

November 8, 2005  
Volume 2 | Number 43

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A Publication of the National Cancer Institute  
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
National Institutes of Health  
NIH Publication No. 05-5498

<http://www.cancer.gov>

## After Treatment: The Needs of Cancer Survivors

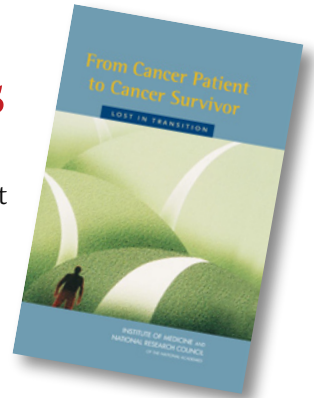
A new report by the Institute of Medicine (IOM) concludes that a growing number of cancer patients are surviving the disease only to face a constellation of new needs and that too often these needs are not met. The 500-page report, based on an extensive review of the scientific literature and interviews with survivors, proposes recommendations for improving the care and quality of life for these individuals.

A primary recommendation is that all cancer patients be given summaries of their medical treatments and instructions for follow-up care once they complete therapy. These survivor care plans would document

which treatments a patient had and which health changes should be monitored closely.

"A care plan is a concrete step that could be taken tomorrow and would provide relief essentially immediately," says Dr. Sheldon Greenfield, who directs the Center for Health Policy Research at the University of California, Irvine, and co-led the panel that produced the report, *From Cancer Patient to Cancer Survivor: Lost in Transition*.

*(continued on page 2)*



Director's Update

Guest Update by Dr. Ernie Hawk



*Dr. Ernie Hawk, Director, NCI Office of Centers, Training, and Resources*

## TRWG Process Moving Forward, Members Named

Since being named by Dr. von Eschenbach earlier this year to chair the Translational Research Working Group

(TRWG), I have come to more fully appreciate the potential of the working group to influence how we approach translational research. We will evaluate the translational research components of the National Cancer Institute's (NCI's) current portfolio and provide a blueprint for

how best to harness our translational research resources. Our goal is to ensure that the processes and programs are in place at NCI to rapidly translate the scientific discoveries of the cancer community's many dedicated scientists into new interventions for preventing, diagnosing, and treating cancer.

There will be broad public input into the TRWG deliberations, including participation in the working group by many of the country's leading translational researchers, as well as representatives from *(continued on page 2)*

*(After Treatment continued from page 1)*

The study focuses on adult survivors from the time they complete initial treatment to a relapse, secondary illness, or death. During this period, survivors may develop any number of problems related to their cancers that prevents them from obtaining adequate health care, often with disastrous results.

The report stresses the need for more communication and coordination among doctors who treat the diverse health problems described in the report, including depression, sexual dysfunction, and heart disease.

The report also calls for the development of clinical care guidelines for every type of cancer, which would allow primary care physicians and other health professionals to help monitor and care for survivors.

“When you consider that there are 10 million cancer survivors in this country, finding these patients and delivering the best possible health care that is targeted to their special needs becomes a large concern for the health care community,” says Dr. Sandra Horning, president of the American Society of Clinical Oncology (ASCO).

“I don’t believe the issues of cancer survivorship have ever been laid out as clearly and comprehensively as in this report,” adds Dr. Horning. ASCO is hosting a conference today to discuss the report and plan strategies for implementing the recommendations.

The study follows a [report](#) on survivors by the President’s Cancer Panel last year, which proposed survivor care plans, and a 2003 IOM study on childhood cancer survivors.

All cancer survivors, the report concludes, have permanent health conditions that may need to be treated like other chronic conditions. But it is not uncommon for friends and relatives of survi-

vors to suggest that normal life should resume once the treatments have ended.

“This idea that a person completes cancer treatment and then returns to normal life as though nothing had happened is outrageous,” says one of the report’s editors Ellen Stovall, who is president of the National Coalition for Cancer Survivorship and one of several survivors on the panel.

The panel emphasized the importance of more research to develop evidence-based survivorship interventions for meeting the unique needs of cancer survivors.

“More people today are living with cancer than dying from it, and we must look critically at issues of quality of life and care for these survivors,” says Dr. Julia Rowland, director of NCI’s Office of Cancer Survivorship. “This report is a powerful blueprint for action.”

*By Edward R. Winstead*

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*(Director’s Update continued from page 1)*

the advocacy community, industry, the Food and Drug Administration (FDA), and NCI staff. In fact, the complete 60-member TRWG roster is now available on the working group’s Web site at [www.cancer.gov/trwg](http://www.cancer.gov/trwg).

In naming the members, I worked with the TRWG co-chairs, Drs. Lynn Matrisian and William G. Nelson, to select as representative a group as possible, while still ensuring it was of a manageable size.

Following in the mold of the Clinical Trials Working Group, TRWG will formulate recommendations for developing an optimized model for a translational research program, as well as an implementation plan for taking those recommended actions. The implementation plan is important because it will lay out the short-term changes to existing programs

the working group believes are needed, as well as what new, longer term initiatives are required. Both the recommendations and the implementation plan will be presented to the National Cancer Advisory Board.

In December, TRWG will have its first planning meeting, which will be preceded by small-group teleconferences where members can engage in preliminary discussions about the issues that need to be addressed and potential models for a comprehensive translational research program.

The TRWG Web site will be an excellent resource for the cancer community to use for following and commenting on the TRWG process. After the December planning meeting, for example, specific questions about issues raised during the meeting will be posted to the Web site, and the public will be invited to submit comments on them.

In February, a larger roundtable meeting will be held involving the entire TRWG and an additional 140 participants, most of whom will be nominated by TRWG members. The February meeting should allow for a robust and fruitful discussion of the issues and potential models raised during the first planning meeting and public comment period.

I encourage those with an interest in the process to participate by submitting comments when materials are posted on the TRWG Web site. If you have questions about the TRWG, they can be submitted via the Web site as well.

I’m excited about TRWG and confident that the process for developing its recommendations and implementation plan will lead to important changes that, first and foremost, will benefit patients and move NCI and the cancer community closer to the 2015 goal. ♦



# Spotlight

## Consortium Modelers Interpret U.S. Trends in Breast Cancer Mortality

Do screening mammography and adjuvant therapy really reduce breast cancer mortality outside of clinical trials? While the benefits of therapy are more clear, a unique consortium of seven biostatistical teams has added important evidence to address the still controversial question regarding mammography. The problem of separating out the impact of mammography and advances in therapy, which occurred at about the same time during the 1980s and 1990s, was addressed by the consortium in their study reported in the October 27 *New England Journal of Medicine*.

This approach used population data to describe the dissemination and usage patterns of mammography and adjuvant therapy that occurred over time in the United States. The usage patterns were then coupled with seven independent modelers' synthesis of all available information on the benefits of these advances. The authors make the case that each factor accounted for half of the historic 24 percent decrease in mortality that was actually observed between 1990 and 2000.

Until now, the debate over mammography included many who questioned the evidence that screening does in fact reduce cancer deaths, one of them being lead author Dr. Donald Berry, head of biostatistics at the University of Texas M.D. Anderson

Cancer Center. "The controlled trials on which the mortality assertion was based were uneven and not without flaws," he says.

Nonetheless, citing more recent papers, screening advocates have said that mammography can reduce mortality by up to 69 percent. But, says Dr. Berry, "Fervor doesn't substitute for evidence. Here we brought the pieces of evidence together in a novel way and separated the effects of screening and treatment. I would say the question is now at least 95 percent settled, in favor of mammography reducing breast cancer mortality."

"The ability to come at important questions like this in a unique way was part of the motivation when NCI formed the Cancer Intervention and Surveillance Modeling Network (CISNET) in 2000," says project director Dr. Eric J. Feuer, chief of NCI's Statistical Research and Applications Branch, who is also one of the study's 10 authors.

The CISNET approach includes bringing together distinct teams—including some of the leading biostatistical investigators in the cancer community—with an interest and expertise in a particular cancer site, framing a common problem, and letting each team develop its own independent model of how to solve it. The network also includes grantee teams that specialize in lung, prostate, and colorectal cancers.

"All models agreed that both screening and treatment reduced breast cancer mortality, and that the observed reduction in the actual population—24 percent during the 1990s—could not be attributed to either one acting alone," says Dr. Kathy Cronin, a mathematical statistician who helped develop the common assumptions all teams used. Just under half of the combined effect came from screening. "There will never be a final piece of evidence on such a complex and tangled question, but this result provides additional evidence for mammography's role in the undeniable progress seen during the 1990s," she adds. "The study also helped refine the population mortality impact of important treatment advances in the use of multiagent chemotherapy and tamoxifen."

The proportion of the total reduction in the death rates from breast cancer attributed to screening varied in the seven models from 28 to 65 percent (with a median of 46 percent), with adjuvant therapy contributing the rest. The variability across models in the absolute contribution of screening was larger than it was for treatment, reflecting the greater uncertainty associated with estimating the benefit of screening.

"Comparative modeling yields a powerful outcome," explains Dr. Feuer, "because you actually produce a meta-result that no single group could achieve. This is a testament not only to the intellectual rigor used to build each of the models, but to the scientists' willingness to collaborate and cooperate."

Links to the journal and more study details can be found at <http://cisnet.cancer.gov/>. ♦

*By Addison Greenwood*



# Cancer Research Highlights

## Studies Test Cervical Cancer Prevention in Underserved Populations

Current medical care provides accurate and economical methods for the detection of cervical cancer and effective removal of precancerous cervical lesions. But standard cervical cancer screening and treatment require several clinic visits over the course of many months, an unfeasible approach for women in underserved, limited-resource communities.

A clinical trial reported in the November 2 *Journal of the American Medical Association (JAMA)* attempted to increase cervical cancer prevention in an underserved population by using a single-visit approach to screening and treatment. Trial participants in California were randomized to either a standard-care or single-visit group. Women in the standard-care group received a conventional Pap test and were immediately discharged home; those with abnormal results were contacted by telephone and urged to return for follow-up. Women in the single-visit group remained in the clinic until their tests were processed, and those with high-grade lesions were offered immediate cervical loop electrosurgical excision. A significantly greater number of women with high-grade lesions in the single-visit group (88 percent) received definitive treatment within 6 months than did women in the standard-care group (53 percent).

A second study reported in the same issue of *JAMA* tested a noncytology-based screen-and-treat approach

in the extremely limited-resource setting of Khayelitsha, South Africa. All participants underwent visual inspection of the cervix with acetic acid (VIA) and human papillomavirus (HPV) DNA testing; 2 to 6 days later, they were randomized to receive treatment based on VIA results, treatment based on HPV DNA results, or delayed evaluation. Women in the VIA and HPV DNA groups with positive test results were immediately offered cryotherapy. Follow-up rates did not differ significantly between groups, but prevalence of high-grade cervical intraepithelial neoplasia and cancer at 6 months were significantly less in both the VIA (2.23 percent) and HPV DNA (0.80 percent) groups compared with the control group (3.55 percent).

In both studies, treatment was offered without definitive diagnosis. But given the very low risk of the interventions and the high likelihood of patients with cervical neoplasia being lost to follow-up, the authors of both studies concluded that these programs are a practical and feasible way to reduce the prevalence of high-grade precancerous cervical lesions in underserved populations.

## Study Shows How 1G8 Antibody Inhibits Prostate Cancer

Prostate stem cell antigen (PSCA) is a cell-surface protein found in most prostate cancers, as well as bladder and pancreatic cancer. The level of this antigen's expression correlates directly with prostate cancer severity and inversely with its prognosis.

Researchers from UCLA's Jonsson Comprehensive Cancer Center have already shown that an antibody against PSCA—1G8, which they developed—inhibits tumor growth and metastasis, and improves survival in mice. Now they have characterized the molecular pathways through which the antibody works, publishing their findings in the October 15 *Cancer Research*.

The team inserted a PSCA expression vector into prostate cancer cells and incubated them in the presence of 1G8. What resulted were weakened plasma membranes, broken nuclei, DNA leakage, and an overall flattened appearance of the cells. However, the cells did not show the usual signs of apoptosis, including chromatin condensation and degradation. When the team tested fragments of the antibody, they found that the full protein and a bivalent (but not monovalent) fragment could induce cell death. Both the bivalent fragment and the full 1G8 antibody slowed tumor growth in mice. The authors concluded that 1G8 acts through a direct antigen cross-linking mechanism that is independent of caspases and of the antibody's cell-attaching Fc domain.

Though these results come from *in vitro* and mouse studies, they have implications for clinical therapy. "In particular," the authors noted, "knowledge of the mechanism...may affect antibody selection, timing of therapy, therapeutic setting, or rational selection of agents for combination therapy."

## Studies Point to Anticancer Potential of Broccoli Sprouts

A chemical in broccoli sprouts may be able to prevent two very different cancers, according to the results of  
*(Highlights continued on page 5)*

(Highlights continued from page 4)

studies presented last week at the American Association for Cancer Research (AACR) “Frontiers in Cancer Prevention Research” meeting. Researchers from Japan reported that people infected with the bacteria *H. pylori*—which has been associated in several studies with gastric cancer—and who ate the sprouts daily for 2 months had reduced levels of *H. pylori* and pepsinogen (a biomarker of gastritis), compared with those who ate alfalfa sprouts for the same period.

While they are virtually identical chemically, broccoli sprouts contain high levels of sulforaphane, while alfalfa sprouts contain none. Two months after the study ended, subjects in the broccoli sprout group saw their *H. pylori* and pepsinogen levels return to baseline. The researchers attributed the broccoli sprouts’ benefit to the protective effect of sulforaphane against cell DNA damage.

To confirm whether the sprouts do indeed have an anticancer effect, the study’s leader, Dr. Akinori Yanaka, said during a news conference that his lab hopes to test the intervention over a longer period to see if it can prevent gastric cancer recurrence in those at high risk.

Also at the AACR meeting, researchers from Johns Hopkins University reported that, in a mouse model of UV-light-induced melanoma, sulforaphane extract applied to the skin significantly reduced the risk of cancerous skin tumors. All of the control mice developed cancerous skin tumors, whereas only half of the mice who received a high dose of the extract did. The high-dose mice that developed tumors had their tumor burden reduced by half.

## Familial Cancer Risk Estimates Affected by Surveillance Bias

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The risk of familial cancer after a parent or sibling is first diagnosed with cancer may be overestimated based on the number of additional cancers found among other family members shortly after the initial diagnosis, according to a study in the November 2 *Journal of the National Cancer Institute*.

Researchers from the German Cancer Research Centre in Heidelberg followed almost 1.7 million offspring and siblings of 846,448 cancer patients in the Swedish Family Cancer Database. They compared the relative risk of those family members against the general population for developing cancers of the breast, prostate, and cervix, as well as other cancers. For most of the cancers, the relative risk for family members was greatest in the first year but “decreased with time after diagnosis of the first familial tumor,” the researchers reported. For example, “daughters of women with breast cancer had a statistically significantly higher relative risk of *in situ* breast cancer during the year of the mother’s diagnosis than they did 5 or more years later,” the study found.

The diagnosis of cancer in a family raises concern among the patient’s relatives, who may seek medical advice in the immediate aftermath of the initial bad news, resulting in increased detection of asymptomatic tumors—a phenomenon called surveillance bias.

Given the possibility of inflated risk estimates, the scientists cautioned that “the possibility of overestimated familial risks of cancer shortly

after diagnosis of the first familial tumor should be considered before a patient’s clinical and genetic counseling is implemented.”

## National Study Shows Relationship of Movies to Kids’ Smoking

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A new study by researchers at Dartmouth Medical School found that young people who watched the most smoking in the movies were almost three times more likely to start smoking than their peers who watched the least amount of smoking in movies. This result was found throughout all regions of the country, regardless of race and ethnic group. The results of this NCI-funded study were published in the November 7 *Journal of Pediatrics*.

The researchers surveyed a total of 6,522 adolescents aged 10 to 14 from across the country using a random-digit telephone dial system. The participants were representative of the U.S. population of adolescents in terms of age, sex, household income, and census region. Using a telephone keypad, respondents indicated which movies they had seen out of 50 that had been randomly selected from among the top 532 U.S. box office hits between 1998 and April of 2003 (74 percent of which included smoking).

The study showed that exposure to onscreen smoking was an independent, primary risk factor even after accounting for the impact of other known risk factors for smoking such as parental and sibling smoking, smoking by friends, and rebelliousness, among other factors. ♦



*The Nation's Investment in Cancer Research: A Plan and Budget Proposal for Fiscal Year 2007* describes

continuing and new activities that NCI believes will accelerate achievement of the 2015 challenge goal to eliminate the suffering and death due to cancer. Current and future activities encompass three key components for a strong cancer research enterprise: capitalizing on powerful scientific opportunities, targeting specific public health needs, and continuing to build a sound research infrastructure and capacity for the future.

The report describes the major components of the NCI research portfolio, infrastructure, and resources. It also details five proposed high-impact strategic investments for 2007 and how they will improve patient care and public health. These investments will foster integration within and among NCI-designated Cancer Centers; respond to recommendations for re-engineering cancer clinical trials; link cancer science and technology; advance and support medical informatics and health information systems; and integrate the disciplines and cultures in cancer science. The FY 2007 budget request comprises the increase required to maintain the present level of operations or "current services," plus the increases required for the five new strategic investments.

The report is available online at <http://plan.cancer.gov>. Print copies will be available in mid-November and may be ordered by e-mailing [cisocc@pop.nci.nih.gov](mailto:cisocc@pop.nci.nih.gov). ♦



## Featured Clinical Trial

### New Targeted Therapy for Solid Tumors and Lymphomas

#### Name of the Trial

Phase I Study of 17-Dimethylaminoethylamino-17-Demethoxygeldanamycin (17-DMAG) in Patients with an Advanced Solid Tumor or Lymphoma (NCI-04-C-0218). See the protocol summary at <http://cancer.gov/clinicaltrials/NCI-04-C-0218>.

#### Principal Investigator

Dr. Martin Gutierrez, NCI Center for Cancer Research

#### Why Is This Trial Important?

Heat shock proteins (HSPs) are found in every cell of the body. HSPs help cells survive stressful conditions (including heat, cold, nutrient starvation, and oxygen deprivation) by protecting other proteins. Under nonstressful conditions, HSPs help proteins achieve and maintain their proper shape. Researchers at NCI are investigating a particular HSP, called HSP-90, as a target for cancer therapy. Many of the proteins implicated in cancer development need HSP-90 to help them achieve their correct functional shape and cellular location.

In this trial, researchers are studying 17-DMAG, an HSP-90 inhibitor developed by NCI, to see if it can help prevent cancer cells from growing in patients with solid tumors or lymphomas. The trial will also be used to determine the maximum dose of 17-DMAG that can be given to patients and examine what side effects the drug may cause.

"Preclinical research results suggest that inhibiting HSP-90 will alter many

of the protein pathways in tumor cells and may result in tumor cell death," said Dr. Gutierrez. "This is the first test of 17-DMAG in humans, and so far, the drug has been well tolerated.

"We think that 17-DMAG's mode of action may represent an important new approach in the treatment of many types of cancer."

#### Who Can Join This Trial?

Researchers seek to enroll 40 patients aged 18 or over with either solid tumor malignancy or lymphoma that is metastatic or inoperable, and for which standard curative or palliative measures do not exist or are associated with minimal survival benefit. See the full list of eligibility criteria at <http://cancer.gov/clinicaltrials/NCI-04-C-0218>.

#### Where Is This Trial Taking Place?

The study will be done at the NIH Clinical Center in Bethesda, Md.

#### Contact Information

Contact the NCI Clinical Studies Support Center (CSSC) at 1-888-NCI-1937. The call is toll free and confidential. ♦

An archive of "Featured Clinical Trial" columns is available at <http://cancer.gov/clinicaltrials/ft-all-featured-trials>.

#### "Understanding NCI" Teleconference

NCI's Office of Liaison Activities will hold an "Understanding NCI" teleconference on the NCI Mouse Models of Human Cancers Consortium November 9 at 3:00 p.m., EST. To join the call, dial 1-800-857-6584 and enter pass code 4683#. ♦

## Buetow Named to New NCI Position

Dr. Kenneth Buetow has been appointed to the new position of NCI Associate Director for Bioinformatics and Information Technologies. Previously, Dr. Buetow served as director of the NCI Center for Bioinformatics.

Dr. Buetow will manage and execute information technology and bioinformatics initiatives that will lead to the usage of common tools, standards, and datasets across NCI; assist internal teams in adopting and leveraging NCI's cancer Biomedical Informatics Grid™ (caBIG™) infrastructure; review and update NCI's existing and planned bioinformatics programs and activities; make recommendations for the creation of a standing group that will provide technical guidance on new projects; and regularly report to the NCI Executive Committee, of which he is a member.

## NCI Announces Biorepository Coordination System

On November 7, NCI announced a cancer biorepository pilot project designed to standardize biospecimen collection and management among investigators at NCI's prostate cancer Specialized Programs of Research Excellence (SPOREs). The project will enhance the quality and availability of biospecimens and associated data for the broader scientific community.

The Biorepository Coordination System (BCS) will link researchers at 11 institutions to enable and accelerate the evaluation of key genes and proteins as potential clinical measures of prostate cancer. The project will create a common biorepository of high-quality, clinically annotated biospecimens, including paraffin-

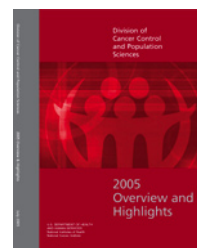
embedded and frozen tissue, serum, and plasma. Researchers will gain the analytical power of combined biorepository resources that will support an Inter-Prostate SPORE Biomarkers Study. This study will provide a scientific framework for testing the BCS model by conducting validation trials on promising prostate cancer prognostic biomarkers.

For more information, visit <http://prostatenbpilot.nci.nih.gov>.

## Science Writers' Seminar Focuses on Pain

On November 2, NCI's Press Office hosted a science writers' seminar on new approaches to treating chronic pain. The seminar highlighted the efforts of the NIH Pain Consortium, which was established to enhance pain research and promote collaboration among researchers across the many NIH institutes, centers, and offices that have programs and activities addressing pain. Speakers included Drs. Andrew Mannes and Michael J. Iadarola from NIDCR; Drs. Ann O'Mara and Blossom Patterson from NCI; Dr. Jeffrey S. Mogil, a NIDA grantee from McGill University; and Drs. Lawrence Tabak (NIDCR), Story Landis (NINDS), and Patricia Grady (NINR), institute directors and co-chairs of the NIH Pain Consortium. The seminar was attended by reporters from *U.S. News and World Report*, *People Magazine*, *Dow Jones Newswires*, and *Knight Ridder*, as well as several trade publications. For more information about the NIH Pain Consortium, visit <http://painconsortium.nih.gov/>. The seminar can be viewed online via archived webcast at <http://videocast.nih.gov/PastEvents.asp>.

## DCCPS Report Available Online



The Division of Cancer Control and Population Sciences' (DCCPS) July report, "2005: Overview and Highlights," was

recently posted online. The report describes DCCPS' initiatives in surveillance, molecular epidemiology, quality of care, tobacco control, behavioral research, energy balance, survivorship, health disparities, dissemination, and diffusion. It is available at <http://cancercontrol.cancer.gov/bb/index.html>.

## CGEMS Funding Opportunity Available

The Cancer Genetic Markers of Susceptibility (CGEMS) program is a 3-year NCI initiative to identify and validate cancer susceptibility genes, and to make such information publicly accessible through NCI's caBIG™. CGEMS recently issued a Request for Proposals titled "Genotyping Service for the Cancer Genetic Markers of Susceptibility (CGEMS) Initiative (RFP S06-072)." The objective of this solicitation is to seek a qualified vendor to perform a high-quality, genome-wide scan of high-density single nucleotide polymorphisms (SNPs). The requirement is to assay 300,000 or more distinct SNP genotypes in each of approximately 2500 high-quality genomic DNA samples within 90 days of the contract execution period. A completion rate of greater than 95 percent per sample and a per locus genotype error rate under 0.3 percent are required. For more information, go to [www.fbo.gov/spg/HHS/NIH/FCRF/Reference%2DNumber%2DS02%2D076/Attachments.html](http://www.fbo.gov/spg/HHS/NIH/FCRF/Reference%2DNumber%2DS02%2D076/Attachments.html). ♦

## FDA Approves Drugs for Pancreatic Cancer and Rare Leukemia

The FDA last week approved drugs for pancreatic cancer and a rare form of leukemia that affects both adults and children.

The agency approved erlotinib (Tarceva), in combination with gemcitabine, as a first-line treatment for patients with advanced, inoperable, or metastatic pancreatic cancer. The approval was based on a single phase III randomized clinical trial in which the combination of erlotinib, an EGFR-inhibitor approved approximately a year ago for the treatment of non-small-cell lung cancer, and gemcitabine, the standard treatment for these patients, resulted in a small but statistically significant improvement in survival compared with gemcitabine alone. The median improvement in survival was only 12.8 days, but the 1-year survival rates favored the addition of erlotinib, 24 percent versus 17 percent.

During a meeting in September, the FDA Oncology Drugs Advisory Committee voted in favor of approving erlotinib for this new indication. Committee members struggled with whether such a small sur-

vival improvement—which could be accompanied by an increase in diarrhea and skin rash—was enough to justify an approval recommendation. In the end, most committee members agreed, as one put it, that the approval would be an important “first step” toward new options for what is an almost uniformly fatal form of cancer.

The agency also approved nelarabine (Arranon) to treat adults and children with T-cell acute lymphoblastic leukemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL), and whose disease is refractory to or has relapsed following at least two chemotherapy regimens. Nelarabine, which was approved under an accelerated approval mechanism and also granted orphan drug status, is the first drug cleared for this rare indication; an estimated 500 patients per year have relapsed or refractory disease.

FDA based the accelerated approval—which requires the drug’s manufacturer, GlaxoSmithKline, to conduct additional studies to verify clinical benefit—on two NCI-sponsored phase II clinical trials. The

nelarabine phase II trial in children was conducted by the Children’s Oncology Group (COG), while the trial in adults was led by the Cancer and Leukemia Group B, in conjunction with the Southwest Oncology Group. In both trials, complete responses were observed in approximately 20 percent of patients. Median overall survival was 21 weeks in adults and 13 weeks in children. The post-approval study will be an NCI-sponsored phase III trial conducted by COG and will include event-free survival at 4 years as an endpoint.

“It is very important to now have this drug available,” said Dr. Kimberly P. Dunsmore, associate professor of pediatrics at the University of Virginia Health System. “It’s proven to be quite effective in the phase I and II settings.” Nelarabine’s effectiveness in the trials to date is welcome, she adds, because patients have typically been refractory to other drugs tested for this indication.

Dr. Dunsmore is the principal investigator for a COG-conducted pilot study testing nelarabine upfront in patients with T-ALL or T-LBL who are at increased risk for relapse. The trial recently closed to accrual. ♦

### Featured Meetings and Events

A calendar of scientific meetings and events sponsored by the National Institutes of Health is available at <http://calendar.nih.gov/cgi-bin/calendar>. ♦

The *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads the national effort to eliminate the suffering and death due to cancer. Through basic, clinical, and population-based biomedical research and training, NCI conducts and supports research that will lead to a future in which we can identify the environmental and genetic causes of cancer, prevent cancer before it starts, identify cancers that do develop at the earliest stage, eliminate cancers through innovative treatment interventions, and biologically control those cancers that we cannot eliminate so they become manageable, chronic diseases.

For more information on cancer, call 1-800-4-CANCER or visit <http://www.cancer.gov>.

*NCI Cancer Bulletin* staff can be reached at [ncicancerbulletin@mail.nih.gov](mailto:ncicancerbulletin@mail.nih.gov).