient preferences, raising public awareness, and communicating to policymakers the impact of policies on cancer. **Conclusions:** The panel methodology illustrates the impact of policy decisions on cancer patients and survivors. Findings provide an unprecedented level of input to the policy process for cancer patients and survivors. Research Sponsor: Bristol Meyers Squibb.

12060 Poster Session (Board #348), Fri, 8:00 AM-11:00 AM

Patterns of the risk for subsequent primary cancer among survivors of adult-onset cancers in the United States. *First Author: Hyuna Sung, American Cancer Society, Atlanta, GA*

Background: The number of cancer survivors who develop new cancers is projected to grow in the US. Few studies, however, have provided a comprehensive overview of the contemporary pattern in the risk of subsequent primary cancer (SPC) among survivors of adult-onset cancers. Herein, we evaluate overall and type-specific risks of SPCs among adult-onset cancer survivors by first primary cancer types and sex. **Methods:** We assessed the excess risk of SPCs among 1,442,374 persons aged 20-84 years who were diagnosed with first primary cancers from 1992-2010 and survived ≥5 years in the 12 Surveillance, Epidemiology, and End Results registries. We expressed the risks using excess absolute risk (EAR) per 10,000 person-years and standardized incidence ratio (SIR) by first primary cancer types and sex, compared to those expected in the general population. We also estimated percent contributions of each specific type of SPCs to the total EAR for all first primary cancers combined by sex. **Results:** The overall risk of SPCs was higher than expected for 24 of the 34 first primary types among male survivors and for 28 of the 35 first primary types among female survivors. The greatest SIR and EAR were estimated after laryngeal cancer in both men (SIR = 1.74, 95%CI = 1.67-1.82; EAR = 159.3, 95%CI = 143.6-175.5) and women (SIR = 2.48, 95% CI = 2.26-2.73; EAR = 202.7; 95%CI = 171.8-236). There were 290 type-specific associations with significantly higher risk of SPC, 36% of which being reciprocal, predominantly among smoking-associated, HPV-associated, and hematologic cancers. The SIRs in men ranged from 1.05 (95%CI = 1.00-1.10; EAR = 1.69) for lung/bronchus cancer after colorectal cancer to 73.9 (95%CI = 58.3-92.3; EAR = 23.3) for anal cancer after Kaposi sarcoma; and in women the SIRs ranged from 1.08 (95%CI = 1.02-1.15; EAR = 0.36) for pancreatic cancer after breast cancer to 19.9 (95%CI = 15.0-26.0; EAR = 39.5) for oral cavity/pharyngeal cancer after laryngeal cancer. For all first primary cancers combined, lung/bronchus cancer comprised the greatest proportion of the total EAR of SPCs, 34.6% in men and 29.1% in women, followed by urinary bladder (11.8%) and oral cavity/pharynx (7.5%) in men and by corpus uterus (12.9%) and colorectum (7.6%) in women. **Conclusions:** Despite the substantial heterogeneity in the risk of SPCs across the first primary types, only a few cancers comprised a considerable proportion of the total excess risk among survivors. Better understanding of contributing factors to these patterns will inform survivorship care plans and care delivery. Research Sponsor: None.

12061 Poster Session (Board #349), Fri, 8:00 AM-11:00 AM

Impact of immune checkpoint and BRAF inhibitors on the incidence of second primary malignancies (SPM) in melanoma. *First Author: Nibash Budhathoki, NYU Winthrop Hospital, Mineola, NY*

Background: Prior studies have shown an increased risk of SPM in melanoma, however there is limited data on the incidence of SPM following the 2011 approvals of immune checkpoint (ipilimumab) and BRAF (vemurafenib) inhibitors, which have become standard of care. We present data comparing SPM rates before and after introduction of these agents for advanced cutaneous melanoma. **Methods:** Adult melanoma patients with regional or distant metastases were identified from SEER-18 database and divided into cohorts: 2005-2010 and 2011-2016. SPM was defined as tumors diagnosed ≥6 months from diagnosis of the primary cancer. SEER*stat was used to calculate SPM by multiple primary standardized incidence ratio based on observed (O) and expected (E) cases. The expected numbers of new cancers of specific types were estimated by assuming that incidence rates for new primary tumors corresponded to sex, age, and calendar time–specific SEER rates for similar invasive primary cancers and applying those rates to the accumulated person-years (PYR) of observation. Excess absolute risk (EAR) of malignancy per 10,000 PYR at risk was calculated as $([O - E]/PYR) \times 10{,}000$. **Results:** As shown in the table, from before 2005-2010, 421 of 7991 patients (5.2%) with advanced melanoma had 444 SPM (O/E ratio 2.2, 95% CI 1.9-2.4, $P < 0.0001$, EAR 157). In comparison, from 2011-2016, 527 of 9341 patients (5.6%) developed 584 SPM (O/E ratio 2.5, 95% CI 2.3-2.7, $P < 0.0001$, EAR 193). Incidence of AML, myeloma, and pancreatic cancer increased in 2005-2010, while soft tissue malignancies increased from 2011-2016. The incidence of thyroid, brain, and small bowel tumors increased in both groups from 2005-2016. **Conclusions:** There is a distinct pattern as well as increased latency of SPM in patients with advanced melanoma in the era of immune checkpoint and BRAF inhibitors. We speculate that reduction in chemotherapy use, augmentation of immunosurveillance, and inhibition of oncogenic pathways may impact the pathogenesis of SPM. Research Sponsor: None.

Summary	2005-2010	2011-2016
Total number of patients	7991	9341
Male	5096 (63.7%)	5996 (64%)
Female	2895 (36.3%)	3345 (36%)
White	7683 (96.1%)	8987 (96%)
Black	122 (1.5%)	127 (1.4%)
Other races	186 (2.3%)	127 (1.4%)
Total number of SPMs	444	584
Total patients with SPM	421 (5.3%)	527 (5.6%)
Patients with 1 SPM	400 (5.0%)	431 (4.6%)
Patients with 2 SPM	19 (0.23%)	35 (0.4%)
Patients with 3 SPM	2 (0.02%)	11 (0.1%)
Median years of age at diagnosis of SPM (range)	66 (20-94)	69 (23-101)
Median latency time to development of SPM (range)	18 months (6-64)	41 months (6-200)

12062 Poster Session (Board #350), Fri, 8:00 AM-11:00 AM

Effects of radiation therapy on clonal hematopoiesis. *First Author: Leslie Ann Modlin, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Clonal hematopoiesis (CH), characterized by recurrent somatic mutations in blood, is a common age-associated condition that portends an increased risk of myeloid neoplasms and cardiac disease. Oncologic therapies appear to promote CH, including ionizing radiation therapy (RT) (OR = 1.4, $p < 10^{-6}$) and systemic DNA-damaging agents (OR = 1.2, $p = 8 \times 10^{-4}$). How various RT parameters (e.g. target site, dose, fractionation, modality) may influence CH is unknown. **Methods:** CH mutations were identified via targeted, deep-coverage next-generation sequencing from paired peripheral blood and tumor samples (MSK-IMPACT). CH was defined as a somatic blood mutation with a minimum variant allele frequency of 2%. Putative driver mutations (CH-PD) were identified from OncoKB and other published sources. Clinical and RT characteristics were abstracted from medical records. To account for differences in RT dose and fractionation, equivalent radiation dose in 2 Gy fractions (EQD_2) with an α/β ratio of 3 for late effects was calculated. Univariate and logistic regression modeling for associations between clinical and treatment parameters and CH were performed. **Results:** We identified 2,195 patients who received RT before blood draw and 7,832 who did not, encompassing 57 histologies. A median of 267 days elapsed between the end of RT and blood draw. After RT, 22% of patients had at least one CH-PD mutation (n = 486). The most common single anatomic sites radiated were pelvis, chest wall/breast, and head and neck. Conventional RT was used in 2% (n = 46), 3D-conformal in 14% (n = 308), intensity modulated RT in 36% (n = 787), volumetric modulated arc RT in 12% (n = 263), multiple techniques in 26% (n = 560), and unknown in 11% (n = 231). There was no association between RT modality and presence of CH-PD ($p > 0.05$ for all between group comparisons of modality). On multivariate regression after controlling for age, race, time from diagnosis to blood draw, smoking status, and for chemotherapy class, cytotoxic, immune, or targeted therapies in the entire cohort, EQD_2 was associated with CH-PD ($p = 0.012 \times 10^{-3}$). Evaluating EQD_2 by irradiated anatomic site, total pelvic dose by EQD_2 in 10 Gy increments remained significantly associated with CH-PD (OR = 1.07, p = 0.0046), as was head and neck EQD_2 (OR = 1.046, p = 0.032). **Conclusions:** CH-PD was associated with higher radiation dose for pelvic or head and neck RT, but not other anatomic sites after controlling for systemic therapies. RT modality was not associated with CH-PD. Ongoing work will directly evaluate the bone marrow dosimetry of various treatment approaches using phantom-based modeling. Research Sponsor: U.S. National Institutes of Health.

12063 Poster Session (Board #351), Fri, 8:00 AM-11:00 AM

Impact of preexisting cardiovascular disease (CVD) on treatments and outcomes of patients with breast or lung cancer. *First Author: Atul Batra, Tom Baker Cancer Center, Calgary, AB, Canada*

Background: Prior cardio-oncology and geriatric oncology research has mainly focused on cancer treatments and their late effects on cardiac health, but little information is known about how cardiac health may influence subsequent cancer treatments. This real-world study aimed to evaluate the associations of pre-existing CVD on treatment adherence and survival in patients with breast or lung cancer. **Methods:** We linked administrative data from the population-based cancer registry, electronic medical records, and billing claims in a large province (Alberta, Canada) over a 10-year time period (2006-2015). Multivariable logistic regression analyses were performed to identify associations of CVD with cancer treatments. Multivariable Cox proportional hazards models were constructed to determine the effect of CVD on overall survival (OS), while adjusting for receipt of cancer treatments. **Results:** We identified 46,227 patients with breast or lung cancer, of whom 77% were women and median age was 65 years. While 82% of patients with breast cancer were early stage, 50% with lung cancer had metastasis. The prevalence of pre-existing CVD was 20% where congestive heart failure was most frequent. In logistic regression, CVD was associated with lower odds of receiving appropriate chemotherapy (OR, 0.60, 95% CI, 0.56-0.65, *P*<.0001), radiotherapy (OR, 0.76, 95% CI, 0.72-0.81, *P*<.0001), and surgery (OR, 0.60, 95% CI, 0.54-0.66, *P* <.0001), irrespective of tumor site (Table). The 5-year OS was lower in patients with baseline CVD as compared to those without (46% vs 58%, *P<0.0001*). Upon adjusting for stage and treatment, CVD continued to correlate with worse OS (HR, 1.23, 95% CI, 1.19-1.26; *P*<.0001). **Conclusions:** Cancer patients with prior CVD were less likely to receive standard cancer therapy. Even among those who underwent cancer treatments, worse outcomes were observed in those with CVD. Early cardio-oncology and geriatric oncology engagement may reduce treatment bias and ensure that carefully selected patients with a cardiac history are still offered appropriate cancer therapy. Research Sponsor: None.

Odds of receiving appropriate cancer therapy in patients with pre-existing CVD (vs. those without CVD).

	Breast Cancer (n=25,527)	Lung Cancer (n=20,700)	Total (n=46,227)
Chemotherapy			
OR	0.56	0.59	0.60
95% CI	0.49-0.65	0.54-0.64	0.56-0.65
***P*-value**	<0.0001	<0.0001	<0.0001
Surgery			
OR	0.66	0.55	0.60
95% CI	0.60-0.72	0.48-0.63	0.54-0.66
***P*-value**	<0.0001	<0.0001	<0.0001
Radiation			
OR	0.69	0.81	0.76
95% CI	0.57-0.83	0.76-0.87	0.72-0.81
***P*-value**	<0.0001	<0.0001	<0.0001

12065 Poster Session (Board #353), Fri, 8:00 AM-11:00 AM

Fatigue in long-term survivors with ovarian cancer: Results of Expression VI – Carolin meets HANNA – Holistic analysis of Long-term survival with ovarian cancer—The international NOGGO, ENGOT and GCIG survey. *First Author: Hannah Woopen, NOGGO and Department of Gynecology, European Competence Center for Ovarian Cancer, Charité, University Medicine of Berlin, Campus Virchow Klinikum, Berlin, Germany*

Background: Long-term survivors (LTS) with ovarian cancer may be cured from cancer but frequently experience long-term toxicities such as fatigue with a huge impact on quality of life. Aim of this study was to evaluate factors associated with fatigue in LTS. **Methods:** Within the study "Carolin meets HANNA" (www.carolinmeetshanna.com) long-term survivors with ovarian cancer (LTS) were recruited since 11/2016. Long-term survival was defined as an ovarian cancer diagnosis more than eight years ago. **Results:** Until 12/2019 473 LTS could be recruited. 211 LTS (44.5%) have experienced fatigue. At the time point of recruitment in 23.4% (111 LTS) fatigue was still present. LTS with fatigue were not more frequently under current treatment compared to LTS without fatigue (p = 0.348). LTS with fatigue were not younger at initial diagnosis (50.4 vs. 51.9 years, p = 0.228). 58.6% of LTS with fatigue compared to 41.5% without fatigue have developed recurrent disease (p = 0.002) and LTS had more frequently more than one recurrence (66.1% vs. 51.7%, p = 0.055). Fatigue was associated with worse health status (2.9 vs. 2.2 on a scale from 1-5, p < 0.001). Fatigue was associated with medical complaints in general (82.0% vs. 43.0%, p < 0.001). Symptoms such as nausea and vomiting (p < 0.001), loss of appetite (p < 0.001), constipation (p < 0.001), diarrhea (p < 0.001), weight loss (p = 0.001) and bloating (p < 0.001) were more frequent in LTS with fatigue. This also accounts for cognitive disorders (39.6% vs. 10.5%, p < 0.001), depression (23.4% vs. 7.4%, p < 0.001), polyneuropathy (39.6% vs. 13.2%, p < 0.001) and cardiovascular disease (11.7% vs. 3.6%, p = 0.002). LTS with fatigue regard themselves more frequently as cancer patient (73.9% vs. 40.8%), p < 0.001). **Conclusions:** Fatigue is still very common in LTS despite the long survival time. Fatigue is associated with worsened health status and other long-term side effects underlining the impact on LTS. There is a high need for survivorship clinics that should ask for and, if necessary, should address still existing side effects such as fatigue. Research Sponsor: German Ovarian Cancer Foundation, Pharmaceutical/Biotech Company.

12066 Poster Session (Board #354), Fri, 8:00 AM-11:00 AM

Efficacy of ear acupuncture on sleep quality in breast cancer survivors: A randomized controlled trial. *First Author: Melanie Désirée Hoextermann, Department of Internal and Integrative Medicine, Evang. Kliniken Essen-Mitte, Faculty of Medicine, University of Duisburg-Essen, Essen, Germany, Essen, Germany*

Background: Among females, breast cancer is the most commonly diagnosed cancer worldwide. Sleep problems impair 40 to 70 % of breast cancer survivors. The aim of this randomized controlled trial was to evaluate the effect of ear acupuncture on sleep quality in breast cancer survivors. **Methods:** Fifty-two female breast cancer survivors (mean age 55.73 ± 8.10) were randomized to either 10 treatments of ear acupuncture within five weeks (N = 26) or to a single session of psycho-education and given an advice booklet concerning insomnia (N = 26). Both interventions were delivered in a group setting. Primary outcome was sleep quality (measured by the Pittsburgh Sleep Quality Index) at week 5 corrected for treatment expectancies. Secondary outcomes were inflammation parameters (interleukin-6) at week 5, sleep quality at week 17, and stress, anxiety, depressive symptoms, quality of life and fatigue 5 weeks and 17 weeks after randomization. **Results:** Intention-to-treat analysis showed a significantly stronger increase of sleep quality in the ear acupuncture group compared to the psycho-education group (p= .031; d = 0.64) at week 5. Furthermore, ear acupuncture improved stress (p= .030; d = 0.64), anxiety (p = .001; d = 0.97), and fatigue (p = .012; d = 0.75) at week 5 compared to psycho-education. No significant group difference was found on any outcome at week 17. No serious adverse events occurred during the study period. **Conclusions:** Group ear acupuncture may be a helpful intervention in tackling sleep problems in breast cancer survivors in the short term and may reduce stress, anxiety and fatigue as well. Long-term effects remain questionable. Clinical trial information: NCT03874598. Research Sponsor: Karl and Veronica Carstens-Foundation.

12068 Poster Session (Board #356), Fri, 8:00 AM-11:00 AM

Lifelong disease burden of chemotherapy in Hodgkin lymphoma (HL): A simulation study from the St. Jude Lifetime (SJLIFE) Cohort and HL International Study for Individual Care (HoLISTIC). *First Author: Susan K. Parsons, Tufts Medical Center, Boston, MA*

Background: Current emphasis for childhood and young adults with HL is to maintain high cure rates while concurrently identifying regimens to reduce excess long-term mortality/morbidity. Thus, understanding the late effects (LE) of contemporary clinical trials (CCT) for HL is critical. **Methods:** We used simulation to estimate the projected life expectancy (LExp), quality adjusted life-expectancy (QALE) & cause of death (COD) in a large cohort of HL CCT patients (pts) in the recently established HoLISTIC consortium by linking long-term risk models from the SJLIFE cohort. Individual patient data (IPD) on bleomycin, alkylating agents and anthracycline were extracted & harmonized for 982 HL pts in 5 prospective CCT (mean diagnosis age 19y, range 3-30y; 51% male; all treated with chemotherapy only; progression-free survival [PFS] >5y) in the HoLISTIC database. LExp, QALE & COD were projected using a previously developed microsimulation model (Bhakta, *Blood [Supplement]*, 2019) that incorporated mortality & incidence of LEs by diagnosis age, sex, race, treatment exposures & attained age estimated from 5,522 adult 10-y survivors of childhood cancers in the SJLIFE cohort (56% male; mean age at last follow-up 35y, range 19-68). Microsimulation was applied to 10,000 randomly selected survivors of HL CCT cohort, from 10y after HL diagnosis until death to project the LExp, QALE & COD. **Results:** Assuming 10-y PFS, LExp and QALEs projected for the HL CCT cohort using adjusted US general population rates linked with the SJLIFE microsimulation model, COD and trial-specific exposures are shown in the Table. **Conclusions:** A novel lifetime simulation approach was used to project LExp, QALE & COD by linking together IPD from CCTs with the long-term risk model of the SJLIFE survivorship cohort. Despite differences in PFS, reflecting in part the variation in risk/stage status, the projected long-term outcomes were similar. Our approach highlights a new opportunity to inform future clinical trial design and aid provider & patient decision-making. Research Sponsor: None.

		Trial				
	US Population	COG AHOD0431	EORTC/LYSA/FIL H10	COG AHOD0031	ECOG2496	Italian HD0607
Number		**139**	**266**	**304**	**73**	**200**
Risk/Stage		**Low**	**Early**	**Intermediate**	**Advanced**	**Advanced**
5-y PFS (%)		90	87	85	77	80
Exposures						
Bleomycin (Yes/No)		N	Y	Y	Y	Y
Alkylators (mg/m^2)		3600	6218	3200	6600	8850
Anthracyclines (mg/m^2)		150	244	200	275	305
Outcomes (y, mean)						
LExp	79	72	71	71	70	70
QALE	69	58	57	58	57	56
COD (%)						
Cardiac		19	20	19	21	22
Pulmonary		1	1	1	1	1
Second Malignancy		7	12	12	13	14
Other		73	67	68	65	64

12069 Poster Session (Board #357), Fri, 8:00 AM-11:00 AM

Long-term follow-up assessment of cardiac safety in SAFE-HEaRt, a clinical trial evaluating the use of HER2-targeted therapies in patients with HER2-positive breast cancer and compromised heart function. *First Author: Katia Khoury, Georgetown Lombardi Cancer Center, Washington, DC*

Background: HER2-targeted therapies are associated with cardiotoxicity, mostly asymptomatic and reversible. The impact of withholding these therapies on breast cancer outcomes is unknown. SAFE-HEaRt trial was the first study to evaluate the safety of HER2-targeted agents in patients with reduced left ventricular ejection fraction (LVEF) receiving concomitant cardioprotective medications and close cardiac monitoring. We report the 3-year follow-up (f/u) results. **Methods:** Thirty patients with stage I-IV HER2-positive breast cancer receiving trastuzumab, pertuzumab or ado-trastuzumab emtansine (TDM-1), with asymptomatic LVEF 40-49%, were started on beta blockers (ß-blockers) and/or ACE inhibitors/ARBs, with the primary endpoint being completion of HER2-targeted therapy without cardiac events (CE) or protocol-defined asymptomatic worsening of LVEF. **Results:** Patients were accrued from 10/2013 to 12/2017 and median f/u as of 2/7/20 is 37 months. The study met its primary endpoint with 27 patients (90%) completing their HER2-targeted therapies without cardiac issues. 24 patients were reconsented for long-term f/u. There were 23 evaluable patients (1 lost for f/u). Off study, 2 patients continued treatment with trastuzumab, 3 with trastuzumab and pertuzumab, and 3 with TDM-1 for metastatic disease. 1 of the 2 patients who had developed a CE with symptomatic heart failure (HF) died of progressive oncological disease, and the second had LVEF recovery on cardiac medications after completion of adjuvant HER2-targeted therapy. Almost 5 years later, she had an asymptomatic decline in her LVEF to 35% after deciding to stop her ß-blocker and ARB. Of the remaining 21 patients, 15 had recovery of their LVEF to $\geq$50%, 9 of whom remain on cardiac medications. 5 patients had stable LVEF 40-49% and remain asymptomatic on cardiac medications. Only 1 patient had symptoms suggestive of HF, with last documented LVEF stable at 45-50%, but she has not sought medical care for the last 15 months since relocating to another country. There were no new CE and no cardiac deaths. Mean LVEF was 45% at baseline, 46% at end of treatment, and 51.5% at long term f/u. **Conclusions:** Long-term f/u of the SAFE-HEaRt study continues to provide safety data of HER2-targeted therapy use in patients with compromised heart function. The late development of cardiac dysfunction is uncommon and continued multi-disciplinary oncologic and cardiac care of patients is essential for improved patient outcomes. Clinical trial information: NCT04143594. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology, Pharmaceutical/Biotech Company, U.S. National Institutes of Health.

12070 Poster Session (Board #358), Fri, 8:00 AM-11:00 AM

Assessing the roles of inflammation and blood brain barrier permeability in cognitive impairment: A nationwide longitudinal study of patients receiving chemotherapy and non-cancer controls. *First Author: Elizabeth Belcher, University of Rochester Medical Center, Rochester, NY*

Background: Cognitive impairment is a prevalent side effect of chemotherapy. We have previously shown that chemotherapy treatment is associated with worse performance on the Rapid Visual Processing test (RVP), an objective measure of sustained attention, over time compared to non-cancer controls. Better understanding of the biologic mechanisms underlying cognitive impairment in cancer patients is needed. The pro-inflammatory cytokine tumor necrosis factor alpha (TNFα) has been implicated in increasing blood brain barrier (BBB) permeability, which in turn is associated with cognitive impairment. This study assessed the relationships of TNFα and S100β, a biomarker of BBB permeability, to each other and to RVP performance over time. **Methods:** We analyzed a subset of participants (n = 89 patients, n = 52 controls, mean age = 60) from a prospective longitudinal study of women with breast cancer receiving chemotherapy and non-cancer controls. TNFα and S100β were measured in serum pre-chemotherapy (T1, $\leq$7 days before first treatment) and post-chemotherapy (T2, $\leq$1 month after last treatment) and at corresponding times for controls. Sustained attention was assessed by total correct rejections on the RVP test at T1 and T2. Separate linear regression models including all participants were used to relate 1) baseline TNFα and S100β levels to change in RVP performance over time, 2) change in TNFα and S100β to change in RVP performance over time, and 3) change in TNFα to change in S100β. Models were adjusted for age. 4) T-tests were used to compare the TNFα and S100β change scores (T1 to T2) of patients vs controls. **Results:** Greater increase (T1 to T2) in the pro-inflammatory cytokine TNFα was associated with worse cognition, measured by performance on RVP over time ($p = 0.02$). Higher baseline S100β, a biomarker of BBB permeability, was associated with worse performance on RVP over time ($p = 0.09$). Increase in TNFα was associated with increase in S100β ($p = 0.11$). S100β increased from T1 to T2 in patients relative to controls ($p = 0.09$). **Conclusions:** These results suggest that higher TNFα may be related to increases in blood brain barrier permeability and worse cognition. Future studies will further define the link between inflammation, blood brain barrier permeability and chemotherapy-related cognitive decline, with the goal of informing the development of new interventions. Funding: R01CA231014, T32CA102618, DP2CA195765, UG1CA189961. Research Sponsor: U.S. National Institutes of Health.

12071 Poster Session (Board #359), Fri, 8:00 AM-11:00 AM

Effects of GC4419 (avasopasem manganese) on chronic kidney disease in head and neck cancer patients treated with radiation and cisplatin. *First Author: Emily J. Steinbach, University of Iowa, Iowa City, IA*

Background: Nephrotoxicity is a major complication of platinum-based chemotherapy and ranges in incidence from 31-68%. The effects of platinum-based chemotherapeutics on long-term renal outcomes (chronic kidney disease, CKD) profoundly affect morbidity and mortality. Concurrent chemoradiotherapy (CRT) including cisplatin is standard for locally advanced squamous cell head and neck cancer (HNC) but is accompanied by the risk of CKD. In a randomized, multi-center, placebo-controlled Phase 2b trial (NCT02508389) of GC4419 (avasopasem manganese) in HNC patients receiving CRT, avasopasem reduced the duration, incidence, and severity of severe oral mucositis (Anderson et al, JCO 2019). Avasopasem did not appear to alter the safety profile of CRT in that trial, including incidence of adverse events of kidney injury or azotemia. **Methods:** Pre- and post-treatment markers of kidney function including blood urea nitrogen (BUN), serum creatinine (sCr), and estimated glomerular filtration rate (eGFR) were retrospectively evaluated for a subset of 52 of the trial patients who received 3 cycles x 100 mg/m^2 cisplatin plus placebo or 30 or 90 mg of avasopasem intravenously prior to RT, and 7 comparator patients who received the same CRT outside the study. Kidney function was evaluated between 3- and 24-months post-completion of cisplatin-radiation therapy by two-way analysis of variance (-ANOVA) as defined by the Kidney Disease Improving Global Outcomes (KDIGO) CKD staging. **Results:** Baseline patient characteristics were skewed towards a male population but were balanced across all treatment arms with regards to baseline kidney function (comparator + placebo, n = 19; 30 mg GC4419, n = 18; 90 mg GC4419, n = 15). Treatment with 90 mg GC4419 demonstrated normal BUN values (10-20 mg/dL) at 3, 6, and 18 months and normal sCr values (0.6-1.2 mg/dL) between 3 and 24 months as compared to the placebo arm + comparator group, which exhibited statistically elevated BUN and sCr ($p < 0.05$). Treatment with 90 mg GC4419 also demonstrated significantly higher eGFR between 3 and 24 months post-chemoradiation ($p < 0.05$) compared to the placebo arm + comparator group. 90 mg GC4419 treatment significantly reduced the incidence of CKD compared to the placebo arm and comparator group, as determined by fold change in sCr values and eGFR measurements $<$ 60 mL/min (stage G3a/b, G4, or G5 CKD). **Conclusions:** Avasopasem has the potential to reduce the incidence and severity of CKD in patients receiving cisplatin therapy. Clinical trial information: NCT02508389. Research Sponsor: Galera Therapeutics, Inc.

12072 Poster Session (Board #360), Fri, 8:00 AM-11:00 AM

Patient reported outcomes in older breast cancer survivors. *First Author: Sharon H. Giordano, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: The majority of breast cancer patients are age 66 years or older at diagnosis, yet little is known about the symptom burden of older breast cancer survivors. **Methods:** Using the same process as for SEER-Medicare, data from the Texas Cancer Registry (TCR) and Medicare claims were linked. From this TCR-Medicare dataset, patients age 65 years and older at diagnosis, with localized or regional breast cancer, diagnosed in 2012 and 2013, and still alive in 2018 were identified. To assess long-term outcomes, a mailed survey, which included selected questions from the NCI's PRO-CTCAE question bank, was sent to 4591 eligible patients along with a $10 gift card. Non-responders were sent a follow-up questionnaire at 4-6 weeks and 8-10 weeks after initial mailing. The percentage reporting symptoms, overall and by treatment received, are described. **Results:** 1594 survivors completed the questionnaire (35% response rate). Median time from diagnosis to survey completion was 67 months. 70% of responders were age 65-74, 26% age 75-84, and 3% age 85+ at diagnosis. 84% were non-Hispanic white, 6% black, and 9% Hispanic. 77% had localized stage disease and 23% had regional disease at diagnosis. 58% had lumpectomy, 36% had mastectomy, and 2% reported no surgery. 77% had ER+ breast cancer. 28% received adjuvant chemotherapy. 48% had Part D claims for adjuvant endocrine therapy. PROs are reported in Table, overall and by use of chemotherapy and endocrine therapy. **Conclusions:** Older breast cancer survivors, particularly those who were treated with chemotherapy, experience a high symptom burden. Research Sponsor: CPRIT, Other Foundation.

PRO-CTCAE	Overall % Reporting in Past 7 Days N = 1594	% Among Chemotherapy Treated N = 454	% Among Endocrine Therapy Treated N = 774
Arm/leg swelling	32	40	33
Any hair loss	36	53	33
Numbness/tingling in hands or feet	40	58	39
Problems with concentration	37	49	37
Problems with memory	49	61	50
Aching muscles	69	77	70
Aching joints	69	76	69
Fatigue/tiredness/lack of energy	72	84	73
Hot flashes	43	49	45

12073 Poster Session (Board #361), Fri, 8:00 AM-11:00 AM

Financial toxicity among breast cancer survivors with health insurance. *First Author: Wendy Landier, University of Alabama at Birmingham, Birmingham, AL*

Background: Cancer treatment and its sequelae have been associated with financial toxicity in breast cancer survivors, particularly those who have no health insurance. However, the prevalence of financial toxicity in the insured survivors, and the underlying factors are not well understood. **Methods:** Breast cancer survivors attending a survivorship clinic (University of Alabama at Birmingham) completed a survey assessing demographics, financial toxicity (i.e., material resources; food/housing/energy insecurity), and health-related quality of life (HRQL: SF-36). Clinical characteristics were abstracted from medical records. A multivariable logistic regression model was developed to understand factors associated with financial toxicity; the model included survivor age, race, socioeconomic status, insurance type, marital status, cancer stage, time since diagnosis, current medications, and physical and mental domains of HRQL. **Results:** The 368 participants (1% male; 67% white, 25% African American, 8% other) were a median of 61y of age (range, 33-86y) and 4.3y post-diagnosis (1-34y) at survey completion; 90% had stage 0-II disease; 34% were single (not currently married/partnered); type of health insurance included private/military (57%), Medicare (39%), and Medicaid/self-pay (4%). Overall, 31% reported financial toxicity; 26% endorsed not being able to live at current standard of living $>$ 2 mo. if they lost all current sources of income; 6% endorsed energy insecurity, 5% endorsed food insecurity, and 4% endorsed housing insecurity. In a multivariable model, financial toxicity was associated with age $\leq$60y at survey (Odds Ratio [OR] 5.1; 95% confidence interval [CI] 2.0-13.3); household income $<$ $50K/y (OR 5.3; 95%CI 2.5-11.2); being single (OR 2.6; 95%CI 1.3-5.4); and lower physical (OR 2.6; 95%CI 1.2-5.4) and mental (OR 2.2; 95%CI 1.2-4.3) HRQL. Cancer stage, race, time from diagnosis, and insurance type were not associated with financial toxicity. The prevalence of financial toxicity among survivors who were single, $\leq$60y at survey, and with household income $<$ $50k/y was 79.3%, compared with 6.7% among those who were older, married/partnered, and with higher income. **Conclusions:** Financial toxicity is prevalent among insured breast cancer survivors several years after cancer diagnosis, and is exacerbated among the younger survivors who are single, with low household income, and endorse poorer physical and mental quality of life. These findings inform the need to develop interventions to mitigate financial toxicity among at-risk breast cancer survivors. Research Sponsor: Breast Cancer Research Foundation of Alabama.

12074 Poster Session (Board #362), Fri, 8:00 AM-11:00 AM

Cutaneous pigmentary changes related to anticancer therapy in African Americans. *First Author: Dulce M. Barrios M.S, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Pigmentary disorders are known to disproportionately affect individuals with darker skin, including African Americans (AAs)— a historically underrepresented population in oncology research. However, reports on the prevalence and characterization of anticancer-therapy related cutaneous pigmentary changes in this population are lacking. **Methods:** A retrospective analysis of AA cancer patients that ever received a hematopoietic stem cell transplantation (HSCT) and/or systemic oncologic therapy within six months prior to diagnosis of cutaneous hypo- or hyperpigmentation at our institution between 4/18/2012 and 8/26/2019 was conducted. Clinical and management characteristics were summarized; severity of pigmentary changes was assessed using the Common Terminology Criteria for Adverse Events version 5.0 (CTCAE v.5.0). **Results:** From a total of 1342 AA patients evaluated by oncodermatologists during the study period, 121 (9%) met inclusion criteria. Average age in this cohort was 52, and 102 (84%) were women. Breast (63, 52%), gastrointestinal (14, 12%), and hematologic malignancies (13, 11%) comprised the majority of cancer diagnoses. Most (93, 77%) patients had skin hyperpigmentation (84, 69%) or hypopigmentation (9, 7%) as a primary CTCAE diagnosis; the rest had secondary post-inflammatory hyperpigmentation (28, 23%). A higher proportion (105, 87%) of pigmentary alterations was attributed to single agents [i.e. chemo- (55, 46%), radiation (16, 13%), targeted (12, 10%), endocrine (9, 7%), and supportive oncologic (6, 5%) therapy] versus combination treatment (16, 13%). Five (4%) patients had graft versus host disease associated with allogeneic HSCT, four (80%) of which presented as cutaneous hypopigmentation. Hand foot syndrome (24, 20%), acneiform rash (24, 20%), and radiation dermatitis (16, 13%) were commonly diagnosed dermatologic adverse events (dAEs), generally classified as mild/grade 1 (67, 55%) in severity. For management, skin lightening agents +/- emollients (36, 30%) or emollients alone (25, 21%) were highly recommended. Topical corticosteroids +/- emollients were prescribed just as frequently as reassurance and/or avoidance of sun exposure (22, 18%). **Conclusions:** Cutaneous pigmentary changes related to cytotoxic chemotherapy, radiation and/or targeted oncologic therapy are common in AA cancer patients. Undertreatment of these dAEs, possibly due to under-recognition in darker skin, warrants further investigation to assess impact on quality of life and help improve management in this population. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

12075 Poster Session (Board #363), Fri, 8:00 AM-11:00 AM

Long-term cancer survival in cohorts of U.S. health professionals. *First Author: En Cheng, Yale University, New Haven, CT*

Background: Few studies have investigated long-term survival and causes of death among men and women diagnosed with major cancers. **Methods:** We estimated overall and cause-specific mortality rates for men diagnosed with prostate, lung and bronchus, colon and rectum, bladder, and melanoma cancer in the Health Professionals Follow-up Study between 1986-2010+, and women with breast, lung and bronchus, colon and rectum, uterine corpus, thyroid, and ovarian cancer in the Nurses' Health Study (NHS) between 1976-2010+ and NHS II between 1989-2010+. Kaplan-Meier curves were used to calculate cumulative mortality rates at 5, 10, 15, 20, and 30 years and competing risk methods were used to calculate cumulative cancer-specific mortality rates of major causes at 5, 10, 15, 20, and 30 years. Additionally, among women 40-year mortality rates were calculated. **Results:** Except for lung and ovarian, most major cancer patients are more likely to die from other causes than the index cancer. We observed two basic patterns for cumulative cancer-specific mortality rates. The first pattern is greatly diminished risk of index cancer-specific mortality 10 years or more following diagnosis - for colorectal cancer, cancer-specific mortality rate increased by less than 3% between 10 to 30- or 40-year following diagnosis (among men, from 35.1% to 36.7%; among women, from 34.8% to 37.7%), and this pattern also applied to bladder, melanoma, or uterine corpus cancer. The second one is sustained, but nevertheless low, excess risk - prostate cancer-specific mortality rate increased gradually and almost linearly from 5.3% to 15.1% after diagnosis from 5 to 30 years, and for breast cancer, it increased likewise from 7.2% to 18.9% after diagnosis from 5 to 40 years. **Conclusions:** Except for lung and ovarian cancers, patients diagnosed with major cancers were more likely to die from causes other than cancer. Colorectal, bladder, melanoma or uterine corpus cancer patients surviving more than 10 years after diagnosis are unlikely to ever die from that disease. Research Sponsor: U.S. National Institutes of Health.

All-cause* and cancer-specific† mortality rates of men (1986-2018) and women (1976-2018) diagnosed with major cancers.

	Men				Women		
		30-year				40-year	
Cancer Types	N	AC	CS	Cancer Types	N	AC	CS
Prostate	6,993	86.5	15.1	Breast	19,904	70.9	18.9
Lung and bronchus	1,309	98.1	83.1	Lung and bronchus	4,251	98.1	80.8
Colon and rectum	1,424	89.5	36.7	Colon and rectum	3,736	88.4	37.7
Urinary bladder	1,570	85.4	21.7	Uterine corpus	1,645	81.7	16.3
Melanoma	3,212	76.1	7.4	Thyroid	1,119	50.8	3.2
				Ovary	1,734	88.6	58.8

Abbreviations: AC, All-cause; CS, Cancer-specific.

12076 Poster Session (Board #364), Fri, 8:00 AM-11:00 AM

Risk of secondary hematologic malignancies in patients with ovarian cancer treated with PARP inhibitors: A combined meta-analysis of seven phase III randomized controlled trials. *First Author: Thura Htut, Department of Haematology, Aberdeen Royal Infirmary, Foresterhill Health Campus, Aberdeen, United Kingdom*

Background: Ovarian cancer (OC) is a leading cause of death from gynecologic cancers in women worldwide. Poly adenosine diphosphate ribose polymerase (PARP) inhibitors prevent the repair of single-strand breaks and generate double-strand breaks in tumor cells and have recently shown survival benefits in OC. Yet, the impact on the risk of secondary hematologic malignancies (SHM) remains uncertain. We performed a combined meta-analysis of randomized controlled trials (RCT) to determine the risk of SHM in patients with advanced OC treated with PARP inhibitors. **Methods:** MEDLINE, EMBASE databases and meeting abstracts from inception through January 2020 were queried. Phase III RCTs utilizing PARP inhibitors maintenance in advanced OC were eligible. Mantel-Haenszel (MH) method was used to calculate the estimated pooled risk ratio (RR) with 95% confidence interval (CI). Heterogeneity was assessed with I^2 and Cochran's Q- statistic. Fixed effects model was applied. **Results:** A total of 4,445 patients with advanced OC from seven phase III RCTs were included. The study arm used olaparib or niraparib or rucaparib or veliparib or olaparib +bevacizumab while the control arm utilized placebo or bevacizumab. Randomization ratio was 2:1 in all studies. The I^2 statistic for heterogeneity was 0, suggesting some heterogeneity among RCTs. The overall SHM incidence was 0.80% in PARP inhibitors group vs 0.47% in control group (RR 1.45; 95% CI: 0.68 – 3.07, P = 0.34). In patients with newly diagnosed OC (n = 3,044), the incidence was 0.59% vs 0.09% in control group (RR 2.7; 95% CI: 0.7—10.37, P = 0.15). In recurrent OC subset (n = 1,401), 1.28% were reported in both study and control arms (RR 0.96; 95% CI: 0.38-2.46, P = 0.94). SHM was noted in 1.3% in the olaparib subgroup compared to 1% in the control with RR of 1.24 (95% CI: 0.46 –3.31, P = 0.67). SHM occurred in 0.7% in the niraparib subgroup compared to 0.47% in the control with RR of 1.28 (95% CI: 0.30-5.45, P = 0.74). **Conclusions:** Our study demonstrated that the risk of SHM was not significantly increased in patients who received PARP inhibitors compared to control arm, despite attaining survival benefits. Further studies and long term follow up are necessary to define the actual relation and definitive incidence. Research Sponsor: None.

12077 Poster Session (Board #365), Fri, 8:00 AM-11:00 AM

High flow oxygen for dyspnea in hospitalized patients with cancer: A 4x4 crossover randomized clinical trial. *First Author: David Hui, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Dyspnea is common in hospitalized cancer patients and highly distressing. High flow oxygen (HFOx) is administered for oxygenation in this setting; however, its effect on dyspnea has not been well examined, particularly among non-hypoxemic patients. In this phase II trial, we assessed the effect of HFOx, high flow air (HFAir), low flow oxygen (LFOx) and low flow air (LFAir) on dyspnea. We hypothesized that HFO and HFA can alleviate dyspnea. **Methods:** This double-blind, 4x4 crossover clinical trial enrolled hospitalized patients with cancer who were dyspneic (NRS $\geq$3 at rest) and non-hypoxemic (SpO2>90% on room air). Patients were randomized to 10 minutes of HFOx, HFAir, LFOx and LFAir in different orders. The flow rate was titrated between 20-60 L/min in the high flow groups and 2 L/min in the low flow groups. The primary outcome was dyspnea 0-10 numeric rating scale (NRS) "now", where 0=none and 10=worst. Secondary outcomes included modified Borg scale dyspnea intensity and unpleasantness, adverse effects, and overall preference. We compared among the interventions with a linear mixed model adjusting for time, treatment effect, period effect and carryover effect. **Results:** 17 patients completed 55 interventions in a random order. Mean age 51, 58% female, mean baseline dyspnea NRS 6.3 (SD 1.7). The absolute change of dyspnea NRS between 0 and 10 minutes was -1.8 (SD 1.7) for HFOx, -1.8 (2.0) for HFAir, -0.5 (0.8) for LFOx and -0.6 (1.2) for LFAir. In mixed model analysis, HFOx group provided greater dyspnea relief than LFOx (mean difference [95% CI] -0.80 [-1.45, -0.15], P=0.02) and LFAir (-1.24 [-1.90, -0.57], P<0.001). HFAir also provided a significantly greater dyspnea relief than LFOx (-0.95 [-1.61, -0.30], P=0.005) and LFAir (-1.39 [-2.05, -0.73], P<0.001). No difference was found between HFOx and HFAir nor between LFOx and LFAir. There was no significant carryover effect. Dyspnea Borg scale intensity and unpleasantness showed similar changes. Oxygen saturation increased in the HFOx group (97.2% to 99.7%) and LFOx group (95.5% to 98.2%) but not HFAir nor LFAir groups. HFOx was well tolerated. At the end of the study, 7 (54%), 4 (31%), 1 (8%) and 1 (8%) patients blindly preferred HFOx, HFAir, LFOx and LFAir, respectively. **Conclusions:** For the first time, we found that HFOx and HFAir provided a rapid and clinically significant reduction of dyspnea at rest in hospitalized cancer patients even when they were non-hypoxemic, supporting a role for high flow devices to provide palliation beyond oxygenation. Larger studies are needed to confirm these findings. Clinical trial information: NCT02932332. Research Sponsor: Sabin Family Foundation Fellowship Award.

12078 Poster Session (Board #366), Fri, 8:00 AM-11:00 AM

Patient controlled analgesia (PCA) vs non-PCA intravenous hydromorphone titration for severe cancer pain: A multi-center, phase III trial, HMORCT09-1. *First Author: Rongbo Lin, Gastrointestinal Medical Oncology, Fujian Cancer Hospital, Fuzhou, China*

Background: The titration of opioid dosage is necessary for adequate pain relief with acceptable side effects among individuals with cancer pain. The titration process can be achieved by non-patient administration or PCA pump. The aim of this study was to evaluate the efficacy of PCA versus non-PAC titration for severe cancer pain. **Methods:** Patients with severe cancer pain (NRS $\geq$ 7/10 at rest) were randomized into PCA or non-PCA titration and stratified by opioid tolerance or intolerance. For PCA, the pump was set as no continuous dose, hydromorphone bolus dose was 10%-20% of the total equianalgesic of past 24h for opioid tolerance, or 0.5 mg for opioid intolerance. The lockout time was 15 min. For non-PCA, initial hydromorphone bolus was the same with PCA. Reassess pain at 15 min. The dose of hydromorphone was increased by 50%-100% if pain unchanged or increased, or repeated if NRS was 4-6, or continue at current dose as needed if NRS$\leq$3. The primary endpoint was the time to successful titration (TST) - time from start to the time of pain controlled at NRS $\leq$ 3 in two consecutive evaluation with 15-min intervals, which was tested by K-M curve. **Results:** A total of 214 patients were randomized (106 in PCA, 108 in non-PCA) in 17 study sites. The most common sites of primary cancer were lung (21.03%), stomach (15.89%), colorectal (14.49%) etc. Median TSTs were 0.50h in PCA, 0.79h in non-PCA, HR 1.64 (95% CI 1.23, 2.17, P = 0.00127). In opioid tolerance, 0.50h in PCA, 1.00h in non-PCA (HR 1.92, 95% CI 1.32, 2.78, P = 0.0025). while in opioid intolerance, 0.50h in PCA and 0.50 in non-PCA (HR 1.35, 95% CI 0.88, 2.04, P = 0.162). The median dosage of hydromorphone for TST was 1.00mg (P_{25}, P_{75} 0.50, 2.00) in PCA, 1.50mg (P_{25}, P_{75} 1.00, 2.50) in non-PCA (P = 0.086). In opioid tolerance, 1.00mg (P_{25}, P_{75} 1.00, 2.00) in PCA, 2.00mg (P_{25}, P_{75} 1.00, 4.00) in non-PCA (P = 0.009). In opioid intolerance, 1.00mg (P_{25}, P_{75} 0.50, 2.00) in PCA and 1.00 mg (P_{25}, P_{75} 0.50, 2.00) non-PCA (P = 0.793). Mean patient satisfaction assessed by ESAS score was significantly superior in PCA to non-PCA (0.62$\pm$0.67 vs 1.27$\pm$0.98 for ITT, 0.66$\pm$0.66 vs 1.39$\pm$1.00 for opioid tolerance, and 0.56$\pm$0.69 vs 1.13$\pm$0.95 for opioid intolerance). Adverse events were similar in both PCA/non-PCA groups. **Conclusions:** PCA IV hydromorphone titration provided quicker analgesic effect, higher patients satisfaction, and a similar tolerability as compared to non-PCA administration in patients with severe cancer pain. Clinical trial information: NCT03375515. Research Sponsor: None.

12079 Poster Session (Board #367), Fri, 8:00 AM-11:00 AM

Using digital engagement to proactively manage symptoms in patients on capecitabine. *First Author: Mandeep Sohal, CVS Health, Woonsocket, RI*

Background: Adherence to oral chemotherapy is a challenge due to the toxic adverse events (AEs) patients' experience. Capecitabine (CAP) may cause patients to experience AEs such as diarrhea and hand and foot syndrome (HFS), leading to therapy non-adherence. Digital patient engagement has successfully improved patient adherence and has been used to monitor AEs in a variety of cancer types. We used proprietary secure messaging to engage specialty patients receiving CAP and to message them at the expected onset of diarrhea and HFS; nurse care management was deployed for patients reporting an AE. The objective of this study was to determine whether nurse engagement using digital tools to manage oncology AEs resulted in improved medication adherence. **Methods:** CAP patients were sent outgoing SMS branching logic messages during November 2019, and respondents reporting AEs were engaged by nurses using a proprietary secure messaging platform. Nurses made clinical interventions in these patients by either making a pharmacologic or non-pharmacologic recommendation or referring the patient to an oncologist. The number of patients responding to outgoing SMS and secure messaging, nurse interventions, and medication fill history were measured. We compared 30-day post-intervention proportion of days covered (PDC) in the intervention group (those that engaged with nurses and received digital adherence and clinical messages) to standard of care (those who received digital adherence and clinical messages but did not engage) using the Student's t-test. **Results:** 1,421 outgoing messages were sent to utilizers of CAP; 95 patients replied indicating the occurrence of either diarrhea or HFS. Nurse care managers reached 49 (52%) unique patients resulting in 54 interventions where care coordination was provided. The majority of engaged patients reached (74%) had symptom resolution as a result of nurse intervention. PDC was 79.3% in the intervention group and 68.8% (p = 0.038) in the standard of care group. **Conclusions:** SMS and secure messaging patients with AEs on CAP resulted in clinical interventions by nurse care managers. Nurse intervention resulted in the majority of patients having symptomatic resolution and therapy continuation. PDC indicated greater medication adherence in the engaged group. These results for one drug suggest that nurse digital engagement can be effective in increasing adherence for patients treated with oral oncolytics suffering from AEs. Proactive symptom tracking supports the early identification of potential AEs and effective nurse care coordination. Research Sponsor: CVS Health.

12080 Poster Session (Board #368), Fri, 8:00 AM-11:00 AM

Relationships between worry about dying in patients with advanced cancer and their illness understanding, treatment preferences, and advance care planning. *First Author: Rachel Rodenbach, University of Pittsburgh Medical Center, Pittsburgh, PA*

Background: Patients with advanced cancer often worry about dying, yet little is known about the role their fears play regarding future care. We aimed to explore relationships between patients' worry about dying and their illness understanding, treatment preference, and advance care planning. **Methods:** This cross-sectional study uses baseline data from a community-based, primary palliative care intervention trial. Patients had metastatic solid tumors, an Eastern Cooperative Oncology Group performance status of 0-2, and their oncologist "would not be surprised" if they died in the next year. Using patients' response to "I worry about dying" (not at all, a little bit, somewhat, quite a bit, or very much) from the Functional Assessment of Chronic Illness - Palliative Care survey instrument, univariate and multivariate analyses assessed associations with illness understanding (report of being terminally ill or not), treatment preference (life-extending vs. symptom-focused), and advance care planning (completion of an advance directive or not). We also performed sensitivity analyses substituting "I feel scared about my future" (strongly disagree, disagree, agree, or strongly agree) from the Herth Hope Index for "I worry about dying." **Results:** Of 672 patients, 54% were female, 94% white, and 69% currently receiving chemotherapy. 47% reported worrying about dying "not at all," while 9.7% worried "quite a bit" or "very much." In regression analysis, those who worried "quite a bit" or "very much" were more likely to describe themselves as terminally ill (adjusted odds ratio (AOR)=1.98, 95% CI=1.10-3.54, p=0.021) and more likely to prefer life-extending treatment over symptom-focused care (AOR=2.61, 95% CI=1.30-5.22, p=0.007) compared with patients who reported not worrying about dying. They also were less likely to have completed an advance directive (AOR=0.49, 95% CI=0.25-0.94, p=0.032). The same relationships were observed using patients' response to "I feel scared about my future." **Conclusions:** Patients with advanced cancer who worry more about dying can affirm they are terminally ill and are more likely to want life-extending treatment over symptom care while less likely to engage in advance care planning. Understanding these patients' decision making is critical to ensuring that their values are known and understood near the end of life. Research Sponsor: U.S. National Institutes of Health.

12081 Poster Session (Board #369), Fri, 8:00 AM-11:00 AM

Results of a randomized, open-label, multicenter trial to assess the safety, dose, and schedule ofRRx-001(001) in reducing incidence, severity and duration of severe oral mucositis (SOM) inpatients receiving concomitant chemoradiation (CRT) for advanced head and neck cancer (HNC). *First Author: Marcelo Raul Bonomi, James Cancer Hospital Solove Research Institute, The Ohio State University, Columbus, OH*

Background: SOM occurs in 70% of patients receiving CRT for HNC with consequent pain, treatment interruptions and increased costs of care. Supraphysiologic levels of oxidative stress are key SOM initiators. 001 activates nuclear factor erythroid related factor 2 (Nrf2) increasing expression of multiple antioxidant genes including superoxide dismutase glutathione peroxidase and glutathione S-transferase. This trial examined the effect of dose and schedule on safety and efficacy of 001. Primary efficacy endpoint was duration of SOM (WHO criteria assessed); secondary endpoints included time to onset, incidence grade 4 through 60Gy and 70Gy. **Methods:** Locally advanced HNC treated with definitive or postoperative CRT (cisplatin + RT) received one of 3 001 schedules: (ARM1) 2 doses/wk for 2 weeks (prior to) CRT. ARMS 2, 3: prior to + 2 doses or 6 doses with CRT respectively or standard of care (SOC). **Results:** 53 patients randomized, 45 evaluable. Benefit trends for endpoints were consistent across all 3 001 arms with greatest effect size in pre-treatment only, ARM1. Compared to SOC, 001 reduced duration of SOM by 45% (40 vs 22 days). Through 60Gy and 70Gy a reduction of 95% and 79% in duration SOM was also observed (17 vs 1 day, and 23 vs 5 days) respectively. No patients in ARM1 developed grade 4, (0% vs SOC 30%). Side effects were comparable to SOC. **Conclusions:** In this small, open label trial, 001 demonstrated a favorable risk-benefit profile supported by reductions in overall SOM duration including through 60Gy and 70Gy with no grade ARM1 was most effective suggesting short periods of Nrf2 activation before CRT oxidative stress generation may increase the threshold and buffering capacity of upregulated antioxidants. Larger, blinded trials, confirming the observed dose, schedule and treatment effects are warranted. Clinical trial information: NCT03515538. Research Sponsor: Prothex Pharma, Inc.

12082 Poster Session (Board #370), Fri, 8:00 AM-11:00 AM

Value of oncologist generated "surprise question" in predicting survival in metastatic cancer. *First Author: Stephen B. Edge, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: Treating patients with metastatic cancer (MCA) requires timely integration of palliative and hospice care (PHC). The Surprise Question (SQ-"Would you be surprised if your patient died in the next year?") may help predict short-term mortality in patients with chronic disease and prompt initiation of PHC. There limited data on the utility of the SQ in oncology and none controlling for age and cancer site (CS). This study evaluates the SQ in MCA. **Methods:** SQ data were collected using a clinical oncology pathway program (COP) in which the treating oncologist is required to answer the SQ for all patients with MCA. The cohort includes MCA patients with SQ entries from 5-1-2018 to 4-30-2019 providing cohorts with 6- and 12-months follow-up (f/u) from the date of the SQ. Vital status was determined as of 1-15-20. Over 90% of deaths are reported with 3 months of death. Models using SQ response (yes/no), cancer site and age were tested with logistic regression (LR) with Akaike Information Criterion (AIC) for model selection (lower number best model) and ANOVA to assess the value of the SQ in predicting mortality. **Results:** There were 655 and 1276 patients with MCA in COP with 1 year and 6 months f/u from the SQ, respectively. The proportion with the SQ response "No" (shorter expected survival) varied by cancer site (range 19% – 82% - e.g. breast 42%; pancreas 81%). The SQ was the best predictor compared to cancer site and age for 6 and 12-month mortality (LR Model A – lowest AIC). The odds ratio of death at one year from SQ-No vs. SQ-Yes was 3.8 (95% CI 2.7, 5.4) with a strong association between SQ response and 1-year and 6-month mortality ($p < 0.001$). See Table. **Conclusions:** Oncologist assessment of survival expectancy by the SQ in MCA is a strong predictor of mortality beyond cancer site and age. The treating oncologist's response to SQ can serve as a simple and reliable predictive tool to identify those with MCA likely to die sooner who may benefit from timely referral to PHC. Research Sponsor: None.

Follow-up Time	6-month	6-month SQ-No	6-month SQ-Yes	1-year	1-year SQ-No	1-year SQ-Yes
Total at Risk	1276	972	604	655	328	327
Mortality	324 (25%)	230 (34%)	94 (16%)	278 (42%)	191 (58%	87 (26%)
Pearson's c^2 test			$p_{val}<$ 0.001			$p_{val}<$ 0.001
Model Description	AIC	Comparison	p_{val}	AIC	Comparison	p_{val}
A: Mortality = SQ	1389.8	D vs A	0.014	828.6	D vs A	0.098
B: Mortality = CS	1426.5	C vs B	< 0.0001	881.6	C vs B	< 0.0001
C: Mortality = SQ + CS	1393.8	C vs A	0.026	836.2	C vs. A	0.096
D: Mortality = SQ + CS + Age	1392.1	D vs C	0.057	837.0	D vs. C	0.281

12083 Poster Session (Board #371), Fri, 8:00 AM-11:00 AM

Assessing the impact of antiemetic guideline compliance on prevention of chemotherapy-induced nausea and vomiting (CINV): Results of the Nausea/Emesis Registry in Oncology (NERO). *First Author: Matti S. Aapro, Clinique de Genolier, Genolier, Switzerland*

Background: Evidence-based antiemetic guidelines offer predominantly consistent recommendations for CINV prophylaxis. However, studies and surveys suggest that adherence to these recommendations is suboptimal. We explored potential inconsistencies between clinical practice and guideline-recommended treatment with a registry evaluating the effect of guideline-consistent CINV prophylaxis (GCCP) on patient outcomes. **Methods:** This was a prospective, non-interventional, observational, multicenter study designed to assess overall (0-120 h) complete response (CR: no emesis/no rescue use) rates in patients who received GCCP or guideline inconsistent CINV prophylaxis (GICP) using diaries for 5 days following chemotherapy. Cycle 1 results are presented in patients who received either 1) anthracycline/cyclosphosphamide (AC) highly emetogenic chemotherapy (HEC), non-AC HEC or carboplatin, with GCCP for all these groups consisting of prophylaxis with an NK_1 receptor antagonist (RA), 5-HT_3RA, and dexamethasone (DEX) prior to chemotherapy or 2) moderately emetogenic chemotherapy (MEC), with GCCP consisting of a 5-HT_3RA and DEX prior to chemotherapy as per MASCC 2016 guidelines. CR rates for cohorts deemed to be GCCP and GICP were compared using a chi-square test. **Results:** A total of 1,089 patients were part of the cycle 1 efficacy evaluation. Overall GCCP was 23% for all patients. CR rates were significantly higher in patients receiving GCCP versus GICP (Table). **Conclusions:** Consistent with prior studies, GCCP was very low. The primary endpoint of the study was achieved as there was a significant benefit of almost 10% improved prevention of CINV when administering GCCP. As per MASCC/ESMO guidelines such an absolute difference should be practice changing. Comprehensive multifaceted strategies are needed to achieve better adherence to antiemetic guidelines. Research Sponsor: Angelini Pharma Oestereich GmbH.

All Patients (N = 1089)	GCCP	GICP
Proportions of Patients who Received GCCP vs. GICP	251/1089 **(23.0%)**	838/1089 **(77.0%)**
Overall CR Rates	156/251 **(62.2%)***	441/838 **(52.6%)**

*Statistically significant difference ($P < 0.05$, chi-square test) between GCCP vs. GICP group

12084 Poster Session (Board #372), Fri, 8:00 AM-11:00 AM

Symptom burden as a predictor of emergency room use and unplanned hospitalization in patients with head and neck cancer: A population-based study. *First Author: Christopher Noel, Department of Otolaryngology Head and Neck Surgery, Faculty of Medicine, University of Toronto, Toronto, ON, Canada*

Background: Symptoms are common in oncology patients, though they remain undetected and untreated by clinicians in up to 50% of cases. Integrating patient reported outcomes (PRO) within routine clinical practice has been suggested as a way to improve detection. In order to inform an effective and efficient PRO symptom screening program, we sought to determine whether outpatient symptom scores could predict emergency room use and unplanned hospitalization (ER/Hosp) in a cancer patient population. **Methods:** This was a population-based study of patients diagnosed with head and neck cancer who had completed at least one outpatient Edmonton Symptom Assessment System (ESAS) assessment between January 2007 and March 2018 in Ontario. Logistic regression models were used to determine the relationship between reported outpatient ESAS scores and ER/Hosp use in the 14-day period following ESAS completion. A generalized estimating equations approach was incorporated to account for possible patient-level clustering. **Results:** There were 11,761 unique patients identified with a total of 73,282 ESAS assessments. There were 5,203 ER/Hosp outcome events. In adjusted analysis, the odds of ER/Hosp use increased log linearly with ESAS score (1.23 per 1 unit increase in index ESAS score, [95% confidence interval (CI) 1.22 – 1.25]). This corresponds to a 9.23 (95%CI 7.22-11.33) higher odds of ER/Hosp use for the maximum index ESAS score of 10. Seven of the nine ESAS symptom scores were significantly associated with ER/Hosp use with pain, appetite and shortness of breath demonstrating the strongest association. **Conclusions:** ESAS scores are independently associated with 14-day ER/Hosp in head and neck cancer patients. Appropriate and timely management of symptom burden may reduce rates of ER/Hosp. Research Sponsor: Canadian Institute of Health Research Terry Fox New Investigator Award, Other Foundation, Other Government Agency.

Logistic regression models for odds of 14-day ER use or unplanned hospitalization (ER/Hosp) by Index ESAS score.

ESAS Score (0-10)	Univariable		Multivariable*		14-day ER/Hosp use (%)
	OR	(95% CI)	OR	(95% CI)	
0	1	REF	1	REF	1.5
1	1.55	(1.21-1.99)	1.51	(1.17-1.95)	2.3
2	1.68	(1.34-2.10)	1.57	(1.24-1.97)	2.4
3	2.60	(2.09-3.23)	2.33	(1.87-2.90)	3.8
4	3.14	(2.52-3.92)	2.68	(2.14-3.35)	4.6
5	3.65	(2.97-4.49)	3.05	(2.48-3.77)	5.3
6	5.05	(4.10-6.23)	4.16	(3.36-5.15)	7.2
7	5.55	(4.52-6.81)	4.52	(3.67-5.56)	7.7
8	7.20	(5.90-8.80)	5.81	(4.74-7.12)	9.9
9	9.63	(7.83-11.84)	7.67	(6.21-9.47)	12.9
10	11.75	(9.61-14.36)	9.23	(7.52-11.33)	15.1

*adjusted for age, sex, rurality, comorbidity, treatment modality, subsite, diagnosis year and treatment centre

12085 Poster Session (Board #373), Fri, 8:00 AM-11:00 AM

Optimizing management of the oncological patient with pulmonary embolism: Validation of the epiphany index—PERSEO study. *First Author: Manuel Sánchez Cánovas, Department of Hematology and Medical Oncology, Hospital G. Universitario Morales Meseguer, IMIB-Arrixaca, Murcia, Spain*

Background: EPIPHANY is the first algorithm to predict serious complications in both suspected and unsuspected cancer-associated pulmonary embolism (PE), overcoming limitations of previous models. **Methods:** PERSEO is a prospective multicenter study. We recruited cancer patients with both incidental and symptomatic PE treated between Oct. 2017 and Dec. 2019. The primary aim was to determine the percentage of serious complications in patients at low predicted risk, with at least 3% accuracy. We also compared the predictive parameters of EPIPHANY with other available scores for prediction 15-day serious complications and 30-day mortality. **Results:** Cohort includes 831 patients (men, 58.6%; median age, 66 years). Most frequent tumors were lung (27.1%), colorectal (19%) and breast (7.8%). 78.6% had stage IV disease, and 77.6% were receiving antineoplastic treatment. EPIPHANY classified 27%, 24% and 49% of patients as low, medium and high risk, respectively. The rate of 15-day serious complications increased significantly across these prognostic categories: 2.67 (95% CI 0.6 - 4.8), 8.9% (95% CI 0.5 - 12.8), and 25.9% (95% CI 21.7 - 30.2), for low, intermediate, and high risk patients, respectively ($p<0.001$, linear-by-linear test). In comparison with other validated scores, EPIPHANY has a higher negative predictive value, lower negative likelihood-ratio, and comparable sensitivity (Table). **Conclusions:** The EPIPHANY index is able to identify a subgroup of patients with cancer-associated pulmonary embolism at very low risk of serious complications or short-term mortality, with potential implications for decision making. Research Sponsor: Leo Pharma.

		EPIPHANY (all patients)	EPIPHANY (patients with non-incidental EP)	RIETE*	PESI*	s-PESI*
15-day serious complications	S	95,3% (CI 95% 91,7 - 99)	97,4% (CI 95% 90,07 - 99,55)	81,67% (CI 95% 69,15 - 90,07)	96,9% (CI 95% 92,7 - 100)	100 %
	E	31,1% (CI 95% 27,6 - 34,5)	5,58% (CI 95% 3,05 - 9,78)	24,46% (CI 95% 18,57 - 31,44)	5,1% (CI 95% 1,9 - 8,4)	0 %
	PPN	97,3% (CI 95% 95,2 - 99,4)	85,71% (CI 95% 56,15 - 97,48)	80,36% (CI 95% 67,17 - 89,34)	81,8% (CI 95% 59 - 100)	0 %
	LR -	0,15	0,44	0,749	0,61	0
30-day mortality	S	99% (CI 95% 94,3 -100)	100 %	97,5% (CI 95% 85,27 - 99,87)	97,9% (CI 95% 93,7-100)	100 %
	E	30,3% (CI 95% 27-33,7)	5,86% (CI 95% 3,36 - 9,85)	26,96% (CI 95% 21,1-33,69)	5,2% (CI 95% 2,1 - 8,3)	0 %
	PPN	99,6% (CI 95% 98,7 - 100)	100 %	98,21% (CI 95% 89,18 - 99,91)	90,9% (CI 95% 73,9 - 100)	0 %
	LR -	0,03	0	0,09	0,41	0

*For the calculation of the SCORE in these models, incidental EPs have not been taken into account since they are scales developed for symptomatic EP.

12086 Poster Session (Board #374), Fri, 8:00 AM-11:00 AM

Frequency and prediction of non-medical opioid use behaviors (NMOU) among advanced cancer patients referred to a supportive care center (SCC). *First Author: Sriram Yennu, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: One of the methodological barriers to conducting research on interventions for NOMU (Aberrant Opioid Use Behaviors) among cancer patients is the lack of data on the frequency of this problem. Although the frequency of risk factors has been established by our group and others, not all the patients with risk factors will be diagnosed with having NMOU behaviors, and some patients with no previous risk factors will engage in NMOU. AIM: To characterize the overall frequency of NMOU for a duration of 3 months, as well independent predictors for NMOU. **Methods:** In this retrospective study, 1558 consecutive patients referred to supportive care clinic (SCC) from 3/18/2016 to 6/6/2018 were reviewed for development of NMOU using established diagnostic criteria. Patients were eligible if they were $\geq$18 years, had a diagnosis of cancer, and were on opioids for pain for at least a week. All patients were assessed with the Edmonton Symptom Assessment Scale (ESAS), SOAPP-14, and CAGE-AID. Descriptive statistics, spearman correlation coefficient, multivariate analysis were performed. **Results:** 299 patients (19%) had $\geq$1 NMOU behavior. The median (IQR) NMOU behavior was 1 (1-2); range 1-10. Most NMOU occurred at 1st and 2nd follow up visits. The most frequent NMOU behavior was unscheduled clinic visit for inappropriate refills. 29/299 (10%) NMOU patients received specialized care for high-risk for aberrant opioid misuse by interdisciplinary team. Results of multivariate logistic regression model showed Marital status (Divorced vs. Married, OR=1.47, 95% CI: 0.98, 2.22, p=0.654 (marginally significant); Single vs. Married, OR=1.68, 95% CI: 1.15, 2.46, p=0.0079), SOAPP (Positive vs. Negative, OR=1.42, 95% CI: 1.05, 1.93, p=0.0238), morphine equivalent daily dose (MEDD) (OR=1.004, 95% CI: (1.003, 1.006), $p<0.0001$) and ESAS pain (OR=1.11, 95% CI: 1.06, 1.17, $p<0.0001$) were independently associated with the presence of NMOU during follow-up visits. **Conclusions:** 19% cancer patients followed at SCC had detectable NMOU behaviors. Being single, SOAPP+, pain severity and high MEDD were independent predictors for NMOU. This information will assist clinicians and investigators designing clinical and research programs in this important field. Research Sponsor: Institutional funds.

12087 Poster Session (Board #375), Fri, 8:00 AM-11:00 AM

Feasibility of olanzapine at reduced dose in highly emetogenic chemotherapy: A randomised controlled trial against aprepitant in triple therapy (FORESIGHT). *First Author: Michelle Chen, CISSS Monteregie-Centre-Hopital Charles LeMoyne, Greenfield Park, QC, Canada*

Background: Olanzapine is used as an adjunct antiemetic in oncology as salvage therapy and in four-drug prophylaxis. Growing literature supports its effectiveness in initial three-drug prophylaxis in highly emetogenic chemotherapy (HEC). **Methods:** This prospective, multi-centre, open-label study evaluated the feasibility of a large-scale randomized controlled trial comparing the effectiveness and tolerability of 5 mg olanzapine once daily for four days (starting the night before chemotherapy) versus standard dose aprepitant (in tritherapy with standard ondansetron and dexamethasone) in treatment-naive patients receiving the first cycle of a HEC. Secondary outcomes included: complete response (no nausea, no emesis, no use of rescue medication), complete remission (no emesis, no rescue medication), intensity of patient-reported nausea and emesis on a visual analog scale, quality of life (scored with the Functional Living Index Emesis [FLIE]), and incidence of adverse events. **Results:** We randomized 30 patients in an intent-to-treat analysis. The large-scale trial was deemed not feasible without support from a research centre. Complete response rates were significantly higher in the olanzapine group in the delayed phase (24-120h post-chemotherapy) (86,7% v 21,4%, $p < 0,001$) and overall phase (0-120h post-chemotherapy) (60,0% v 21,4%, $p = 0,04$). Similar results were observed for complete remission. Intensity of patient-reported nausea was significantly lower in the olanzapine group in the delayed phase ($p = 0,001$). FLIE scores were significantly lower for the nausea domain (mean 62,3 v 60,9, $p = 0,004$) and overall score (124,3 v 108,8, $p = 0,006$). Depression on the ESAS-R was more common in the aprepitant group (0% v 38%, $p = 0,01$). Other adverse events were not significantly different. **Conclusions:** Support from a research centre must be ensured for study feasibility. Tritherapy olanzapine significantly improved complete response and remission in the delayed and overall phases post-chemotherapy among patients receiving HEC. It was also associated with higher quality of life and a reassuring safety profile. This feasibility trial, despite its small sample size, is one of the first prospective randomised trials to suggest similar efficacy of 5 mg olanzapine to aprepitant and to measure a difference in patient quality of life with this regimen. Clinical trial information: NCT04075955. Research Sponsor: Funding was provided by the Pharmacy department of the CISSS Monteregie-Centre.

12088 Poster Session (Board #376), Fri, 8:00 AM-11:00 AM

Efficacy and safety of direct oral anticoagulants (DOACs) and low molecular weight heparin (LMWH) for primary prevention of venous thromboembolism (VTE) in ambulatory cancer patients. *First Author: Mina Shenouda, Tampa General Hospital, Tampa, FL*

Background: Active malignancy is a well described risk factor for thrombosis. Randomized clinical trials (RCT) have evaluated anticoagulation (AC) with DOACs or LMWH for prevention of VTE in ambulatory cancer patients. This objective of this meta-analysis is to evaluate the efficacy and safety of DOACs and LMWH thromboprophylaxis in adult patients with active solid organ malignancy or lymphoma. **Methods:** We conducted a search of MEDLINE, EMBASE, and CENTRAL from 10/31/2009-11/31/2019. Data for meta-analysis was extracted from studies that met inclusion criteria (RCT, ambulatory patients age >18 years with active solid organ malignancy or lymphoma, prophylactic AC with DOAC or LMWH). Risk ratio (RR) were calculated for primary (efficacy) end point of VTE occurrence and secondary (safety) end points of major bleeding (MB) and clinically relevant non-major (CRNMB). Subgroup analyses of efficacy and safety endpoints were conducted based on AC and cancer types. **Results:** Eleven trials met inclusion criteria with total of 7741 participants. Two trials evaluated DOACs and nine trials evaluated LWMH for thromboprophylaxis. Efficacy results are noted in Table. Safety outcomes for MB and CRNMB for AC were RR 1.83 (95% CI 1.26, 2.65), p=0.001 and RR 1.36 (95% CI 1.05, 1.76), p=0.02. Safety outcomes for MB and CRNMB for DOAC were RR 1.95 (95% CI 0.88, 4.30), p=0.10 and RR 1.35 (95% CI 0.80, 2.27), p=0.26. Safety outcomes for MB and CRNMB for LMWH were RR 2.05 (95% CI 1.19, 3.51), p=0.009 and RR 1.44 (95% CI 1.01, 2.05), p=0.04. **Conclusions:** Both DOACs and LMWH decrease risk for VTE development in ambulatory adult cancer patients. MB and CRNMB were significantly increased in patients taking LMWH but not in patients taking DOACs. A large clinical trial using DOACs for thromboprophylaxis would help elucidate the thrombosis and bleeding event rate in ambulatory cancer patients. Research Sponsor: None.

Efficacy outcomes.

Intervention	Outcome/ Subgroup	# Studies	Participants	Risk Ratio (95% CI)	p-value
AC	VTE	11	7741	0.74 (0.36, 061)	<0.00001
DOACs	VTE	2	1404	0.55 (0.34, 0.90)	0.02
LMWH	VTE	9	6337	0.44 (0.32, 0.61)	<0.00001
AC	VTE/ Pancreas	5	1011	0.33 (0.13, 0.81)	0.02
AC	VTE/ Lung	5	2502	0.42 (0.28, 0/62)	<0.0001
AC	VTE/ Stomach	2	587	0.34 (0.09, 1.23)	0.10

12089 Poster Session (Board #377), Fri, 8:00 AM-11:00 AM

Improving cancer pain control: Potential impact of *CYP2D6* pharmacogenomic (PGx) testing in oncology (Onc) patients. *First Author: Natalie Reizine, University of Chicago Medical Center, Chicago, IL*

Background: Several opioid analgesics have well-known germline PGx associations which may predict either inefficacy or exaggerated (toxic) responses, depending on the patient's genotype. Despite this, germline PGx testing has not been routinely incorporated into oncology care. We hypothesized that *CYP2D6* germline PGx profiling offers the potential to improve oncology patients' pain control by identifying individuals at increased risk for inadequate analgesia with standard opioid dosing. **Methods:** We retrospectively analyzed the medication histories of over 81,000 adult oncology patients treated at the University of Chicago from 2012-2018 for exposure to opioids. *CYP2D6* genotype (permitting assignment of metabolizer phenotype: normal metabolizer [NM], intermediate metabolizer [IM], or poor metabolizer [PM]) was determined post-hoc for 127 patients who were genotyped for other reasons unrelated to pain prescribing. The primary endpoint was the number of opioids required for pain control over the course of longitudinal care, comparing PM/IMs with NMs. The secondary endpoint was the number of hospitalizations for pain control. **Results:** Over 47,000 oncology patients were exposed to opioids, with an average of 2.67±1.6 different opioid medication exposures per patient. Thirteen percent of genotyped patients were IM/PM, who were at risk for inadequate analgesia. IM/PM patients demonstrated an increased number of different opioid exposures (4.5±2.1) compared to NM (2.7±2.1, P value = 0.002). IM/PM patients were also more likely to have a pain related hospitalization (OR 4.17, CI 1.3-13.2, P = 0.016). **Conclusions:** Based on population prevalence, we estimate that > 6000 oncology patients (1000 patients/year) who received opioids at our center were IM/PM and thus at risk for inadequate analgesia due to genetic predisposition. CYP2D6 germline PGx profiling offers the potential to improve oncology patients' pain management. Research Sponsor: Benjamin McAllister Fellowship, Clinical Therapeutics Training Grant â€“ T32GM007019.

12090 Poster Session (Board #378), Fri, 8:00 AM-11:00 AM

Phase II randomized controlled trial (RCT) of medical intensive nutrition therapy (MINT) to improve chemotherapy (CT) tolerability in malnourished patients with solid tumor malignancies. *First Author: Michael Shusterman, Weill Cornell Medicine, New York-Presbyterian Hospital, New York, NY*

Background: Malnutrition is an underrecognized predictor of inferior cancer related outcomes. Subjective global assessment (SGA), a brief validated survey for malnutrition, may predict increased CT toxicity. This phase II RCT was performed to validate SGA as a predictive tool for malnutrition and to evaluate the impact of MINT on CT associated toxicity. **Methods:** CT naive pts screened by SGA were assigned to well-nourished (SGA A) or malnourished (SGA B/C) cohorts. Both cohorts were followed for CT delivery, toxicity, quality of life (QOL) by FACT-G, biomarkers, radiology, and survival. SGA B/C pts, stratified by regimen/disease, were randomized 1:1 to MINT vs. usual care. The MINT cohort received weekly registered dietician counseling and symptom assessment over the 8-week study period. Percent standard and planned CT doses were calculated. Wilcoxon rank sum tests were used for differences between groups, log-rank tests for survival, and multivariable linear regression for adjusted comparisons. **Results:** 186 eligible pts were enrolled (94 SGA A, 92 SGA B/C). SGA A were younger (median age [range]; 63 [22, 89] vs. 70 [22, 91], p = 0.011) and more fit (ECOG 0-1; 96.8% vs. 72.8%, p < 0.001). Baseline QOL was higher for SGA A (median [range], 87 [34, 115]) vs SGA B/C (70 [31, 101], p < 0.001). SGA A was associated with higher CT delivery: median proportion of planned CT (1 [Q1 0.87, Q3 1] vs 0.94 [0.70, 1], p = 0.022) and standard CT (0.91 [0.72, 1] vs. 0.74 [0.57, 0.95] p < 0.001). Adjusted for age/ECOG, SGA A remained associated with > 80% of planned (OR 2.32, p = 0.05) and standard (OR 2.33, p = 0.04) CT. SGA B/C pts (n = 92) were randomized to MINT vs usual care: median nutrition encounters MINT 5.5 vs. usual care 0.5; we observed no differences in CT delivery: median proportion of planned CT (0.91 [0.69, 1] vs. 0.94 [0.74, 1], p = 0.84) and standard CT (0.75 [0.58, 0.96] vs 0.71 [0.52, 0.99], p = 0.59). SGA A was associated with a longer 12-month survival (77.8% [95% CI 69.6%, 86.9%]) vs. B/C (53.3% [42.8%, 66.4%], p < 0.0001; 12-month survival was similar for MINT (52.3% [38.1%, 71.9%]) vs usual care (54.4% [40.2%, 73.6%], p = 0.58). **Conclusions:** SGA is a validated tool to characterize malnutrition in pts receiving CT. Malnourished pts received significantly less CT, experienced worse baseline QOL, and had worse 12-month survival. Intensive medical nutrition therapy was not associated with differences in CT associated toxicity. Novel nutritional interventions are still needed to improve pt outcomes. Research Sponsor: Sandra and Edward Meyer Cancer Center Internal Grant.

12091 Poster Session (Board #379), Fri, 8:00 AM-11:00 AM

A systematic review of evidence for cannabis and cannabinoids as adjuvant therapy in palliative and supportive oncology care. *First Author: Sebastian Jugl, Department of Pharmaceutical Outcomes & Policy, College of Pharmacy, University of Florida; Center for Drug Evaluation and Safety (CoDES), Gainesville, FL*

Background: Medical cannabis use is increasing significantly in the United States as states reduce restrictions. However, ambiguity concerning the evidence for medical cannabis efficacy and safety, especially in the field of oncology, is persistent. Clinicians therefore face challenges in examining benefits and risks of medical cannabis as adjuvant treatment for cancer patients. This study identifies and evaluates the most recent available evidence for the efficacy of cannabis and cannabinoids as adjuvant in supportive and/or palliative use in patients with cancer. **Methods:** Electronic databases searched included PubMed, Embase, Web of Science, and Cochrane Library to identify studies published following the latest available systematic review, between July 2016 through October 2019. Studies conducted outside the United States, studies not evaluating cannabis or cannabinoids in Oncology care, and preclinical studies were excluded. Findings were organized in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) framework. Lastly, qualitative synthesis was used to generate summary statements about the role of cannabis and cannabinoids as adjuvant in supportive and/or palliative cancer care. **Results:** We screened 2,267 articles and included 96 studies in our qualitative synthesis. Among those were 2 RCT's (1 completed), 6 Systematic reviews with Meta-analysis, 4 Systematic reviews without Meta-analysis, 71 other types of reviews and 13 observational studies. The most frequently reported outcomes assessed were efficacy of cannabis and cannabinoids for: pain (40 of 96; 17 indicating improvement), nausea and vomiting (26 of 96; 20 indicating improvement), cachexia (22 of 96; 2 indicating improvement), and utilization patterns of cannabis and/or cannabinoids among cancer patients (8 of 96). **Conclusions:** Latest available prevalence estimates indicate that a significant proportion of patients in the United States with cancer use cannabis and/or cannabinoids (18.3-40.0%). There is substantial evidence for the effectiveness of cannabis and cannabinoids in treating cancer-related pain; specifically, oromucosal THC/CBD spray. There is conclusive evidence for the effectiveness of cannabis and cannabinoids in relieving chemotherapy-induced nausea and vomiting; specifically, oral THC. There is inconclusive evidence regarding the effectiveness of cannabis and cannabinoids in treating cancer-related cachexia. Research Sponsor: Consortium for Medical Marijuana Clinical Outcomes Research.

12092 Poster Session (Board #380), Fri, 8:00 AM-11:00 AM

Quality of life in patients with locally advanced head and neck cancer undergoing chemoradiation with once-a-week versus once-every-three-weeks cisplatin. *First Author: Nandini Sharrel Menon, Tata Memorial Hospital, Mumbai, India*

Background: This trial was conducted to compare the efficacy of low dose once-a-week cisplatin with once-every-3-weeks cisplatin with radiation in locally advanced head and neck squamous cell carcinoma (LAHNSCC). The current analysis focuses on the quality of life (QoL) of patients in this trial. **Methods:** In this phase III randomized trial, patients with stage III or IV non-metastatic LAHNSCC were randomized to receive cisplatin 30 mg/m^2 once a week or cisplatin 100 mg/m^2 once every 3 weeks concurrently with curative intent radiotherapy. The primary endpoint was locoregional control. QoL was a key secondary endpoint. QoL was assessed using the EORTC QLQ-C30 (v.3) and EORTC QLQ-H&N35 (v.1). QoL data were assessed at baseline and days 22 and 43 during treatment; at the end of chemoradiation and at each follow-up. The linear mixed effects model was used for longitudinal analysis of QoL domains to determine the impact of treatment (arm) and time on QoL scores. **Results:** Three hundred patients were enrolled, 150 in each arm. QoL data from 283 patients with at least one assessable questionnaire were analyzed. The pretreatment QoL scores were similar in both the arms in all domains. There was no significant difference in the global health status/QoL with respect to the treatment arm (P=0.608) or time (P=0.0544). There was no significant difference in the longitudinal QoL scores between the two treatment arms in all domains except the physical function (P= .0074), constipation (P= .0326), trouble with social contact (P= .0321) and sexuality (P= .0004). There was a decline in the QoL scores in all domains in both arms during treatment. After completion of treatment, the QoL scores started improving steadily up to 1 year and plateaued thereafter in both arms. **Conclusions:** The use of once-every-three weeks cisplatin significantly improved the locoregional control without adversely impacting the quality of life as compared to once-a-week cisplatin in combination with radical radiotherapy in locally advanced HNSCC. Clinical trial information: CTRI/2012/10/ 003062.. Research Sponsor: Tata Memorial Centre Research Administration Council.

12093 Poster Session (Board #381), Fri, 8:00 AM-11:00 AM

Patient-reported distress and healthcare utilization in patients with advanced cancer. *First Author: Jordan Danielle Hildenbrand, Duke University School of Medicine, Durham, NC*

Background: The National Comprehensive Cancer Network (NCCN) defines distress as an unpleasant, multidimensional experience that may interfere with patient behavior, emotions, and ability to cope with illness. Distress screening is a critical aspect of comprehensive cancer treatment, but the relationship between patient-reported distress and healthcare utilization remains unclear. We assessed this relationship in patients with advanced cancers historically associated with high utilization, specifically non-small cell lung cancer (NSCLC) and non-colorectal gastrointestinal (NCRGI) cancer. **Methods:** We extracted data from the electronic medical record of adult patients with metastatic NSCLC and NCRGI cancers who were receiving active treatment, visited outpatient Duke Cancer Institute clinics between July 2013 and January 2017, and completed at least two self-report NCCN Distress Thermometer (DT) and Problem List (PL) surveys as part of routine clinical care between July 2013 and March 2019. Mixed effects logistic regression was used to estimate the odds of hospitalization or emergency room (ER) visit within either 3 or 6 months after each self-reported DT, with adjustment for age at first distress score, sex, primary tumor site, race (white vs. non-white) and duration of participation (i.e., time from first distress score to 3 months after the last distress score) information from the EMR. **Results:** A total of 11,027 DT scores were collected from 848 patients, with 508 (60%) having NSCLC, 340 (40%) having NCRGI cancer, and 192 (23%) reporting actionable distress (i.e., DT score $\geq$4). Actionable distress was associated with higher odds of hospitalization or visiting the ER within 3 months (OR = 1.37; 95% CI = 1.19, 1.58; $p < 0.001$) and 6 months (OR = 1.19; 95% CI = 1.03, 1.37; p = 0.019) after DT self-report. Patients who had an average DT score of $\geq$4 were more likely to report the following problems at least once: worry (89% of patients), nervousness (79%), fatigue (95%), pain (92%), sleep problems (79%), and eating problems (79%). **Conclusions:** Patient-reported distress is associated with greater healthcare utilization in patients with advanced NSCLC and NCRGI cancers who are receiving active treatment. These patients report high burden of physical and emotional problems. Actionable distress may be a useful indicator of patients in need of specialist palliative care interventions. Research Sponsor: None.

12094 Poster Session (Board #382), Fri, 8:00 AM-11:00 AM

A community oncology palliative care program: Pain-related inpatient utilization in oncology care model (OCM) patients. *First Author: Adil Jamal Akhtar, Michigan Health Professionals, Sterling Heights, MI*

Background: Oncology Division of Michigan Health Professionals (MHP) participates in OCM. A comprehensive community oncology program for early and timely involvement of palliative care (PC) was launched in September 2017 to help achieve the OCM program goals of high-quality, cost-effective, coordinated care. PC provides a single point of care for all-cause pain management. PC program included pre-program training and continuous education for early and timely involvement of PC. This study aims to assess the educative effect of PC to reduce pain-related inpatient admissions (Pain IP) in all MHP OCM patients, irrespective of PC-referral. **Methods:** This initiative was led by palliative care physicians and included continuous education and reinforcement of the benefits, every 2-4 weeks, by sharing PC outcomes data with MHP physicians. Physician feedback was part of the program enhancements that were regularly reviewed during monthly MHP physician meetings. Retrospective claims review was performed with OCM episodes from Oct 2016 – Mar 2019. Monthly Pain IP utilization (based on diagnosis code) per 1000 OCM patients (UPK) was analyzed within pre- and post- PC Program start (Sep 2017). Cost per Pain IP included mean of 30-day follow-up skilled nursing facility (SNF) stay and 30-day outpatient facility expenses. Monthly historical Pain IP (pre-PC UPK) was compared to post-PC Pain IP UPK to calculate OCM savings from PC education at MHP. **Results:** Pain IP peaked at 7.12 UPK in September 2017 when PC program training and education started, then fell as low as 0.87 UPK in January 2019. Unit cost per Pain IP was $12,473. Post-PC (Sep 2017 – Mar 2019), there were 40 fewer Pain IP admissions compared to Pre-PC Pain IP for a total cost savings of $498,920. **Conclusions:** After PC Program, Pain IP decreased in MHP OCM population (PC-referred and PC not referred). This trend suggests PC training and continuous education for OCM providers is reducing IP utilization. This also translated to a significant cost saving for OCM/Medicare of $498,920. Study was limited by OCM claims available as of December 2019. Results may be refreshed as more data becomes available. Research Sponsor: None.

12095 Poster Session (Board #383), Fri, 8:00 AM-11:00 AM

Antiemetic prophylaxis with NEPA: Final results of the German AKYPRO study. *First Author: Joerg Peter Schilling, Onkologische Schwerpunktpraxis, Berlin, Germany*

Background: NEPA is a fixed combination antiemetic of the NK_1-receptor-antagonist (RA) netupitant and the 5-HT_3-RA palonosetron. Primary objective of this prospective non-interventional study in Germany was to assess quality of life of cancer patients (pts) undergoing moderately (MEC) or highly (HEC) emetogenic chemotherapy (CT) who received NEPA for prophylaxis of nausea and vomiting (CINV). Secondary objectives were patient reported outcomes as well as effectiveness and safety of NEPA. Here we report final data of the quality of life analysis. **Methods:** The study included 2.405 pts in 162 centers receiving 3 consecutive cycles of CT as one or two day MEC or HEC. Primary endpoint was impact of quality of life (QoL) due to vomiting or nausea, documented by Functional Living Index–Emesis (FLIE) questionnaires. Effectiveness was reported in patient diaries. Complete response (CR) was defined as no emesis and no rescue medication (RM). Non-significant nausea (NSN) was no or mild nausea. Adverse events (AEs) were reported on d1–21 of each cycle. **Results:** 2.173 patients were included in the final analysis (full analysis set; FAS). The majority of patients (n = 1976; 91%) received 1-day chemotherapy, 64% HEC, 36% MEC. Median age was 58 years and the majority (85%) was female. Cancer diagnoses: breast 66%, gastrointestinal 10%, ovarian 7% or lung 5%, other 12%. Chemotherapy: AC 57%, carboplatin 19%, cisplatin 8%, oxaliplatin 8% and other 8%. 84% of pts with HEC and 82% with MEC felt no impact on daily life due to vomiting in cycle 1 remaining constant in C2 and C3. 54% HEC patients and 59% MEC patients reported no impact on daily life due to nausea in cycle 1. CR rates ranged between 81-84% and were comparable between different HEC or MEC. NSN rates in MEC ranged from 75% (MEC) to 62% (HEC). Drug-related AEs were rare with constipation, fatigue, insomnia, and nausea as the most common (in $>$ 1% pts). **Conclusions:** NEPA was highly effective in the prevention of CINV and maintenance of QoL in this real world study. Over 80% of pts reported that their daily live was not influenced by emesis while nausea was more difficult to control. Effectiveness was high and patients and physicians estimate was comparable**.** Research Sponsor: Riemser Pharma.

12096 Poster Session (Board #384), Fri, 8:00 AM-11:00 AM

Myelopreservation and reduced use of supportive care with trilaciclib in patients with small cell lung cancer. *First Author: Jared Weiss, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC*

Background: Chemotherapy (CT) is a mainstay of cancer treatment; however, its side effects, notably myelosuppression, cause significant suffering. Trilaciclib (T) is an IV CDK4/6 inhibitor that protects hematopoietic stem and progenitor cells by preventing proliferation during CT administration. Results from three randomized, double-blind, placebo (P)-controlled phase II trials in patients (pts) with extensive-stage small cell lung cancer (ES-SCLC) have previously been reported. Data from these studies were pooled to understand the effects of T on specific myelosuppression endpoints with greater statistical precision. **Methods:** All pts received standard CT (etoposide/carboplatin [E/C], E/C/atezolizumab, or topotecan) plus T or P. Analyses were conducted on pooled intent-to-treat datasets from three ES-SCLC studies (NCT02499770; NCT03041311; NCT02514447). **Results:** 123 pts were treated with T and 119 with P. Median age in both groups was 64 years. Addition of T decreased measures of myelosuppression and the need for supportive care interventions (Table). From the pooled dataset, median OS and PFS (months [95% CI]) were comparable between pts treated with T vs P (OS: 10.6 [9.1, 11.7] vs 10.6 [7.9, 12.8]; PFS: 5.3 [4.6, 6.1] vs 5.0 [4.4, 5.5], respectively). Fewer pts on T had grade 3/4 hematologic events (54 [44.3%]) vs P (91 [77.1%]). Among pts who continued after cycle 1, 11 pts (9.2%) treated with T had $\geq$1 CT dose reduction vs 36 (30.8%) with P. **Conclusions:** T significantly and meaningfully reduced both CT-induced myelosuppression and its consequences, with no detrimental effect on PFS or OS, thus improving the patient experience with CT in ES-SCLC. T has potential to become a new standard of care for preventing myelosuppression in SCLC. Research Sponsor: G1 Therapeutics, Inc.

	T + CT (n=123)	P + CT (n=119)	P value
Mean duration of severe neutropenia in cycle 1, days (SD)	0 (1.8)	4 (5.1)	<0.0001*
Severe neutropenia, n (%)	14 (11.4)	63 (52.9)	<0.0001
Febrile neutropenia, n (%)	4 (3.3)	11 (9.2)	0.089
G-CSF administration, n (%)	35 (28.5)	67 (56.3)	<0.0001
Grade 3/4 anemia, n (%)	25 (20.3)	38 (31.9)	0.028
RBC transfusion on/after Week 5, n (%)	18 (14.6)	31 (26.1)	0.025
ESA administration, n (%)	4 (3.3)	14 (11.8)	0.025
Grade 3/4 thrombocytopenia, n (%)	24 (19.5)	43 (36.1)	0.0067
Platelet transfusion, n (%)	10 (8.1)	11 (9.2)	0.96

*Two-sided p value calculated using nonparametric ANCOVA; other p values calculated using modified Poisson method.

12097 Poster Session (Board #385), Fri, 8:00 AM-11:00 AM

Development and validation of a risk prediction model for poor performance status and severe symptoms among cancer patients. *First Author: Hsien Seow, McMaster University, Hamilton, ON, Canada*

Background: Existing cancer predictive tools focus on survival, but few incorporate patient-reported outcomes to predict quality-of-life domains, such as symptoms and performance status. The objective was to develop and validate a predictive cancer model (called PROVIEW) for poor performance status and severe symptoms over time. **Methods:** We used a retrospective, population-based, cohort study of patients, with a cancer diagnosis, in Ontario, Canada between 2008-2015. We randomly selected 60% of patients for model derivation and 40% for validation. Using the derivation cohort, we developed multivariable logistic regression models with baseline characteristics, using a backward stepwise variable selection process. The primary outcome was odds of having poor performance status six months from index date, as measured by a score $<=30$ out of 100 on the Palliative Performance Scale. The index date for each model was diagnosis (Year 0), which was then re-calculated at each of 4 annual survivor marks after diagnosis (up to Year 4). Secondary outcomes included having severe pain, dyspnea, well-being, or depression, as measured by a score of $>=7$ out of 10 on the Edmonton Symptom Assessment System. Covariates included demographics, clinical information, current symptoms and performance status, and healthcare utilization. Model performance was assessed by AUC statistics and calibration plots. **Results:** Our population-based cohort identified 125,479 cancer patients for the performance status model in Year 0. The median diagnosis age was 64 years, 57% were female, and the most common cancers were breast (24%), lung (13%), and prostate (9%). 32% had Stage 3 or 4 disease. In Year 0 after backwards selection, the odds of having a poor performance status in 6 months was increased by more than 10% when the patient had: COPD, dementia, diabetes; radiation treatment; a hospital admission in the prior 3 months; high pain or depression; a current performance status $<=30$; any issues with appetite; or received end-of-life homecare. Generally, these variables were also associated with a $>10\%$ increased odds in other years and for the secondary outcomes. The average AUC across all 25 models is 0.7676 which indicates high model discrimination. **Conclusions:** The PROVIEW model accurately predicts risk of having a poor performance status or severe symptoms over time among cancer patients. It has the potential to be a useful online tool for patients to integrate earlier supportive and palliative care. Research Sponsor: Canadian Institutes of Health Research.

12098 Poster Session (Board #386), Fri, 8:00 AM-11:00 AM

The impact of the use of opioids among older breast cancer survivors and adverse events. *First Author: Aaron N Winn, Medical College of Wisconsin, Milwaukee, WI*

Background: Older adults and cancer survivors are underrepresented in the literature underpinning recent opioid prescribing guidelines. As prevention of unnecessary persistent opioid use and inadvertent opioid-related harms gains importance in clinical practice, it is necessary to fully capture the risks of opioid related adverse events among patients with cancer pain. The objective of this study was to determine the association between opioid use after cancer diagnosis and comprehensive opioid-related adverse events among older adult breast cancer survivors. **Methods:** We conducted a retrospective cohort study using Surveillance, Epidemiology, and End Results tumor registry data linked with Medicare administrative claims data from 2007-2016 of women with newly diagnosed non-metastatic breast cancer. The study observation period was the year following a patient's end of active cancer treatment. The primary exposure was a daily measure of opioid exposure based on Part D prescription claims. The primary outcomes were daily indicators of all-cause hospitalization, substance use event and a composite of other opioid-related adverse events (infections, gastrointestinal events, falls/fractures, cardiovascular events) and each component of the composite adverse event. We estimated the association of current opioid use and the immediate risk of an outcome event the following day using modified Poisson generalized estimating equation models. We adjusted for patient demographics, cancer characteristics and cancer treatments received. **Results:** We found that opioid exposure more than doubled the immediate risk of all-cause hospitalization (aRR = 2.77; 95%CI = 2.57, 2.99; $p < 0.001$) and having a composite adverse event (aRR = 2.50; 95%CI = 2.18, 2.87; $p < 0.001$) and dramatically increases the immediate risk of a substance use event (aRR = 14.26; 95%CI = 7.11, 28.59; $p < 0.001$). We find consistent results when looking at individual components of the composite adverse event measure. **Conclusions:** Older adult breast cancer survivors with continued prescription opioid use in the year after completing active cancer treatment experienced an immediate increased risk of all-cause hospitalization, substance use events, and myriad opioid-related adverse effects. Research Sponsor: None.

12099 Poster Session (Board #387), Fri, 8:00 AM-11:00 AM

Inflammatory and clinical risk factors for chemotherapy-induced peripheral neuropathy (CIPN): A nationwide longitudinal study in 143 cancer patients during chemotherapy. *First Author: Ian Kleckner, University of Rochester Medical Center, Rochester, NY*

Background: CIPN is a common dose-limiting side effect of taxane and platinum chemotherapy. It is difficult for clinicians to predict who will experience CIPN before initiating chemotherapy, partly because the etiology of CIPN is poorly understood. Specifically, although inflammation putatively plays a role in CIPN, there is limited evidence of the role of inflammation in CIPN in humans. Here, we identified the strongest predictors of CIPN using variables measured before taxane or platinum chemotherapy, including serum inflammation. **Methods:** 143 sedentary patients with cancer (81% breast, 7% colon, 5% lung; 7% other; mean age 56 years) receiving taxane or platinum chemotherapy rated the severity of (a) numbness and tingling, and (b) hot/coldness in hands/feet on 0-10 point scales before and after their first 6 weeks of chemotherapy. Linear regression models were fit to predict CIPN symptom severity at 6 weeks using variables related to inflammation (serum IL-1β, IL-6, IL-8, IL-10, IFN-γ, sTNFR1; 69 patients who gave blood), clinical factors (cancer stage, baseline neuropathy, fatigue, anxiety, depression, using diabetes medications), behavior (daily pedometer steps), and demographics (age, race) measured before chemotherapy. The final model was identified by the smallest AIC goodness of fit. **Results:** The strongest pre-chemotherapy predictors of numbness and tingling after 6 weeks of taxane and/or platinum chemotherapy were worse patient-reported fatigue/anxiety/depression (explaining 25% of variance), platinum chemotherapy (7%), and older age (5%). The strongest predictors of hot/coldness in hands/feet included worse baseline neuropathy (13%), platinum chemotherapy (8%), and fatigue/anxiety/depression (6%). In the 69 patients with serum data, a more pro-inflammatory state was a risk factor for CIPN as higher levels of pro-inflammatory IL-1β (7%) predicted numbness/tingling, and lower levels of anti-inflammatory IL-10 (7%) predicted hot/coldness in hands/feet. **Conclusions:** The strongest pre-chemotherapy predictors of CIPN included worse fatigue/anxiety/depression and platinum chemotherapy in this sedentary population of cancer patients (mostly breast). A pro-inflammatory state before chemotherapy may also increase risk for CIPN, suggesting that inflammation may underlie the etiology of CIPN in humans. Clinicians should consider assessing these factors to inform the patient's risk for CIPN. Funding: NCI UG1CA189961, NCI K07 K07CA221931, T32CA102618. Clinical trial information: NCT00924651. Research Sponsor: U.S. National Institutes of Health.

12100 Poster Session (Board #388), Fri, 8:00 AM-11:00 AM

Depression, anxiety, and patterns of mental health care among men with prostate cancer on androgen deprivation therapy (ADT). *First Author: Phoebe A. Tsao, Department of Hematology/Oncology, University of Michigan Medical School, Ann Arbor, MI*

Background: ADT is associated with an increased risk of depression and anxiety, raising the concern that a substantial portion of men with prostate cancer need mental health care. We sought to investigate the development of depression or anxiety and subsequent patterns of mental health care in men with prostate cancer on ADT. **Methods:** Clinformatics DataMart, a claims database of commercially insured patients, was used to identify men with prostate cancer who received ADT between 2001-2015 and had continuous enrollment for 1 year before and 2 years after starting ADT. We determined the rate of incident diagnoses of depression or anxiety and the incident use of mental health treatments - psychotherapy and psychiatric medications ($\geq$ 5 day supply) - after the start of ADT. **Results:** Among 37,388 men in the final analytic cohort, 11.3% (n=4239, 95% confidence interval (CI) 11.0-11.6%) received new diagnoses of depression or anxiety: 5.8% depression (95% CI, 5.5-6.0%), 3.7% anxiety (95% CI 3.5-3.9%), and 1.8% both (95% CI, 1.7-1.9%). Those who received a diagnosis of depression or anxiety were more likely to be white (68% v. 64%, $p<0.01$); no differences were noted in age, education, or household income. Among those with a new diagnosis of depression or anxiety, 0.07% received psychotherapy (95% CI, 0.02-0.23%), 34.9% a selective serotonin reuptake inhibitor (95% CI, 33.5-36.4%), 11.6% a serotonin norepinephrine reuptake inhibitor (95% CI, 10.7-12.6%), and 19.9% a benzodiazepine (95% CI, 18.7-21.1%). **Conclusions:** Among men with prostate cancer receiving ADT, more than 1 in 10 received a new diagnosis of depression or anxiety. Of those, 1 in 5 were introduced to a benzodiazepine, a drug class with risks of dependence, cognitive impairment, falls, and fractures, whereas receipt of psychotherapy was rare. Further investigation into how to improve the mental health care of men on ADT is needed. Research Sponsor: None.

Depression and anxiety among men with prostate cancer on ADT.

	No depression or anxiety N = 33,149 n (%)		Depression or anxiety N = 4239 n (%)		p-value*
Age (mean, standard deviation)	73	(8.1)	73	(8.7)	0.39
Race					
White	21,204	(64)	2869	(68)	<0.01
Black	4278	(13)	343	(8)	
Hispanic	2442	(7)	306	(7)	
Other/Unknown	5225	(16)	721	(17)	
Education					
< 12th grade	306	(1)	38	(1)	0.11
High school diploma	9731	(29)	1226	(29)	
< Bachelor degree	17,021	(51)	2191	(52)	
Bachelor degree plus	4574	(14)	554	(13)	
Unknown	1517	(5)	230	(5)	
Household income					
< $50,000	10,043	(30)	1286	(30)	<0.01
$50,000-99,000	9658	(29)	1178	(28)	
> $99,000	5369	(16)	623	(15)	
Unknown	8079	(24)	1152	(27)	

*Two sample t-test or chi-square test

12101 Poster Session (Board #389), Fri, 8:00 AM-11:00 AM

Scalp cooling to prevent chemotherapy induced alopecia (CIA) in black patients: Differences in efficacy? *First Author: Asma Ali Dilawari, MedStar Washington Cancer Institute, Lombardi Comprehensive Cancer Center, Washington, DC*

Background: The Paxman scalp cooling device has been used for over 20 years to prevent CIA, obtaining FDA clearance in the U.S. in 2017. Prior studies reported 50-80% success and high patient satisfaction yet included few or no black patients. In the U.S. this may reflect disparities in access due to cost, awareness, or availability. We opened a prospective observational study combining patient-reported outcomes with clinical assessments of alopecia and planned to deliver scalp cooling to 30 black patients receiving chemotherapy for breast cancer. **Methods:** Patients who self-identified racially as black, had a new diagnosis of stage I-III breast cancer, and planned to receive chemotherapy with taxane-containing regimens were eligible. Anthracycline (AC) and non-anthracycline (NAC) chemotherapy agents were included; costs for the intervention were covered by Paxman and internal philanthropic funding. Patients who declined scalp cooling were approached for enrollment as controls. Primary endpoints were grade of alopecia as measured by providers and patient self-report using Modified Dean Scale and Visual Analog Scale (VAS) respectively. Hair preservation was defined as <50% hair loss (<grade 2) by Dean and score < 50 on VAS. Secondary endpoints were alopecia by NCI grading scale and psychosocial from CADS and EORTC QLQ BR45 questionnaires. **Results:** 15 out of 30 planned participants enrolled by February 2020 with interim analysis and hold in accrual due to lack of efficacy. Four patients remain on treatment. Of 11 scalp cooling patients who completed chemotherapy, 0 prevented significant alopecia. Nine discontinued use of scalp cooling before completion (1 due to scheduling, 8 due to >grade 3 alopecia). The 2 patients who used scalp cooling for the duration had >grade 3 alopecia before the last cycle of treatment. **Conclusions:** Scalp cooling is an important supportive therapy that can reduce chance of alopecia, a bothersome side effect for patients. Our experience indicates decreased efficacy in black patients with both AC and NAC regimens. This is an important negative result to explore. Discussions with the Paxman team and providers with expertise in alopecia are underway to explore contributing factors such as hair thickness, prior hair treatments, and cap design. Research Sponsor: Paxman Scalp Cooling Company and Four Seasons Washington Cancer Institute Philanthropic Fund.

Alopecia in scalp cooling patients by chemotherapy.

	AC	NAC*	Total
Completed Chemotherapy	4	7	11
# with Grade> 3 alopecia prior to completion	4	7	11 (100%)
Mean # sessions before Grade >3 alopecia	2.2	2.5	2.5

*Taxotere, Cytoxan = 5, Taxotere/Carboplatin/Trastuzumab/Pertuzumab = 2

12102 Poster Session (Board #390), Fri, 8:00 AM-11:00 AM

Palliative referrals in advanced cancer patients: Utilizing the Supportive and Palliative Care Indicators Tool and Rothman Index. *First Author: Abigail Sy Chan, Sinai Hospital of Baltimore, Baltimore, MD*

Backgroun1d: Timely identification of palliative care needs have the ability to reduce hospitalizations and improve QOL. The Supportive & Palliative Care Indicators Tool (SPICT) is used to identify patients with advanced stage medical conditions who may need special care planning. The Rothman Index (RI) detects patients at high risk of acutely decompensating in the inpatient setting and has been validated to assess 24-hour mortality risk. We used SPICT and RI in cancer patients admitted to the hospital and evaluated their roles in recognizing early palliative care needs and 6-month mortality. **Methods:** Advanced/metastatic cancer patients admitted to our institution from Jan 1, 2019 to June 30, 2019 were retrospectively reviewed. Patient demographics, length of hospital stay (LOS), comorbidities, palliative/hospice care referrals, vital status, initial RI score, and computed SPICT scores were obtained. Worse clinical indicators were defined as SPICT positive if it met > 2 clinical indicators or RI < 60. Univariate and bivariate analyses were performed. **Results:** A total of 227 patients were included, mean age 68, 34% Caucasians, 63% Blacks, 59% female, median comorbidities of 3, with majority having lung and GI malignancies. A total of 137 (60%) were SPICT +, 47 (21%) had RI < 60, and 38 (17%) concurrent SPICT + and RI < 60. SPICT + patients were more likely to have longer hospital stay, change in code status, more palliative/hospice referrals, and increased mortality. Those with RI < 60 had similar results (Table). SPICT + patients are more likely to have RI < 60 (p = 0.0013). **Conclusions:** SPICT and RI are valuable tools in predicting 6-month mortality and palliative/hospice care referrals. These can also be utilized to initiate early palliative and goals of care discussions in patients with advanced cancer. Research Sponsor: None.

Comparison of SPICT and RI in clinical outcomes.

	SPICT +	SPICT -	P-value	RI < 60	RI > 60	P-value
LOS, mean in days	9.6	5.7	P < 0.001	11	7	P = 0.0187
Code status change, %	33	7	P < 0.001	47	16	P < 0.001
Palliative referrals, %	45	3	P < 0.001	55	21	P < 0.001
Hospice referrals, %	31	1	P < 0.001	47	12	P < 0.001
6-month mortality, %	66	20	P < 0.001	70	42	P = 0.0006

12103 Poster Session (Board #391), Fri, 8:00 AM-11:00 AM

Impact of embedded palliative care providers compared to externally available palliative care services on the number of patients receiving palliative care referrals in a large community oncology practice. *First Author: Garrett Young, OneOncology, Nashville, TN*

Background: Palliative care improves quality of life and may increase overall survival in patients with solid tumor malignancies. Despite having the ability to refer patients to in-home and external palliative care services, we observed low palliative care referral rates in our practice of 90 oncologists across 30 clinics. We tested whether embedding palliative care providers directly in clinic would improve palliative care referral rates for solid tumor patients. **Methods:** Between 2017 and 2020, we embedded an independent palliative care provider into five clinics across middle Tennessee. Access to external palliative care services was present both before and after the intervention. Using data from our EHR and billing systems, we performed a pre-post analysis measuring palliative care referrals in the six-month periods immediately before (pre-intervention period) and after (post-intervention period) a palliative care provider was embedded in each clinic. Statistical significance was assessed using Welch's two sample t-test. **Results:** 8,636 unique solid tumor patients were seen in the five clinics during the study periods (Table). Despite having the ability to refer patients to external palliative care services in the pre-intervention period, the placement of a palliative care provider into clinic increased the number of solid tumor patients that received a palliative care referral per month at all clinics (min.: 200%; max.: 990%; median: 600%). Four of the five increases were statistically significant (p-values < 0.05). **Conclusions:** Even when external palliative care services are available, embedding palliative care providers into community oncology clinics significantly increases the rate of palliative care referrals for solid tumor patients. Research Sponsor: None.

Change in palliative care order rates after placing a palliative care provider in clinic.

Clinic	Solid tumor patients seen during study period	Patients referred to palliative care per month: pre-intervention	Patients referred to palliative care per month: post-intervention	Percent change	p-value
1	753	1	5	600%	< 0.01
2*	752	4	13	200%	0.16
3*	1,502	4	37	796%	0.03
4	2,939	2	18	990%	0.01
5**	2,690	3	15	444%	0.01

*Only three months of post-intervention data available; **Only three months of pre-intervention data available

12104 Poster Session (Board #392), Fri, 8:00 AM-11:00 AM

A highly effective and practical desensitization regimen: Results in comparable clinical outcomes for multiple myeloma patients with skin rash after immunomodulatory drugs. *First Author: Amin Firoozmand, University Hospitals Seidman Comprehensive Cancer Center, Cleveland, OH*

Background: Immunomodulatory drugs (IMiDs) are backbone of myeloma therapy for patients with Multiple Myeloma (MM). The incidence of IMiD-associated rash is up to 27% in some reports impeding maximal benefit of this agent. The optimal management of IMiDs-associated skin is unclear. The concurrent weekly Dexamethasone (Dex) does not diminish the incidence of skin eruptions with IMiDs (Sviggum, et al. 2006), therefore we designed a low dose daily and tapering corticosteroid regimen to tame this immune response upon restarting IMiDs and allow desensitization and reinstitution of the same IMiD. Furthermore, we assessed the impact of this desensitization regimen on clinical outcome. **Methods:** A total of 160 patients were evaluated. The incidence of rash was found to be 13% (n = 21). A cohort of age- and gender-matched without rash (n = 39) was randomly selected. The effects of rash on overall and progression free survival (OS and PFS) were further estimated using Cox regression controlling the effects of age and gender. **Results:** Median time to development of rash after IMiD initiation was 28 days (range, 2-232). Rashes were graded as low (I-II) in 89% (n = 17) and high (III-IV) in 19% of pts. All pts were managed by temporary treatment interruption and upon clearance of rash, re-institution of the same IMiD concomitantly with a standardized 3-week steroid rash prophylaxis protocol (prednisone at 10 mg daily for 10 days, followed by 5 mg daily for 10 days, followed by 5 mg on alternate days for 10 days). As a result, all patients were able to restart the same IMiD with none re-experiencing any dermatologic adverse effect afterward. Comparing to no-rash controls, there was no significant difference in PFS (0.13) or OS (p = 0.12) in multivariate regression model. **Conclusions:** Proposed 3-week corticosteroid regimen showed 100% success rate in reinstituting IMiDs in our cohort. It may provide a highly effective and practical short term immunosuppression required to enable patients to restart IMiDs and enjoy comparable outcome to pts without skin rash. Research Sponsor: None.

12105 Poster Session (Board #393), Fri, 8:00 AM-11:00 AM

High-dose vitamin D supplementation for cancer-treatment-induced bone loss in 164 breast and prostate cancer patients: A pooled analysis of two randomized controlled trials (RCTs). *First Author: Luke Joseph Peppone, University of Rochester Medical Center, Rochester, NY*

Background: Aromatase Inhibitor (AI) therapy and androgen deprivation therapy (ADT) significantly accelerate bone loss and increase fracture risk. Vitamin D (VITD) protects against bone loss, but it is unclear whether the recommended daily allowance (RDA; 600 IU/day for ages 51-70) of VITD is sufficient for cancer patients. Data from two RCTs were pooled to examine the safety and efficacy of high-dose VITD versus the RDA of VITD on bone mineral density (BMD). **Methods:** 164 breast and prostate cancer patients on AIs and ADT, respectively, with low VITD (<32 ng/ml) were randomized to either high-dose VITD (50,000 IU/week; n=99) or placebo (n=65) for 24 weeks. All subjects received 600 IU/day of VITD. Of the 99 subjects assigned to high-dose VITD, 38 breast subjects also received the Exercise for Cancer Patients (EXCAP) program combining walking and resistance training. Serum VITD and calcium were assessed at weeks 0, 6, 12, 18, and 24. BMD was assessed at the hip and spine via DXA at weeks 0 and 24. The effect of high-dose VITD was tested via ANCOVA model adjusted for cancer type, baseline BMD and VITD. **Results:** High-dose VITD significantly reduced the amount of hip BMD loss versus the RDA of VITD (high-dose VITD: −0.8% vs placebo: −2.6%; p<0.01) over 24 weeks. Hip BMD loss was greater for subjects on ADT (high-dose VITD: −1.5% vs placebo: −4.1%; p=0.03) than subjects on AI therapy (high-dose VITD: −0.2% vs placebo: −1.7%; p=0.02). Among the high-dose VITD group, there was no BMD difference at the total hip between those who received EXCAP exercise vs no EXCAP (p=0.96). The largest differences in BMD were for those with lower baseline VITD levels (<27 ng/ml) for both total hip (high-dose VITD: −0.6% vs placebo: −3.2%; p<0.001) and femoral neck (high-dose VITD: +0.2% vs placebo: −2.4%; p=0.03). No between-group pooled differences were noted for total spine BMD (high-dose VITD: −0.2% vs placebo: −0.1%; p=0.82). High-dose VITD increased serum VITD without negatively affecting serum calcium (Table). **Conclusions:** High-dose VITD was safe and effective in significantly reducing hip BMD loss, with the largest benefit in those with lower baseline VITD levels. A phase III RCT is needed to confirm these findings. NCI Funding: K07 CA168911/R21 CA175793/UG1 CA189961/T32 CA102618 Clinical trial information: NCT02064946, NCT01419730. Research Sponsor: U.S. National Institutes of Health.

	Week				
	0	6	12	18	24
Mean serum VITD					
High-dose VITD	26.8	52.5	57.8	59.3	61.0
Placebo	27.9	30.6*	33.5*	30.2*	32.2*
Mean Serum Calcium					
High-dose VITD	9.22	9.36	9.42	9.39	9.37
Placebo	9.22	9.31	9.35	9.31	9.41

*p<0.05, high-dose VITD vs. placebo

12106 Poster Session (Board #394), Fri, 8:00 AM-11:00 AM

Safety and effectiveness of medical cannabis as a complementary option for supportive cancer care: Results from the Cannabis Pilot Project. *First Author: Antonio Vigano, McGill University Health Centre, Montréal, QC, Canada*

Background: Access to medical cannabis (MC) is a common request by patients and caregivers in supportive cancer care (SCC). However, health-care professionals require more evidence on MC safety and effectiveness. **Methods:** The Cannabis Pilot Project (CPP) was implemented at the Cedars Cancer Centre of the McGill University Health Centre to evaluate MC as a complementary option for symptom control in SCC. Referral to the CPP was reserved for patients who were receiving SCC but had not obtained adequate symptom relief. An interdisciplinary team (physician, nurse and research coordinator) was established to systematically assess patients, prescribe and monitor MC treatments and record data on their safety and effectiveness. Patients were enrolled in the CPP between February 2018 and December 2019 and reassessed at intervals of one to six months. **Results:** Ninety-six cancer patients (mean age 60.0y (±13.9); 41 (42.7%) males) had at least one follow-up (FUP) and were included in the study. The main cancer types were breast (19.8%), lung (9.4%) and colorectal (9.4%). Adverse events (top three: drowsiness, low energy and nausea) were reported in 28% of patients, with 9% having to stop MC. Mean Brief Pain Inventory scores significantly improved between baseline, FUP-2 and FUP-3 for worst pain (5.4± SEM 0.3 vs 4.3±0.3 and 3.7±0.4) and average pain severity (4.2±0.2 vs 3.2±0.3 and 3.2±0.4). Anorexia improved (3.4±0.3 vs 2.2±0.4 and 1.7±0.4), as measured via the revised Edmonton Symptom Assessment System (ESAS-r). ESAS-r wellbeing improved significantly between baseline and FUP-1 (4.4±0.2 vs 3.7±0.2). Between baseline and each FUP, approximately a third of patients dropped their use of concurrent medications (including analgesics, antidepressants and anxiolytics), as measured by the Medication Quantification Scale. **Conclusions:** The CPP data support the safety and effectiveness of MC as a complementary option for improving pain control, appetite and quality of life in SCC. Research Sponsor: Cedars Cancer Foundation - Rossy Cancer Network.

12107 Poster Session (Board #395), Fri, 8:00 AM-11:00 AM

Validity of patient-reported outcomes to describe the symptom experience of patients enrolled on phase I clinical trials. *First Author: Ramy Sedhom, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD*

Background: Symptoms are common among patients enrolled in phase I trials. To integrate the patient perspective, the National Cancer Institute developed a patient-reported outcomes version of the CTCAE (PRO-CTCAE) to capture symptomatic adverse events (AEs) directly from patients; however, the tool has not been used often in early phase trials or in palliative care studies. Our overall objective was to assess the validity of PRO-CTCAE items to previously validated assessments of quality of life (FACT-G) and psychological distress (Distress Thermometer). We utilized data from a randomized trial testing a palliative care intervention for patients with cancer enrolled on phase I trials. **Methods:** Patients (n = 481) were accrued to the parent study prior to initiating a Phase I clinical trial with data collected at baseline, 4, and 12 weeks. We determined the correlation of PRO-CTCAE with Distress Level, FACT-G total and subscale domain scores. Aggregate scores using PRO-CTCAE were calculated to explore the effect of overall symptom frequency, severity, and interference by calculating the total of all scored items classified within each of those domains. We used these metrics to identify associations between this and other validated tools. **Results:** Patients were predominantly female (56.8%), over age 60, and 30.7% were minority populations. Correlations between PRO-CTCAE items and corresponding FACT-G (total and subscales) and Distress levels reached statistical significance for all items ($p < 0.001$). Importantly, many of symptoms captured would have been missed using HRQOL assessment tools. Some of these symptoms affected nearly 50% of patients and were frequently rated as severe or very severe. The correlation coefficient for Distress Level for all PRO-CTCAE items was small to moderate (Pearson $r = 0.33$ to 0.46). Pearson's correlation coefficient for FACT-G total was moderate ($r = -0.45$ to -0.69). Mood items of the PRO-CTCAE had stronger associations (Pearson $r > 0.5$). PRO-CTCAE symptom interference scores had the strongest correlation with Distress (Pearson $r = 0.46$) and FACT-G Total (Pearson $r = -0.69$). **Conclusions:** Patients entering Phase I trials are willing to report on symptoms they experience as a result of advancing disease and adverse effects from experimental treatment. Evidence demonstrates favorable validity of PRO-CTCAE in a heterogeneous US sample of patients undergoing cancer treatment on phase I trials. The granular assessment of symptomatic AEs may be on increasing importance as we enter a new therapeutic era in oncology. Clinical trial information: NCT01828775. Research Sponsor: U.S. National Institutes of Health.

12108 Poster Session (Board #396), Fri, 8:00 AM-11:00 AM

A survey of cannabis use for symptom palliation in breast cancer patients by age and stage. *First Author: Marisa C. Weiss, Breastcancer.org, Ardmore, PA*

Background: Most US states have legalized medical cannabis for the treatment of serious conditions, including cancer. It is not well known which symptoms breast cancer patients seek to control with cannabis. **Methods:** Members of the Breastcancer.org and Healthline communities were invited to participate in this survey between 12/16/2019 and 1/19/2020. Eligibility criteria included age ≥18 years, resident of the US and a breast cancer diagnosis within the past 5 years. Eligible respondent data were analyzed for the symptomatic profile of cannabis users. Symptoms were compared between two groups using a Chi-square test of independence. The survey was led by Socanna, conducted by Outcomes Insights, and supported by a grant from Ananda Health/Ecofibre. **Results:** Among the 832 respondents who completed screening, 725 met the eligibility criteria, and 612 (84%) completed the survey. The median age of respondents was 57 years, and 85% had non-metastatic disease An estimated 42% of respondents have used medical cannabis to treat symptoms or side effects of breast cancer. Medical cannabis users reported using cannabis to treat insomnia (70%), joint and muscle aches, discomfort, stiffness, or pain (59%), anxiety (57%), and stress (51%). The medical cannabis users less than 50-year-old were more likely to use cannabis to treat these symptoms than their over 50-year-old counterparts, however, the differences were not statistically significant. Medical cannabis users under age 50 used cannabis significantly more than over 50 to treat nausea/vomiting (58% vs 40%; p = 0.010) and inflammation (34% vs 20%; p = 0.021). Medical cannabis users with metastatic disease were more likely to use medical cannabis to treat chronic pain 60% vs 41%; p = 0.017) than non-metastatic users. Post-surgery patients were most likely to use cannabis for nerve pain; and those who were beyond treatment, for stress. Patients suffered an average of 5 symptoms. **Conclusions:** A significant proportion of breast cancer patients reported using cannabis to treat a combination of symptoms from their cancer and its treatment. Although younger patients are somewhat more likely to use this form of palliative management, older patients are suffering from the same symptoms and their use is nearly as high. More research is needed on the personalization of safe and effective symptomatic management with medical cannabis, for people of all ages, stages, and forms of treatment. Research Sponsor: Ananda Hemp/Ecofibre.

12109 Poster Session (Board #397), Fri, 8:00 AM-11:00 AM

The Quebec Cannabis Registry: a pharmacovigilance and effectiveness study on the use of medical cannabis in cancer patients. *First Author: Antonio Vigano, McGill University Health Centre, Montréal, QC, Canada*

Background: The Quebec Cannabis Registry (QCR) was launched in 2015 to allow physicians to prescribe medical cannabis (MC) in the province of Quebec, Canada. This study aimed to investigate the safety and effectiveness of MC in cancer patients using pharmacovigilance data prospectively collected for up to 24 months. **Methods:** Patients were enrolled in the QCR between May 2015 and October 2018 and followed every 3 months. Study outcomes included adverse events (AE), pain severity and interference (Brief-Pain Inventory), wellbeing (Revised-Edmonton Symptom Assessment Scale) and overall health scale (EQ5D5L) at baseline and at each follow-up (F-UP). Significance of changes over time were assessed using repeated-measures ANOVA. **Results:** Out of the 2991 patients enrolled in the QCR, 358 (12.8%) were cancer patients (mean age 57.7 ($\pm$ 14.6); 171 (47.8%) males). The main cancer types were breast (16.2%), lung (11.7%), leukemia (11.5%) and colorectal (11.2%). MC was prescribed primarily for pain (72.1%), anxiety (4.7%), nausea (4.5%), anorexia (3.9%), and insomnia (3.1%). A total of 13 patients (3.6%) reported AE with only three being serious (one unrelated to MC: stroke; and two possibly related: diarrhea, from CBD oil overdose and pneumonia from smoking MC). Mean scores significantly ($p < 0.05$) improved between baseline and 3 months F-UP for pain severity (4.8 ± 1.5 vs 4.1 ± 1.8), pain interference (4.6 ± 1.8 vs 3.8 ± 1.7), and the overall health scale (60 ± 21 vs 71 ± 18). Well-being scores also significantly improved between baseline and 6 months F-UP (4.4 ± 2.1 vs 3.5 ± 2.8). **Conclusions:** Population-based data shows that cancer patients can benefit safely and effectively from MC as a complementary treatment, when prescribed and monitored under medical-nursing supervision. Research Sponsor: College des Medecins de Quebec - Canadian Consortium for the Investigation of Cannabis - Canopy Growth.

12110 Poster Session (Board #398), Fri, 8:00 AM-11:00 AM

Questions prompt lists used by palliative care teams help trigger discussions on prognosis and end-of-life issues with advanced cancer patients. *First Author: Carole Bouleuc, Supportive Care Department, Institut Curie, Paris, France*

Background: Accuracy of prognosis perception is a key element to allow advanced cancer patients to make informed decisions and to reflect on their end-of-life priorities. This study aims to explore whether a question prompt list can promote discussions on prognosis and end-of-life issues during palliative care consultations for advanced cancer patients. **Methods:** In this multicentric randomised study, patients assigned in the interventional arm receive a question prompt list during the first palliative care consultation (T1) after referral by oncologists. The primary endpoint is the number of questions asked by patients during the second palliative care consultation (T2) one month later. Secondary objectives are anxiety and depression, quality-of-life, satisfaction with care, coping assessed at baseline (T1) and at two months (T3). Palliative care teams from 3 french comprehensive cancer centers participate in the study. Main inclusion criteria were adult patients with metastatic non-haematological cancer referred to the palliative care team and with an estimated life expectancy less than one year. **Results:** Patients (n = 71) in the QPL arm asked more questions (mean 21.8 versus 18.2, p-value = 0.03) during the palliative care consultations compared to patients in the control arm (n = 71). These questions addressed palliative care (mean 5.6 versus 3.7, p-value = 0.012) and end-of-life issues (mean 2.2 versus 1, p = 0.018) more frequently than in the control arm. At two months, compared to baseline, there was no change in anxio-depressive symptoms or quality of life. **Conclusions:** QPL favours discussion on prognosis and end-of-life care during the palliative care consultations for advanced cancer patients. Clinical trial information: NCT02854293. Research Sponsor: INCA.

12111 Poster Session (Board #399), Fri, 8:00 AM-11:00 AM

A prospective analysis of chemotherapy-induced nausea and vomiting in gastrointestinal cancers: Results from a tertiary cancer center. *First Author: Akhil Kapoor, Tata Memorial Hospital, Mumbai, India*

Background: Chemotherapy-induced nausea and vomiting (CINV) is a bothersome side-effect associated with cancer chemotherapy which adversely impacts both quality of life and the ability to carry out the activities of daily living. This study was conducted to assess the proportion of patients developing CINV after receiving chemotherapy for gastrointestinal (GI) cancers, in spite of receiving antiemetic prophylaxis as per the standard guidelines. **Methods:** Consecutive patients with GI malignancy who had not received previous chemotherapy were eligible for enrollment in the study if they were scheduled to receive at least one cycle of chemotherapy. SPSS version 20 was used for all statistical calculations. **Results:** 701 patients fulfilling the eligibility criteria were included in this study, out of which 55.4% were males, median age was 51 years (range 22-77). Biliary tract cancer (34%) was the most common diagnosis followed by colorectal (30.2%) and gastric cancer (19.6%). As per MASCC guidelines, 22.1% patients received highly emetogenic chemotherapy, 56.0% moderately emetogenic chemotherapy (MEC) while 19.9% received regimen with low emetogenicity. Failure to achieve complete response (CR, absence of acute and delayed CINV) was found in 27.4% patients. On separately analysing MEC group, overall CR was not achieved in 33.8% with failure in acute settings in 17.8% and delayed in 16.0% patients. Only significant factor for not achieving CR was use of oxaliplatin based chemotherapy (p = 0.018 for acute and p = 0.014 for delayed CINV). **Conclusions:** More than one fourth patients failed to achieve complete response for CINV in gastrointestinal cancers despite using prophylaxis as per standard guidelines. Use of oxaliplatin based therapy is an important factor for MEC causing CINV. There is urgent need to update the guidelines for prophylaxis in this setting. Research Sponsor: None.

	Acute	Delayed
Nausea		
Across All Chemo Groups	98 (14.0%)	89 (12.7%)
Minimal	1 (7.7%)	1 (7.7%)
Low	11 (7.8%)	10 (7.1%)
Moderate	68 (17.3%)	62 (15.8%)
High	18 (11.6%)	16 (10.3%)
Vomiting		
Across All Chemo Groups	49 (7.0%)	41 (5.8%)
Minimal	0 (0%)	0 (0%)
Low	3 (2.1%)	3 (2.1%)
Moderate	41 (10.4%)	33 (8.4%)
High	5 (3.2%)	5 (3.2%)
Complete Response Not Achieved		
Across All Chemo Groups	101 (14.4%)	91 (13.0%)
Minimal	1 (7.7%)	1 (7.7%)
Low	12 (8.6%)	11 (7.8%)
Moderate	70 (17.8%)	63 (16.0%)
High	18 (11.6%)	16 (10.3%)

Complete Response Not Achieved	Overall
Across All Chemo Groups	192 (27.4)
Minimal	2/13 (15.4%)
Low	23/140 (16.4%)
Moderate	133/393 (33.8%)
High	34/155 (21.9%)

12112 Poster Session (Board #400), Fri, 8:00 AM-11:00 AM

Overall survival (OS) and healthcare utilization results of a randomized controlled trial (RCT) assessing a patient navigation (PN) intervention to increase early access to supportive care (SC) for patients with metastatic cancer in a resource-limited setting. *First Author: Miguel Araujo, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Delegacion Tlalpan, Mexico*

Background: We previously reported improvements in access to SC, advance directive completion, and pain control in a RCT comparing a patient navigator-led early SC intervention vs. usual care among patients with newly-diagnosed metastatic cancer in Mexico (NCT03293849). We now present results on healthcare utilization and OS. **Methods:** Patients were randomized to PN or usual oncology care. Patients in the PN arm received SC interventions by a navigator-led multidisciplinary team (palliative care, physical therapy, geriatrics, psychology) in the first 12 weeks after diagnosis. At 12-weeks, patients allocated to usual care were able to cross-over to PN and receive multidisciplinary SC. We analyzed the number (no.) of emergency room (ER) visits, their cause, and whether they were potentially avoidable (as determined by expert consensus), using descriptive statistics and X2 tests. OS was estimated using the Kaplan-Meier method and the log-rank test. **Results:** 133 patients (median age 60, range 23-93; 52% male) were randomized (66 PN, 67 control) from 08/17 to 04/18. Median follow-up was 22.8 months. 61% had gastrointestinal tumors, and 45% had a calculated life expectancy $\leq$6 months. 69% of patients randomized to usual care crossed-over to PN and received SC interventions. 80% of patients attended the ER $\geq$once (median no. of visits = 2). No difference was found between patients randomized to early SC or usual care in ER visits (2.4 vs. 2.3, p = 0.58). Out of a total 316 ER visits, the most common reason was infections (n = 69, 22%), followed by pain (n = 40, 13%), and indwelling catheter-related complications (n = 23, 7%). 41% of ER visits were considered as potentially avoidable, with no difference in avoidable visits found between arms (1.7 vs. 1.7, p = 0.49). No differences between arms were found in no. of hospitalizations (0.8 vs. 0.6 p = 0.82). Survival results were assessed after 64% of patients had died (n = 85), finding no statistically significant OS difference between the early SC intervention and the usual care arms (11.0 vs 13.0 months, p = 0.77) **Conclusions:** In the context of a limited-resource healthcare system, the early delivery of SC did not improve healthcare utilization, reduce avoidable ER visits, or prolong OS compared to the implementation of SC at a later time, which might be partially explained by the unavailability of hospice or home care, and by high rates of cross-over between arms. Clinical trial information: NCT03293849. Research Sponsor: Global Cancer Institute.

12113 Poster Session (Board #401), Fri, 8:00 AM-11:00 AM

Evaluation of the incidence of acute nausea and vomiting after administration of an amino acid solution containing only arginine and lysine with lutetium Lu-177 dotatate. *First Author: Nicholas Alonzo, Stanford Health Care, Stanford, CA*

Background: Lutetium Lu-177 dotatate is used to treat patients with gastroenteropancreatic neuroendocrine tumors, and an amino acid (AA) solution must be administered concurrently to mitigate nephrotoxicity. AA solutions may lead to increased rates of nausea and vomiting (NV) due to the inclusion of unnecessary non-essential and essential AA. **Methods:** This study is a single academic center retrospective chart review from October 6th, 2015 to December 17th, 2019 evaluating the incidence of acute NV in adult patients after administration of an AA solution containing only arginine 25 grams and lysine 25 grams in 1 liter of normal saline (Arginine-Lysine amino acid [AL AA]) with lutetium Lu-177 dotatate. The incidence of acute NV will be compared to the historical incidence in patients administered Parenteral amino acids 10%, Aminosyn II 10% or Clinisol 15% (commercial AA). Secondary endpoints include the incidence of rescue anti-emetic usage and the percentage of patients that require interruption of the AA infusion. Acute NV are defined as any occurrence of NV within twenty-four hours of the AA infusion. **Results:** 53 patients received a total of 164 treatments with the AL AA, while 18 patients received a total of 48 treatments with the commercial AA. The AL AA significantly decreased the incidence of acute NV, the mean AA infusion time, the interruption of the AA infusion, and the utilization of rescue anti-emetics compared to the commercial AA (Table) in patients on lutetium Lu-177 dotatate. **Conclusions:** The study findings support the use of an AL AA to be administered concurrently with lutetium Lu-177 dotatate to minimize commercial AA related acute NV. Research Sponsor: None.

Infusion specific outcomes.

	AL AA, (n = 164)	Commercial AA, (n = 48)	P-Value
Incidence of acute nausea, n (%)	33 (20.1)	31 (64.6)	< 0.0001
Incidence of acute vomiting, n (%)	2 (1.2)	5 (10.4)	0.0072
Amino acid infusion time, mean minutes	252.8	403.6	< 0.0001
Interruption or prolonged amino acid infusion, n (%)	2 (1.2)	15 (31.3)	< 0.0001
Rescue anti-emetic use within 24 hours of treatment, n (%)	33 (20.1)	31 (64.6)	< 0.0001

n = number of AA infusions

12114 Poster Session (Board #402), Fri, 8:00 AM-11:00 AM

Associations of functional, psychosocial, and medical factors with cognitive impairment in older, chemotherapy-naïve patients with early breast cancer. *First Author: Zev Nakamura, University of North Carolina at Chapel Hill, Chapel Hill, NC*

Background: Cognitive decline related to cancer and its treatments is a common concern among patients receiving treatment for cancer. Routine cognitive screening in oncology practice has been limited by the absence of a reliable, cancer-specific cognitive test. The Blessed Orientation Memory Concentration Test (BOMC) [1], has been incorporated in cancer-specific geriatric assessments, but there is no established cutpoint for cancer-related cognitive impairment. Recent research suggests that BOMC scores ≥ 5 may represent cognitive impairment in older patients with cancer. The purpose of this study was to identify cognitive impairment and associated characteristics in chemotherapy-naïve patients with breast cancer. **Methods:** Women with stage I-III breast cancer were recruited between 2009 and 2018. The BOMC (range 0-28, higher is worse function) was administered prior to chemotherapy. Associations between cognitive dysfunction (BOMC ≥ 5) and functional, psychosocial, medical variable were assessed using log binomial regression analysis. **Results:** In a sample of 331 women with breast cancer, the mean age was 65.2 years and 68.6% were 65 and older. Twenty-seven percent demonstrated cognitive impairment prior to treatment. Patients with Time Up and Go Test (TUG) ≥ 14 had increased risk of cognitive impairment compared to those with TUG < 14 (44% vs. 23%, p = 0.0002). After controlling for demographic factors, the estimated increase in risk was 66% (RR: 1.66, 95% CI (1.20, 2.31), p = 0.002). For Medical Outcomes Survey (MOS) Physical Function, after controlling for demographic factors, each 1 point increase in physical function (range 0-20, higher is better function) was associated with a 5% decrease in risk of cognitive impairment (p = 0.0004). **Conclusions:** Using a newly proposed BOMC cutpoint of ≥ 5, our study identified cognitive impairment in over 25% of older, chemotherapy naïve women with breast cancer. This is similar to what has been reported using rigorous neuropsychological testing in comparable populations. Additionally, we found that this degree of cognitive dysfunction was associated with both patient-reported and clinician-assessed impairment in physical function, further supporting the clinical relevance of this new cutpoint. Reference: [1] Katzman et al. Am. J. Psychiatry. 140 (1983) 734–739. Research Sponsor: Kay Yow Foundation, Other Foundation, U.S. National Institutes of Health.

12115 Poster Session (Board #403), Fri, 8:00 AM-11:00 AM

CIFeR: A novel Clinician-lead Intervention to address Fear of cancer Recurrence (FCR) in breast cancer survivors. *First Author: Jia Liu, Psycho-Oncology Co-operative Research Group, Camperdown, Australia*

Background: FCR affects 50-70% of cancer survivors. There are no validated oncologist-delivered FCR interventions. This multicentre, single-arm study sought to determine the helpfulness, feasibility and efficacy of an oncologist-delivered FCR intervention. **Methods:** Women were invited to participate if they had completed local treatment, chemotherapy and/or HER2 targeted therapy for early stage breast cancer and had a FCR score >0 on the 42-item FCR Inventory. The brief intervention, delivered by their medical oncologist at routine follow-up, entailed 1) FCR normalisation; 2) provision of personalised prognostic information; 3) take-home education sheet on recurrence symptoms; and 4) advice on managing worry. Consultations were audio-recorded. FCR, need for help, depression and anxiety were assessed before the intervention (T0), and at one week (T1) and three months (T2) after the intervention. Satisfaction with the intervention was assessed at T1. The primary outcome was participant-rated helpfulness. Secondary outcomes included feasibility (response rate, time taken for intervention) and efficacy. **Results:** Five oncologists delivered the intervention to 61 women (255 women invited; response rate 24%). The mean age was 57 $\pm$ 13 years. The mean time since breast cancer diagnosis was 2.5 $\pm$ 1.3 years. Forty-three (72%) were on adjuvant hormonal therapy. Overall, 58 women (95%) found the intervention helpful and 59 (98%) would recommend it to others. FCR severity, and the proportion of women with clinically significant FCR decreased significantly over time. There were no significant changes in unmet need, depression, or anxiety. Forty (66%) of consultations were recorded. Mean consultation length was 22 minutes (range 12-37 minutes) and mean intervention length was 9 minutes (3-20 minutes). The intervention was perceived as useful and feasible by oncologists, all of whom have used components of the intervention to help manage FCR in other breast cancer patients. **Conclusions:** A brief oncologist-delivered intervention to address FCR is helpful and feasible, and has shown preliminary efficacy in reducing FCR. Plans for an implementation study amongst oncologists in Australia are underway. Clinical trial information: ACTRN12618001615279. Research Sponsor: Sydney Breast Cancer Foundation, AVANT Foundation.

	T0 (n=61)	T1 (n=52)	T2 (n=33)	P-value
FCR Severity (mean $\pm$ SD)[1]	15.5 $\pm$ 6.3	13.3 $\pm$ 5.8	10.9 $\pm$ 4.6	$p<0.0001$[2] $p<0.0001$[2]
Proportion with clinically significant FCR (≥13)[1]	39 (64%)	27 (52%)	12 (36%)	$p=0.016$[3] $p=0.006$[3]

[1]Measured using the severity subscale of 42-item validated FCR Inventory [2]Repeated measures ANOVA [3]McNemar's test (exact significance)

12116 Poster Session (Board #404), Fri, 8:00 AM-11:00 AM

Nonconscious nonverbal synchrony and patient and physician affect and rapport in cancer treatment discussions with black and white patients. *First Author: Lauren M. Hamel, Karmanos Cancer Center, Wayne State University, Detroit, MI*

Background: Clinical communication is poorer with Black patients than with White patients, but most studies are limited to verbal communication. Nonverbal synchrony, the subtle, nonconscious coordination of movement between individuals, has been shown to reflect relationship quality. We investigated nonverbal synchrony's association with patient and physician affect and rapport in cancer treatment discussions, and if those associations differed by patient race. **Methods:** We used motion detection software to measure overall synchrony and synchrony based on who is leading in the interaction (similar to leading in dancing) in video recordings of 68 Black patients and 163 White patients discussing treatment with their non-Black physicians. Additionally, naïve observers rated the interaction for six constructs: patient and physician positive and negative affect and patient-physician positive and negative rapport. We examined associations between nonverbal synchrony and the six constructs. **Results:** In interactions with Black patients, overall synchrony was positively associated with patients' positive affect and positive patient-physician rapport and negatively associated with patients' negative affect and negative patient-physician rapport. When the physician was leading, synchrony was positively associated with patients' positive affect and positive patient-physician rapport and negatively associated with patients' negative affect and negative patient-physician rapport. When the patient was leading, synchrony was positively associated with patients' and physicians' positive affect and positive patient-physician rapport, and negatively associated with patients' negative affect and negative patient-physician rapport. In interactions with White patients, overall synchrony was positively associated with patient positive affect; when the physician was leading, synchrony was negatively associated with patient negative affect. **Conclusions:** This is the first study to use an innovative measure of dynamic communication in patient-physician cancer treatment discussions. Nonverbal synchrony was related to patient and physician affect and rapport in interactions with Black patients, but only patient affect in interactions with White patients, suggesting *nonverbal synchrony is particularly important in interactions with Black patients.* Next steps include investigating associations with patient outcomes (e.g., satisfaction). Findings could contribute to physician training. Research Sponsor: U.S. National Institutes of Health.

12117 Poster Session (Board #405), Fri, 8:00 AM-11:00 AM

Health and cancer concerns among siblings of childhood cancer survivors: A report from the Childhood Cancer Survivor Study (CCSS). *First Author: Sonia Morales, Children's Hospital of Orange County, Orange, CA*

Background: Siblings of long-term survivors of childhood cancer can be at risk for persistent concerns regarding their future health and risk for cancer. We examined self-perceived future health and cancer risk concerns among such siblings. **Methods:** 3,969 siblings (median age 29 [range 18–56] years) of 5+ year matched pair cancer survivors (n= 3,969; age 25 [6–48] years; time since diagnosis 19.6 [9.6-33.8] years) in the CCSS self-reported physical/psychosocial problems, including concerns regarding future health and cancer risk (dichotomized as concerned vs not concerned). Chronic health conditions (CHC) were graded using the Common Terminology Criteria for Adverse Events system: mild (grade 1), moderate (grade 2), severe/disabling (grade 3),or life-threatening (grade 4). Sibling demographics, their matched survivor's diagnosis, era and treatment components, complications (death, relapse, disfigurement) as well as self-reported health status and CHCs for siblings and survivors were examined as potential risk factors for concern using multivariable logistic regression. Adjusted odds ratios (OR) and 95% confidence intervals (CI) are reported. **Results:** The prevalence of siblings reporting concerns regarding health and cancer risk decreased based on decades of matched survivor diagnosis: 1970-79 (73.3%; 63.9%), 1980-89 (67.2%; 62.6%), 1990-99 (45.7%; 52.3%). Risk factors for concerns included sibling poor/fair current health (future health OR 3.65, 95% CI 2.37-5.62; cancer risk OR 1.54, 1.12-2.13) compared to good/very good/excellent health. Sibling grade 2 (future health OR 1.46, 1.23-1.74; cancer risk OR 1.20, 1.01-1.42) or grade 3-4 CHCs (future health OR 1.37, 1.09-1.71; cancer risk OR 1.28, 1.03-1.58) were associated with greater concerns compared to those with less than grade 2 CHCs. Survivor treatment with chemotherapy/radiation was associated with elevated cancer risk concerns (OR 1.51, 1.13-2.02) compared to surgery/no therapy. Siblings of survivors with grade 3-4 CHCs (OR 1.35, 1.12-1.63) had greater future health concerns compared to those with less than grade 2 CHCs. Sibling bereavement was a risk factor for future health (OR 1.45, 1.04-2.03) and cancer risk (OR 1.44, 1.05-1.99) concerns. **Conclusions:** The prevalence of sibling concerns regarding future health and cancer have diminished in more recent decades. Subgroups of siblings are at-risk for concerns over future health and cancer risk, partially determined by medical characteristics of their survivor and their own health status. Research Sponsor: None.

12118 Poster Session (Board #406), Fri, 8:00 AM-11:00 AM

Defining patient-elicited concepts unique to adolescents and young adults with cancer. *First Author: Viswatej Avutu, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Adolescents and young adults (AYAs) require a multidisciplinary approach to cancer care due to complex biopsychosocial variables and varied developmental maturity. Currently, age and diagnosis determine referral to pediatric or adult oncology with differing care paradigms and service utilization. These issues, in conjunction with differences in tumor biology and lower accrual to clinical trials, have contributed to marginal improvements in outcomes for AYAs. Compounding this dilemma is a lack of validated patient-reported outcome measures (PROs) for AYAs. Tracking standardized PROs longitudinally is a crucial step in understanding psychosocial variables, identifying tailored needs, improving outcomes and standardizing care. However, developing a PRO tool for AYAs first requires identifying AYA-unique domains. **Methods:** Three, 90-minute focus groups were conducted with AYAs treated at Memorial Sloan Kettering in the context of 1) pediatric oncology, 2) medical oncology, and 3) either service. Topics explored included: experiences of cancer care as an AYA; physical, social and emotional concerns; and information needs, including appropriateness, timing, and depth of information. Thematic content analysis of transcripts was performed by four interdisciplinary coders in weekly iterative consensus rounds. Phase one consisted of identification of key domains to guide line-by-line coding with NVivo software. Phase two consisted of independent review and categorization of codes, followed by three successive consensus meetings to identify distinct themes. **Results:** A mean of 6 patients (range 5-7) participated in each of the 3 groups; the total sample (n = 17) included 9 males and 8 females, ages 19-35 years (median 26). Four AYA-unique themes were identified: 1. AYAs have an uncertain sense of the future and desire more engagement in conversations pertaining to survivorship, long-term effects and transition to outpatient life. 2. Cancer as an AYA is a socially-isolating experience, prompting a strong desire to connect with peers during and post-treatment. 3. AYAs want control over who can be present during discussions with their care team as the presence of loved ones can impede or facilitate communication. 4. AYAs may be living far away from loved ones during treatment and lack supports needed to help them navigate treatment and daily life. **Conclusions:** Concept elicitation via focus groups identified novel themes related to survivorship, isolation, communication and social support, which can inform development of AYA-specific PROs. Research Sponsor: Memorial Sloan Kettering Cancer Center Patient and Family Advisory Council for Quality Grant.

12119 Poster Session (Board #407), Fri, 8:00 AM-11:00 AM

An intervention RCT-study aimed at improving mental health and increasing understanding of fertility preservation with Oncofertility! Psycho-Education And Couple Enrichment (O!PEACE) therapy. *First Author: Nao Suzuki, Department of Obstetrics and Gynecology, St. Marianna University School of Medicine, Kawasaki, Japan*

Background: Although ASCO revised Guidelines (2013) recommends referring to psychological professionals if cancer patients show concerns or anxiety about fertility, there is no evidence regarding the efficacy of psychotherapy. The aim of this study is to examine whether the Psycho-Education And Couple Enrichment (O!PEACE) therapy can reduce psychiatric symptoms and improve stress coping and marital relationship in breast cancer patients. **Methods:** Trial design: multicenter randomized controlled trial, pre-post design. Subjects were women aged 20–39 years with breast cancer before cancer treatment and their husbands. Couples were randomly assigned to receive O!PEACE therapy (n = 37) or not (usual care: n = 37). Assessments of PTSD symptoms, depression and anxiety were made as the primary end points at baseline and at the end of therapy before cancer treatment. Stress coping strategies, resilience, marital relationships, and marital communication were examined as secondary end points. **Results:** Four participants in O!PEACE therapy and one participant in the usual care withdrew from the trial. Intention-to-treat analyses were conducted using analysis of covariance after multiple imputation by R and SPSS. Series of ANCOVAs were integrated according to Rubin's rule. A significant decrease was observed in the primary outcome of PTSD symptoms, from baseline to post-intervention, in women who participated in O!PEACE therapy ($p = .011$, $\eta_p^2 = .089$). According to post-hoc analyses, for patients with a higher baseline IES-R-J score, O!PEACE therapy resulted in a significantly higher reduction in follow-up assessment IES-R-J score when compared with usual care ($U = 172.80$, $p = .027$, $r = .258$): 59.3% of the women in O!PEACE therapy showed a 5-point or greater reduction, whereas in usual care, 30.0% showed a 5-point or greater reduction. For husbands, the O!PEACE therapy also showed a significant improvement of giving up and blaming others as the stress coping strategy and escape-avoidance coping strategy in their marital communication. For breast cancer patients, the O!PEACE therapy significantly improved support from husbands and the patients' knowledge level of oncofertility compared with those receiving usual care. **Conclusions:** Only two counseling sessions of O!PEACE therapy can reduce patients' distress, improve their husbands' coping style, and may build a better cooperative relationship for couples in terms of fertility preservation and cancer treatment. Clinical trial information: UMIN000017754. Research Sponsor: Health Labour Sciences Research Grant #H26-Cancer-017, The Ministry of Health Labour and Welfare in Japan.

12120 Poster Session (Board #408), Fri, 8:00 AM-11:00 AM

Relationship between caregiver burden and psychological distress among stem cell transplant (SCT) recipients prior to transplant. *First Author: Carlisle Topping, Massachusetts General Hospital, Boston, MA*

Background: SCT is a potentially curative therapy for patients with hematologic malignancies that involves prolonged hospitalization, intensive follow-up, and a considerable risk of morbidity and mortality. Family and friends caring for SCT recipients experience substantial caregiving burden as they prepare for SCT. Previous research demonstrates caregiver distress is highest pre-transplant and is comparable to or higher than patient-reported distress. However, the extent of this distress and its relationship to certain domains of quality of life (QOL) and caregiving burden is currently unknown. **Methods:** We conducted a secondary analysis of cross-sectional data from two supportive care studies focused on caregivers of SCT recipients. Caregivers completed the Hospital Anxiety and Depression Scale (HADS) and the CareGiver Oncology QOL questionnaire to assess their psychological distress and QOL prior to SCT. Scores >8 on the HADS anxiety and depression subscales indicated clinically significant symptoms. We selected eight domains from the CareGiver Oncology QOL questionnaire including social support, physical wellbeing, self-efficacy, coping, leisure time, financial stability, private life concerns, and caregiving burden. Multivariate regression models adjusted for age, sex, caregiver relationship, and SCT type were used to examine associations between these domains and caregivers' anxiety and depression symptoms. **Results:** A total of 193 caregivers (age *M*= 57 years, 70% female, 52% allogeneic transplant) were enrolled with a majority caring for their spouse (80%), parent (8%) or child (5%). Overall 47% and 16% of caregivers reported clinically significant anxiety and depression symptoms, respectively. Low social support, physical well-being, coping and leisure time as well as high caregiver burden, private life concerns and financial distress were associated with both caregiver anxiety and depression symptoms ($p < .05$). Low self-efficacy was associated with higher anxiety symptoms ($p < .05$). **Conclusions:** Caregivers of SCT recipients experience substantial anxiety and depression symptoms prior to SCT. Impairments across multiple QOL domains are associated with caregiver's psychological distress. Psychosocial interventions designed to improve coping, reduce caregiving burden, and enhance QOL are needed for caregivers prior to transplant. Research Sponsor: Lymphoma and Leukemia Society.

12121 Poster Session (Board #409), Fri, 8:00 AM-11:00 AM

Effect of linguistic acculturation on self-efficacy and anxiety in caregivers of Latina breast cancer survivors. *First Author: Ilana Schlam, Medstar Washington Cancer Institute, Washington, DC*

Background: Latina breast cancer survivors and their caregivers face unique challenges. Acculturation is the acquisition of the cultural elements of a dominant society. Higher acculturation in Latino survivors is positively correlated with self-efficacy in patient-provider communication and improved patient-reported outcomes. There is a paucity of research on how language acculturation affects caregiver and patient outcomes. We examined associations over time between linguistic acculturation among caregivers of Latina survivors and outcomes of caregiver self-efficacy and anxiety. **Methods:** We partnered with four community-based organizations that serve Latino families facing cancer. We enrolled 136 Latina breast cancer survivors and their caregivers for a randomized trial comparing a dyadic coping intervention to usual care (e.g., support groups). Participants completed surveys including demographic and clinical information, the short acculturation scale for Hispanics, caregiver inventory to assess self-efficacy and PROMIS domains of anxiety at baseline and 6-months after the intervention. **Results:** In multivariate linear regressions models, we examined the effect of acculturation on caregiver self-efficacy and anxiety, controlling for demographics (patient and caregiver age, caregiver education, employment), patient treatment history (chemotherapy and surgery) patient and caregiver language preference (Spanish or English) and intervention arm (intervention vs. usual care). Greater caregiver self-efficacy at 6-months was associated with younger patient age (t=-2.93, p=.004), older caregiver age (t=2.63, p = .01), female caregiver gender (t=2.79, p = .006) and higher acculturation (t=2.01, p=.04), controlling for baseline self-efficacy, patient language and randomization group. Caregiver anxiety was not related to caregiver acculturation or patient language preferences. **Conclusions:** Caregivers' language acculturation was significantly associated with their self-efficacy over time, suggesting that caregivers with lower acculturation experience lower confidence in their provision of care for Latina survivors. These findings are particularly salient because participants for this study were enrolled from organizations with bilingual services. Caregivers of Latina survivors without access to these community resources may face even more striking challenges. Future work can explore how caregivers' confidence relates to survivors' adherence to care and patient outcomes over time. Research Sponsor: None.

12122 Poster Session (Board #410), Fri, 8:00 AM-11:00 AM

Enhanced coping and self-efficacy in caregivers of hematopoietic stem cell transplant (HCT) recipients: Identifying mechanisms of a multimodal psychosocial intervention. *First Author: Madeleine Elyze, Massachusetts General Hospital, Boston, MA*

Background: A brief multimodal psychosocial intervention (BMT-CARE) for caregivers of HCT recipients demonstrated promising efficacy for improving caregiver quality of life (QOL), mood, coping skills, and self-efficacy. We examined whether improvements in coping and self-efficacy mediated the intervention effects on QOL and mood. **Methods:** We conducted a randomized clinical trial of BMT-CARE for caregivers of patients undergoing autologous or allogeneic HCT at a single institution. Caregivers were randomly assigned to BMT-CARE or usual care. BMT-CARE was tailored to the HCT trajectory and integrated treatment-related education and self-care with cognitive-behavioral skills and caregiving-specific strategies to promote coping. Caregivers completed self-report measures of QOL (CareGiver Oncology QOL), depression and anxiety symptoms (Hospital Anxiety and Depression Scale), coping skills (Measure of Current Status), and self-efficacy (Cancer Self-Efficacy Scale-Transplant) at enrollment and 60 days post-HCT. We used causal mediation regression models to examine whether changes in coping and self-efficacy mediated intervention effects on QOL, depression and anxiety symptoms. **Results:** Caregivers randomized to BMT-CARE reported improved self-efficacy (adjusted means: 156.20 vs. 147.06, P=0.023) and coping skills (adjusted means: 36.54 vs. 25.41, P<0.001). Improved coping and self-efficacy partially mediated the intervention effects on 60-day QOL (indirect effect=6.93, SE=1.85, 95% CI [3.71, 11.05]). Similarly, improved coping and self-efficacy partially mediated reductions in 60-day depression and anxiety symptoms (indirect effect depression=-1.19, SE=0.42, 95% CI [-2.23, -0.53]; indirect effect anxiety=-1.46, SE=0.55, 95% CI [-2.52, -0.43]). Combined improvements in coping and self-efficacy accounted for 67%, 80%, and 39% of the total intervention effect on QOL and depression and anxiety symptoms, respectively. **Conclusions:** A brief multimodal intervention for caregivers of HCT recipients may improve QOL and mood by enhancing coping skills and self-efficacy. These findings offer important insights into the mechanisms by which caregiver-directed interventions may enhance caregiver QOL and reduce their psychological distress. Research Sponsor: Lymphoma and Leukemia Society.

12123 Poster Session (Board #411), Fri, 8:00 AM-11:00 AM

Video conference intervention for distance caregivers (DCGs) of patients with cancer: Improving psychological outcomes. *First Author: Sara L Douglas, Case Western Reserve University and Case Comprehensive Cancer Center, Cleveland, OH*

Background: Family caregivers are increasingly involved in providing care and support for patients with cancer. Approximately 20% of caregivers live > 1 hour away from the patient and are considered DCGs. DCGs report higher distress and anxiety than local caregivers—often due to lack of first hand information and a high degree of uncertainty regarding the patient's condition. **Methods:** This RCT was conducted at a large, urban comprehensive cancer center. Patients of all cancer types were eligible if they had monthly oncologist appointments and were receiving treatment. DCGs were randomized to one of three arms. Arm 1 received 4 monthly videoconference coaching sessions with a nurse practitioner or social worker focused upon information and support, participated in patient's appointments with the oncologist via videoconference over the 4 month study period, and had access to a website designed for DCGs. Arm 2 did not receive the coaching sessions but received the other 2 components of Arm 1. Arm 3 received access to the DCG website only. Primary variables of interest were DCG distress and anxiety. DCGs completed online surveys prior to randomization and at the completion of the intervention period. PROMIS Anxiety and the NCCN distress thermometer were used. **Results:** Between November, 2016 and October, 2019, 441 patient-dyads were enrolled. Mean DCG age was 47 years; 71% were female, 65% Caucasian, 63% were the child of the patient and 81% were employed. Mean patient age was 65 years, 60% were female, 30% had GI cancer and 18% had hematologic cancer. For patients with solid tumor cancers, 59% were Stage IV. RMANOVA was used to examine the change in anxiety t-scores over time by arms of the intervention, controlling for DCG age, race, and gender. There was a significant anxiety by group interaction (p = .03) with Arm 1 being the only group that showed a significant reduction in anxiety over time (21.2% improved, ES = .57). Distress followed a similar pattern with a significant distress by group interaction (p = .02) with Arm 1 demonstrating the greatest improvement in distress over time (54.3%). **Conclusions:** These data suggest that the use of a coaching videoconference intervention made significant and clinically meaningful differences in anxiety and distress for these important members of the family caregiving team. Clinical trial information: NCT02666183. Research Sponsor: U.S. National Institutes of Health.

TPS12124 Poster Session (Board #412), Fri, 8:00 AM-11:00 AM

The effect of longitudinal exercise programming in breast cancer patients. *First Author: Jami Aya Fukui, University of Hawaii Cancer Center, Honolulu, HI*

Background: Obesity and weight gain are significant concerns for breast cancer survivors. Obesity at diagnosis is an established negative prognostic factor and studies suggest that post-diagnosis weight gain may increase risk for recurrence and decrease disease free survival. Various interventions such as dietary modification, physical activity, individualized counseling, cognitive behavioral therapy, and combinations of these interventions have been studied in order to identify strategies for weight loss in breast cancer survivors. However, one of the main challenges have been to show sustainability in these interventions. Given the adverse consequences of weight gain after diagnosis, continued efforts to identify appropriate weight management interventions aimed at promoting overall health and long term survivorship are needed. **Methods:** We have opened an investigator initiated Breast Cancer Exercise Study that provides a tailored exercise program and body health assessments for breast cancer patients along their treatment journey. We are enrolling women diagnosed with breast cancer up to 2 years after their diagnosis into a two 12-week exercise program. Participants' biometrics and physical assessments will be assessed at baseline to determine the appropriate exercise intensity to implement. Women will attend private 1:1, 90min sessions, 3 days/week. At the end of the initial 12-week program, biometric assessments are again performed and participants are then randomized to either: a) continue with individual exercise classes, 2 days/week or b) continue with group exercise classes, 2 days/week. The study follows their long term outcomes including cancer recurrence, exercise adherence as well as quality of life symptoms. The functional health assessment and subsequent personalized exercise program utilizes kinesiology students from University of Hawaii-Manoa during their clinical practicum and is based at our community partner facility the Rehabilitation Hospital of the Pacific. Body assessments and other biomarkers are evaluated through expertise at University of Hawaii Cancer Center. Collectively, our study exemplifies our partnership with community facilities, utilizes cutting edge research and incorporates local students, to provide an important health program for cancer patients all the while enriching our understanding of the unique patient population. The results of this project may help to develop standardized exercise protocols for breast cancer survivors and provide insights to other important health concerns. Clinical trial information: NCT04013568. Research Sponsor: None.

TPS12125 Poster Session (Board #413), Fri, 8:00 AM-11:00 AM

A phase Ib adaptive study of dasatinib for the prevention of oxaliplatin-induced neuropathy in patients with metastatic colorectal cancer receiving FOLFOX chemotherapy and bevacizumab. *First Author: Anne M. Noonan, The Ohio State University Comprehensive Cancer Center, Arthur G. James Cancer Hospital, Columbus, OH*

Background: Neurotoxicity is one of the most significant and disabling side effects of oxaliplatin and frequently limits the cumulative amount that can be used. The mechanism of oxaliplatin-induced neurotoxicity remains uncertain, although our preliminary studies suggest that oxaliplatin uptake by organic cation transporter 2 (OCT2) into mouse and rat dorsal root ganglion is a prerequisite for oxaliplatin-induced peripheral neuropathy. The activity of OCT2 is dependent on tyrosine phosphorylation by the SRC-kinase family member Yes1, which is highly sensitive to inhibition by several FDA-approved, small molecule kinase inhibitors such as dasatinib. We have previously shown that pre-treatment with oral dasatinib prevented acute and chronic oxaliplatin-induced peripheral neuropathy in mouse and rat models. **Methods:** This is a phase Ib dose-finding study of dasatinib given in combination with mFOLFOX6 with or without bevacizumab. The study explores the hypothesis that the addition of dasatinib prior to oxaliplatin will inhibit OCT2 activity and reduce oxaliplatin-induced neuropathy. This hypothesis will be tested in a Bayesian Phase 1b trial with adaptive dose selection using efficacy-toxicity trade-offs (modified toxicity-efficacy probability interval dose-finding design) in patients with confirmed stage IV colorectal cancer who are candidates for mFOLFOX6 with bevacizumab therapy. Patients who have documented peripheral neuropathy or prior exposure to oxaliplatin will be excluded. The primary objective is to determine the recommended Phase 2 dose which is defined as the lowest intermittent dose of dasatinib that affects serum biomarkers of OCT2, including methylnicotinamide and creatinine, by $\geq$2-fold without influencing the clearance of oxaliplatin by $>$ 20%. The following doses will be used: oxaliplatin 85mg/m^2 IV, 5FU bolus 400mg/m^2 IV bolus with Leucovorin 400mg/m^2, bevacizumab 5mg/kg, followed by infusional 5FU 2400mg/m^2 IV over 46 hours given on a day 1 and 15 schedule every 28 days. Dasatinib will be administered at one of 2 dose levels – 100mg or 140mg po. Dasatinib will be given 24 hours and 30 mins prior to oxaliplatin on C1D14, C1D15 respectively and repeated on C1D28 and C2D1. Secondary objectives include evaluation of the influence of dasatinib on the pharmacokinetics of oxaliplatin and vice versa. Quality of life will be explored using the CIPN20 questionnaire. The trial opened to enrollment in Dec 2019 (NCT04164069) and is accepting patients. Clinical trial information: NCT04164069. Research Sponsor: Pelotonia IDEA grant.

TPS12126 Poster Session (Board #414), Fri, 8:00 AM-11:00 AM

Feasibility of a digital medicine program in optimizing opioid pain control in cancer patients (SWOG S1916). *First Author: Sherry Shen, Columbia University Medical Center, New York, NY*

Background: The undertreatment of pain in patients with advanced or metastatic cancer is well described in cancer research. Overcoming barriers that prevent successful use of opioid analgesics for cancer pain requires a clear understanding of how individuals use oral medications at home. The Proteus Discover is a digital medicine program (DMP) consisting of an FDA-approved ingestible sensor made of dietary minerals co-encapsulated with patients' medications, a wearable sensor patch, and a mobile device app that enables patients to electronically transmit their medication adherence patterns. Use of the DMP has demonstrated improved clinical outcomes vs. usual care in patients with diabetes and hypertension, shown superiority over directly-observed therapy in tuberculosis and has been studied in the treatment of patients with hepatitis C, HIV, cancer and severe mental illness, but it has not been previously studied with opioids or in monitoring cancer-related pain. **Methods:** We are conducting a multicenter pilot study at SWOG NCORP sites to test the feasibility of using the DMP to monitor opioid use in the treatment of metastatic cancer pain. Eligible patients must have a diagnosis of metastatic cancer, have a baseline Brief Pain Inventory worst pain score of $\geq$3, be deemed by their physician to need initiation or up-titration of oxycodone-acetaminophen for pain control, and be able to read English. Primary outcomes include: (1) study accrual of 60 patients within six months of study activation at all participating sites; (2) patient retention defined as $\geq$50 patients completing the study, and; (3) adherence to the DMP defined as $\geq$66% of patients wearing the sensor patch for $\geq$28 days of the 42-day observation period. Secondary outcomes include change in Brief Pain Inventory pain scores, opioid medication consumption, number of safety alert triggers for high consumption, hospital or emergency room visits for pain, activity levels, and frequency of changes to the pain control regimen. The study will enroll patients at six sites; the first patient was enrolled on 1/20/2020. If successful, this study will inform design of a randomized controlled trial of the DMP vs. usual care in optimizing medication utilization and controlling cancer-related pain. Clinical trial information: NCT04194528. Research Sponsor: U.S. National Institutes of Health, Proteus Digital Health.

TPS12127 Poster Session (Board #415), Fri, 8:00 AM-11:00 AM

An oro-buccal nanoparticle delivered cannabis medicine for pain management in cancer: A clinical trial in progress. *First Author: Stephen John Clarke, Northern Cancer Institute, Sydney, Australia*

Background: Cannabinoid molecules derived from Cannabis sativa L. have been posited to ameliorate conditions, including pain, chemotherapy induced nausea and multiple sclerosis associated spasticity. The clinical use of cannabinoids refers to a wide variety of formulations and extracts that may contain different active ingredients and adulterants as well as inter batch variability. Novel matrix formulations (e.g., water-soluble nanoparticles) for cannabis delivery may add further efficacy and tolerability to standard routes of administration (e.g., oral / gastrointestinal, inhaled, sublingual). This is further emphasized by the dysbiotic effects on the intestinal microbiome reported for oral formulations of medicinal cannabis, and which resulted in reduced efficacy. Similar results have been reported for other psychotropic compounds, such as alcohol and nicotine. Therapeutic use of cannabinoid formulations may be mode of delivery dependent in order to achieve safe, tolerable and effective doses. **Methods:** A water soluble oro-buccal nanoparticle spray with a racemic 1:1 mixture of Delta9Tetrahydrocannabinol (D9THC) and Cannabidiol (CBD), which bypasses the gastrointestinal system and first pass metabolism by accessing the systemic circulation via the facial lymphatics system, was investigated in patients with advanced cancer and unrelieved pain in a single ascending dose and multiple ascending dose in a first-in-human study. **Results:** The THC / CBD combination delivered as a submicron particle demonstrated safety, tolerability and a pharmacokinetic profile suitable for maintenance analgesic therapy. Preliminary analysis found an overall (n = 25) improvement in pain scores, especially in the subgroup of patients with bone metastases (n = 8), who obtained a greater than 30% average reduction in pain severity. 1 Clinical trial information: ACTRN12617001480370. Research Sponsor: Medlab Clinical.

TPS12128 Poster Session (Board #416), Fri, 8:00 AM-11:00 AM

A phase Ib study of the safety and pharmacology of nilotinib to prevent paclitaxel-induced peripheral neuropathy in patients with breast cancer. *First Author: Elizabeth J. Adams, Ohio State University Wexner Medical Center, Columbus, OH*

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating adverse effect of paclitaxel, but convincing evidence for a preventative technique founded on mechanistic rationale is lacking. We previously report that paclitaxel accumulation is mediated by the murine organic anion transporting polypeptide, OATP1B2 in mice (OATP1B1 and OATP1B3 in humans) (Leblanc, J Clin Invest, 2018). We found that paclitaxel induces acute and chronic neurotoxicity in mice in an OATP1B2-dependent manner, which is reversed by pre-treatment with FDA-approved tyrosine kinase inhibitor, nilotinib. **Methods:** This phase Ib dose finding study of nilotinib in combination with weekly paclitaxel is investigating the hypothesis that intermittent dosing of nilotinib 24 hours before paclitaxel infusion (excluding C1D1) and again 30 minutes before paclitaxel infusion will inhibit OATP1B1 and prevent CIPN. This hypothesis will be assessed using an adaptive Bayesian method for dose finding based on efficacy-toxicity trade-offs in patients with breast cancer stages I-III who qualify for paclitaxel therapy. Patients with previous $\geq$ grade 2 neuropathy on breast cancer therapies will be excluded. The primary objectives are to find the recommended phase II dose of nilotinib in combination with paclitaxel for early stage breast cancer, defined as the lowest intermittent dose of nilotinib that temporarily inhibits OATP1B1 function without affecting paclitaxel plasma pharmacokinetics (PK), and to determine the toxicity profile of nilotinib in combination with paclitaxel. OATP1B1 inhibition by nilotinib will be assessed via validated surrogate endogenous substrates, glycochenodeoxycholate sulfate (GCDGA-S) and chenodeoxycholate-24-glucuronide (CDCA-24G). Effective OATP1B1 inhibition will be $\geq$5-fold increase in AUC of GCDCA-S from pre- to post- treatment or detectable CDCA-24G levels post-treatment. The 4 nilotinib dose levels are 50 mg (dose level -1), 100 mg (dose level 1), 200 mg (dose level 2), 300 mg (dose level 3). IV paclitaxel dose of 80 mg/m^2 on D1,8,15 for 12 total weekly doses will be used. Oral nilotinib will be administered 24 hours before paclitaxel infusion on C1D7,D14 and again 30 minutes before infusion on C1D8,D15. Secondary objectives are to determine paclitaxel's effect on PK of nilotinib and vice versa. Quality of life via CIPN-20 survey, disease free survival, event free survival, overall survival are exploratory objectives. NCT04205903 enrollment opened February 2020 and is accepting patients. Clinical trial information: NCT04205903. Research Sponsor: U.S. National Institutes of Health.

TPS12129 Poster Session (Board #417), Fri, 8:00 AM-11:00 AM

Use of simulation for training family caregivers of patients receiving radiation therapy. *First Author: Susan R Mazanec, Case Western Reserve Univ, Cleveland, OH*

Background: Positive treatment outcomes and avoidance of complications are dependent to a large extent on the care provided by family members. However, family caregivers report feeling unprepared to assume the multiple, complex tasks of caregiving, including tracheostomy care, tube feedings, wound and colostomy care, pain management, and emotional support. Despite being a critical extension of the oncology healthcare team, training of caregivers to manage symptoms, deal with communication issues with the care recipients, and take care of their own physical and emotional health as caregivers, is not integrated into clinical practice. The purpose of this clinical trial is to measure the effect of a psychoeducational caregiver intervention that incorporates simulation techniques focused on skill development to improve caregiver and patient outcomes. Simulation, commonly used in training healthcare professionals, is a form of experiential learning that creates events or situations to mimic clinical situations. Use of simulation for skills training in family caregivers of patients with cancer is rarely studied. **Methods:** This two-group, randomized clinical trial, which opened to accrual in December 2019, will recruit 180 caregivers from University Hospitals Seidman Cancer Center. Patients must be receiving radiation therapy for a diagnosis of stage I - III cancers of the rectum, anus, and esophagus; stage III NSCLC; or stage I – IV A/B head/neck cancer. Adult caregivers must be identified by the patient as their primary caregiver, who is providing daily assistance and/or emotional support. The intervention involves three in-person, one-on-one sessions during radiation treatments. The control group is usual care. Data will be collected at baseline, at the end of radiation treatment, and 4 and 20 weeks post-radiation treatment. The primary outcome is caregiver anxiety at 20 weeks postradiation treatment. Other caregiver outcomes include depression, health-related quality of life [HRQOL], and fatigue. Patient outcomes (HRQOL and interrupted treatment course) and healthcare utilization outcomes (unplanned hospital admission, emergency room visits, and use of intravenous fluids) will be measured. The analysis will consist of linear mixed model repeated measures, mediation and moderation tests, and Poisson regression methods. Clinical trial information: NCT04055948. Research Sponsor: U.S. National Institutes of Health.

TPS12130 Poster Session (Board #418), Fri, 8:00 AM-11:00 AM

Effects of an e-home based symptom management and mindfulness training program on quality of life in breast cancer survivors. *First Author: Karis Kin-Fong Cheng, National University of Singapore, Singapre, Singapore*

Background: The first five years post-treatment for breast cancer are a critical phase, when the survivors may face a multitude of problems, including persistent and/or late-emerging symptoms following the cancer and its treatment, psychosocial distress associated with the risk of cancer recurrence, chronic uncertainty and social disruption. Thus, this trial will answer the research questions of 'Will the combined symptom management and mindfulness-based training programme be a promising approach to assist women with breast cancer in transition from treatment to survivorship?', and 'Since breast cancer survivors have infrequent clinical follow-up, will e-Home based system provide a feasible option for post-treatment care?' **Methods:** We aim to develop an e-Home based symptom management and mindfulness training programme for breast cancer survivors and to determine its effects on the endpoints including quality of life, symptom distress, psychosocial adjustment, psychological morbidity, and unplanned outpatient attendance or hospitalisation in breast cancer survivors. (ClinicalTrials.gov Identifier: NCT02931864) We employ a randomised clinical trial with four study arms (with 47 subjects, who have completed cancer treatment for stage 0 to 3 breast cancer between 6 months to 5 years previously, in each arm) together with a process evaluation; group 1 (usual care), group 2 (experimental group: five weekly sessions of online symptom management + mindfulness training programme and usual care), group 3 (comparison group 1: online symptom management programme and usual care), and group 4 (comparison group 2: online mindfulness training programme and usual care). Subjects will complete questionnaires measures of 6-item Social Support Questionnaire, Breast Cancer Survivor Self- Efficacy Scale, the Quality of Life-Cancer Survivor Scale, Memorial Symptom Assessment Scale, Psychosocial Adjustment to Illness Scale, short version of the Fear of Recurrence Scale, Hospital and anxiety Depression Scale, and Five Facet Mindfulness Questionnaire at baseline, at 8 weeks from time 1 (time 2), at 12 weeks from time 1 (time 3) and at 24 weeks from time 1 (time 4). Intention-to-treat approach will be used. Repeated measures analysis of variance will be used to examine the differences on outcome measures among the experimental, comparison, and control groups across study time points. Currently, 162 of 188 planned subjects have been enrolled and the trial continues as planned. Clinical trial information: NCT02931864. Research Sponsor: Singapore Cancer Society Research Fund.

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