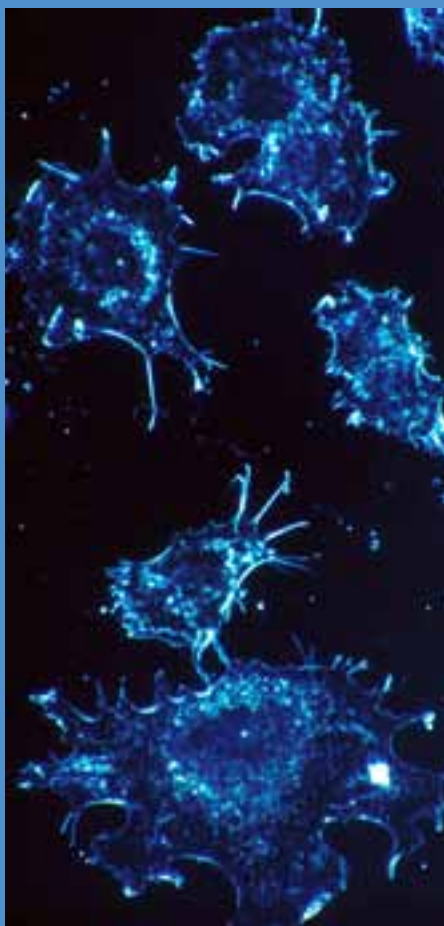


CLINICAL CANCER ADVANCES 2010

ASCO's
Annual Report
on Progress
Against
Cancer



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CLINICAL CANCER ADVANCES 2010

ASCO's Annual Report on Progress Against Cancer

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A Letter from ASCO's President

PATIENTS. PATHWAYS. PROGRESS.

Like many health professionals who care for people with cancer, I entered the field because of specific patients who touched my heart. They still do. In an effort to weave together my personal view of what the American Society of Clinical Oncology stands for and the purpose the organization serves, my presidential theme this year is "Patients. Pathways. Progress."

"Patients" come first. Caring for patients is the most important, rewarding aspect of being an oncology professional. At its best, the relationship between doctor and patient is compassionate and honest, and one of mutual respect. Many professional organizations have an interest in cancer, but no other society is so focused on the entire spectrum of cancer care, education and research. Nor is any other society particularly interested in bringing new treatments to our patients through clinical trials as ASCO's. Clinical trials are the crux to improving treatments for people with cancer and are critical for continued progress against the disease.

"Pathways" has several meanings. Some pathways are molecular—the cancer cell's machinery of destruction, which we have only begun to understand in recent years. But there are other equally important pathways, including the pathways new therapies follow as they move from bench to bedside, and the pathways patients follow during the course of their disease. Improved understanding of these pathways will lead to new approaches in cancer care, allowing doctors to provide targeted therapies that deliver improved, personalized treatment.

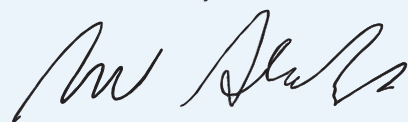
The best pathway for patients to gain access to new therapies is through clinical trials. Trials conducted by the National Cancer Institute's Cooperative Group Programs, a nationwide network of cancer centers and physicians, represent the United States' most important pathway for accelerating progress against cancer. This year, the Institute of Medicine released a report on major challenges facing the Cooperative Group Program. Chief among them is the fact that funding for the program has been nearly flat since 2002. ASCO has called for a doubling of funding for Cooperative Group Research over five years and supports the full implementation of the Institute of Medicine (IoM) recommendations to revitalize the program.

ASCO harnesses the expertise and resources of its 28,000 members to bring all of these pathways together for the greater good of patients.

"Progress" against cancer is being made every day—measurable both in our improved understanding of the disease and in our ability to treat it. A report issued in December 2009 by the National Cancer Institute (NCI), the Centers for Disease Control and Prevention (CDC), the American Cancer Society (ACS) and the North American Association of Central Cancer Registries (NAACR) found that rates of new diagnoses and rates of death from all cancers combined declined significantly in recent years for men and women overall and for most racial and ethnic populations in the United States.

The pace of progress can and needs to be hastened. Much remains to be done. Sustained national investment in cancer research is needed to bring better, more effective, less toxic treatments to people living with cancer. Pathways to progress continue in the clinic as doctors seek to find the right treatments for the right patients, understand what represents the right treatments, and partner with patients and caregivers on access to those treatments.

This report demonstrates that significant progress is being made on the front lines of clinical cancer research. But, while our nation's investment in this research is paying off, we must never forget the magnitude of what lies ahead. Cancer remains the number two killer of Americans. Future progress depends on continued commitment, from both ASCO and the larger medical community.



George W. Sledge Jr., MD

President

American Society of Clinical Oncology

Executive Summary

Hard-To-Treat Cancers

Treatment Shows Promise

Quality of Life

Reducing Cancer Recurrence

New Drug Approvals

Cancer Cases, Death Rates Decline

Palliative Care

PROGRESS AGAINST CANCER

Effective Prevention

Lower Rate of Diagnosis

Research

Chemotherapy Combination

Targeted Therapies and Personalized Medicine

Clinical Trials

Improved Survival

SUMMARY OF FINDINGS

The American Society of Clinical Oncology conducts an annual, independent review of advances in clinical cancer research to identify those that have had the greatest impact on patient care. *Clinical Cancer Advances 2010: ASCO's Annual Report on Progress Against Cancer* features 53 of the most significant studies, 12 of which the report's editors consider major advances.

Despite the 2009 National Cancer Institute (NCI) report of overall cancer rates on the decline in the United States, more than 1.5 million new diagnoses are expected in 2010, and nearly 570,000 Americans are expected to die from the disease this year alone. *Clinical Cancer Advances 2010* outlines recommendations for increasing the rate of progress against cancer and for a significant increase in funding and improvements to the clinical research system to accelerate the pace of discoveries that will lead to improved mortality rates and quality of care.

1. CANCER CASES, DEATH RATES DECLINE

A new report issued by leading health and cancer organizations in late 2009 found that overall rates of new diagnoses and death resulting from all cancers combined declined significantly in recent years for most racial and ethnic populations in the United States.

The report, issued by NCI, the U.S. Centers for Disease Control and Prevention, the American Cancer Society, and the North American Association of Central Cancer Registries showed the number of new cancer cases declined, on average, by nearly 1 percent per year between 1999 and 2006. In addition, death rates dropped 1.6 percent annually from 2001 to 2006, mainly due to reductions in new cases and death rates for the three most common cancers in men (lung, prostate, and colorectal cancers) and for two of the three leading cancers in women (breast and colorectal cancer).

2. HARD-TO-TREAT CANCERS

While some cancers defy early detection, and are more often diagnosed in advanced stages, many cancers are simply inherently resistant to therapy. Advances in such hard-to-treat cancers in the last year include:

Chemotherapy Combination Increases Survival in Advanced Lung Cancer in the Elderly

The same combination of chemotherapy drugs (carboplatin and paclitaxel) that is commonly used in younger lung cancer patients improved survival over single agent therapy (gemcitabine or vinorelbine) in elderly patients. Although older patients are often given less aggressive forms of therapy, the researchers reported in a multicenter, phase III study that the more aggressive combination therapy was both more effective and well-tolerated.



News for Patients from the 2010 ASCO Annual Meeting

www.cancer.net/ascoannualmeeting

Chemotherapy Combination Dramatically Improves Survival for Patients with Metastatic Pancreatic Cancer

A randomized, phase III trial in patients with metastatic pancreatic cancer is the first, to our knowledge, to demonstrate a significant survival improvement in individuals with stage IV adenocarcinoma of the pancreas. It found that treatment with FOLFIRINOX—a combination of the chemotherapy drugs 5-fluorouracil, leucovorin, irinotecan and oxaliplatin—resulted in better response rates, progression-free survival and overall survival compared to standard single-drug treatment with gemcitabine (Gemzar).

Bevacizumab Extends Progression-Free Survival for Women with Advanced Ovarian Cancers

A phase III trial found that adding the anti-angiogenesis drug bevacizumab—which targets tumor blood vessel growth and development—to the standard chemotherapy drug combination carboplatin and paclitaxel helped women with advanced ovarian cancers live significantly longer without their disease progressing than chemotherapy alone. These extremely difficult-to-treat types of cancers include epithelial ovarian cancer, primary peritoneal ovarian cancer and fallopian tube cancer. Researchers found that giving chemotherapy and bevacizumab, followed by longer-term treatment with bevacizumab, was the most effective strategy.

ABOUT THIS REPORT

Every year significant progress is made in the fight against cancer. Because hundreds of cancer clinical trials are completed each year, identifying the most notable advances in cancer research in any given year can be challenging. Six years ago, ASCO stepped in to fill this information gap and undertook the compilation and publishing of *Clinical Cancer Advances*.

Developed under the direction of a 14-person editorial board comprised of prominent oncologists, only studies that significantly altered the way a cancer is understood or had a direct effect on patient care were included. The editors—including specialty editors for each of the disease- and issue-specific sections—reviewed research presented at major scientific meetings and studies published in peer-reviewed scientific journals over a one-year period (October 2009-September 2010).

Although important research is underway in all cancer types, advances that met the above criteria were not demonstrated in all types of cancer over the past year. Studies included

in this year's report are grouped as follows:

- Blood and lymphatic cancers
- Breast cancers
- Cancer disparities
- GI cancers
- Genitourinary cancers
- Gynecologic cancers
- Head and neck cancers
- Lung cancers
- Melanoma
- Pediatric cancers
- Prevention and screening
- Quality of life and quality of care

The advances detailed in each section are categorized as "major" and "notable," depending on their impact on patient care and survival. The research considered for this report covers the full range of clinical cancer issues:

- Epidemiology
- Prevention
- Screening
- Early detection
- Traditional treatment (surgery, chemotherapy, radiation)
- Targeted therapies
- Immunotherapy
- Genetic research
- Personalized medicine
- Access to care
- Quality of life
- End-of-life care

Antibody Ipilimumab Improves Survival in Advanced Melanoma

In the first-ever phase III randomized trial to show a survival benefit for advanced melanoma, researchers found that an experimental immune therapy, ipilimumab—a human monoclonal antibody that keeps the immune system's T cells activated, including those that target melanoma cells—resulted in patients living 34 percent longer after two years. The study also found that the melanoma was kept in check for six months in nearly 30 percent of those receiving the drug, compared to 11 percent of controls.

3. REDUCING CANCER RECURRENCE

While many cancers can be treated successfully at first, staving off the return of cancer may be a daunting challenge. When a cancer recurs, it often is resistant to treatment and leads to death. There was a major advance over the last year in reducing recurrence in breast cancer.

Briefer Course of Radiation Just as Effective in Preventing Recurrence in Early Stage Breast Cancer

A shorter, three-week course of higher-dose radiation—an approach called

hypofractionated therapy—was just as effective as the standard five-week course for women with early-stage breast cancer. After 10 years, the risk of local recurrence among two groups of more than 600 women randomly assigned to receive the shortened course or the standard radiation course was nearly the same.

4. TARGETED THERAPIES AND PERSONALIZED MEDICINE

As researchers continue to better understand the basic biology and behavior of cancers, they are also increasingly successful in developing treatment strategies that are tailored to the genetics of individual patients and their tumors. Major advances in personalized medicine and targeted therapies in the past year include:

Novel ALK Inhibitor Shows High Response in Group of Patients with Lung Cancer

A phase I trial showed that a high percentage of patients with a specific *ALK* gene mutation (about one in 20 patients with lung cancer) responded to treatment with the *ALK* inhibitor, crizotinib, with more than two thirds having some tumor shrinkage. Phase I trials typically are aimed at gauging toxicity and rarely show dramatic clinical activity. More than 90 percent of the 82 patients enrolled in the study responded to the drug—either their disease stopped growing or there was some tumor shrinkage.

New Targeted Treatment Shows Promise for Advanced Melanoma Patients with *BRAF* Gene Mutation

In a study that bodes well for the future use of targeted therapies against melanoma, researchers showed that the majority of advanced melanoma patients with a specific *BRAF* gene mutation (V600E mutant *BRAF*) responded to a new *BRAF* inhibitor, PLX4032. In the second part of a phase I trial, tumors either completely or partially regressed, including metastases in the bone and liver, in 81 percent of patients.



PHILIPPE GARO / PHOTO RESEARCHERS, INC

5. QUALITY OF LIFE

Several important studies this year contributed to improving the lives of people with cancer.

Adding Palliative Care to Chemotherapy Improves Survival in Patients with Lung Cancer

A randomized clinical trial of patients with advanced lung cancer showed that those individuals who received standard chemotherapy coupled with palliative care immediately after diagnosis lived significantly longer and had a better quality of life than those who received chemotherapy alone. Patients who regularly saw palliative care specialists reported less depression and pain, better mobility and were less likely to undergo fruitless and expensive aggressive therapy at the end of life than individuals who had chemotherapy alone. This research was supported by an American Society of Clinical Oncology Career Development Award.

Sleep Problems Impact Large Majority of Cancer Patients Taking Chemotherapy

In the first large study to evaluate the prevalence of insomnia in patients undergoing chemotherapy, researchers found that more than three-quarters of patients have insomnia and other sleep disorders—nearly three times the rate found in the general population. The researchers showed that sleep problems

SPECIAL UPDATE:

National Lung Screening Trial (NLST) Shows 20 Percent Decrease in Lung Cancer Deaths

On November 4, 2010, NCI released initial results from the National Lung Screening Trial, which found 20 percent fewer lung cancer deaths among trial participants screened with low-dose chest CT than those screened with a chest X-ray. (See page 33)



chemotherapy drug available for men with advanced, hormone-refractory prostate cancer who have already received treatment with the chemotherapy drug docetaxel.

SUMMARY OF RECOMMENDATIONS

This year's Clinical Cancer Advances report highlights the most significant advances that have been made in cancer research in 2010. For the past 50 years, the NCI Cooperative Group Program has served as one critical link between these scientific discoveries and improved treatment for patients with cancer. Unfortunately, stagnant funding and numerous administrative and oversight challenges threaten the program's ability to continue to serve in this role.

In conjunction with the release of the Institute of Medicine (IoM) report, "*A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the National Cancer Institute (NCI) Cooperative Group Program*," ASCO makes the following recommendations:

Double Funding for Cooperative Clinical Research: ASCO calls on NCI to double funding for Cooperative Group trials in the academic and community settings from its current level of \$250 million to \$500 million by 2015. Funding for Cooperative Clinical Research has been virtually flat since 2002, forcing NCI Cooperative Groups to limit patient enrollment in clinical trials. A recent ASCO survey found that one-third of Cooperative Group Program participants plan to limit participation in federally funded clinical trials as a result of inadequate patient reimbursement.

Implement IoM Report Recommendations: ASCO urges all stakeholders affected by the report's recommendations to implement them. The IoM's recommendations focus on improving the speed, efficiency and flexibility of Cooperative Group clinical trials, while maximizing their involvement of patients and physicians.

were more prevalent in patients under age 58, and patients reporting insomnia were also significantly more likely to report depression and fatigue than those without insomnia.

6. NEW DRUG APPROVALS

Important clinical studies resulted in new drug approvals by the U.S. Food and Drug Administration this year, including two for prostate cancer.

Sipuleucel-T (Provenge) Approved for Treating Advanced Prostate Cancer

The FDA approved Sipuleucel-T (Provenge), a cancer vaccine for metastatic hormone-refractory prostate cancer early in 2010. Unlike a preventive vaccine, which is given to stimulate the immune system to fight off infections and prevent disease, Provenge is a therapeutic vaccine that boosts the body's immune system to attack cancer cells in the body.

Cabazitaxel (Jevtana) Approved for Advanced Prostate Cancer

Cabazitaxel (Jevtana) became the first

Cancer Research Advances

BLOOD AND LYMPHATIC CANCERS

Cancers of the blood and lymphatic system include leukemia, lymphoma and multiple myeloma. During the past year, several important studies were reported. A pair of studies showed two second-generation drugs were more effective than the current standard for chronic myeloid leukemia. Another reported on the potential benefit of maintenance therapy for multiple myeloma, a disease in which relapse is a constant threat. Two more reports described the potential benefits of adding antibody therapy to established treatments for follicular lymphoma. Lastly, the past year also brought several new FDA approvals of drugs to treat rare forms of lymphoma and leukemia.

NOTABLE ADVANCES

Tyrosine Kinase Inhibitors Provide Additional Options to Imatinib for Front-Line CML

For the vast majority of patients with chronic myeloid leukemia (CML), imatinib (Gleevec), the current standard drug, is extremely effective. Yet a small but growing number of patients either don't respond or develop resistance to imatinib. Therefore, researchers have sought alternatives for those in whom imatinib is ineffective.

Two separate studies this year showed the second generation tyrosine kinase inhibitors dasatinib (Sprycel) and nilotinib (Tasigna)—which target the same genetic pathway as imatinib—may provide even more effective options against CML as first-line therapies. These treatments were previously found to be effective in CML patients where disease persisted despite imatinib, or in those patients who cannot tolerate imatinib. In both cases, the newer drugs elicited faster and stronger responses and were better tolerated than imatinib.

- In one phase III trial, 519 newly diagnosed patients with chronic phase CML were randomly assigned to receive either dasatinib or imatinib. The researchers measured the patients' complete cytogenetic response (CCyR)—considered a good marker for long-term survival—and rate of major molecular response (MMR), another marker of drug effectiveness.

After one year, 77 percent of dasatinib patients reached a CCyR compared to 66 percent of those receiving imatinib. The rate of major molecular response was also higher for dasatinib (46 percent) versus imatinib (28 percent). Researchers plan to follow these patients to assess long-term overall survival and progression-free survival.¹

- In the other trial, called the ENESTnd (Evaluating Nilotinib Efficacy and Safety in Clinical Trials of Newly Diagnosed Philadelphia Chromosome-positive CML Patients) trial, 846 newly diagnosed chronic phase CML patients were randomized to receive either nilotinib (two different doses, either 300 mg or 400 mg) or imatinib. (Fig 1.) By a median follow up time of 18 months, both nilotinib patient groups had experienced more MMRs: 69 percent for the 300 mg group and 63 percent for those receiving 400 mg. Only 36 percent of the imatinib patients had MMRs. By 24 months, the patients who received nilotinib were still doing better: the corresponding MMR rates were 86 percent, 88 percent and 48 percent respectively. Patients treated with nilotinib were less likely to progress to more dangerous phases compared with patients treated with imatinib.²

CCyR complete cytogenetic response
MMR major molecular response

After one year, 77 percent of dasatinib patients reached a CCyR compared to 66 percent of those receiving imatinib.

Source: Dasatinib versus imatinib in newly diagnosed chronic phase chronic myeloid leukemia.

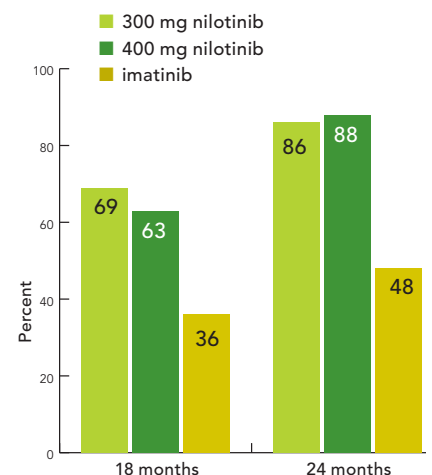


Fig 1. ENESTnd Trial: CML patient MMR rates



autologous stem cell transplantation

a procedure in which some of a patient's own blood stem cells are removed and returned after treatment to rebuild the immune system

The results of both trials offer more choices for patients with newly diagnosed CML in chronic phase. Nilotinib was granted accelerated approval by the FDA in 2010 and is now indicated for use in front-line chronic phase CML. These data suggest that second-generation inhibitors could become the new standard of care for chronic phase CML. However, many experts caution that longer follow-up is needed before either nilotinib or dasatinib universally replace imatinib for this indication.

Side effects are common with all tyrosine kinase inhibitors. Compared to imatinib, nilotinib more frequently caused rash, headache, liver function abnormalities, high cholesterol, hyperglycemia, elevated serum lipase and abnormal electrolytes. Dasatinib was more likely than imatinib to cause thrombocytopenia and pleural effusions. All three agents can cause significant myelosuppression.

Lenalidomide Maintenance Therapy Slows Myeloma Progression

Multiple myeloma, a cancer of plasma cells in the bone marrow, is typically treated with high-dose chemotherapy and autologous stem cell transplantation—a procedure in which some of a patient's own blood stem cells are removed and returned after treatment to rebuild the immune system. Despite this aggressive approach, more than 90 percent of patients eventually relapse.

New findings from a phase III trial showed that adding "maintenance" therapy with the drug lenalidomide (Revlimid) in patients who had achieved remission after initial therapy slowed disease progression by 54 percent. Maintenance therapy is longer-term treatment given after patients successfully complete initial therapy with the goal of prolonging their remission.

In this study, investigators evaluated more than 600 patients who were randomly assigned to receive maintenance lenalidomide or placebo until their cancer relapsed. All patients had received previous treatment with high-dose therapy and autologous stem cell transplantation, followed by two months of lenalidomide treatment after initial therapy to achieve a complete remission. Investigators found that adding lenalidomide maintenance therapy almost doubled three-year progression-free survival: 68 percent of patients in the lenalidomide maintenance group did not experience disease progression, compared with 35 percent of the placebo group.

Two-year overall survival was similar in both groups (95 percent), and analysis is ongoing. These findings suggest that this approach can improve quality of life for patients with multiple myeloma by delaying the need for intensive therapy to treat a relapse.³

New Chemotherapy Agent, Better Use of Rituximab, May Improve Survival, Delay Relapse in Follicular Lymphoma

Two studies this year provided important new insights on potential advances

in treating follicular lymphoma, a slow-growing, but usually incurable cancer.

- A phase III German trial showed that bendamustine (Trenda), a novel chemotherapeutic agent, plus the antibody rituximab (Rituxan), increased the rate of complete response in follicular and other types of lymphomas compared to the commonly used CHOP and rituximab regimen. CHOP includes the drugs cyclophosphamide, doxorubicin, vincristine, and prednisone.

In the study, 513 patients with late-stage, slow-growing lymphomas (most of which were follicular lymphoma) were randomly assigned to treatment with either the bendamustine-rituximab or CHOP-rituximab combination. (Fig 2.) Researchers found that the bendamustine-rituximab group lived significantly longer without the disease progressing (54.9 months) compared to the CHOP-rituximab patients (34.8 months). The bendamustine patients had better overall responses than the CHOP group, but there were no differences in overall survival. The CHOP/rituximab combination had significantly more toxicities and complications from infections than did the bendamustine regimen. Bendamustine is not toxic to the heart, whereas doxorubicin is known to be cardiotoxic and may increase the risk of heart failure. These findings suggest that the bendamustine-rituximab combina-

tion could become a new standard of care for previously untreated follicular lymphoma patients.⁴

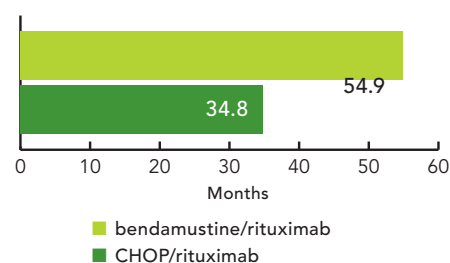
- The phase III international PRIMA (Primary Rituximab and Maintenance) trial found that two years of rituximab (Rituxan) maintenance therapy reduces the risk of follicular lymphoma recurrence by 50 percent in patients who responded to initial chemotherapy plus rituximab.

Patients with stage III or stage IV follicular lymphoma whose disease was reduced or eliminated by rituximab-based combination chemotherapy were randomly assigned to receive two additional years of rituximab maintenance therapy (505 patients) or no maintenance therapy (513 patients). After a median follow-up time of 25 months, the lymphoma progressed in 18 percent of the rituximab maintenance group compared with nearly double that (34 percent) among those who didn't receive the drug. The researchers noted that longer follow-up is needed to confirm the benefits of maintenance rituximab therapy for reducing the risk of lymphoma relapse. Rituximab maintenance therapy was well tolerated, and quality of life was similar between the two groups. Based on these findings, the manufacturer of rituximab has applied for approval in the U.S. and Europe for an expanded indication for rituximab as maintenance therapy in these patients.⁵

CHOP

includes the drugs cyclophosphamide, doxorubicin, vincristine, and prednisone

Fig 2. Phase III: Bendamustine vs. CHOP Head to head progression-free survival



ASCO Answers:
Chronic Myeloid Leukemia
www.cancer.net/cmifactsheet

ASCO Answers:
Chronic Lymphocytic Leukemia
www.cancer.net/cllfactsheet

ASCO Answers:
Multiple Myeloma
www.cancer.net/multiplemyelomafactsheet

ASCO Answers:
Non-Hodgkin Lymphoma
www.cancer.net/nhlfactsheet



A scientist preparing white blood cells from donated bone marrow for a transplant

“Major milestones have been achieved in the management of blood cancers in the past decade. Several important highlights have been the advent of effective immunotherapy, active oral agents, and the use of high throughput technology to better understand underlying biology. We continue to need funding and support to move to the next level of care where personalized therapies based on biologic differences are available to every patient.”

—SONALI SMITH, MD



**Cancer.Net Guide to
Chronic Myeloid Leukemia**
www.cancer.net/cml

**Cancer.Net Guide to
Chronic Lymphocytic Leukemia**
www.cancer.net/cll

**Cancer.Net Guide to
Multiple Myeloma**
www.cancer.net/myeloma

**Cancer.Net Guide to
Non-Hodgkin Lymphoma**
www.cancer.net/nhl

New Targeted Therapies Approved for Peripheral T-Cell Lymphoma and Recurrent Chronic Lymphocytic Leukemia

Two new drugs were approved by the FDA this year for extremely difficult-to-treat cancers—peripheral T-cell lymphoma and recurrent chronic lymphocytic leukemia (CLL). The approvals were based on significant response data in small numbers of patients.

- Pralatrexate (Folotyn) received FDA approval as a single-agent therapy for relapsed or refractory peripheral T-cell lymphoma, a relatively rare and aggressive type of non-Hodgkin lymphoma that occurs in nearly 9,500 Americans annually. This first drug approved for peripheral T-cell lymphoma works by inhibiting RFC-1, a protein that is overexpressed in T-cell lymphoma cells. The approval was based on findings from the phase II PROPEL (Pralatrexate in Patients with Relapsed or Refractory Peripheral T-cell Lymphoma) trial, which showed that 29 of 109 peripheral T-cell lymphoma patients (27 percent) who received pralatrexate had some tumor shrinkage.⁶
- The FDA approved ofatumumab (Arzerra), a monoclonal antibody drug targeting the CD20 protein on B cells, for treating relapsed or resistant chronic lymphocytic leukemia (CLL). The approval was based on findings from a single-arm trial of 154 patients with relapsed or resistant CLL. In a subgroup of 59 CLL patients who were resistant to two drugs, fludara-

bine and alemtuzumab, researchers found that treatment with ofatumumab resulted in a 42 percent overall response rate, with a median response duration of 6.5 months. This response rate is encouraging in a population of patients that has been heavily pretreated and immunocompromised and that who have few non-myelosuppressive options.⁷

REFERENCES

1. Kantarjian, H, et al. Dasatinib versus imatinib in newly diagnosed chronic phase chronic myeloid leukemia. *N Engl J Med*. 2010; 362:2260-2270.
2. Larson, RA, et al. Comparison of nilotinib and imatinib in patients with newly diagnosed chronic myeloid leukemia in chronic phase (CML-CP): ENESTnd beyond one year. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.
3. Attal, M, et al. Lenalidomide maintenance after transplantation for myeloma. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.
4. Rummel, MJ, et al. Bendamustine plus rituximab is superior in respect of progression free survival and CR rate when compared to CHOP plus rituximab as first-line treatment of patients with advanced follicular, indolent, and mantle cell lymphomas: final results of a randomized phase III study of the StiL (Study Group Indolent Lymphomas, Germany). Presented at the 51st ASH Annual Meeting and Exposition; December 2009; New Orleans, LA.
5. Salles, GA, et al. Rituximab maintenance for 2 years in patients with untreated high tumor burden follicular lymphoma after response to immunochemotherapy. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.
6. FDA Approves First Drug for Treatment of Peripheral T-cell Lymphoma. Press release, U.S. Food and Drug Administration. September 25, 2009.
7. Wierda, WG, et al. Ofatumumab as single-agent CD20 immunotherapy in fludarabine-refractory chronic lymphocytic leukemia. *J Clin Oncol*. 2010; 28:1749-1755.

BREAST CANCERS

Breast cancer remains the most commonly diagnosed cancer among women in the United States and significant progress continues to be made against the disease. Women are living longer, healthier lives, thanks to improvements in surgery, chemotherapy and radiation therapies. Recent insights into the molecular pathways critical to the behavior of specific breast cancers, and the sub-classification of breast cancers based on genomic profile—as opposed to histological features seen under the microscope—have been key to advancing understanding and treatment of the disease. But many challenges remain, as certain forms of breast cancer continue to be very difficult to treat.

Important advances of the past year include smarter radiation therapy approaches for early-stage disease; a new chemotherapy agent for women with advanced breast cancer whose disease has progressed despite other treatments; and new information on the most effective, least invasive way to detect cancer spread in the under-arm lymph nodes.

MAJOR ADVANCE

Briefer Course of Radiation Just as Effective in Preventing Recurrence in Early Stage Breast Cancer

Radiation of the entire breast after breast-conserving surgery significantly reduces breast cancer deaths compared with surgery alone. Yet, as many as 30 percent of women who have such surgery in North America don't opt for radiation, partly due to its inconvenience.

But this year, Canadian researchers reported that a shorter, three-week course of higher-dose radiation—an approach called hypofractionated therapy—may be just as effective as the standard five-week course for women with early-stage disease. After 10 years, the risk of local recurrence among 622 women randomly assigned to receive



the shortened course was 6.2 percent compared to 6.7 percent among 612 women given the standard radiation course. In addition, 71.3 percent of patients in the standard radiation group experienced good or excellent cosmetic outcomes after 10 years compared to 69.8 percent of women receiving the briefer therapy.¹

NOTABLE ADVANCES

Removing Fewer Lymph Nodes in Sentinel Node-Positive Breast Cancer Does Not Impair Survival

When cancer is detected in the sentinel node, the surgeons frequently remove additional lymph nodes (axillary node dissection) under the arm to look for more cancer there. While this has been shown to control breast cancer spread locally, its effect on survival has been controversial. New findings suggest that despite evidence of cancer in the sentinel lymph node, removing axillary lymph nodes may not provide a survival benefit.

In the largest phase III study of axillary node dissection in sentinel node-positive women to date, researchers randomly assigned into two groups 891 women who had clinically node negative disease; fewer than three cancer-positive sentinel nodes; breast-conserving

hypofractionated therapy

is radiation treatment in which the total dose of radiation is divided into large doses and treatments are given less than once a day. Also called hypofractionation.

surgery and radiation. The first group received further sentinel node biopsy and the second was treated with both sentinel node biopsy and axillary node dissection.

After a median follow-up of six years, the researchers found no survival advantage to removing more lymph nodes. The five-year survival for those who had extra lymph nodes removed was 91.9 percent compared to 92.5 for women who had only the sentinel node removed. Disease-free survival was similar as well: 82.2 percent for the axillary node group versus 83.8 for sentinel node only.

The study closed early because of lower-than-expected enrollment and further study is needed. However, the results raise the possibility that for selected individuals, such as the elderly and women with certain accompanying conditions or diseases, doctors could safely forgo additional lymph node removal.²

Novel Drug based on Marine Sponge Chemical Improves Overall Survival in Metastatic Breast Cancer

Metastatic breast cancer kills approximately 40,000 women in the United States each year, but there are currently no curative treatments. For the first time, researchers have found that a chemotherapy agent, eribulin mesylate, a new type of microtubule inhibitor that is an analogue of a chemical derived from a marine sponge, helped patients with recurrent or metastatic disease live longer compared to the physician's choice of other standard treatments.

The phase III international study, called EMBRACE (Eisai Metastatic Breast Cancer Study Assessing Physician's Choice Versus Eribulin E7389), found that women who received eribulin had a median overall survival of 13.1 months, versus 10.7 months for women who received their physician's choice of therapy. After one year, 53.9 percent of patients were alive after treatment with

eribulin compared to 43.7 percent of those receiving the physician's choice. The results could potentially establish eribulin as a new standard for this group of patients.³

Immunohistochemistry to Find Micrometastases in Bone Marrow and Sentinel Lymph Nodes Unnecessary

Doctors frequently use an extra-sensitive test called immunohistochemistry (IHC) to detect the spread of hidden breast cancer, with the goal of predicting risk of recurrence and guiding therapy choices. However, a large observational trial of women with early-stage breast cancer found that using IHC to find micrometastases in both the bone marrow and sentinel lymph nodes did not have an impact on survival. These results argue against the frequent use of IHC testing, which could save money and spare women from potentially unnecessary therapy based on such tests.

In this prospective, multicenter study, researchers examined the potential clinical significance of IHC-detected cancer in the bone marrow and sentinel node in more than 5,500 women with early stage, clinically node-negative disease. All underwent sentinel node biopsies and bone marrow aspiration to look for micrometastases, and those who were found to be negative by these standard pathology tests were tested with IHC. Standard pathology detected cancer in 23.9 percent of the sentinel nodes, and IHC found cancer in an additional 10.5 percent.

Despite the fact that IHC detected more cancer, the five-year survival rate was statistically similar between the two groups. In the IHC group, 95.1 percent of the women with positive sentinel nodes lived five years, compared to 92.8 with positive nodes found by standard pathology. For patients with bone marrow metastases detected by IHC, median five-year overall survival was lower (90.2 percent compared to 95.1 percent for women with IHC-negative bone



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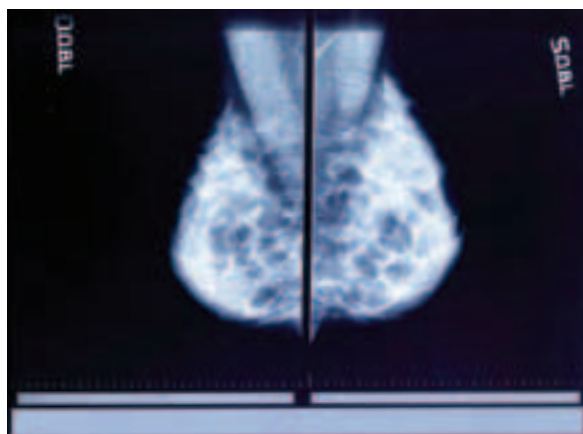
An estimated 207,090 new cases of invasive breast cancer are expected to be diagnosed among women in the U.S. during 2010; about 1,970 cases are expected in men.

PERSPECTIVE ON BREAST CANCERS

“We have long recognized that breast cancer is not one disease. It neither behaves like one disease in the clinic, nor does it appear as one disease morphologically under the microscope.

A future challenge will be the definition of a molecular marker or profile to select patients who may be most likely to benefit from targeted strategies. With the exception of the use of estrogen receptor and HER2 testing, this has thus far been elusive.”

—ANDREW SEIDMAN, MD



marrow) and statistically significant. While the detection of bone marrow metastases by IHC identified patients with an increased risk for death, it was not predictive of overall survival in a multivariate analysis.⁴

Negative Sentinel Node Adequate to Confirm Lack of Cancer Spread

In recent years, the standard practice has been to examine the breast's sentinel lymph node—usually under the woman's arm—to look for hidden cancer that may have spread there. This procedure can avoid the need for axillary node dissection in women who have no palpable disease or evidence of spread to the lymph node. Axillary node dissection, which is a surgical procedure to remove all axillary lymph nodes under the arm, can cause pain, swelling and scarring.

A National Surgical Adjuvant Breast and Bowel Project trial randomly assigned 5,611 women with clinically node-negative breast cancer to either have both sentinel and axillary nodes removed (Group 1), or have only sentinel node surgery, with axillary dissection only if cancer was found (Group 2). Of the 5,611 women, only the 3,989 in groups 1 and 2 who were found to be sentinel node-

negative were followed—for an average of 95 months. The researchers did not find any statistically significant differences in local and regional recurrence or in overall survival between groups 1 and 2.⁵

REFERENCES

1. Whelan, BM, et al. Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer. *N Engl J Med.* 2010; 362:513-520.
2. Giuliano AE, et al. ACOSOG Z0011: A randomized trial of axillary node dissection in women with clinical T1-2 N0 M0 breast cancer who have a positive sentinel node. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.
3. Twelves C, et al. A phase III study (EMBRACE) of eribulin mesylate versus treatment of physician's choice in patients with locally recurrent or metastatic breast cancer previously treated with an anthracycline and a taxane. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.
4. Cote R, et al. ACOSOG Z0010: A multicenter prognostic study of sentinel node (SN) and bone marrow (BM) micrometastases in women with clinical T1/T2 N0 M0 breast cancer. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.
5. Krag DN, et al. Primary outcome results of NSABP B-32, a randomized phase III clinical trial to compare sentinel node resection (SNR) to conventional axillary dissection (AD) in clinically node-negative breast cancer patients. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.



Cancer.Net Guide to Breast Cancer
www.cancer.net/breast

What to Know: ASCO's Guideline on Sentinel Lymph Node Biopsy for Early-Stage Breast Cancer
www.cancer.net/whattoknow

After Treatment for Breast Cancer: Preventing Lymphedema
www.cancer.net/preventinglymphedema



ASCO Answers: Breast Cancer
www.cancer.net/breastfactsheet

CANCER DISPARITIES

While progress continues to be made in cancer detection, screening and treatment, these advances do not necessarily benefit all groups to the same degree. Disparities in cancer outcomes are well documented between various racial and ethnic groups in the United States, and ongoing research seeks to better understand the complex causes of these differences. While socioeconomic disadvantages in access to cancer care and services are more prevalent among racial and ethnic minorities—and are widely assumed to account for most of these cancer outcome differences—increasing attention has focused on the potential effects of newly discovered inherited susceptibilities to certain cancers.



Key studies published over the past year showed that equal cancer treatment results in equal outcomes, regardless of racial or ethnic identity for most cancers. However, several recent breast cancer studies have demonstrated provocative differences in the biologic characteristics and survival rates in women with African ancestry both within the United States and in continental Africa, compared to white women. Other research provided new perspective on the underlying factors affecting racial differences in survival for patients with colon cancer.

NOTABLE ADVANCES

Disparities in Cancer Survival Most Significant in Hormonally-Driven Cancers

In a ground-breaking study examining the root causes of racial disparities in cancer survival among patients in clinical trials, researchers found that cancer outcomes were indeed similar for cancer patients receiving equal treatment within the context of a clinical trial, regardless of racial-ethnic identity. This was true, with the exception of trials designed for hormonally-driven cancers, such as breast, prostate, and ovarian cancer. For this category of disease, survival rates were worse for African American patients than for white patients. These differences persisted even after controlling for prognostic, treatment and socioeconomic factors.

Investigators closely examined the records of nearly 20,000 adult patients with cancer, including 2,308 African Americans from 35 Southwest Oncology Group (SWOG) phase III trials that were conducted during a 27-year period. They studied outcomes for cancers of the breast, lung, colon, ovaries and prostate, along with lymphoma, leukemia and multiple myeloma. Results were stratified according to cancer pathology and stage. The study findings showed African American heritage was associated with increased risk of death in patients with early-stage premenopausal and postmenopausal breast cancer, advanced-stage ovarian cancer and advanced-stage prostate cancer. The 10-year survival rates for African American versus all other patients were 68 percent and 77 percent, respectively, for early-stage, premenopausal breast cancer; 52 percent versus 62 percent for early-stage, postmenopausal breast cancer; 13 percent versus 17 percent for advanced ovarian cancer; and 6 percent versus 9 percent for advanced prostate cancer. These findings suggested that tumor biological, hormonal and other inherited factors could be contributing to race- and ethnicity-associated survival differences in hormonally-driven cancers.¹ (Fig 3.)

Two Studies Reveal an Association Between African Ancestry and Risk of Triple-Negative Breast Cancer

African American women have a lower lifetime incidence of breast cancer compared to white women, but they have significantly higher breast cancer mortality rates. A key to explaining the mortality disparity is the fact that African American women are more likely to be diagnosed with tumors that are negative for the estrogen receptor, the progesterone receptor, and the HER2/neu protein—known as “triple-negative” breast cancer. Triple-negative breast cancers are also highly correlated with the inherently aggressive basal breast cancer subtype, and they do not respond to targeted, biologic systemic treatment for breast cancer, such as endocrine therapy or the drug trastuzumab (Herceptin).

This year, two studies added important new insights to the body of knowledge on the association between racial and ethnic identity and the risk for triple-negative breast cancer. Both studies evaluated breast tumors of Western African women, which is particularly relevant to inherited breast cancer risk in contemporary African American women because of the hypothesized shared ancestry with Western African women.

- In a first-of-its-kind study, researchers assessed the distribution of molecular subtypes of invasive breast cancers in native West African women by creating tissue microarrays from the tumors of 507 Nigerian and Senegalese women. They found that approximately three-quarters of these tumors were hormone receptor-negative, and more than half were either a basal subtype or an unclassified triple-negative subtype.²
- Another study concluded that the extent of African ancestry is associated with risk for developing triple-negative breast cancer, based upon a comparative analysis of 581 African

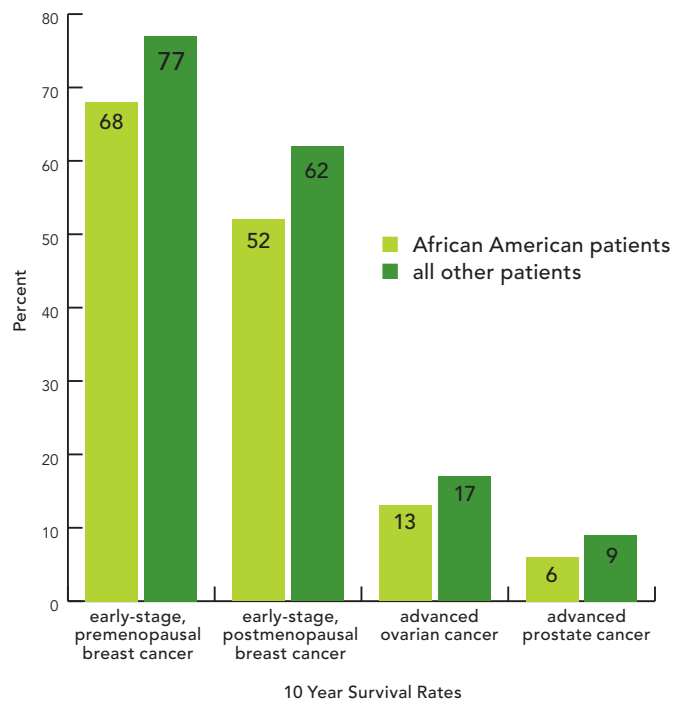


Fig 3. Hormonally-driven cancer disparities

American, 1008 White American, and 75 Ghanaian breast cancer patients. The highest proportion of triple-negative breast cancer was seen among the Ghanaian women (82 percent), and the lowest frequency was seen among the white women (16 percent); African American women had an intermediate frequency of 26 percent. A similar pattern was observed for proportions of estrogen receptor-negative tumors, where the frequencies were 76 percent, 36 percent, and 22 percent among Ghanaian, African American, and white women, respectively.³

These studies strengthen the understanding of breast cancer outcome disparities, and they may ultimately contribute to the clinical applications of targeted breast cancer treatment and risk assessment.

Study Confirms Socioeconomic Status Plays Major Role in Racial Disparities in Colon Cancer Outcomes

Past studies have shown differences between stage-specific colon cancer treatments delivered to African American and white patients. These disparities in care have been presumed to be

These findings suggested that tumor biological, hormonal and other inherited factors could be contributing to race- and ethnicity-associated survival differences in hormonally-driven cancers.

PERSPECTIVE ON CANCER DISPARITIES

“Although it is very disappointing that inequities in cancer treatment and outcome persist, it is exciting to witness progress in disparities research as an independent field of study. Disparities research now includes data from prospective multicenter clinical trials as well as advanced molecular biology and behavioral science studies.”

—LISA NEWMAN, MD



Health Disparities and Cancer

www.cancer.net/disparities

Managing the Cost of Cancer Care

www.cancer.net/managingcostofcare

Patient Navigation: Getting Help With Cancer Care

www.cancer.net/patientnavigation

related to socioeconomic disadvantages and poorer healthcare access, thereby at least partially explaining the higher colon cancer mortality rates that are observed among African Americans. A recent analysis supports this theory, demonstrating that in a population of colon cancer patients with similar socioeconomic status and insurance coverage, patients received the same quality of care regardless of race and had similar outcomes, confirming that socioeconomic status plays a major role in race or ethnicity-associated disparities in colon cancer outcomes.

To examine the effects of race on colorectal cancer outcomes in a single hospital, investigators retrospectively analyzed records from 365 patients (175 African Americans and 190 whites) diagnosed with stage II, III or IV colon cancer. After adjusting for demographics such as socioeconomic status, health insurance coverage, gender, age and marital status, they examined racial differences in the quality (timeliness and effectiveness) of stage-specific colon cancer therapy. They found no difference in patient care or outcomes between African Americans and whites.⁴

Race Associated with Response to Chemotherapy for Advanced Colorectal Cancer

Another study offered further clues to disparities in colon cancer mortality rates by evaluating differences in

response to chemotherapy. Researchers studied race- and ethnicity-related variation in pharmacogenetics by analyzing a group of participants in the North Central Cancer Treatment Group trial N9741, a randomized controlled trial comparing three different colon cancer regimens: 1) irinotecan and fluorouracil, 2) fluorouracil and oxaliplatin and 3) irinotecan and oxaliplatin.

Investigators compared adverse events, response rates, time to progression and overall survival in 1,412 white and African American trial participants. In addition, pharmacogenetic analyses were performed on 486 patients for whom blood samples were available. After controlling for stage at diagnosis and treatment arm, they found overall survival and time to disease progression were similar for the two groups. However, response rates were significantly higher among the white participants (41 percent) compared to the African Americans (28 percent).

Additionally, several highly significant associations were identified between racial and ethnic identity and drug-metabolizing enzyme genotypes, but no definitive conclusions could be drawn regarding the impact of these associations on drug toxicity and effectiveness due to inadequate sample size.⁵

REFERENCES

1. Albain KS, et al. Racial disparities in cancer survival among randomized clinical trials patients of the Southwest Oncology Group. *J Natl Cancer Inst.* 2009; 101:984-992.
2. Huo D, et al. Population differences in breast cancer: survey in indigenous African women reveals over-representation of triple-negative breast cancer. *J Clin Oncol.* 2009; 27:4515-4521.
3. Stark A, et al. African ancestry and higher prevalence of triple-negative breast cancer: findings from an international study. *Cancer*, n/a. doi:1002/cncr.25276.
4. Berry J, et al. A black-white comparison of the quality of stage-specific colon cancer treatment. *Cancer* 2010; 116:713-722.
5. Sanoff HK, et al. Racial differences in advanced colorectal cancer outcomes and pharmacogenetics: a subgroup analysis of a large randomized clinical trial. *J Clin Oncol.* 2009; 27:4109-4115.

GASTROINTESTINAL CANCERS

GI cancers include those of the esophagus, stomach, liver, pancreas, biliary tract, colon, rectum and anus. Important advances in the past year included a pair of studies showing progress against two types of metastatic pancreatic cancer, and reports showing the potential value of analyzing gene mutations in GI stromal tumors and metastatic colon cancer.

MAJOR ADVANCE

Chemotherapy Combination Dramatically Improves Survival for Patients with Metastatic Pancreatic Cancer

Adenocarcinoma of the pancreas (the most common type of pancreatic cancer) is extremely aggressive and often detected after it has spread to other parts of the body. Treatment options for patients diagnosed with stage IV pancreatic cancer are limited, making treatment challenging. But a recent, randomized phase III trial of 250 patients with metastatic pancreatic cancer is the first to demonstrate a significant survival improvement in this population. It found that first-line treatment with FOLFIRINOX—a combination of the chemotherapy drugs fluorouracil, leucovorin, irinotecan and oxaliplatin—resulted in better response rates, progression-free survival and overall survival compared to standard single-drug treatment with gemcitabine. The trial was halted early at an interim analysis, based on these positive results.

The median overall survival for patients treated with FOLFIRINOX was 11.1 months, compared with 6.8 months for those on gemcitabine—marking the longest-ever survival advantage observed in a clinical trial for advanced pancreatic cancer. Approximately 48 percent of patients on FOLFIRINOX were alive at one year compared with 20 percent of patients who received gemcitabine. Patients on the FOLFIRINOX arm also lived nearly twice as long without a worsening of their disease—median progression-free survival was 6.4 months for those on FOLFIRINOX



and 3.3 months for those treated with gemcitabine.

Although common in the FOLFIRINOX group, side effects were not severe enough that patients had to stop treatment. Patients who received FOLFIRINOX had longer preservation of their quality of life, although toxicities were higher compared with gemcitabine.¹

NOTABLE ADVANCES

Sunitinib Delays Cancer Spread for Patients with Pancreatic Neuroendocrine Tumors

An international study showed that patients with advanced pancreatic neuroendocrine tumors lived twice as long without disease progression when treated with the tyrosine kinase inhibitor sunitinib (Sutent) as did those who received placebo. Pancreatic neuroendocrine tumors, which sometimes secrete excessive amounts of various hormones, make up only about five percent of all pancreas tumors and they are more slow-growing than adenocarcinoma of the pancreas.

In this multicenter, phase III trial, 171 patients whose tumors had progressed in the previous 12 months were randomly assigned to receive either sunitinib or

Factoid:

Adenocarcinoma of the pancreas is the most common type of pancreatic cancer.



ASCO Answers: Pancreatic Cancer
www.cancer.net/pancreaticfactsheet

ASCO Answers: Colorectal Cancer
www.cancer.net/colorectalfactsheet

New chemotherapy combination yields the longest-ever survival advantage observed in a clinical trial for advanced pancreatic cancer.



Cancer.Net Guide to Pancreatic Cancer

www.cancer.net/pancreatic

Cancer.Net Guide to Neuroendocrine Tumor

www.cancer.net/neuroendocrine

Cancer.Net Guide to Colorectal Cancer

www.cancer.net/colorectal

Cancer.Net Guide to Gastrointestinal Stromal Tumor

www.cancer.net/gist

ASCO Expert Corner: KRAS Testing in People With Colorectal Cancer

www.cancer.net/krastesting

News for Patients from the 2010 Gastrointestinal Cancers Symposium

www.cancer.net/gisymposium

placebo. All patients received supportive care, which could include anti-nausea medication, nutritional support, and antibiotics for infections. Overall, patients in the sunitinib group were more likely to be alive after six months than those treated with placebo (92.6 percent versus 85.2 percent). Researchers also found that median progression-free survival was longer in the sunitinib group than in the placebo group (11.4 months, vs. 5.5 months). The trial was halted early due to the superiority of sunitinib over placebo. The results suggest that sunitinib can delay disease progression and help patients live longer.²

BRAF Status Prognostic Marker for Metastatic Colon Cancer Survival with Chemotherapy Plus Cetuximab

Two large trials, the CRYSTAL (Cetuximab Combined With Irinotecan in First-Line Therapy for Metastatic Colorectal Cancer) and the OPUS (Oxaliplatin and Cetuximab in First-Line Treatment of Metastatic Colorectal Cancer) studies, showed that adding the targeted drug cetuximab (Erbix) to initial chemotherapy improved outcomes compared to chemotherapy alone for those patients with metastatic colon cancer tumors that do not have KRAS gene mutations.

In a follow-up analysis, researchers pooled data from both trial populations

(which included 1,645 patients, though only 1,378 evaluable samples) and assessed outcomes based on both KRAS and BRAF gene mutation status. They found that adding cetuximab to chemotherapy improved outcomes for all patients with normal forms of KRAS, regardless of BRAF status, but that those with normal forms of both the KRAS and BRAF genes benefited most.

Median survival for patients with normal KRAS and BRAF treated with chemotherapy and cetuximab was 24.8 months, versus 21.1 months for chemotherapy alone. For patients with normal KRAS and BRAF mutations, adding cetuximab increased median survival from 9.9 months to 14.1 months. These data demonstrate that BRAF mutations are prognostic; patients whose tumors harbor BRAF mutations have significantly shorter progression-free and overall survival. However, patients with a normal KRAS gene and a BRAF mutation still seem to benefit from cetuximab, and treatment decisions regarding the use of cetuximab should not be made based on the presence of BRAF mutations.³

GIST Mutations Predict Recurrence Risk, May Guide Treatment Choices

An American College of Surgeons Oncology Group (ACOSOG) trial—the largest trial of patients with gastrointestinal stromal tumors (GIST) followed

prospectively after surgery—found that patients whose tumor cells have certain gene mutations are at higher risk of recurrence and are more likely to benefit from adjuvant therapy with the tyrosine kinase inhibitor imatinib (Gleevec). The findings suggest that analyzing GIST mutations may help guide treatment strategies after surgery.

Researchers previously had shown that one year of imatinib therapy after surgery significantly prolonged survival without recurrence for GIST patients, compared to placebo. In this study, researchers analyzed tumor and molecular characteristics in 513 patients with GIST who were randomized to receive either imatinib or placebo. Researchers found that high mitotic rate, small bowel location, and large tumor size were associated with worse recurrence-free survival. Patients whose tumors expressed exon 11 mutations and who were treated with adjuvant imatinib were significantly less likely to suffer disease recurrence within two years than those who received placebo (91 percent of those with exon 11 mutations were relapse-free compared to 65 percent). Likewise, patients with mutations in the *PDGFRA* gene were also less likely to have recurrence when treated with imatinib. In contrast, imatinib did not seem to influence recurrence for patients with wild-type tumors.⁴

***BRAF* Status, Tumor Site, Time to Relapse Help Predict Overall Survival After Colon Cancer Relapse**

Researchers have previously evaluated the prognostic value of eight selected molecular markers on relapse-free survival in stage II and stage III colon cancer. In this study, they examined the prognostic value of the same eight markers on survival after relapse in 392 of 990 patients with relapse. They found that while *BRAF* gene status and tumor

site had no prognostic value in relapse-free survival, both, along with time to relapse, were strong determinants of overall survival in colon cancer after relapse. In their data set, patients with *BRAF* mutated tumors had a median survival of 7.5 months compared to 25.2 months for patients with *BRAF* wild-type tumors. The median survival after relapse of patients with right-sided tumors was 16.2 months compared to 28.4 for those patients with left sided tumors. Finally, patients with late relapse lived more than 2.5 years compared to 1.5 years for those who had early relapse. Researchers suggest that the markers evaluated in this study should be used in stratifying metastatic colon cancer patients for clinical trials.⁵

REFERENCES

1. Conroy T, et al. Randomized phase III trial comparing FOLFIRINOX (F: 5FU/leucovorin [LV], irinotecan [I], and oxaliplatin [O] versus gemcitabine (G) as first-line treatment for metastatic pancreatic adenocarcinoma (MPA): Preplanned interim analysis results for the PRODIGE4/ACCORD 11 trial. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.
2. Raymond E, et al. Updated results of the phase III trial of sunitinib (SU) versus placebo (PBO) for treatment of advanced pancreatic neuroendocrine tumors (NET). Presented at the 2010 Gastrointestinal Cancers Symposium; January 2010; Orlando, FL.
3. Bokemeyer C, et al. Cetuximab with chemotherapy (CT) as first-line treatment for metastatic colorectal cancer (mCRC): Analysis of the CRYSTAL and OPUS studies according to *KRAS* and *BRAF* mutation status. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.
4. Corless CL, et al. Relation of tumor pathologic and molecular features to outcome after surgical resection of localized primary gastrointestinal stromal tumor (GIST): Results of the intergroup phase III trial ACOSOG Z9001. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.
5. Roth A, et al. Molecular and clinical determinants of survival following relapse after curative treatment of stage II-III colon cancer (CC): Results of the translational study on the PETACC 3-EORTC 40993-SAKK 60-00 trial. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.

PERSPECTIVE ON GASTROINTESTINAL CANCERS

“We are moving the treatment of GI cancers forward through a deeper understanding of the molecular basis of our treatments. Multiple predictive markers now tell us which patients have the potential to respond to our medical therapies. In the future, we will continue to develop personalized treatment for GI malignancies so that we can choose the right therapy for the right patient.”

—JENNIFER OBEL, MD

GENITOURINARY CANCERS

Factoid:

Prostate cancer is the most common cancer among men. In 2010, an estimated 217,730 U.S. men will be diagnosed.

The findings also suggested that watchful waiting is particularly feasible and safe for men older than age 70 who have low-to-intermediate risk prostate cancer. In this group, the risk of death from other causes was almost 19-fold greater than that of prostate cancer.



ASCO Answers: Prostate Cancer
www.cancer.net/prostatefactsheet

This past year saw important advances in the treatment and understanding of genitourinary cancers, which include those in the prostate, bladder, kidney, testes, ureters and urethra. A major study provided evidence on the feasibility of “watchful waiting” for prostate cancer and the importance of regular biopsies. The U.S. Food and Drug Administration also approved two new drugs for metastatic hormone-resistant prostate cancer: a first-ever therapeutic vaccine and a new chemotherapy drug for patients whose disease progressed despite other forms of chemotherapy. In addition, the FDA also approved a drug for advanced renal cell cancer.

MAJOR ADVANCES Sipuleucel-T Approved for Treating Advanced Prostate Cancer

The FDA approved sipuleucel-T (Provenge), a cancer vaccine for metastatic hormone-refractory prostate cancer, in April 2010. Unlike a standard vaccine, which is given to stimulate the immune system to fight off infections and prevent disease, sipuleucel-T is a therapeutic vaccine that boosts the body’s immune system to attack cancer cells in the body.

The approval of sipuleucel-T was based on results from a randomized, phase III trial of 512 patients with metastatic prostate cancer that was resistant to other therapies. Those who received the vaccine had a 4.1 month improvement in their median survival when compared to patients receiving placebo (25.8 months versus 21.7 months).¹

Cabazitaxel Approved for Advanced Prostate Cancer

Cabazitaxel (Jevtana), the first second-line chemotherapy drug for advanced, hormone-refractory prostate cancer in men who have already received treatment with the chemotherapy drug docetaxel, was approved by the FDA in June 2010. Prior to this approval, there were no effective treatments in this setting.

The approval was based on data from the randomized, phase III TROPIC (Treatment of Hormone-Refractory Metastatic Prostate Cancer Previously Treated With a Taxotere-Containing Regimen) clinical trial, conducted among 755 patients in 26 countries. All patients had advanced hormone-refractory prostate cancer and all had previously been treated with docetaxel. In the clinical trial, patients were randomized to receive either cabazitaxel or another cancer drug, mitoxantrone. Men who received cabazitaxel lived a median of 15.1 months, a 30-percent increase in survival, compared with a median of 12.7 months for those who received mitoxantrone.²

NOTABLE ADVANCES Watchful Waiting an Option for Low-Risk Patients, Better Tools Needed to Identify Aggressive Disease

Early stage, low-risk prostate cancer can be a very slow-growing disease, in some cases taking as long as 25 years to require any treatment. As a result, many men opt for a “watchful waiting” approach, in which surgery or treatment is delayed, and men instead undergo frequent prostate-specific antigen (PSA) testing and occasional biopsy to determine when and if treatment is needed.

In a single-arm study reported this year, researchers assessed the feasibility of watchful waiting by prospectively observing 450 low-risk prostate cancer patients. In the study, the decision to treat was based on rising PSA or changes in tumor pathology (based on a biopsy). PSA testing was performed every three months for two years. All men underwent confirmatory biopsy six to 12 months after an initial biopsy, then every three to four years, with a median follow-up of 6.8 years. Those whose PSA levels doubled in three years or less were offered treatment.

Investigators found that overall, 30 percent of patients—based on PSA doubling rates—had to be reclassified

“Future bladder, prostate and kidney cancer care will increasingly use genetic and epigenetic signatures to define the lethal phenotype. These signatures will become increasingly refined and will predict patterns of metastases and sensitivity to the increasing number of pathway inhibitors, disruptors or stimulators that are emerging from the vibrant laboratories of many pharmaceutical companies. These agents will noticeably and measurably alter the natural progression of GU cancer metastatic disease, and will enter trials in earlier stage disease. Each year over the next decade I expect to see two to three new active agents available for our patients.”

—NICHOLAS J. VOGELZANG, MD

as higher risk and offered treatment. Of the 117 patients treated with surgery, 50 percent of them (or 13 percent of patients overall) experienced rising PSA scores again and a recurrence of their cancer—implying that they may have benefited from earlier, more aggressive treatment. Still, researchers found that men in this trial were more likely to die of causes other than prostate cancer, reporting a prostate cancer-specific survival rate of 97.6 percent (overall survival of patients in the study was 78.6 percent).

The findings also suggested that watchful waiting is particularly feasible and safe for men older than age 70 who have low-to-intermediate risk disease. In this group, they reported that the risk of death from other causes was almost 19-fold greater than that of prostate cancer.

The researchers concluded that while watchful waiting was feasible and very few men died of prostate cancer, more regular biopsies could be helpful in better detection of progressing cancer, and additional studies, including genetic tests of the tumors, are needed to better identify patients who have more aggressive disease, despite initial low-risk status.³

Pazopanib Approved for Patients with Kidney Cancer

The FDA approved pazopanib (Votrient) for the treatment of advanced renal cell cancer in October 2009. Pazopanib is an oral drug that blocks multiple cancer cell receptors that are associated with tumor growth and angiogenesis (development of blood vessels that feed tumors). This approval was based on data from a phase III study of 435 patients with advanced renal cell carcinoma which showed that patients who received pazopanib lived significantly longer without their disease progressing (9.2 months) compared to those who had placebo (4.2 months).⁴

REFERENCES

1. Kantoff, PW, et al. Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer. *N Engl J Med.* 2010; 363:411-422.
2. Sartor, AO, et al. Cabazitaxel or mitoxantrone with prednisone in patients with metastatic castration-resistant prostate cancer (mCRPC) previously treated with docetaxel: Final results of a multinational phase III trial (TROPIC). Presented at the 2010 Genitourinary Cancers Symposium; March 2010; San Francisco, CA.
3. Klotz, L, et al. Clinical results of long-term follow-up of a large, active surveillance cohort with localized prostate cancer. *J Clin Oncol.* 2010; 28:126-131.
4. Sternberg CN, et al. Pazopanib in locally advanced or metastatic renal cell carcinoma: results of a randomized phase III trial. *J Clin Oncol.* 2010; 28:1061-1068.



Cancer.Net Guide to Prostate Cancer

www.cancer.net/prostate

Cancer.Net Guide to Kidney Cancer

www.cancer.net/kidney

ASCO Answers: Kidney Cancer

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ASCO Expert Corner: Talking With Your Doctor About PSA Screening

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News for Patients from 2010 Genitourinary Cancers Symposium

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ASCO Answers: Ovarian Cancer

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Angiogenesis and Angiogenesis Inhibitors to Treat Cancer

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GYNECOLOGIC CANCERS

Gynecologic cancers include cancers of the cervix, uterus, ovaries, fallopian tubes, vagina and vulva. Two reports this year could have important implications for treating and screening for ovarian cancer, which is the most deadly form of gynecologic cancer. In one study, researchers reported on the first effective targeted therapy—bevacizumab—for advanced ovarian cancer, while other research showed promising results from a novel screening technique in women at normal risk for ovarian cancer.

MAJOR ADVANCE Bevacizumab Extends Progression-Free Survival for Women with Advanced Ovarian Cancer

While two chemotherapy drugs—carboplatin and paclitaxel—have been the standard treatment for advanced ovarian cancer for the past decade, this cancer has remained extremely difficult to treat and most women eventually

die of their disease. But a new strategy for treating epithelial ovarian cancer, primary peritoneal ovarian cancer and fallopian tube cancer, has shown promising results. A Gynecologic Oncology Group trial has found that adding the anti-angiogenesis drug bevacizumab to the standard chemotherapy drug combination helped women live significantly longer without their disease progressing. The Gynecologic Oncology Group is part of the National Cancer Institute (NCI) Cooperative Group Program that serves as one critical link between these scientific discoveries and improved treatment for cancer patients.

In this double-blind, phase III study, researchers treated nearly 1,900 women with stage III or stage IV disease who had not undergone previous treatment to one of three groups: standard chemotherapy (paclitaxel plus carboplatin) and placebo plus placebo maintenance; standard chemotherapy with bevacizumab plus placebo maintenance; or standard chemotherapy with bevacizumab followed by bevacizumab maintenance. Maintenance therapy is defined as longer term treatment given after standard chemotherapy, with the goal of extending cancer progression-free survival.

In conclusion, the researchers found that patients in the third group lived a median of 14.1 months without disease progression, compared to 10.3 months for patients in the group that received chemotherapy alone. Patients who received initial chemotherapy and bevacizumab with placebo maintenance did not experience a significant benefit, compared with those who were treated with chemotherapy alone.¹

NOTABLE ADVANCE New Ovarian Cancer Screening Strategy Promising for Post-Menopausal Women at Average Risk

More than 70 percent of ovarian cancers are diagnosed at an advanced stage, and researchers would like to identify

“In the future it can be predicted that innovative strategies in the management of the gynecologic malignancies will be based on specific molecular markers demonstrated to be present in individual cancers (“personalized medicine”). Preliminary data supporting a potential role for PARP inhibitors in women with ovarian cancer who possess BRCA-1 and BRCA-2 abnormalities support this hypothesis. Based on the provocative information regarding the use of bevacizumab when employed in the primary treatment of advanced ovarian cancer, it is also highly likely this class of agents will continue to be extensively evaluated as components of care in female pelvic malignancies.”

—MAURIE MARKMAN, MD

a reliable screening test for early-stage disease. For years, levels of the CA-125 protein, found through a blood test, have been known for years to rise during ovarian cancer development. But the CA-125 protein test has not proved to be a reliable indicator for documenting the presence of early-stage ovarian cancer. A recent study, however, showed the feasibility of a novel and promising new screening approach for post-menopausal women at average risk of ovarian cancer. The new approach uses a mathematical model, called the “Risk of Ovarian Cancer Algorithm” (ROCA), that combines trends in CA-125 blood test results and a patient’s age, followed by transvaginal sonogram (TVS) and finally referral to a gynecologic oncologist, as necessary.

The study included 3,238 postmenopausal women aged 50 to 74 with no significant family history of breast or ovarian cancer who were followed for up to eight years. On an annual basis, researchers found that less than 1 percent of women required TVS. Eight women underwent surgery based on

the ROCA results; three of whom had invasive but early-stage ovarian cancers; two had borderline ovarian tumors and three had benign ovarian tumors. The specificity of ROCA followed by TVS for referral to surgery was 99.7 percent, indicating that very few false-positives resulted from this approach.

A large-scale study of ROCA involving more than 200,000 women is under way in the United Kingdom; the results are expected in 2015.²

REFERENCES

1. Burger, RA, et al. Phase III trial of bevacizumab (BEV) in the primary treatment of advanced epithelial ovarian cancer (EOC), primary peritoneal cancer (PPC), or fallopian tube cancer (FTC): A Gynecologic Oncology Group study. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010, Chicago, IL.
2. Lu, KH, et al. A prospective U.S. ovarian cancer screening study using the risk of ovarian cancer algorithm (ROCA). Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010, Chicago, IL.

Types of Ovarian Cancer

Epithelial carcinoma

Epithelial carcinoma makes up 85% to 90% of ovarian cancers. This type of cancer begins in cells on the outer surface of the ovary.

Germ cell tumor

This uncommon type of ovarian cancer develops in the egg-producing cells of the ovaries. This type of tumor is more common for women ages 10 to 29.

Stromal tumor

This rare form of ovarian cancer develops in the connective tissue cells that hold the ovaries together and make female hormones.

The incidence of head and neck cancer is increasing globally and is now the fourth most common malignancy in the world, with more than 70 percent of all cases found in developing countries.



ASCO Answers: Oral and Oropharyngeal Cancer

www.cancer.net/oralfactsheet



Cancer.Net Guide to Oral and Oropharyngeal Cancer

www.cancer.net/oral

HPV and Cancer

www.cancer.net/hpv

HEAD AND NECK CANCERS

Head and neck cancers—including those commonly found in the mouth, larynx, pharynx and sinus-nasal tract—account for approximately five percent of all diagnosed cancers in the United States. The incidence of head and neck cancer is increasing globally and is now the fourth most common malignancy in the world, with more than 70 percent of all cases found in developing countries.

This year, the most significant research included two large clinical trials that demonstrated the importance of human papillomavirus (HPV) infection on head and neck cancer prognosis and treatment outcomes. Other studies reported promising results in using “accelerated” radiotherapy to improve outcomes in resource-limited countries and demonstrated the usefulness of sentinel node biopsies to determine the spread of oral cavity cancers. Finally, a study showed the influence of radiation quality on overall head and neck cancer survival.

NOTABLE ADVANCES

Survival is Better with HPV-Related Oropharyngeal Tumors

Most head and neck cancers have been closely linked to excessive tobacco and alcohol use. More recently, there has been a rise in HPV-related head and neck cancers, which are caused by infections with the same high-risk HPV subtypes that cause cervical cancer. Prior studies have suggested a link between tumor HPV status to overall survival and progression-free survival among patients with oropharyngeal cancer.

- Researchers examined the connection between the HPV status of oropharyngeal cancer and survival among patients with stage III or stage IV tumors who participated in two large, randomized clinical trials. One trial compared two types of radiotherapy (standard seven-week course versus accelerated six-week course); they were both delivered together with the chemotherapy drug, cisplatin. They found that patients with HPV-positive oropharyngeal cancer

had significantly better three-year overall survival (82.4 percent versus 57.1 percent) than those with HPV-negative tumors.¹

- The second trial compared standard radiotherapy and cisplatin versus the same treatment plus a second drug, tirapazamine, which is a cytotoxin. Although this study noted that the outcome of the experimental treatment was not better than that of the standard treatment, it found that patients with HPV-positive oropharyngeal cancer had significantly better overall survival than those with HPV-negative tumors.²

As a result of these large studies, future head and neck trials will enroll patients according to the tumor’s HPV status. HPV-positive trials will focus on treatment de-intensification and thus allow improved quality of life in those patients who are likely to have a better prognosis; whereas HPV-negative trials will focus on intensifying treatment to improve survival in this patient group that appears to have a poorer prognosis.

Accelerated Radiotherapy Schedule is More Effective in Head and Neck Cancer in Resource-Poor Countries

Several large, randomized studies in Western countries have shown that accelerated fractionated radiotherapy, which shortens the overall radiation course without compromising the total dose, can improve local and regional tumor control in patients with locally advanced head and neck cancer. A large, multicenter, randomized trial in nine centers located in countries with limited resources showed that this treatment was more effective than conventional fractionation and can be feasibly delivered to a large number of patients without requiring additional resources.

In the trial, 908 patients with squamous cell carcinoma of the larynx, pharynx or oral cavity were randomly assigned to receive either an accelerated regimen of six radiation fractions per week

“Although we used to treat all squamous cell carcinomas (SCCs) of the head and neck the same way, we now know that they are quite different from each other with regards to etiology, biology and treatment response. To improve outcomes, we will need to design separate clinical trials for SCCs arising from different head and neck sites as well as for HPV positive and HPV negative oropharyngeal carcinomas. Less invasive surgery is a future direction to improve organ function and quality of life in head and neck cancer patients.”

—QUYNH-THU LE, MD

over six weeks (median 40 days) or the conventional schedule of five fractions per week over seven weeks (median 47 days). After five years of follow up, the accelerated radiation treatment was superior to the conventional treatment in local and regional control (42 percent versus 30 percent) and 5 year disease-specific survival (50 percent versus 40 percent). There was also a trend for improved overall survival with the accelerated treatment (35 percent versus 28 percent). Accelerated treatment was associated with more side-effects (skin reaction, mucosal inflammation and temporary feeding tube use) but not with increased late toxicity.³

Sentinel Node Biopsy Shows Potential for Early Stage Oral Cancer

For patients with early stage oral cavity cancer that has a high risk for spreading to the lymph nodes in the neck, standard treatment is surgery without necessarily checking the sentinel nodes. Sentinel node biopsy has been shown to be highly accurate and useful in the management of early stage breast cancer and melanomas, but it has not been well tested in squamous cell carcinoma of the head and neck.

This year, a prospective, multicenter trial tested this concept in 140 patients with early stage oral cavity cancer. The study found that sentinel node biopsy could serve as a useful tool for staging oral cavity cancer, rather than performing a larger, more invasive neck surgery to determine if the cancer has spread. These findings are important because such neck surgery can be disfiguring

and also associated with swallowing and shoulder dysfunction.

In the study, researchers found that of 106 sentinel node biopsies that were pathologically negative for cancer, 100 patients had no other pathologically positive lymph nodes, yielding a negative predictive value of 94 percent. Through additional testing, a negative sentinel lymph node biopsy correctly predicted a lack of metastases to the neck in 96 percent of cases. Experts caution that although these results are very promising, it is too early to call for the routine use of such testing, and more research is needed.⁴

Radiotherapy Quality and Protocol Compliance are Keys to Head and Neck Cancer Survival

In the context of an international phase III clinical trial of radiotherapy and chemotherapy in patients with locally advanced head and neck cancer, researchers for the first time showed that radiation quality and adherence to radiotherapy guidelines impact tumor control and translate into a survival difference. The trial aimed to test the benefit of adding a hypoxic cell cytotoxin, tirapazamine, to concurrent cisplatin-based chemotherapy and radiation. Participating centers submitted imaging and radiation treatment plans to a centralized quality assurance center for initial review and feedback after one week of starting radiation treatment, and then submitted for final review after treatment was completed.

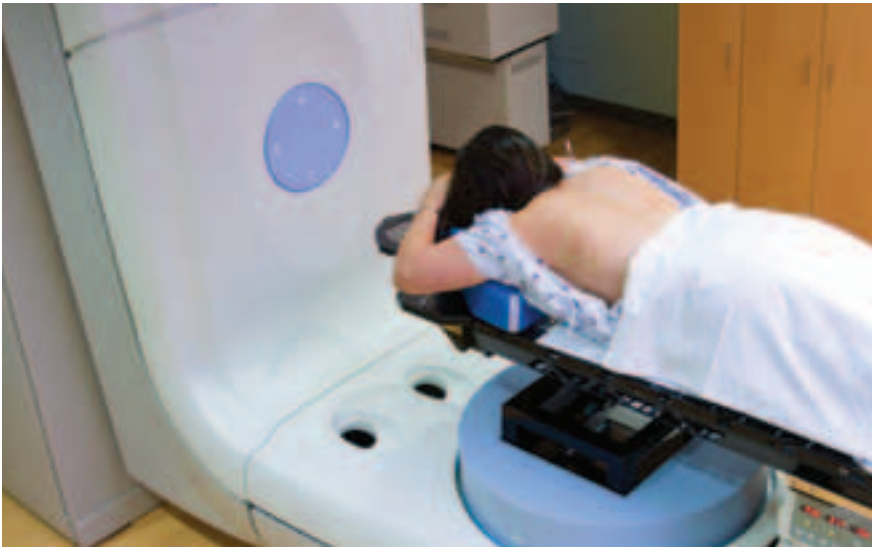
In the study, 208 (approximately 25 percent) of 820 patients received radia-

tion treatment that was non-compliant with the protocol. Of these, 87 patients received doses under 60 Gy and had radiation treatment deficiencies that were predicted to have an adverse impact on tumor control. These patients had significantly poorer tumor control rate and, more importantly, worse two-year overall survival (50 percent versus 70 percent) than those with compliant plans.

Researchers also found that centers with low patient enrollment in the trial were more likely than centers with high enrollment to have non-compliant plans. Centers that enrolled fewer than five patients in the trial had 29.8 percent of the submitted radiation plans that were predicted to have an adverse impact on tumor control, whereas those enrolling more than 20 patients only had 5.4 percent of such plans.⁵

REFERENCES

1. Ang KK, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med.* 2010; 363:24-35.
2. Rischin D, et al. Prognostic significance of p16 INK4A and human papillomavirus in patients with oropharyngeal cancer treated on TROG 02.02 phase III trial. *J Clin Oncol.* 2010; 28: 4142-4148.
3. Overgaard J, et al. Five versus six fractions of radiotherapy per week for squamous-cell carcinoma of the head and neck (IAEA-ACC study): a randomized, multicentre trial. *Lancet Oncol.* 2010; 11:553-560.
4. Civantos FJ, et al. Sentinel lymph node biopsy accurately stages the regional lymph nodes for T1-T2 oral squamous cell carcinomas: Results of a prospective multi-institutional trial. *J Clin Oncol.* 2010; 10;28:1395-1400.
5. Peters L, et al. Critical impact of radiotherapy protocol compliance and quality in the treatment of advanced head and neck cancer: Results from TROG 02.02. *J Clin Oncol.* 2010; 28:2996-3001.



provided rare insight into this group. It showed that the same combination of chemotherapy drugs commonly used in younger patients improved survival over the single agent therapy in elderly patients. (Fig 4.)

This phase III study compared the effectiveness of carboplatin and paclitaxel to therapy with gemcitabine or vinorelbine in 451 patients with advanced non-small cell lung cancer between the ages of 70 and 89. Researchers found that the patients treated with the combination therapy had better overall survival (10.4 months) compared to those who received a single drug (6.2 months). Those receiving the combination lived nearly twice as long without disease progression (6.3 versus 3.2 months) as well.¹

LUNG CANCERS

Over the past year, research has focused on personalizing treatment approaches based on age, specific gene mutations, and extent of disease. These findings will help physicians refine the use of existing cancer treatments and offer promising new tools for groups of patients. One trial found that elderly patients with lung cancer can tolerate the same treatment as younger patients, while another focused on the role of specific genetic mutations and the effectiveness of a targeted agent. A third study found that patients with lung cancer benefitted from early palliative care given with chemotherapy. Finally, research showed the dramatic effect of a form of radiotherapy for early-stage patients with inoperable disease.

Crizotinib Shows High Response Rate in Patients with Lung Adenocarcinoma with *EML4-ALK* Translocations

A phase I trial showed that a high percentage of patients with lung adenocarcinoma with a specific *ALK* gene mutation responded to an investigational *ALK* inhibitor, crizotinib. More than half of these patients demonstrated some tumor shrinkage. Phase I trials are typically aimed at gauging toxicity of an experimental agent and rarely show dramatic clinical activity.

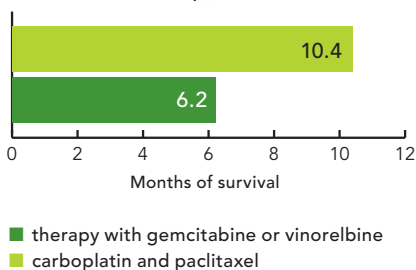
When the *ALK* gene fuses with another gene, it promotes lung cancer cell growth by encoding the production of a tumor-specific protein called anaplastic lymphoma kinase, or *ALK*—an enzyme that is instrumental to cancer cell growth and development. Crizotinib, which is taken orally, inhibits the *ALK* enzyme. About one in 20 patients with lung cancer, or approximately 11,000 people, in the United States are estimated to be diagnosed with *ALK*-positive lung cancer each year.

In the study, more than 90 percent of the 82 patients enrolled responded to the drug—either their disease stabilized or there was some tumor shrinkage. Based on these findings, phase III trials comparing crizotinib to chemotherapy are ongoing.²

Factoid:

Lung cancer continues to be the leading cause of cancer death among men and women in the United States.

Fig. 4. Overall survival in advanced lung cancer in the elderly with chemotherapy combination



MAJOR ADVANCES Chemotherapy Combination Increases Survival in Advanced Lung Cancer in the Elderly

Most patients with lung cancer are over age 70, yet there are few new clinical trials evaluating therapies in this population. This year, a French study

“These trials explore many areas of ongoing research in the field of lung cancer to help alleviate the pain and suffering associated with this disease. While we still need to focus additional research on prevention and early detection of lung cancer to help bring down the high mortality rate of this deadly disease, these studies show that radiation, chemotherapy, and newer targeted treatments can help prolong survival. Improved supportive and palliative care can also help reduce the symptoms attributable to this cancer and improve their quality of life. As we move forward, our ongoing efforts to help these patients through innovative science and translational clinical research will help to manage this difficult disease more effectively.”

—GREG MASTERS, MD

Adding Routine Management by a Palliative Care Team to Chemotherapy Improves Survival in Lung Cancer Patients

A randomized clinical trial of patients with advanced lung cancer showed that those individuals who received standard chemotherapy, coupled with palliative care immediately after diagnosis, lived significantly longer and had a better quality of life than those who received chemotherapy alone. Patients who regularly saw palliative care specialists reported less depression and pain, better mobility, and were less likely to undergo aggressive therapy at the end of life than individuals who had chemotherapy alone.

In the study, 151 patients with the most common form of lung cancer were randomized within eight weeks of diagnosis to receive either chemotherapy with palliative care—including pain relief and other supportive measures—or chemotherapy alone. The investigators found that the median survival in the palliative care group was improved by three months, compared with the patients who had chemotherapy alone (11.6 months compared to 8.9 months). Individuals whose symptoms were managed by palliative care specialists reported a better quality of life. Only 16 percent, versus 38 percent of the chemotherapy group, reported symptoms of depression over three months. Despite living longer, fewer patients receiving palliative care (33 percent) chose aggressive end-of-life care (which

does not improve quality of life) over those receiving only chemotherapy (54 percent). This research was supported by an American Society of Clinical Oncology Career Development Award.³

NOTABLE ADVANCE Stereotactic Radiation a Potential Alternative for Patients with Inoperable Early-Stage Lung Cancer

For patients with early stage lung cancer who cannot undergo surgery, conventional radiotherapy fails to control the primary lung tumor in 60 to 70 percent of patients, with only 20 to 35 percent of patients surviving after three years. However, a recent study found that stereotactic radiation, which involves delivering highly focused radiation beams to the tumor, is a good alternative for early stage lung cancer patients whose tumors cannot be surgically removed.

A Radiation Therapy Oncology Group, phase II study found that 48.3 percent of patients with inoperable, stage I, non-small cell lung cancer who received stereotactic body radiation therapy were alive without disease symptoms after three years, and overall, 55.8 percent were still alive. Median disease-free survival and overall survival for all patients were 34.4 months and 48.1 months, respectively. Overall, patients had a high rate of local disease control (97.6 percent), with moderate treatment-related side effects. The Radiation Therapy Oncology Group is part of the NCI

Cooperative Group Program that serves as one critical link between scientific discoveries and improved treatment for patients with cancer nationwide.⁴

REFERENCES

1. Quoi EA, et al. Weekly paclitaxel combined with monthly carboplatin versus single-agent therapy in patients age 70 to 89: IFCT-0501 randomized phase III study in advanced non-small cell lung cancer (NSCLC). Presented at the 46th Annual Meeting of the American Society of Clinical Oncology: June 2010; Chicago, IL.
2. Bang Y, et al. Clinical activity of the oral ALK inhibitor PF-02341066 in ALK-positive patients with non-small cell lung cancer (NSCLC). Presented at the 46th Annual Meeting of the American Society of Clinical Oncology: June 2010; Chicago, IL.
3. Temel JS, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*: 2010; 363:733-742.
4. Timmerman R, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA*: 2010; 303 (11):1070-1076.



ASCO Answers: Lung Cancer
www.cancer.net/lungfactsheet



Cancer.Net Guide to Lung Cancer
www.cancer.net/lung

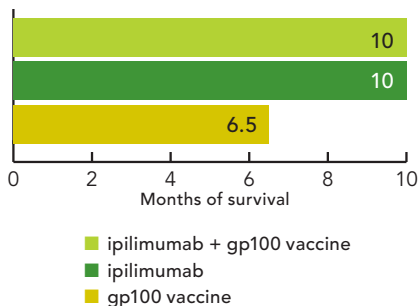


Factoid:

While melanoma accounts for less than 5 percent of skin cancer cases, it accounts for the majority of skin cancer deaths.

Ipilimumab is among the first of a new class of drugs called checkpoint inhibitors that sustains activation of the immune system's T-cells that then seek and destroy melanoma cells.

Fig 5. Overall Survival with ipilimumab for advanced melanoma



MELANOMA

The incidence of melanoma—the deadliest form of skin cancer—has climbed faster than any other cancer type in the past three decades and is becoming a major public health concern.

Over the past year, several studies have advanced the understanding and treatment of melanoma, with a particular focus on the approaches that activate the immune system against the disease. In a study that could have major implications for advanced melanoma, researchers found that an immune therapy extended survival in this difficult-to-treat disease. Another study that also focused on advanced melanoma showed promising results for a new targeted therapy. A third report confirmed the strong connection between tanning bed use and melanoma. Finally, a study analyzed results from several adjuvant trials and demonstrated that adding the immune-boosting agent interferon alfa improves survival in patients with high risk.

MAJOR ADVANCES Monoclonal Antibody Ipilimumab Improves Survival in Advanced Melanoma

In what is to our knowledge the first-ever phase III trial to exhibit a survival benefit for advanced melanoma, researchers found that an immune therapy

shows great promise. Unlike most traditional cancer treatments that target the cancer cell, ipilimumab is among the first of a new class of drugs called checkpoint inhibitors. Ipilimumab is a fully human monoclonal IgG1 antibody that sustains activation of the immune system's T-cells, including tumor-specific T-cells that then seek and destroy melanoma cells.

In this phase III study, researchers compared ipilimumab with ipilimumab plus the gp100 vaccine (an experimental therapeutic vaccine designed to induce tumor-specific T-cells), and the gp100 vaccine alone, among 676 patients with stage III or IV melanoma whose disease had progressed on an earlier therapy. (Fig 5.) They found that the two groups of patients who received ipilimumab lived 34 percent longer than those who received the gp100 vaccine alone (a median of 10 months versus 6.5 months). At two years, 24 percent of the patients who received ipilimumab and 22 percent of those who received the combination treatment were alive, compared to 14 percent of patients who received only the vaccine.

At six months, the melanoma did not progress in nearly 30 percent of those receiving ipilimumab, compared to 11 percent of patients treated with the vaccine alone. About two-thirds of patients developed immune-related adverse effects from ipilimumab, such as skin rashes, diarrhea or endocrine imbalances. Most complications, although they were severe in some patients, were manageable with corticosteroids.¹

Targeted Treatment Shows Promise for Advanced Melanoma Patients with Gene Mutation

A recent study showed that the majority of advanced melanoma patients with a specific *BRAF* gene mutation (V600E mutant *BRAF*) responded to a new *BRAF* inhibitor, *PLX4032*, providing evidence that the targeted therapy may have a promising future in treating melanoma.

Approximately 50 percent of melanomas harbor a mutation in the cancer cell growth-promoting *BRAF* gene. In a phase I trial, researchers initially examined optimal dosing for *PLX4032* based on toxicity in a group of 55 patients with cancer, most of whom had melanoma. After the optimal dose had been established, an “extension” cohort of 32 patients with metastatic melanoma carrying the V600E *BRAF* gene mutation was treated.

In the extension cohort, 24 patients (81 percent) responded to *PLX4032*—their tumors either completely or partially regressed, including metastases in the bone and liver. Cancer-related symptoms improved in as early as one week, and the median length of response was found to be greater than seven months. Tumor shrinkage was not observed in patients with tumors not carrying the *BRAF* mutation. These findings provide clinical validation of the V600E mutation as an important therapeutic target in melanoma.²

NOTABLE ADVANCES

Indoor Tanning Raises Melanoma Risk

A study confirmed the link between indoor tanning and melanoma risk. This review, comparing more than 1,000 melanoma patients to more than 1,000 matched controls, found that tanning bed users were 74 percent more likely to develop melanoma than non-users. This population-based case-control study overcomes some of the limitations of earlier reports and provides strong support for the recent declaration by the International Agency for Research on Cancer that tanning devices are carcinogenic in humans.

This study also found that frequency of indoor tanning increased melanoma risk: individuals who tanned the most—for 10 or more years—had more than twice the risk of melanoma compared with people who never used tanning beds. Those risks did not change when

researchers accounted for a number of variables, including age, sex, income, family history, education, skin and eye color, freckles, moles, sunscreen use or time in the sun. The type of tanning bed used did not matter; the risks were the same.³

Meta-Analysis Shows Adding Interferon Alpha After Surgery Improves Overall Survival in Patients With Melanoma

The benefit of the immune booster interferon alpha is often questioned because of its significant side effects and the lack of certainty of whether the treatment improves overall survival in patients with resected, high-risk melanoma. Previous studies have shown that adding interferon alpha after surgery for high-risk melanoma improved disease-free survival, though its effects on overall survival have been unclear. Now, a large meta-analysis of randomized controlled clinical trials conducted between 1990 and 2008 showed that interferon alpha treatment improved overall survival, supporting its use in the adjuvant setting.

The analysis of 14 clinical trials involving 8,122 high-risk melanoma patients showed improved survival and outcomes for patients with high-risk melanoma. Interferon alpha therapy led to improved overall survival in four of 14 trials, and improved disease-free survival in 10 of 17 studies.⁴

REFERENCES

1. Hodi, FS, et al. Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med* published online June 5, 2010, p 1-13.
2. Flaherty, KT, et al. Inhibition of mutated, activated *BRAF* in metastatic melanoma. *N Engl J Med*. 2010; 363: 809-19.
3. Lazovich, D, et al. Indoor tanning and risk of melanoma: A case control study in a highly exposed population. *Cancer Epidemiol Biomarkers Prev*. 2010; 19(6): 1557-68.
4. Mocelin, S, et al. Interferon alpha adjuvant therapy in patients with high-risk melanoma: A systematic review and meta-analysis. *J Natl Cancer Inst*. 2010; 102: 493-501.

PERSPECTIVE ON MELANOMA

“Remarkable progress has been made in the treatment of metastatic melanoma over the past year with two new agents, the immune checkpoint blockade inhibitor ipilimumab and the *BRAF*V600E specific tyrosine kinase inhibitor *PLX4032*. Both compounds have shown promising results in clinical trials; they raise optimism that immune and targeted therapies will transform metastatic melanoma into a controllable disease and lead to increased survival in the advanced and possibly also the adjuvant setting.”

—SYLVIA ADAMS, MD



ASCO Answers: Melanoma
www.cancer.net/melanomafactsheet



Cancer.Net Guide to Melanoma
www.cancer.net/melanoma

Protecting Your Skin From the Sun
www.cancer.net/sunprotection

PEDIATRIC CANCERS

Based on self-reported data from childhood cancer survivors and their siblings, investigators found that cancer survivors were six times more likely to report congestive heart failure; five times more likely to report a myocardial infarction; and about five times more likely to report heart valve disease than their cancer-free siblings.



An estimated 38,000 childhood cancer deaths have been averted in the United States between 1975 and 2006. Improved treatment strategies and fewer deaths from acute toxicity both contribute to this success. Although long-term survival rates for childhood cancer increased from 58 percent to nearly 80 percent during that same 30-year period, approximately 2,000 children still die from cancer every year.

The next step for progress against pediatric cancers will be to identify more effective agents that take advantage of increased knowledge of individual genetic differences between tumors. Rather than a one-size-fits-all approach, this will mean more personalized therapies aimed at specific pediatric subtypes of cancer.

A key study this year reported that adult survivors of pediatric cancers have a risk of heart disease many years after childhood treatment. Other important research described the role of genetics in hearing loss susceptibility, while another study evaluated a drug combination in pediatric brain tumors that had been found effective for treating adults showing the later-in-life effects of childhood cancer therapies can significantly reduce life expectancy. Lastly, a report showed the benefit of adding a targeted agent to chemotherapy in treating a rare form of leukemia in children and adolescents.

MAJOR ADVANCE Study Reveals Long-Term Risks for Cardiac Problems among Childhood and Adolescent Cancer Survivors

An analysis of more than 14,000, five-year adult cancer survivors from the Childhood Cancer Survivor Study—a study of adult childhood cancer survivors that compiled information on cancer recurrence, secondary cancers, other illnesses and conditions, and psychosocial and other outcomes—showed higher risks of many types of cardiovascular disease when compared to a

sibling control group. The findings are important reminders to healthcare providers caring for the growing numbers of long-term childhood cancer survivors about the potentially life-threatening late effects of cancer treatment.

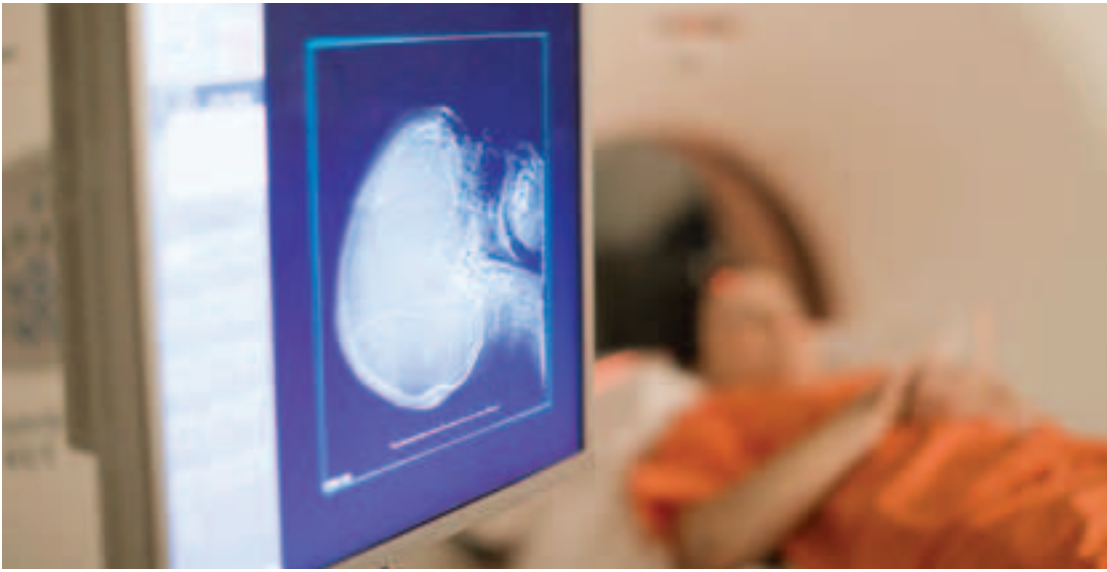
Based on self-reported data from survivors and their siblings, investigators found that cancer survivors—all of whom were under age 21 at diagnosis and were treated between 1970 and 1986—were six times more likely to report congestive heart failure; five times more likely to report a myocardial infarction; and about five times more likely to report heart valve disease than their cancer-free siblings.

The investigators also found that anthracycline drugs or radiation treatment to the chest increased the risk of cardiovascular problems two- to six-fold among survivors compared with those who did not receive anthracyclines or chest radiation. Pediatric oncologists currently attempt to limit the use of anthracyclines and chest radiation, and also to use agents that may protect the heart from damage associated with chemotherapy.¹

NOTABLE ADVANCES Genetic Variants Linked to Hearing Loss in Children Who Received Cisplatin

While the chemotherapy drug cisplatin can be effective against a number of cancers, it comes with a caveat: the threat of permanent hearing loss, particularly in children. As many as 60 percent of children receiving the drug may be affected, and they may be at increased risk for communication and learning problems as a result.

Researchers studied the possibility that specific variants of proteins associated with cisplatin drug metabolism may predispose certain patients to develop hearing loss, while others escape this side effect. By studying a large number of variations in 220 genes that encode these proteins, the research-



ers found that specific variants of two genes—*TPMT* and *COMT*—are highly associated with severe hearing loss after cisplatin exposure. Patients with certain variants (known as single nucleotide polymorphisms) may have up to 17 times the risk of developing cisplatin-associated hearing loss as those without the variants.²

The findings are important because understanding genetic susceptibility to hearing loss may improve the ability to personalize therapies and better weigh treatment selection against potential side effects. They also raise the larger question of whether the genetic background of the patient, not just the tumor genetics, should be evaluated to identify the safest drugs to use.

Effective Drug Combination for Adult Brain Tumors Does Not Work in Children

Brain tumors, gliomas in particular, are extremely difficult to treat. However, in adults, the anti-angiogenesis drug bevacizumab, in combination with the chemotherapy drug irinotecan (Campotovar), has shown success in delaying the progression of gliomas.

One common biological feature of pediatric brain tumors, including malignant gliomas, is the overexpression

of vascular endothelial growth factor (VEGF), which fosters the development of tumor-feeding blood vessels—and which bevacizumab targets. Pediatric Brain Tumor Consortium researchers evaluated the effectiveness of the drug combination in a phase II trial of 31 children with either recurrent malignant glioma or brainstem glioma. Although the therapy was well tolerated, the treatment had little effect against the tumors, with no sustained responses seen. The reasons why childhood gliomas (in comparison to adult gliomas) are not responsive to this combination are not clear, but may be associated with tumors in children having more resistance to anti-angiogenic agents in general or bevacizumab in particular.³

Late Effects of Childhood Cancer Substantially Reduce Life Expectancy

The growing population of long-term childhood cancer survivors—now numbering more than 300,000—faces a higher risk of dying from a subsequent cancer, heart disease or pulmonary problems than the general population.

Using data from the Childhood Cancer Survivor Study, investigators modeled the overall effect of the disease and its treatment on life expectancy of childhood cancer survivors. They found

The growing population of long-term childhood cancer survivors—now numbering more than 300,000—faces a higher risk of dying from a subsequent cancer, heart disease or pulmonary problems than the general population.

PERSPECTIVE ON
PEDIATRIC CANCERS

“Childhood cancer treatment successes over the last two decades have left clinical researchers in pediatric oncology with a number of challenges, including understanding how to maintain excellent cure rates with reductions in therapy, how to incorporate new agents into current regimens, and how to study late health effects in survivors. Recent successes in identifying patients or survivors with specific risks, such as genetic changes predisposing them to late effects, or treatments linked to adult-onset diseases or exposures associated with adult-onset diseases will assist in development of more “personalized” cancer therapy and follow-up health care.”

—LISA DILLER, MD

that the life expectancy for a group of 15-year-old five-year cancer survivors was 50.6 years, a loss of 10.4 years of life (17.1 percent) compared with the general population. Researchers also showed that reductions in life expectancy varied by diagnosis, ranging from a 4-year reduction for kidney tumor survivors to more than 17.8 years for brain and bone cancer survivors. Additionally, they reported that approximately one in four survivors is estimated to die of a cancer recurrence later in life, of a new cancer that has occurred or a heart condition.

The study also found that after cancer recurrence, the development of a new, second cancer is the most important factor in reduced life expectancy. The researchers underscore the need for long-term monitoring of the health of childhood cancer survivors and the evaluation of new therapies that might have fewer toxic effects later in life.⁴

Adding Imatinib to Chemotherapy Improves Event-Free Survival in High-Risk ALL

Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) accounts for three to five percent of childhood ALL and is extremely difficult to treat. Fewer than 40 percent are cured by intensive chemotherapy, including blood and marrow transplant. A new study showed that adding imatinib to intensive chemotherapy for patients with this form of ALL may be more effective than treatment with intensive chemotherapy alone. The current standard of care for Philadelphia chromosome-positive ALL patients is blood and marrow transplant, which can be an invasive and more toxic therapy. The results of this study suggest that patients receiving chemotherapy plus continuous imatinib do just as well as those patients receiving blood and marrow transplant.

In this Children’s Oncology Group study, researchers examined treatment with imatinib added to intensive chemotherapy in 92 newly diagnosed, high-risk children and adolescents with Philadelphia chromosome-positive ALL. All patients received two cycles of chemotherapy, after which those patients

with blood and marrow donor matches had transplants, whereas the remaining patients were divided into five groups, and doses and length of treatment with imatinib were progressively increased.

Investigators found that three-year event-free survival (EFS) rate was 80 percent in the group who received chemotherapy and continuous imatinib, compared to 35 percent for historical control patients who had been treated with chemotherapy alone. Chemotherapy and continuous imatinib also resulted in an EFS at three years that was similar to (or slightly better than) that seen in patients who received sibling donor transplants, along with standard chemotherapy. Further long-term follow up is necessary, but these results are encouraging, particularly for patients without bone marrow transplant donors.⁵

REFERENCES

1. Mulrooney, D, et al. Cardiac outcomes in a cohort of adult survivors of childhood and adolescent cancer: retrospective analysis of the Childhood Cancer Survivor Study cohort. *BMJ* 2009; 339: b4606.
2. Ross, C, et al. Genetic variants in *TPMT* and *COMT* are associated with hearing loss in children receiving cisplatin chemotherapy. *Nature Genetics* 2009; 41:1345-1349.
3. Gururangan, S, et al. Lack of efficacy of bevacizumab plus irinotecan in children with recurrent malignant glioma and diffuse brainstem glioma: A pediatric brain tumor consortium study. *J Clin Oncol.* 2010; 28:3069-3075.
4. Yeh, J, et al. A model-based estimate of cumulative excess mortality in survivors of childhood cancer. *Ann Intern Med.* 2010; 152:409-417.
5. Schultz, KR, et al. Improved early event-free survival with imatinib in Philadelphia chromosome-positive acute lymphoblastic leukemia: A Children’s Oncology Group study. *J Clin Oncol.* 2009; 27:5175-5181.



**Cancer.Net Guide to
Childhood Cancer**

www.cancer.net/childhood

Childhood Cancer Survivorship

www.cancer.net/survivorship

Late Effects of Childhood Cancer

www.cancer.net/lateeffects

PREVENTION AND SCREENING

While screening for breast, colon and cervical cancers has been extremely successful in reducing the risk of cancer-related death through early detection, there are no effective screening tools for the early detection of major cancer killers, such as lung, pancreatic and ovarian cancers, which are often found in advanced stages.

A major report published this year found reductions in cancer incidence and death rates, due in part to improvements in prevention and early detection. In an important advance for cancer prevention and screening, another study showed that one-time screening with flexible sigmoidoscopy reduces colon cancer incidence and death, and may offer a lower-cost, less invasive alternative to colonoscopy. Lastly, a significant report on screening, issued by the U.S. Preventive Services Task Force, questioned the value of routine screening for breast cancer in women under the age of 50, raising substantial controversy.

NOTABLE ADVANCES

Report Describes Declines in Cancer Incidence, Death Rates in United States

A report issued in December 2009 found that rates of new diagnoses and rates of death from all cancers combined declined significantly in recent years for men and women overall and for most racial and ethnic populations in the United States.

The report, issued by the National Cancer Institute, the U.S. Centers for Disease Control and Prevention, the American Cancer Society, and the North American Association of Central Cancer Registries, showed the number of new cancer cases declined, on average, by nearly 1 percent per year be-

SPECIAL NEWS FEATURE:

National Lung Screening Trial (NLST) Shows 20 Percent Decrease in Lung Cancer Deaths

On November 4, 2010, NCI released initial results from the National Lung Screening Trial, which found 20 percent fewer lung cancer deaths among trial participants screened with low-dose chest CT than those screened with a chest X-ray. The NLST is a national trial involving more than 53,000 Americans ages 55-74 who had smoked the equivalent of a pack of cigarettes per day for 30 years. This is the first study to provide clear evidence of a significant reduction in lung-cancer deaths with a screening chest CT in a randomized controlled trial.

"These findings show lung cancer screening in high-risk patients can save nearly as many lives as the number of people who die from breast cancer per year. We as a medical community now need to figure out how to do this in a way that the cost is acceptable to the public," said ASCO official Bruce E. Johnson, MD, ASCO Board Member, Director, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute.

At the time of this publication, the full analysis of the trial was in development for peer-reviewed journal publication.

tween 1999 and 2006. In addition, death rates dropped 1.6 percent annually from 2001 to 2006, mainly attributed to reductions in new cases and death rates for the three most common cancers in men (lung, prostate, and colorectal cancers) and for two of the three leading cancers in women (breast and colorectal cancer).

The report also created a model suggesting that there could be an overall reduction in colorectal cancer mortality by 50 percent in 2020, citing improvements in treatment and early detection for the progress.¹

One-Time Sigmoidoscopy Screening Reduces Colon Cancer Incidence, Death

A large trial involving more than 170,000 individuals in the United Kingdom found that one-time screening by flexible sigmoidoscopy reduced colorectal cancer incidence by one third and related deaths by more than 40 percent. Flexible sigmoidoscopy examines only the lower half of the colon, as opposed to a colonoscopy that examines the full length of a patient's colon. The purpose of these tests is to identify patients with

Factoid:

Flexible sigmoidoscopy examines only the lower half of the colon, as opposed to a colonoscopy that examines the full length of a patient's colon.

“Prevention and screening continues to represent an area of active research. Molecular screening techniques involving the study of serum, stool and sputum continue to evolve. Compliance continues to improve in the screening of certain cancers. Small advances have been made in prevention and screening and 2010 witnessed a major controversy in breast cancer screening guidelines.”

—MORTON S. KAHLENBERG, MD



Cancer Screening

www.cancer.net/screening

Sigmoidoscopy—What to Expect

www.cancer.net/sigmoidoscopy

Mammography—What to Expect

www.cancer.net/mammography

Expert Perspective from ASCO on Mammography Screening for Breast Cancer

www.cancer.net/expertsoncancernews

precancerous polyps and/or early-stage cancers before they grow and spread. While colonoscopy may be superior to flexible sigmoidoscopy in detecting cancer, the latter requires less preparation and discomfort, which may result in better compliance.

In the study, a group of 170,432 patients between ages 55 and 64 were randomized to either the intervention group (40,674), which received a single flexible sigmoidoscopy, or to a control group (113,195), which received no intervention. After a median follow-up of 11.2 years, the incidence of colorectal cancer was reduced by 33 percent in the intervention group compared to the control group. Sigmoidoscopy also cut cancer death rates by 43 percent compared to controls. In all, the incidence of colorectal cancer in the rectum and sigmoid colon—the area directly examined by the sigmoidoscope—was reduced by 50 percent.²

Federal Task Force Provides Recommendations on Routine Breast Screening Mammography for Women 40 to 49

A report by the U.S. Preventive Services Task Force, a group of independent health experts convened by the Department of Health and Human Services, recommended against routine mammography screening for women under the age of 50, saying that the risks of mammography—including unnecessary follow-up tests and treatment, and related anxiety—outweighed the potential benefits for this age group. The report instead urged women ages 40 to 49 to



MAURO FERMARIELLO / PHOTO RESEARCHERS, INC

talk with their doctors about the risks and benefits of the test, and before deciding if they want to be screened.

For women ages 50 to 74, the task force recommended routine mammography screenings every two years. Risks and benefits for women age 75 and older are unknown, it said. The group’s previous recommendation was for routine screenings every year or two for women aged 40 and older.

Overall, the report says the modest benefit of mammograms—reducing the breast cancer death rate by 15 percent—must be weighed against the risk of harm. The task force concluded that one cancer death is prevented for every 1,904 women aged 40 to 49 who are screened for 10 years, compared with one death for every 1,339 women aged 50 to 59, and one death for every 377 women aged 60 to 69. The guidelines are not meant for women considered at increased risk for breast cancer, such as those who have a *BRCA1* or *BRCA2* gene mutation or who have had extensive chest radiation.³

REFERENCES

1. Edwards, BK, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. *Cancer*. 2010; 116:544-573.
2. Atkin, WS, et al. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: A multicentre randomized controlled trial. *Lancet*. 2010; 375:1624-1633.
3. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2009; 151:716-726.

QUALITY OF LIFE, QUALITY OF CARE

While scientists attempt to better understand the behavior and underpinnings of cancer in developing new treatments, other research focuses on ways to improve patient care and quality of life.

This year, research provided new insights into the prevalence of sleep disorders among cancer patients and the benefits of adding palliative care to chemotherapy after a diagnosis in advanced lung cancer. Other studies focused on the use of yoga in improving sleep and quality of life for cancer survivors, techniques to remotely manage a patient’s depression and pain, and factors affecting the decision to undergo surgery for early-stage lung cancer.

MAJOR ADVANCE Sleep Problems Impact Most Patients with Cancer Taking Chemotherapy

In what is to our knowledge the first large study to evaluate the prevalence of insomnia in patients undergoing chemotherapy, researchers found that more than three-quarters of such patients have insomnia and other sleep disorders—nearly three times the rate found in the general population.

In the study, 823 persons with cancer completed questionnaires following two rounds of chemotherapy. They found that nearly 37 percent (301 patients) had insomnia symptoms and another 43 percent (362 patients) had difficulty falling asleep and staying asleep for at least three nights a week. (Fig 6.)

The researchers showed that sleep problems were more prevalent in younger patients, with 85.6 percent under age 58 reporting symptoms compared to 75.5 percent 58 or older.

Insomnia also differed by cancer diagnosis: breast cancer patients reported the highest number of overall insomnia complaints, and lung cancer patients were most likely to report insomnia of any group. Patients reporting insomnia were also significantly more likely to report depression and fatigue than those without insomnia.¹

NOTABLE ADVANCES Adding Palliative Care to Chemotherapy Improves Survival, Quality of Life in Patients with Lung Cancer

A randomized clinical trial found that patients with advanced lung cancer who received standard chemotherapy coupled with palliative care immediately after diagnosis lived significantly longer

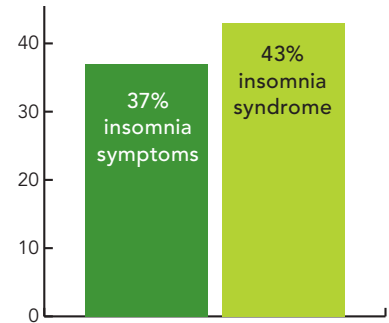


Fig 6. Sleep problems among cancer patients

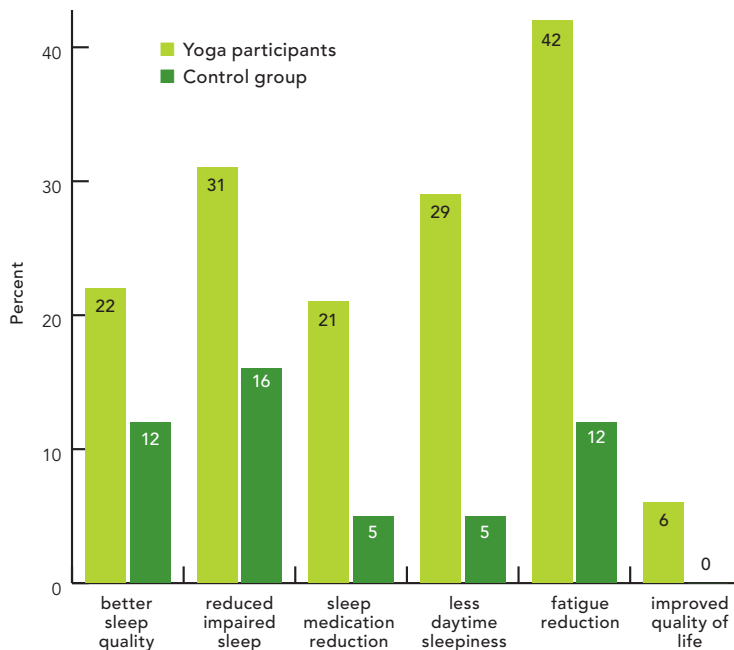


Fig 7. Benefits of yoga for cancer survivors

and had a better quality of life than those who received only chemotherapy. Patients who regularly saw palliative care specialists reported less depression and pain, better mobility and were less likely to have aggressive therapy at the end of life than those who had chemotherapy alone (see *Lung Cancer* section for full report).

Yoga Improves Sleep and Quality of Life, Lessens Fatigue for Cancer Survivors

The largest study to date examining the value of yoga designed specifically



for cancer survivors found that a four-week yoga program helped them sleep better, experience less fatigue, and improved their quality of life. (Fig 7.)

Sleep problems and fatigue are among the most prevalent side effects experienced by cancer survivors. Approximately 80 percent of patients report sleep problems during treatment and as many as 65 percent experience problems after therapy ends. Few effective treatments are available. In a randomized, multicenter, phase II/III trial, the benefits of yoga were assessed in 410 survivors of early-stage cancers (96 percent women, 75 percent breast cancer patients) who reported sleeping problems between two and 24 months

after completing adjuvant therapy for their cancer. Participants received either usual care and standard monitoring or standard monitoring plus a four-week, twice-weekly YOCAS® (Yoga for Cancer Survivors) program, consisting of mindfulness exercises, such as breathing, meditation, visualization, and poses in standing, seated and lying-down positions.

Patients in the yoga group reported greater improvement in sleep quality (22 percent versus 12 percent); reduced incidence of clinically impaired sleep (31 percent versus 16 percent); greater reduction in sleep medication use (21 percent versus 5 percent); and less daytime sleepiness (29 percent compared to 5 percent) compared to patients in the control group. Yoga participants reported a 42 percent reduction in fatigue, while the control group reported only a 12 percent reduction in fatigue. The former also reported an improved quality of life (6 percent), while the control group reported no change.²

Telephone-Based Patient Management Improves Cancer Depression, Pain

A recent trial found that a telephone-based care management program delivered by a nurse with physician-psychiatrist consultation, coupled with an automated symptom monitoring system, improved pain and depression outcomes in cancer patients receiving care in geographically dispersed oncology practices.

In the study, 405 patients with depression and/or pain, who were receiving treatment from one of 16 urban and rural oncology practices, were randomly assigned the “intervention” or “usual care” (regular care delivered by their own physicians and no special calls or monitoring). Patients in the intervention group received periodic telephone calls from a nurse care manager trained in assessing symptoms, and in providing pain and depression education. These patients were also regularly monitored for depression and/or pain via an auto-

mated system that involved interactive phone calls or Internet-based surveys.

Of the 405 participants, 131 had depression only, and 96 had only pain, and 178 had both. Of the 274 with pain, those in the intervention group had greater improvements in pain severity after one year compared to the usual care group. Similarly, of the 309 with depression, patients in the intervention arm reported improvements in depression, compared to the usual care group. In addition to improving pain and depression among participants, the study proved the feasibility of a telephone-based care management system.³

Poor Communication, Other Medical Conditions Affect Decision-Making about Surgery for Early Stage Lung Cancer

Surgery for early-stage lung cancer is the most effective treatment for this type of cancer, and those who do not have surgery generally live less than one year following their diagnosis. Historically, African Americans have particularly low surgical rates, but the reasons why they and other patients forgo surgery have been unclear.

In an attempt to find out, investigators surveyed 437 patients diagnosed with early-stage lung cancer who had not yet decided on a course of treatment. Patients were asked questions about trust in their physician, patient-physician communication, attitudes toward cancer and their ability to function in daily physical activities. The survey identified a number of factors associated with a patient's decision not to have surgery, including poor communication with health professionals, distrust about their diagnosis and the value of surgery, other concurrent medical conditions, and a lack of a consistent source of medical care.

Surgery rates were higher among white patients. Of 386 surgery-eligible patients, 66 percent of whites (179 out of 273) and 55 percent of blacks (62 of 113) underwent surgery. This gap occurred

PERSPECTIVE ON QUALITY OF LIFE, QUALITY OF CARE

“There are many persistent symptoms or problems that patients have after a cancer diagnosis, including difficulties with sleep, fatigue, mood and pain. Research described here shows that cancer patients need not suffer with these symptoms if we apply what is learned from interventions that have been tested and are effective in controlling or improving outcomes. It is important that these services be accessible to patients and be a standard part of quality cancer care.”

—PATRICIA GANZ, MD

despite lower age of the black patients. Researchers found that surgery rates among blacks were particularly low (13 percent) for patients who had two or more concurrent illnesses, versus 62 percent for one or no other medical conditions, compared to 39 percent and 70 percent for white patients, respectively. And the number of surgeries among African Americans who did not see a doctor regularly for their care was 42 percent compared to 57 percent for those who had regular care.⁴

REFERENCES

1. Palesh, OG, et al. Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. *J Clin Oncol*. 2009; 28:292-298.
2. Mustian, KM, et al. Effect of YOCAS yoga on sleep, fatigue and quality of life: A URCC CCOP randomized, controlled clinical trial among 410 cancer survivors. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010, Chicago, IL.
3. Kroenke, K, et al. Effect of telecare management on pain and depression in patients with cancer. *JAMA* 2010, 304 (2):163-171.
4. Cykert, S, et al. Factors associated with decisions to undergo surgery among patients with newly diagnosed early-stage lung cancer. *JAMA* 2010, 303 (23): 2368-2376.



Managing Side Effects
www.cancer.net/sideeffects

Understanding Chemotherapy
www.cancer.net/chemotherapy

Coping with Cancer-Related Fatigue
www.cancer.net/copingwithfatigue

Depression and Anxiety
www.cancer.net/depressionanxiety

Making Decisions About Cancer Treatment
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Policy Recommendations

On April 15, 2010, the Institute of Medicine (IoM) released the report, “*A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the National Cancer Institute (NCI) Cooperative Group Program*,” which provides comprehensive recommendations to strengthen NCI’s Cooperative Group Program. On that same day, ASCO called on NCI to implement the recommendations and double its funding for Cooperative Clinical Research.

This year, ASCO’s public policy recommendations are focused squarely on two goals that call for NCI to double its funding for Cooperative Clinical Research and for the full implementation of the recommendations of the IoM report.

THE STATE OF THE NCI COOPERATIVE GROUP PROGRAM

“If our expectations are fulfilled, the stimulus provided by the Congress may result in a truly national effort toward a cooperative and integrated search for agents useful in the treatment of cancer in humans.”

—W.H. Sebrell, Jr., MD, Director, National Institutes of Health, on the formation of the NCI Cooperative Group Program, May 4, 1954

The NCI Cooperative Group Program is designed for the purpose of developing and conducting clinical trials in academic and community settings across the country and around the world. It consists of 10 Groups, involving more than 3,100 institutions and 14,000 investigators, who enroll more than 25,000 patients each year. Each of the Groups differs in disease focus, geographic setting, and types of treatment. For example, the Children’s Oncology Group focuses on the medical specialty of pediatric cancers, while other Groups focus on specific cancers or therapeutic

approaches. All of the Groups’ research largely centers on areas that the private sector has little incentive to investigate, such as comparative effectiveness of treatments made by different companies, cancers that affect a small patient population and quality of life after treatment. These federally-funded trials build on industry breakthroughs to discover new uses for cancer treatments and are crucial to our long-term progress against cancer.

Since the program was established in the 1950s when Congress provided \$5 million and directed NCI to expand the research of chemotherapy in cancer, Cooperative Group trials have provided or enabled virtually all of the important scientific advances in cancer prevention, treatment and quality of life. As NCI continues to lead the way in our growing understanding of the cancer genome, the Cooperative Group Program will be the critical link to translate laboratory discoveries into improved treatments for cancer patients. Unfortunately, this program is not currently positioned to serve in this crucial role. Funding for Cooperative Clinical Research has been virtually flat since 2002, which in real dollars means that total funding is less today than a decade ago. In addition, numerous administrative and oversight challenges threaten the program’s ability to continue conducting innovative clinical trials needed to demonstrate the effectiveness of new cancer treatments.

DOUBLE FUNDING FOR COOPERATIVE CLINICAL RESEARCH

The first step in reinvigorating NCI’s Cooperative Group Program comes in increased funding. Administrative changes alone will not sustain this vital research system. Currently, NCI devotes \$250 million to Cooperative Group



trials in the academic and community settings and provides approximately \$2,000 to sites in order to enroll a patient in a Cooperative Group trial. However, a 2003 *Journal of Clinical Oncology* study and 2005 C-Change study determined that the actual cost of conducting NCI trials was \$5,000-\$6,000 per case. Since these studies were completed, the cost and complexity of Cooperative Group trials has increased.

These payments are insufficient to cover research costs, forcing Cooperative Group research sites to limit patient enrollment in clinical trials. An ASCO survey of Cooperative Group participants published in the April 2010 *Journal of Oncology Practice* found that one-third of participating sites plan to limit participation in federally funded clinical trials due to inadequate patient reimbursement .

To cover the true costs of conducting research without decreasing the number of trials or patients enrolled, ASCO has called on the NCI to double funding for Cooperative Clinical Research from its current level of \$250 million to \$500 million by 2015.

THE IOM REPORT RECOMMENDATIONS

ASCO also supports the IoM report's recommendations, which are consolidated into four goals. The society urges all stakeholders affected by these recommendations to immediately begin taking the necessary steps to implement them.

GOAL I: Improve the speed and efficiency of the design, launch and conduct of clinical trials

- **Recommendation 1:** NCI should facilitate some consolidation of Cooperative Group front office operations by reviewing and ranking the Groups

with defined metrics on a similar timetable and by linking funding to review scores.

- **Recommendation 2:** NCI should require and facilitate the consolidation of administration and data management operations across all of the Cooperative Groups (the back office operations) and, working with the extramural community, make process improvement in the operational and organizational management of clinical trials a priority.
- **Recommendation 3:** The U.S. Department of Health and Human Services should lead a transagency effort to streamline and harmonize government oversight and regulation of cancer clinical trials.
- **Recommendation 4:** NCI should take steps to facilitate more collaboration among the various stakeholders in cancer clinical trials.

A clinical trial must be developed and launched as efficiently as possible to ensure that it keeps pace with scientific findings, but recent studies have indicated that the average time to develop and launch a phase III Cooperative Group trial often exceeds two years. For patients diagnosed with or battling cancer, this is unacceptable. Redun-



dancy amongst the Groups, iterative oversight by agencies all within the U.S. Department of Health and Human Services (HHS) and bureaucratic challenges create inefficiencies that can cause significant delays.

While the methods of vetting concepts and statistical designs for trial and data management duties may vary amongst the Groups, a consolidated effort based on merit and efficiency will help to speed the launch of clinical trials. In addition, parallel, concurrent, or—ideally—joint reviews conducted by the various HHS agencies that oversee clinical trials, including NCI, the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP), and the Office for Civil Rights (OCR), will help reduce the number of repetitive reviews. Finally, steps like developing standard forms for data collection and contract templates for intellectual property ownership and more closely aligning the regulatory requirements of NIH, FDA, OHRP, and OCR can lead to improved efficiency in the development and launch of trials.



GOAL II: Incorporate innovative science and trial design into cancer clinical trials

- **Recommendation 5:** NCI should mandate the submission of annotated biospecimens to high-quality, standardized central biorepositories when samples are collected from patients in the course of Cooperative Group trials and should implement new funding mechanisms and policies to support the management and use of those resources for retrospective correlative science.
- **Recommendation 6:** Cooperative Groups should lead the development and assessment of innovative designs for clinical trials that evaluate cancer therapeutics and biomarkers (including combinations of therapies).
- **Recommendation 7:** In cooperation with other agencies, NCI should establish a consistent, dynamic process to oversee the development of national unified standards as needed for oncology research.

An effective Cooperative Group trial must be able to incorporate emerging discoveries, such as biomarkers, and alternative trial designs. However, few standards and resources are in place to ensure this happens in a consistent manner and in accordance with regulatory requirements. For example, biospecimens from patients who participate in clinical trials have proven invaluable to developing molecularly-based testing for appropriate cancer therapies. Yet, it can be difficult for investigators in one Cooperative Group to access biospecimens taken from patients participating in another Cooperative Group trial without having to seek additional funds. NCI and the Groups can address this by promoting standardization of collection and maintenance techniques and providing adequate resources. NCI, FDA, OHRP, and OCR should also promote common approaches to deal with privacy, access, and ownership concerns.

GOAL III: Improve the means of prioritization, selection, support and completion of cancer clinical trials

- **Recommendation 8:** NCI should reevaluate its role in the clinical trials system.
- **Recommendation 9:** NCI, Cooperative Groups, and physicians should take steps to increase the speed, volume, and diversity of patient accrual and to ensure high-quality performance at all sites participating in Cooperative Group trials.
- **Recommendation 10:** NCI should allocate a larger portion of its research portfolio to the Clinical Trial Cooperative Group Program to ensure that the Program has sufficient resources to achieve its unique mission.

To further combat the delays Cooperative Group trials face, NCI must reevaluate its role in the clinical trials process. Since 1980, NCI has conducted oversight of every aspect of the Groups' clinical trials process, which can become repetitive considering the additional layers of oversight. There are instances where this oversight is necessary, such

as trials where NCI has filed an investigational new drug (IND) application for a Group. In contrast, when NCI has not filed an IND application for a trial, NCI and the Group would be better served if NCI uses its limited resources to support the group.

In addition to doubling the funding for Cooperative Clinical Research, NCI, Cooperative Groups and physicians can make an across-the-board push to improve patient accrual for clinical trials. Methods for doing this include encouraging patient eligibility criteria that ensure the broadest participation possible, partnerships with patient advocacy organizations and working with private and federal payers to promote clinical trial participation.

GOAL IV: Incentivize the participation of patients and physicians in clinical trials

- **Recommendation 11:** All stakeholders, including academic medical centers, community practices, professional societies, and NCI, should work to ensure that clinical investigators have adequate training and mentoring, paid protected research time, the necessary resources, and recognition.
- **Recommendation 12:** Health care payment policies should value the care provided to patients in clinical trials and adequately compensate that care.

Participation in clinical trials exists because patients, investigators, and research staff believe in and have personal pride in the contributions they are making toward advancing the science of treatment. For investigators, the most important factors that would preserve and enhance volunteerism are having an impact on the trial development process and getting credit for participation. The Groups play an important role in providing investigators the opportunity to participate in the development and leadership of nationally conducted trials. The Groups also provide important mentorship, training, and career opportunities for the next generation of clinical investigators. The credit for participation comes in the form of



protected time to conceive, design and conduct clinical trials. For patients, it means ensuring that their costs for participating in a clinical trial, excluding those covered by a drug manufacturer, will be covered. The Patient Protection and Affordable Care Act—which passed following the completion of the IoM report—now guarantees insurance coverage for individuals participating in clinical trials. However, additional measures, such as collaboration with insurance providers to encourage trial participation, must be taken .

For more information about ASCO's policy priorities, visit www.asco.org/ascoaction.

REFERENCES

1. Emanuel EJ, Schnipper LE, Kamin DY, et al: The costs of conducting clinical research. *J Clin Oncol* 2003; 21:4145-4150.
2. C-Change: A Guidance Document for Implementing Effective Cancer Clinical Trials Executive Summary: Version 1.2. http://www.cchangetogether.org/pubs/reports/GuidanceDocument_ES.pdf.
3. Runowicz CD, Blayney DW, Bruinooge SS, et al: Challenges to National Cancer Institute–Supported Cooperative Group Clinical Trial Participation: An ASCO Survey of Cooperative Group Sites. *JOP* 200028, vol. 6 no. 3 114-117, 2009.
4. IoM (Institute of Medicine). 2010. *A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program*. Washington, DC: The National Academies Press.

Cancer Statistics

CANCER INCIDENCE & MORTALITY—2010*

Cancer Type	Estimated New Cases	Estimated Deaths
All Sites	1,529,560	569,490
Tongue	10,990	1,990
Mouth	10,840	1,830
Pharynx	12,660	2,410
Other Oral Cavity	2,050	1,650
Esophagus	16,640	14,500
Stomach	21,000	10,570
Small Intestine	6,960	1,100
Colon	102,900	51,370
Anus, Anal Canal & Anorectum	5,260	720
Liver & Intrahepatic Bile Duct	24,120	18,910
Gallbladder & Other Biliary	9,760	3,320
Pancreas	43,140	36,800
Larynx	12,720	3,600
Lung & Bronchus	222,520	157,300
Bones & Joints	2,650	1,460
Soft Tissue (Including Heart)	10,520	3,920
Melanoma—Skin	68,130	8,700
Breast	209,060	40,230
Uterine Cervix	12,200	4,210
Ovary	21,880	13,850
Vulva	3,900	920
Vagina & Other Genital—Female	2,300	780
Prostate	217,730	32,050
Testis	8,480	350
Penis & Other Genital—Male	1,250	310
Urinary Bladder	70,530	14,680
Kidney & Renal Pelvis	58,240	13,040
Ureter & Other Urinary Organs	2,490	830
Eye & Orbit	2,480	230
Brain & Other Nervous System	22,020	13,140
Endocrine System	46,930	2,570
Thyroid	44,670	1,690
Hodgkin Lymphoma	8,490	1,320
Non-Hodgkin Lymphoma	65,540	20,210
Myeloma	20,180	10,650
Acute Lymphocytic Leukemia	5,330	1,420
Chronic Lymphocytic Leukemia	14,990	4,390
Acute Myeloid Leukemia	12,330	8,950
Chronic Myeloid Leukemia	4,870	440

* Rounded to the nearest 10; estimated new cases exclude basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

Source: American Cancer Society, *Cancer Facts and Figures 2010*.

TRENDS IN 5-YEAR RELATIVE SURVIVAL RATES*, 1975-2005 (SELECT CANCERS)

Cancer Type	1975-77	1984-86	1999-2005	Cancer Type	1975-77	1984-86	1999-2005
All sites	50%	54%	68% [§]	Non-Hodgkin Lymphoma	48%	53%	69% [§]
Brain	24%	29%	36% [§]	Oral cavity and pharynx	53%	55%	63% [§]
Breast (female)	75%	79%	90% [§]	Ovary	37%	40%	46% [§]
Colon	52%	59%	66% [§]	Pancreas	3%	3%	6% [§]
Esophagus	5%	10%	19% [§]	Prostate	69%	76%	100% [§]
Hodgkin Lymphoma	74%	79%	86% [§]	Rectum	49%	57%	69% [§]
Kidney	51%	56%	69% [§]	Stomach	16%	18%	27% [§]
Larynx	67%	66%	63% [§]	Testis	83%	93%	96% [§]
Leukemia	35%	42%	54% [§]	Thyroid	93%	94%	97% [§]
Liver and bile duct	4%	6%	14% [§]	Urinary bladder	74%	78%	82% [§]
Lung and bronchus	13%	13%	16% [§]	Uterine cervix	70%	68%	72% [§]
Melanoma of the skin	82%	87%	93% [§]	Uterine corpus	88%	84%	84% [§]
Myeloma	26%	29%	37% [§]				

* Survival rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 9 areas from 1975-77, 1984-86, 1999-2005, and followed through 2006.

[§] The difference in rates between 1975-1977 and 1999-2005 is statistically significant (p<0.05).

Source: American Cancer Society, Cancer Facts and Figures 2010.

FDA APPROVALS OF ANTI-CANCER AGENTS, SEPTEMBER 2009–SEPTEMBER 2010

Newly Approved Agents

Generic Name	Trade Name	Indications	Date of Approval
Cabazitaxel	Jevtana	Metastatic hormone-refractory prostate cancer ¹	June 17, 2010
Sipuleucel-T	Provenge	Asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer ²	April 29, 2010
Romidepsin	Istodax	Cutaneous T-cell lymphoma (CTCL) ³	November 5, 2009
Ofatumumab	Arzerra	For treatment of patients with chronic lymphocytic leukemia (CLL) refractory to fludarabine and alemtuzumab	October 26, 2009
Pazopanib	Votrient	Advanced renal cell carcinoma	October 19, 2009
Pralatrexate	Folotyn	For relapsed or refractory peripheral T-cell lymphoma (PTCL) ⁴	September 25, 2009

Expanded Indications For Existing Agents

Generic Name	Trade Name	Indications	Date of Approval
Nilotinib	Tasigna	For adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia	June 17, 2010
Erlotinib	Tarceva	Maintenance treatment for patients with locally advanced or metastatic non-small cell lung cancer (NSCLC)	April 16, 2010
Lapatinib	Tykerb	For use with letrozole to treat certain postmenopausal women with hormone receptor positive metastatic breast cancer	January 29, 2010
Rasburicase	Elitek	For the initial management of plasma uric acid levels in adult patients with leukemia, lymphoma and solid tumor malignancies	October 16, 2009
Ibritumomab Tiuxetan	Zevalin	For use in patients with chemotherapy relapsed or refractory follicular non-Hodgkin's lymphoma	September 3, 2009

¹ FDA approved for use in combination with prednisone for treatment of patients with metastatic hormone-refractory prostate cancer (mHRPC) previously treated with a docetaxel-containing regimen.

² FDA approved autologous cellular immunotherapy for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer.

³ FDA approved for cutaneous T-cell lymphoma (CTCL) in patients who have received at least one prior systemic therapy

⁴ The Office of Oncology Drug Products granted accelerated approval to pralatrexate injection (FOLOTYN™, Allos Therapeutics, Inc.) for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL).

COOPERATIVE GROUP STUDIES FEATURED IN 2010 CCA REPORT

Research Conducted Directly By Cooperative Groups

Cooperative Group	Cancer Type	Research
National Surgical Adjuvant Breast and Bowel Project	Breast	Negative Sentinel Node Adequate to Confirm Lack of Cancer Spread Krag DN, et al. Primary outcome results of NSABP B-32, a randomized phase III clinical trial to compare sentinel node resection (SNR) to conventional axillary dissection (AD) in clinically node-negative breast cancer patients. <i>Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.</i>
American College of Surgeons Oncology Group	Breast	Immunohistochemistry to Find Micrometastases in Bone Marrow and Sentinel Lymph Nodes Unnecessary Cote R, et al. ACOSOG Z0010: A multicenter prognostic study of sentinel node (SN) and bone marrow (BM) micrometastases in women with clinical T1/T2 N0 M0 breast cancer. <i>Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.</i>
American College of Surgeons Oncology Group	Breast	Removing Fewer Lymph Nodes in Sentinel Node-Positive Breast Cancer Does Not Impair Survival Giuliano AE, et al. ACOSOG Z0011: A randomized trial of axillary node dissection in women with clinical T1-2 N0 M0 breast cancer who have a positive sentinel node. <i>Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.</i>
American College of Surgeons Oncology Group	Gastrointestinal	GIST Mutations Predict Recurrence Risk, May Guide Treatment Choices Corless CL, et al. Relation of tumor pathologic and molecular features to outcome after surgical resection of localized primary gastrointestinal stromal tumor (GIST): Results of the intergroup phase III trial ACOSOG Z9001. <i>Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010; Chicago, IL.</i>
Gynecologic Oncology Group	Gynecologic	Bevacizumab Extends Progression-Free Survival for Women with Advanced Ovarian Cancer Burger, RA, et al. Phase III trial of bevacizumab (BEV) in the primary treatment of advanced epithelial ovarian cancer (EOC), primary peritoneal cancer (PPC), or fallopian tube cancer (FTC): A Gynecologic Oncology Group study. <i>Presented at the 46th Annual Meeting of the American Society of Clinical Oncology; June 2010, Chicago, IL.</i>
American College of Surgeons Oncology Group	Head and Neck	Sentinel Node Biopsy Shows Potential for Early Stage Oral Cancer Civantos FJ, et al. Sentinel lymph node biopsy accurately stages the regional lymph nodes for T1-T2 oral squamous cell carcinomas: Results of a prospective multi-institutional trial. <i>J Clin Oncol. 2010; 28:1395-1400.</i>
Radiation Therapy Oncology Group	Lung	Stereotactic Radiation a Potential Alternative for Patients with Inoperable Early-Stage Lung Cancer Timmerman R, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. <i>JAMA: 2010; 303:1070-1076.</i>
Children's Oncology Group	Pediatrics	Adding Imatinib to Chemotherapy Improves Event-Free Survival in High-Risk ALL Schultz, KR, et al. Improved early event-free survival with imatinib in Philadelphia chromosome-positive acute lymphoblastic leukemia: A Children's Oncology Group study. <i>J Clin Oncol. 2009; 27:5175-5181.</i>

Using Data From Cooperative Group Studies

Cooperative Group	Cancer Type	Research
North Central Cancer Treatment Group	Cancer Disparities	Race Associated with Response to Chemotherapy for Advanced Colorectal Cancer Sanoff HK, et al. Racial differences in advanced colorectal cancer outcomes and pharmacogenetics: a subgroup analysis of a large randomized clinical trial. <i>J Clin Oncol. 2009; 27:4109-4115.</i>
Southwest Oncology Group	Cancer Disparities	Disparities in Cancer Survival Most Significant in Hormonally-Driven Cancers Albain KS, et al. Racial disparities in cancer survival among randomized clinical trials patients of the Southwest Oncology Group. <i>J Natl Cancer Inst. 2009; 101:984-992.</i>
Radiation Therapy Oncology Group	Head and Neck	Survival is Better with HPV-Related Oropharyngeal Tumors Ang KK, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. <i>N Engl J Med. 2010; 363:24-35.</i>
North Central Cancer Treatment Group	Melanoma	Meta-Analysis Shows Adding Interferon Alpha After Surgery Improves Overall Survival in Patients With Melanoma Mocelin, S, et al. Interferon alpha adjuvant therapy in patients with high-risk melanoma: A systematic review and meta-analysis. <i>J Natl Cancer Inst. 2010; 102: 493-501.</i>

ASCO Resources

Oncologist-approved cancer information from the American Society of Clinical Oncology



Basic Cancer Information

www.cancer.net/cancertypes

Comprehensive information on more than 120 cancer types and cancer-related syndromes

- Risk factors
- Staging
- Diagnosis
- Questions to ask the doctor
- Treatment
- Spanish language section
- Symptoms



Coping Resources

www.cancer.net/coping

Resources to help people with cancer and those who care for them

- Caregiving
- Sexuality
- Personal stories
- End-of-life care
- Relationships
- Mental health



Cancer Clinical Trials

www.cancer.net/clinicaltrials

How to participate in studies of promising new treatments

- Finding a clinical trial
- Deciding to participate
- Questions to ask the research team
- Patient safety
- Phases of clinical trials

ASCO Progress Reports

www.cancer.net/cca

Clinical Cancer Advances: ASCO's Annual Report on Progress Against Cancer (2006–present)



www.cancer.net/progresstimeline



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