THE CANCER LETTER

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FDA News

ODAC Nixes Sanofi's VTE Drug in 14-1 Vote, Setting High Bar For Adjunctive Therapies

By Paul Goldberg

If it's ever approved, the Sanofi drug semuloparin could become one of the most widely used drugs in oncology.

The company sought a truly gigantic indication for its low-molecular-weight heparin: prophylaxis of venous thromboembolism in patients receiving chemotherapy for locally advanced or metastatic solid tumors.

Even after FDA pressured the sponsor to narrow down the proposed indication to metastatic pancreatic or lung cancer or for locally advanced or metastatic solid tumors with a VTE risk score of 3 or above, the indication would have changed everyday practice of oncology.

This change is now unlikely to occur. On June 20, the FDA Oncologic Drugs Advisory Committee resoundingly voted down semuloparin, sending a message to everyone developing adjunctive therapies for cancer:

Define the population of patients who stand to benefit from your therapy. A clinician's intuition is not good enough. Sorry.

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News Analysis

Legislation on Drug Shortage Crisis Moves Toward Passage on Capitol Hill

By Rena Conti

In recent weeks, Congress made significant progress on identifying plausible causes of widespread and persistent drug shortages and addressing the ongoing crisis.

On June 4, less than a week after the Senate passed its version of a bill amending the user fee provisions of the Food, Drug and Cosmetic Act for funding FDA review of innovator and generic drugs, medical devices and

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Appropriations

Senate Increases NIH Funding for 2013, Rejects President's $200+ Million Increase For Program Evaluation Activities

By Matthew Bin Han Ong

The Senate Appropriations Committee slated $30.7 billion for NIH in the next fiscal year—a $100 million increase over the current level—and recommended an appropriation of $5.08 billion for NCI.

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ODAC: Semuloparin Application Failed To Define Target Population

(Continued from page 1)

By voting 14-1 with one abstention against approval, ODAC set a high bar—perhaps an impossibly high bar—for approval of supportive therapies.

"Cancer patients have a lot to deal with, just in treating their cancer with chemotherapy," said committee member Mikkael Sekeres, associate professor of medicine at the Department of Hematologic Oncology and Blood Disorders at the Cleveland Clinic Taussig Cancer Institute. "When we add adjunctive medicines to prevent potential complications, we have to be particularly careful in not also adding harm. I was not convinced that this drug prevented clinically significant clots, and I was not convinced that the bleeding that it did cause wasn't equally harmful."

Both the underlying cancer and the drugs used to treat it contribute to the formation of blood clots, and no drug is used for routine prophylaxis of these clots. Sanofi's strategy in its massive 3,212-patient, placebo-controlled trial was to focus on patients at the time when they receive chemotherapy, when clotting associated with treatment is added on to the clotting caused by the underlying disease.

"What would I do in my practice?" said Paul Bunn, the Dudley professor at the University of Colorado Cancer Center, who testified for Sanofi. "In my practice, when they stop their platinum doublet and they are getting maintenance, they are not going to get this drug. In my practice, for the high-risk patients, when they recur, I would put them on it. But the trial had people who had it in first-line and people who had second-line, and there was benefit in both."

The application was based on a single trial—SAVE-ONCO—a multinational, phase III, randomized, double-blind trial of patients who were to undergo chemotherapy for locally advanced or metastatic cancer of the lung, pancreas, stomach, colon/rectum, bladder, or ovary.

This would likely have produced the largest cancer indication in history. However, FDA officials had serious doubts, in part because some major tumor types—for example, breast and prostate cancers—weren't represented in the company's mixed-bag trial.

In the overall trial population, for every 1,000 patients treated, the drug prevented 22 VTEs or VTE-related deaths, while causing fewer than one major bleeding, the company said.

The company then conducted a post hoc analysis to isolate a population that FDA was willing to consider for an indication. Focusing on the metastatic pancreatic and lung cancer patients with a VTE risk score of 3 or above, the company found that for every 1,000 patients treated, the drug prevented 33 VTEs or VTE-related deaths, while causing fewer than one major bleeding.

Since the overall trial was positive, the committee didn't challenge validity of the post hoc analysis. However, both ODAC and FDA focused on clinical significance of the findings. At one point during the discussion, Richard Pazdur, director of the Office of Hematology and Oncology Products in the FDA Center for Drug Evaluation and Research, rattled off his list of big questions raised by the application:

"What is chemotherapy? Does this include oral chemotherapy drugs? Does it include only IV drugs? Does it include newer classes of drugs? How long does one give this? If you got it first-line, should you get it second-line, and what is the safety? What if you got it third-line?

"All approvals need to be put in a clinical context. It is not just the p-value."

One might argue that prophylaxis of VTE would be a logical thing to do. Alas, logic has been known to get oncologists into trouble both in cancer treatment and in supportive care.

Nearly two decades ago, in 1993, FDA approved red blood cell growth factors based on data pooled from six randomized, double-blind, placebo-controlled trials that, altogether, enrolled 131 patients. The patients had a mixed bag of cancers, and the data on that drug's

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detrimental impact on survival and disease progression wasn't measured until much later, in part due to FDA's eagerness to address the big questions and its skepticism about this class of drugs.

Regarding semuloparin? "This might be a really good drug," said ODAC's temporary member Tito Fojo, head of the Experimental Therapeutics Section of the NCI Center for Cancer Research. "I don't know that any drug could have succeeded in this setting. It was just too tall an order. You learn from experience, and this is one of those cases."

Fojo focused on the drug's harm, which includes the inconvenience of daily injections.

"The elephant in the room was never addressed, and that's the fact that you have to administer this subcutaneously every day," said Fojo before the vote was taken. "No patient likes that. We have been talking about death, about bleeding, but that's going to affect very few patients, but every single patient is going to have their quality of life impacted by these subcutaneous injections."

Focusing on Oncology

Sanofi has tried semuloparin in several indications for VTE prophylaxis. The company tested it in six phase III trials.

A seventh trial, in acutely ill medical patients, was initiated but stopped early. Overall, semuloparin was successful against placebo in the SAVE-ONCO and SAVE-HIP3 trials. However, the drug failed to meet the primary efficacy endpoint of any VTE or all-cause death in three of the four completed enoxaparin-controlled trials, including both superiority and non-inferiority study designs.

These trials were conducted in patients undergoing orthopedic surgery, including knee replacement (SAVE-KNEE) and hip fracture surgery (SAVE-HIP2), and in patients undergoing major abdominal surgery (SAVE-ABDO).

One of the four enoxaparin-controlled trials (SAVE-HIP1) met the primary efficacy endpoint (any VTE or all-cause death), but did not meet the secondary efficacy endpoint (major VTE or all-cause death).

The proportion of patients with under-planned dosing was larger in the enoxaparin group (10.6 percent) than in the semuloparin group (4.5 percent) for the safety population in this study.

If anything, oncology is more complicated than these other indications, FDA and ODAC members pointed out.

"We know in clinical practice that the longer patients live the more they become moribund, the more blood clots they get, and they die," said committee member Patrick Loehrer, director of the Indiana University Melvin and Bren Simon Cancer Center.

"In clinical practice, most people are not going to treat with three months of this drug while they are on one course of chemotherapy. They are going to go on to another course of chemo and put this drug with this other course of chemo. My concern is that this is no different from some of the other low-weight heparins.

"The bleeding episodes, the longer you are on, are going to separate."

FDA's Pazdur said the agency's staff struggled to define the population that could be treated based on SAVE-ONCO.

"One of the problems we had when we initially saw this indication was this broad indication of all cancer patients on chemotherapy," he said.

"There were big patient groups that were not represented. For example, there were no breast cancer patients. There were no prostate cancer patients. How possibly could we have approved the drug for an indication where you had huge populations of patients—probably the ones that were most likely to get it—not receiving the drug [in the trial]?

"That's why we asked the sponsor to come back and redefine the population.

"Still, we have a lot of unanswered questions. What chemotherapy are we talking about here? Not all chemotherapy is created equal. Not al chemotherapy has the same chance of being thrombogenic.

"The population of patients is somewhat disturbing. The major problem we are having is not only do we have to demonstrate favorable risk/benefit, but we also have to define in labeling a patient population that most likely is going to benefit.

"This has been the crux of the reason why we brought it to the committee.

"For most of the other prophylactic anticoagulants—for hip or knee [surgery]—we are talking about a very limited period of time. You have surgery. You are going to get this drug for a period of a couple months, and it's well understood that these people are going to be immobile, and that's why they are being anti-coagulated.

"This is heterogeneous population of first-line, second-line, potentially, third-line treatment. Is it the chemotherapy or is it the disease that we are dealing with? Is it a constructed indication rather than a real indication?

"Remember, in treatment of DVTs [in other indications], this drug went head-to-head with

enoxaparin and did not meet the non-inferiority endpoint.

"We have 25-years-plus of low-molecular-weight heparins. To say that this drug reduces deep venous thrombosis, compared to a placebo, is not a surprise.

"The issue is how you put this into the clinical context."

Committee chair Wyndham Wilson, chief of the Lymphoma Therapeutics Section of the NCI Center for Cancer Research Metabolism Branch, echoed Pazdur's misgivings.

"We see a trial here, where a drug is used in what is now considered not to be a standard clinical setting: during the use of chemotherapy and only during the time when chemotherapy is given," Wilson said. "The overall trial did, in fact, show a very significant p-value, but the question before us is not a matter of whether there is a statistically significant effect, but whether there is a clinically meaningful effect.

"For the overall trial, that really translated into a 2-percent absolute incidence reduction in VTEs. I cannot get my hand around whether this reduction led to any overall reduction in quality of life, other safety issues further down line, because that data was not collected.

"What we do know is that there was major bleeding into organs on the treatment arm. The problem I am having is that we have already seen that the indication has been narrowed in a secondary analysis, which always makes me uncomfortable.

"And, as a number of members of the committee have pointed out, the incidence of clots probably increases over time with cancer, but the hypothesis here is that the increased incidence of clots due to chemotherapy—on top of the cancer—is what they are really targeting."

Kyprolis Gets a Nod in Multiple Myeloma

In another action, which signals that single-arm studies can still convince ODAC, the committee voted 11-0 [with one abstention] to recommend approval of Kyprolis (carfilzomib) for relapsed and refractory multiple myeloma.

The drug's sponsor, Onyx Pharmaceuticals Inc., is seeking an accelerated approval for the multiple myeloma patients who received at least two prior lines of therapy that included a proteasome inhibitor and an immunomodulatory agent.

The Prescription Drug User Fee Act date for completion of FDA review for accelerated approval of the Kyprolis NDA is July 27.

The Kyprolis NDA is based on the 003-A1 study, an open-label, single-arm Phase IIb trial, as well as supportive data from additional studies.

The 003-A1 trial evaluated 266 heavily-pretreated patients with relapsed and refractory multiple myeloma who had received at least two prior therapies, including bortezomib, and either thalidomide or lenalidomide.

According to the company, Kyprolis is being studied in several clinical trials either as a single-agent or in combination with other therapies, including:

• A global phase III clinical trial, ASPIRE, has completed enrollment and is evaluating the combination of lenalidomide and low-dose dexamethasone with or without Kyprolis in patients with relapsed multiple myeloma who have received one to three prior therapies. The company has an agreement with the FDA on a Special Protocol Assessment and has received scientific advice from the European Medicines Agency on the design and planned analysis of the trial.

• A phase III clinical trial, FOCUS, is evaluating single-agent Kyprolis in patients with relapsed and refractory myeloma who have received three or more prior therapies. The trial is designed to facilitate regulatory approvals around the world.

• A global phase III clinical trial, called ENDEAVOR, is planned to begin enrolling patients in mid-2012. The head-to-head trial will evaluate the combination of Kyprolis and low-dose dexamethasone versus the combination of bortezomib and low-dose dexamethasone.

• A phase I/II study being conducted by Onyx's partner, Ono Pharmaceutical Co. Ltd., is evaluating Kyprolis in Japanese patients with relapsed/refractory multiple myeloma.

In another development, four members have rotated off ODAC. They are: Wilson; Loehrer; Kevin Kelly, director of the Division of Solid Tumor Oncology and associate director of translational research at Thomas Jefferson University; and Ralph Freedman, clinical professor at the Department of Gynecologic Oncology at MD Anderson Cancer Center.

News Analysis

Drug Shortage Legislation Moves Toward Completion

(Continued from page 1)

biosimilars (S. 3187; Food and Drug Administration Safety and Innovation Act), the House passed its version of the bill (H.R. 5651; Food and Drug Administration Reform Act of 2012).

Like the Senate bill, the House version reauthorizes prescription drug (PDUFA; Title I) and medical device (MDUFA; Title II) user fees, as well as establishing new user fees for generic drugs (GDUFA; Title III) and biosimilars (BsUFA; Title IV) and includes specific provisions aimed at ameliorating current and future drug shortages.

There are some differences in the House and Senate bills, which will need to be reconciled before it is ready for President Barack Obama's signature.

On June 15, the House of Committee on Oversight and Government Reform released its final report on the economic causes of the drug shortages (http://oversight.house.gov/wp-content/uploads/2012/06/6-15-2012-Report-FDAs-Contribution-to-the-Drug-Shortage-Crisis.pdf).

The committee report contains some under-substantiated claims of the shortages' causation that should be the subject of future empirical study.

The legislation now moving through Congress calls for the generic drug industry to pay $299 million annually in user fees for the next five years, beginning Oct. 1. This funding is supplemental to what Congress appropriates to FDA each year and will enable the FDA's Office of Generic Drugs to provide timely approval of generic medicines, and increase funding for inspections of generic manufacturer facilities, which are required before new generics can be approved.

The bill will act to lower the costs of production and generic manufacturers' risk of producing specialty injectable and infusible drugs, substantially ameliorating causes of the widespread, persistency of the crises in four ways.

First, the GDUFA part of the bill will speed generic abbreviated new drug approvals. Both the House and Senate versions the bill call on FDA to review 90 percent of ANDAs within 10 months of submission—almost two years faster than the current practice.

Recent reports document an increase in the number of new ANDAs for cancer drugs between 2006 and 2011, preceding and coincident with shortages. Generally, the manufacturing of new ANDAs is undertaken by existing generic manufacturers with experience in the manufacturing of similar drugs given the complexity of their manufacturing and attendant investment risks.

These new opportunities appear to entail their own risks, in part because of FDA backlogs in the approval process. These forces have been linked to increasing the costs of manufacturing specialty injectable or infusible drugs to generic manufacturers, contributing to the widespread and persistent crises among these drug types.

Second, the bill provides increased resources to the FDA to conduct facility inspections and re-certifications in domestic and abroad manufacturing facilities. It enhances the FDA's ability to conduct risk-adjusted, biennial, current Good Manufacturing Practice surveillance inspections of active pharmaceutical ingredient manufacturers and finished drug products, with the goal of achieving parity of inspection frequency between foreign and domestic firms in fiscal year 2017.

Since it is clear the proximal cause of the shortages are significant lapses in facility maintenance among manufacturers, this program will help ensure that noncompliant finished product or intermediate manufacturers within the drug supply chain, wherever they are based, are identified in order to ensure the safety of drugs in the U.S.

Third, GDUFA addresses the unintended consequences of the 30-month forfeiture provision in the Medicare Modernization Act of 2003. The average approval time for an ANDA is now stretching beyond 30 months, five times longer than the statutory six-month review time.

While GDUFA will help to lower this approval time to 10 months over the next five years, in the short-term this delay is causing some generic manufacturers to forfeit the 180-days of market exclusivity period they would gain by successfully challenging a branded drug's patent under Hatch-Waxman provisions.

This likely contributed to delays in the entry of willing manufacturers to supply drugs, including some reported to be in short supply preceding and coincident with the crises unfolding.

Finally, the parts of the bill addressing drug shortages will require manufacturers to notify the FDA six months in advance of a reduction in supply and/or quality of control problems. It will also increase the transparency of potential supply interruptions and improve the timeliness of identifying and coordinating the willingness and ability of existing domestic manufacturers to increase production in case of shortfalls by the FDA.

This will directly address some problems

encountered by the FDA in anticipating short term supply interruptions, and proactively working with current drug manufacturers to increase supply, precipitating persistent shortages among many drugs.

The House Committee's report also acknowledges increases in the regulatory costs and risks of producing these drugs may have led to the widespread and persistent nature of the shortages.

Specifically, it argues increases in the FDA's regulatory enforcement of facility certification and recertification in accordance with good manufacturing practices may have led to widespread reductions in the supply of many drugs and their persistence. This is consistent with the provisions of the passed legislation increasing resources to the FDA to consistently enforce current safety statutes.

The report also argues that changes in Medicare's reimbursement to physicians, enacted in the MMA, precipitated the shortages. This contention is only partially supported by currently available empirical evidence.

The report relies for justification largely on a recent unpublished economic analysis.

The analysis argues that drugs commonly used by Medicare beneficiaries are more affected by the shortages than those which are not, and therefore alterations in Medicare payment policy enacted in 2003 are largely to blame for increasing shortage reports among these drugs in 2008-2011.

The analysis is fundamentally flawed since it ignores other alterations in costs and risks of manufacturing these drugs which occurred preceding and coincident with the shortages including the increase in the number of ANDAs and the FDA's backlog in approving them, increases in FDA regulatory enforcement of facility certification and recertification starting in 2008, increases in the prices of approved pharmaceutical ingredients due to increasing worldwide demand for pharmaceutical products and quality interruptions.

These factors among others could have plausibly affected the willingness and ability of generic manufacturers to produce these drugs, resulting in the emergence of concentrated supply in many of these markets. Some of these concerns are in part addressed in the recently passed legislation.

However, the unpublished economic analysis perpetuates a misunderstanding regarding the link between Medicare reimbursement policies and generic manufacturers' willingness to produce these drugs. In theory, decreases in revenue (due to decreases in the prices paid for these drugs) could induce manufacturers to skimp on the quality of products produced, decrease the volume produced or exit the supply of some drugs altogether.

Unlike the oral drug market, physicians and hospitals should be considered the direct consumers of these drugs; they purchase the drugs from wholesalers and distributors, and, in turn, are reimbursed by insurers when the drugs are administered to patients.

Outpatient oncology practice revenues have been traditionally tied to the difference between insurer reimbursement for infused specialty drugs and their wholesale acquisition cost negotiated on their behalf by the purchasing channels including group purchasing organizations. The difference is commonly called cost recovery.

It is true that reimbursement to physicians for the administration of generic specialty injectable and infusible drugs by the Centers for Medicare and Medicaid has declined over the past decade.

The MMA switched the reimbursement benchmark for these drugs from average wholesale price (or in some cases 95 percent of AWP) to 106 percent of the Average Sales Price (commonly referred to as ASP+6%) effective January 1, 2005. ASP represents the final price end users paid for each product averaged over most purchasers, reported directly to the CMS by each manufacturer starting in April 2004. Payments for existing drugs given to patients by physician practices in the outpatient setting were switched over to the ASP payment system with a two-quarter lag in January 2005.

It is also clear these reimbursement declines have put pressure on oncologists' practice revenues. These pressures have been linked to decreases in the number of private medical specialty practices observed between 2005 and 2008. These pressures have also been linked to the emergence of group purchasing organizations in the past two decades to negotiate the prices and quantity of bundles of drugs on their members behalf.

There is limited empirical evidence to support (or reject) the proposition that physicians and hospitals are

passing down the reimbursement deceases for generic specialty drugs to manufacturers through existing contracting arrangements in whole or in part. Whether this is occurring largely depends upon the bargaining power of the manufacturers to wring prices from purchasing groups for the bundle of drugs they produce.

Markets with limited suppliers would likely have more bargaining power than those with significant generic entry and competition all else equal. Understanding trends in the bargaining power of physicians, hospitals and group purchasing organizations to obtain price concessions from largely generic drug manufacturers is a critical avenue for empirical work on the economic foundations of the shortages.

There is another way MMA reimbursement changes could affect the supply of these drugs—by rewarding physicians for the use of higher priced patent protected therapies that offer physicians higher cost recovery over generic substitutes. Recent empirical work suggests physicians do appear to make prescribing decisions in part based upon variations and alterations in the reimbursement they receive from payers, holding patient benefit from a given therapy constant.

Alas, empirical work in this area is in its infancy. This rationale's contribution to the shortages also controverts observed increases in the demand for oncology and immunology drugs previous to the shortages. Myself and other independent observers believe that these increases in demand are, in part, related to the use of generic drugs in combination with newer branded therapies—in effect, acting as complements in treatment rather than substitutes. It is very difficult in empirical work to robustly separate out changes in guideline adherent therapy due in part to the introduction of new branded specialty pharmacotherapies from changes in these reimbursement incentives.

This is also a critical avenue for future empirical investigation.

Rena Conti is a health economist in the University of Chicago Section of Hematology/Oncology, Department of Pediatrics, and is a faculty affiliate at the University of Chicago Comprehensive Cancer Center.

Appropriations

Senate To Increase NIH Funding By $100 Million in Fiscal 2013

(Continued from page 1)

The committee rejected the Obama administration's proposal for an increase on a program evaluation "tap" on Public Health Service agencies from 2.5 percent to 3.2 percent, maintaining the tap at 2.5 percent.

Called the PHS Program Evaluation Transfer, the budget tap is used to fund program evaluation activities**.** The NIH, as well as other PHS agencies, are subject to allocating a certain percentage of their budget to fund these activities.

The committee noted that over $200 million would be cut from NIH's net appropriation had the tap increase been implemented in the administration's budget proposal—a 0.65 percent cut, which would have brought NIH's 2013 budget below the level of the current year.

Recommended funding levels for some NIH institutes and centers dropped below the fiscal 2012 levels, reflecting reallocation and redistribution of funding in the budget request, but funding for most increased by the same percentage for fiscal 2013.

Of the $5.08 billion allocated for NCI, $8 million is available for repairs and improvements to the NCI facility in Frederick, Md.

The committee encouraged NCI to continue to fund and support research on a number of fronts, including breast, liver, pancreatic and pediatric cancers.

The NIH budget level has remained mostly flat for the past decade—and when factoring in the rate of biomedical inflation, the agency has lost about $6 billion in purchasing power—according to a press release from the American Association for Cancer Research. As a result, the chances that a researcher will be awarded an NIH grant are at an all-time low, the press release said

Senators Dianne Feinstein (D-Calif.) and Kay Bailey Hutchison (R-Texas), of the Senate Cancer Coalition, said in a recent breast cancer forum that a majority of senators are advocating for an increase in funding for cancer research—in spite of a flagging economy and a march against increases government spending.

"I cannot say whether as much as $6 billion (that the NIH lost) can be regained, but I know we're making it a priority where funding for cancer research is concerned," Hutchison said Tuesday.

The text of the Senate report follows:

The Committee provides $30,731,459,000 for NIH

activities within the jurisdiction of this bill, including $8,200,000 in transfers available under section 241 of the PHS Act. The budget request is $30,631,459,000, the same as the fiscal year 2012 level.

The Committee notes that the net amount for NIH in the budget request would actually be a cut of more than $200,000,000 below the fiscal year 2012 level following implementation of the administration's proposal to increase the program evaluation tap on PHS agencies from 2.5 percent to 3.2 percent. As explained in the introduction to the HHS title in this report, the Committee rejects that proposed increase and maintains the tap at 2.5 percent.

The Institute and Center appropriation levels listed below for fiscal year 2012 reflect the transfers announced by HHS in April to increase funding for Alzheimer's disease research.

Recommended funding levels for some ICs are slightly below the fiscal year 2012 levels, or increase less than others, due to small reallocations or changes in scientific opportunity reflected in the administration's budget request. For example, the Committee agrees with the administration that all of the funding for public access activities and the National Center for Biotechnology Information should be provided directly to NLM beginning in fiscal year 2013 instead of partly through direct funding to NLM and partly through contributions from other ICs. This change accounts for the relatively large apparent increase for NLM and some minor reductions to other ICs. In addition, as in prior years, the recommended levels for the ICs reflect a redistribution of funding for AIDS research, as some ICs increase their work in this area and others do less.

Other than these reallocations, funding for most of the ICs is increased over the fiscal year 2012 levels by the same percentage.

NATIONAL CANCER INSTITUTE

Appropriations, 2012	$5,067,396,000
Budget estimate, 2013	5,068,864,000
Committee recommendation	5,084,227,000

The Committee recommends an appropriation of $5,084,227,000 for NCI. Of this amount, $8,000,000 is available for repairs and improvements to the NCI facility in Frederick, Maryland.

Angiogenesis - The Committee commends NCI for planning a scientific workshop to explore the effect of medication, diet, and lifestyle on angiogenic levels. The Committee encourages NIH to use this workshop to engage with the Trans-Institute Angiogenesis Research Program on implementing a vigorous agenda that examines current angiogenesis therapies in order to improve outcomes. The Committee also encourages NCI to examine angiogenic levels in the body prior, during, and after treatments. In addition, all relevant Institutes are urged to coordinate efforts to study the correlation of platelet proteomes to angiogenesis with the goal of developing a health marker.

Breast Cancer - The Committee remains concerned about the toll of triple negative breast cancer and urges NCI to collaborate with ORWH, NIMHD, OMH, and OWH to help improve treatment and survival rates.

Cancer Disparities - The Committee urges NCI to fund basic, translational, and clinical research on cancer disparities in regions of the country that have a high predominance of economically disadvantaged African Americans. Specifically, the Committee urges further research on novel immune therapeutics intervention in cancer areas relevant to human papilloma virus and genomics etiologies in cancer areas relevant to smoking and obesity.

Liver Cancer - The Committee recognizes NCI's efforts in the area of liver cancer, but encourages a stronger effort to include funding of a specialized program of research excellence on this disease as well as liver cancer program projects focusing on pathogenesis, detection, and/or therapeutics.

Lung Cancer - The Committee commends NCI for its National Lung Screening Trial and urges the Institute and partner agencies to move forward in translating these findings into public health recommendations. The Committee requests an update in the fiscal year 2014 congressional budget justification about the benefits of screening among high-risk groups including women, African-American men, and those with other co-morbidities.

Melanoma - The Committee continues to encourage NCI to support research directed at the biology of tumor initiation including UV radiation as a carcinogen, the immunologic and addictive effects of UV radiation, host risk factors, and risk reduction strategies. Research into the relative utility of novel early detection strategies is encouraged, including leveraging recent advances in imaging technology. Despite two recent drug approvals for advanced melanoma, cures are rare. Research strategies with

curative potential that build on these advances should be supported, including examining mechanisms of drug resistance to molecularly targeted therapies such as BRAF gene inhibitors. The Committee also urges more research on treatment strategies for the 50 percent of patients without BRAF mutations, as well as on predictive biomarkers that correlate with immune response to ipilimumab. Finally, the Committee urges NCI to promote collaborations between industry, the extramural program, and foundations that will accelerate translational and clinical research.

Minority Communities - The Committee continues to remain concerned at the disproportionately high rate at which minority populations suffer from virtually every form of cancer. The Committee requests that NCI and NIMHD prepare a joint report on efforts to end this disparity and effective ways to communicate with minorities on this important issue.

Neuroblastoma - The Committee encourages NCI to expand its research portfolio on this deadly pediatric cancer, including the development of new treatment options for children suffering from central nervous system [CNS] relapses. The Committee requests an update on this research, including the potential utilization of chimeric antibody immunotherapy for CNS-relapsed neuroblastoma, in the fiscal year 2014 congressional budget justification.

Pancreatic Cancer - While survival rates for many types of cancer have steadily improved, the rate for pancreatic cancer has remained in the single digits for over 40 years. With the number of new cases of pancreatic cancer projected to increase 55 percent between 2010 and 2030, the Committee urges NCI to create a comprehensive, long-term research strategy for this disease that focuses on increasing survival. The plan should not be simply a summary of recent and ongoing research activities. Rather, it should set out concrete goals for the future. The Committee requests an update in the fiscal year 2014 congressional budget justification on the steps NCI is taking to create such a plan.

Pediatric Cancer - The Committee continues to urge NCI to devote more of its funding specifically for research on pediatric cancer, including pediatric low-grade astrocytoma. The Committee requests an update in the fiscal year 2014 congressional budget justification, including efforts that could result in more effective, less toxic treatments.

Robotic Biorepository Technology - In order to determine the genetic differences in the development, progression, and response to treatment of individuals with cancer, biospecimens (e.g. blood, urine, tumor tissue) must be collected and evaluated. Under some circumstances, high throughput, robotic instruments for the processing and storage of biospecimens can improve the efficiency and consistency of handling and distribution of these samples. In an effort to adequately address the increasing demand for these specimens, an automated approach should be considered when appropriate. Robotic biorepositories may also allow researchers to expand the collection of tissue specimens. A related goal is to ensure an adequate supply of high-quality human biospecimens from multiethnic communities for research to understand and overcome cancer health disparities. The Committee encourages NCI to explore the applicability of robotic biospecimen collection technologies and the establishment of regional robotic biorepositories in an effort to advance cancer research.

Shared Medical Decisionmaking - The Committee encourages NCI's collaboration with OBSRR to study shared medical decisionmaking and to identify ways to improve communications between healthcare providers and their patients

Tumor Lysis Syndrome - The Committee understands that identifying high-risk patients, taking preventive measures, and closely monitoring patients are all key in fighting TLS, a life-threatening oncologic emergency that is frequently encountered during and/or after the treatment of a variety of cancers. The Committee encourages NCI to convene an expert panel or working group to evaluate current risk assessment models, recommend a standardized assessment tool, and develop a plan of action to validate and disseminate the tools in clinical practice.

In Brief

William Riley Appointed Chief Of NCI DCCPS Research Branch

WILLIAM RILEY was named chief of the **Science of Research and Technology Branch** in the Behavioral Research Program within **NCI's Division of Cancer Control and Population Sciences**.

He will help lead the institute's behavioral science methodologies, analytics, and approaches; theory development and application; and the application of technological advances to health behavior measurement and intervention.

Riley's research is in the application of new technologies, particularly mobile and wireless technologies, in behavioral measurement and intervention—and the potential of these technologies to assess and intervene with broad reach and scalability.

"Bill's experience and expertise fits well within SRTB's mission in the development and application of innovative research approaches, theories, methods, measures, analytic tools, and technologies to advance social and behavioral science in the context of cancer prevention and control," said Robert Croyle, DCCPS director. "His contributions to measurement science are impressive, including his recent work on the Patient-Reported Outcomes Measurement Information System."

Before his current NCI appointment, he was a health scientist administrator and deputy director in the Division of AIDS and Health Behavior Research at the National Institute of Mental Health and a program director at the National Heart, Lung, and Blood Institute. He also serves as a professorial lecturer in the School of Public Health at George Washington University.

JOSEPH PAUL EDER was appointed director of experimental therapeutics and the Phase I Research Group at **Yale Cancer Center and Smilow Cancer Hospital** at Yale-New Haven. He will begin July 1.

Currently, Eder serves as senior director of the Clinical Discovery Team at AstraZeneca, focusing on the design of Phase I clinical trials. He is also the medical science director of AstraZeneca's Boston site.

Eder also holds an appointment as an associate clinical professor at Harvard Medical School.

He is on the board of directors for the International Symposium on Drug Development and on the scientific advisory board for the International Symposium on Cancer Chemotherapy.

LAJOS PUSZTAI was named head of the breast cancer medical oncology team at **Smilow Cancer Hospital** and as director the breast cancer research group and co-director of the Cancer Genetics Research Program. He will begin Aug. 1.

He joins **Yale Cancer Center** from MD Anderson Cancer Center, where he currently serves as professor in the Department of Breast Medical Oncology in the Division of Cancer Medicine.

Pusztai's research focuses on the developing pharmacogenomic markers of response to breast cancer therapy and identifying methods to select the optimal treatment for each patient.

He is a member of the NIH Breast Cancer DataMart Steering Committee and the NCI Breast Cancer Groups Correlative Science Committee.

A. KIM RITCHEY was named president of the **American Society of Pediatric Hematology/ Oncology**.

Ritchey, chief of the division of pediatric hematology/oncology at the Children's Hospital of Pittsburgh, will take the place of Jeffery Lipton, chief of hematology/oncology at Cohen Children's Medical Center of New York.

Ritchey is the hospital's principal investigator for the Children's Oncology Group. He oversees clinical research trials in different types of childhood malignancy. The hospital is one of 20 COG institutions approved to perform Phase I studies for children.

MARGARET FOTI received the **Biotechnology Industry Organization's 2012 Biotech Humanitarian Award**.

Foti, CEO of the American Association for Cancer Research, is being honored for her efforts to foster cancer research and team science.

The award and a prize of $10,000 was presented during the keynote address at the 2012 BIO International Convention in Boston.

During her time as CEO, AACR's membership has grown from 3,000 to more than 34,000 laboratory, translational and clinical researchers; health care professionals; students; cancer survivors; and research and patient advocates.

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