THE CANCER LETTER

PO Box 9905 Washington DC 20016 Telephone 202-362-1809

Vol. 38 No. 31
Aug. 3, 2012

SPECIAL ISSUE

An Earmark for Pancreatic Cancer

Advocacy Group Amasses Support For Bill That Threatens Integrity of NCI Peer Review

By Matthew Bin Han Ong and Paul Goldberg

A bill moving rapidly through Congress directs NCI to spend $887.8 million over five years for pancreatic cancer research.

In addition to moving resources out of NCI's control at a time of flat budgets, the legislation gives NCI only a minor role in deciding how the massive new program would use institute resources.

The institute would have only one vote on a critically important 13-member panel that would allocate the funds.

According to opponents, the measure amounts to a vote of no confidence in NCI's ability to oversee pancreatic cancer research. It would catastrophically undermine the peer review system, touching off a round of what some on Capitol Hill call "disease olympics."

The Pancreatic Cancer Action Network, the advocacy group that launched the aggressive drive that resulted in the legislation, said the old approach hasn't produced results, citing small budgets for pancreatic cancer research and alleging that NCI has failed to respond to congressional mandates. The bill would roughly double the institute's spending on the disease.

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Conversation with The Cancer Letter

PanCAN CEO Denies Bill Would Undermine NCI's Role in Directing and Funding Research

The Pancreatic Cancer Research and Education Act, if passed in its current form, downgrades NCI to the status of a minority player in carrying out a congressionally mandated pancreatic cancer research agenda.

Though the language of the bill indicates that the institute would have little control over strategic decisions, Julie Fleshman, CEO of the Pancreatic Cancer Action Network, the organization behind the bill, said NCI's peer review system would remain intact.

"Our understanding is that authorizations are often written to the HHS secretary as a way to convey how important a priority the subject is," Fleshman said in an interview with The Cancer Letter. "But as a practical matter, the responsibility is subsequently delegated to the NIH or NCI director as the law is implemented."

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In-Your-Face Campaign Succeeds By Showcasing Morgue Toe Tags

(Continued from page 1)

PanCAN hired a lobbyist, put together a glossy fact sheet and staged an "advocacy day" on Capitol Hill. Legislators were handed morgue-style toe tags with the names of constituents who died from pancreatic cancer. A child recounted a family member's death from the disease, sources said.

The result: the bill, called the Pancreatic Cancer Research and Education Act (H.R.733 and S.362), has amassed the support of 279 House members and 58 Senate members. This means that some kind of a pancreatic cancer bill has an excellent chance of passing during the current legislative session.

The measure was introduced February 2011 by Reps. Anna Eshoo (D-Calif.), Leonard Lance (R-N.J.) and Sen. Sheldon Whitehouse (D-R.I.).

This political momentum makes critics—including many on the NIH campus in Bethesda—cringe at the prospect of interest groups competing for Congressional earmarks that would be doled out based on severity of disease and the advocates' ability to mobilize political clout, without regard for the quality of science or the opportunity to bring about clinical advances.

The bill specifically paves the way for other patient groups to seek similar approaches to bypassing NCI authority.

"This is not a disease-specific bill," PanCAN proclaimed in documents distributed on the Hill at the advocacy day June 26. "It includes a recommendation that the NCI develop a new grant program to focus on the other deadly cancers. The program would be piloted with pancreatic cancer (the deadliest major cancer), but could be expanded to include any cancer with a five-year survival rate below 50 percent, including brain, esophageal, liver, lung, myeloma, ovarian and stomach cancers."

To direct pancreatic cancer activities, the bill requires the HHS secretary to establish a 13-member coordinating committee including academics and a pancreatic cancer advocate. The panel will conduct evaluations and make recommendations to the HHS secretary regarding the prioritization and awarding of NIH grants. NCI will have only one vote on this panel.

"While I have tremendous sympathy for patients and families affected by pancreatic cancer, I find this bill quite disturbing," said Charles Sawyers, cancer research physician and scientist at Memorial Sloan Kettering Cancer Center, investigator at the Howard Hughes Medical Institute, and president-elect of the American Association for Cancer Research. "As a cancer researcher, I feel strongly that the existing NIH peer review system is an effective way to identify promising science across diseases.

"Any proposal that allows a separate committee that would exist outside the existing NIH peer review system to prioritize and make funding recommendations puts the entire peer review process at risk," said Sawyers, speaking only for himself, and not for any of the organizations with which he is affiliated. "Furthermore, this bill would establish a dangerous precedent that could balkanize our field at precisely the wrong moment.

"We are learning that different cancers share molecular features and that treatments developed for one disease can be quickly leveraged to impact others. Unfortunately, certain provisions in this bill run the risk of losing that synergy. What we really need is a commitment of sustained NIH funding across cancers."

A Lack of "Funding, Focus, and Commitment"

The pancreatic cancer legislation criticizes NCI for a lack of "funding, focus, and commitment" on the institute's part to implement pancreatic cancer initiatives over the past decade and for allocating only two percent of its federal funding to pancreatic research.

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202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $405 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

Though the bill plainly states that it would shift coordination and prioritization of pancreatic cancer research away from NCI, Julie Fleshman, CEO of PanCAN, said that the NCI peer review system would continue to function as it does.

"The Pancreatic Cancer Action Network reads the bill as creating a committee that provides recommendations to the NCI director, but does not change the NCI's peer review process," Fleshman said in an email exchange with The Cancer Letter.

"Our understanding is that authorizations are often written to the HHS secretary as a way to convey how important a priority the subject is," Fleshman said. "But as a practical matter, the responsibility is subsequently delegated to the NIH or NCI director as the law is implemented." The interview appears on p. 1.

PanCAN's advocacy day documents accuse NCI of being insufficiently interested in the disease and unresponsive to concerns from legislators.

"It is time for the National Cancer Institute to develop a long-term and comprehensive research strategy that specifically addresses pancreatic cancer," one PanCAN handout alleged. "Congress has repeatedly asked the NCI to address this issue, but the NCI has failed to respond to Congressional requests. It is time for Congress to take action, as it has done for other diseases, by requiring the NCI to develop a strategic plan for one of our nation's leading cancer killers."

Recently, while updating an NCI advisory committee, NCI Director Harold Varmus said the controversy over pancreatic cancer had come up at NIH appropriations hearings.

The institute has, in fact, increased funding for pancreatic cancer research, Varmus said to a joint meeting of the National Cancer Advisory Board and the Board of Scientific Advisors June 25.

"I personally had six friends who died from this disease in the last five years," Varmus said to the two boards. "We have increased our funding of pancreatic cancer research by 300 percent in the last 10 years, despite a flat budget.

"Of course, we can't just pour all of our money into pancreatic cancer research, but there is no doubt that there is significant concern, and I'd like to kind of meet those concerns in an equitable way," said Varmus, whose lab at NCI is involved in pancreatic cancer research.

In a recent press release, bill sponsors Eshoo and Lance cited past earmarked funds for research on breast cancer, Alzheimer's, autism, diabetes and HIV/AIDS as precedent for enacting a similar legislation for pancreatic cancer.

"While the strategic plan required by the bill would provide a critical tool for making progress in this terrible disease, nothing in the bill specifically requires NCI to allocate taxpayer dollars for disease-specific research," wrote Eshoo and Lance in a letter to the Committee on Energy and Commerce. "NCI would continue to set priorities, and grants would continue to be awarded on a peer-reviewed basis."

This is, at least in part, correct. The bill authorizes spending funds on pancreatic cancer. Appropriations would be determined through a separate legislative process. However, in the era of flat budgets, it is inconceivable that funds can come from any place other than the NCI budget, thereby lowering the amount of funds available for other research.

Effort Differs from Defense Department Program

The fact that a relatively small advocacy group like PanCAN, based in Manhattan Beach, Calif., was able to amass so much congressional support demonstrates just how vulnerable NCI is to earmarking.

PanCAN raised $13.3 million in 2010, according to tax documents, and spent $1.5 million on "government affairs and advocacy."

The group's lobbyist, Joel White, is a former Republican Capitol Hill staff member, whose other clients include the Pharmaceutical Research and Manufacturers of America and a coalition seeking to maintain Medicare Part D coverage.

He appears to be representing PanCAN pro bono: http://www.opensecrets.org/lobby/firmsum.php?id=F27076.

The group's public relations campaign is handled by AK PR Group.

During this legislative session, PanCAN published an advertisement showing a pair of feet, presumed to belong to a dead pancreatic cancer patient, with a morgue toe tag attached. Penciled in on the tag is the number of U.S. pancreatic cancer-related deaths over the past five years and the disease's low survival rate. The text of the ad reads: "Pass this bill so thousands more won't pass away."

PanCAN provided similar toe tags to the 650 participants of the June 26 advocacy day. Each of these tags contained a blank that could be filled in with the name of a patient who had died of pancreatic cancer.

The participants were instructed to leave the tags with the congressional offices after their meetings with all 100 Senate members and 371 of 435 House members.

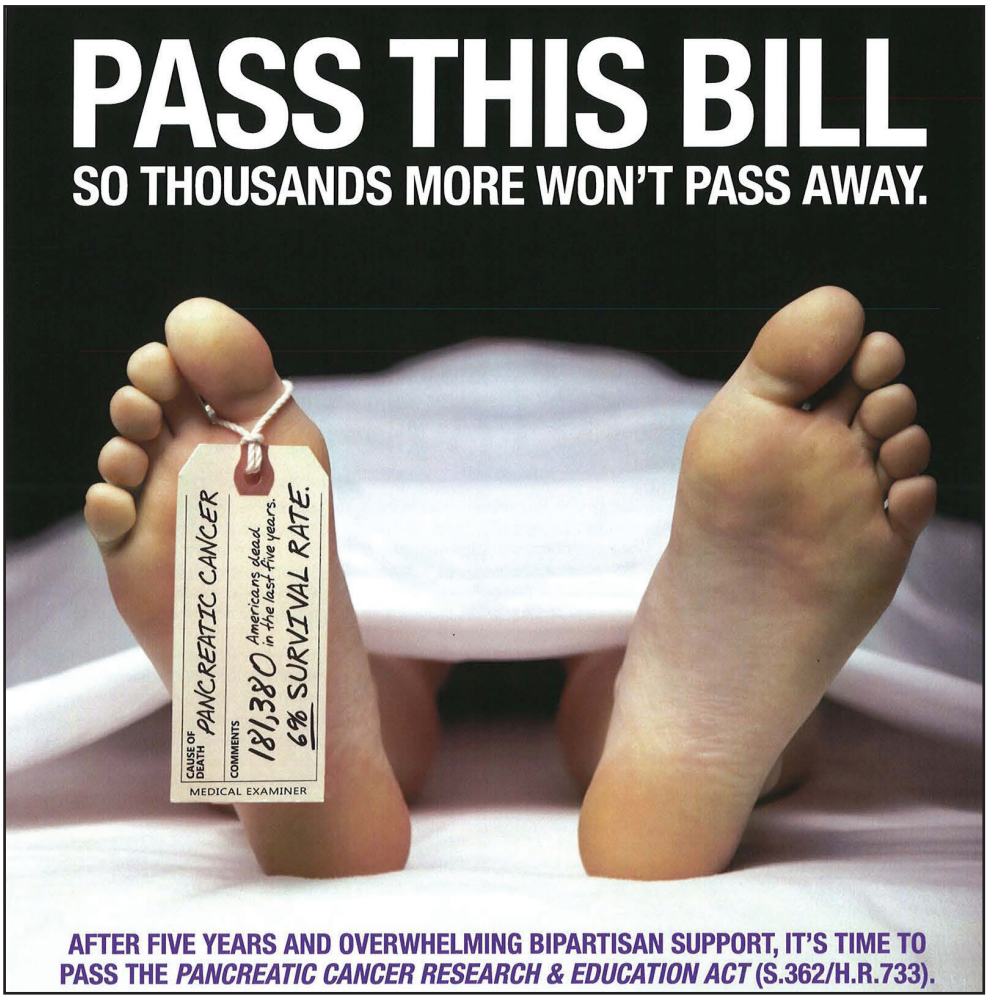
"I feel strongly, as does the Pancreatic Cancer Action Network, that we must be aggressive and

even shocking to get our message heard above all of the others that legislators hear each day," said Richard Orr, PanCAN advocate and pancreatic cancer survivor, in a letter published on PanCAN's website: http://bit.ly/QnnPxr.

"We expect members of the Congress and their staff to be shocked by this tactic and believe that this is a good thing as it will be impossible to ignore," Orr wrote. "As a result, they will not be able to ignore our message that they must pass the bill this year."

PanCAN isn't the only cancer organization to employ in-your-face tactics.

The Lung Cancer Alliance has been advocating changing current practices to include screening for early-stage lung cancer, working closely with the International Early Lung Cancer Action Program. LCA's "No One Deserves To Die" campaign of public service announcements, is similarly designed to shock: http://www.noonedeservestodie.org/.



The Pancreatic Cancer Action Network distributed this image to shock and provoke legislators into passing the Pancreatic Cancer Research and Education Act. PanCAN provided similar toe tags to 650 participants at the June 26 advocacy day—each had a blank that could be filled in with the name of a patient who had died of pancreatic cancer. A packet of PanCAN's advocacy materials can be downloaded at http://www.cancerletter.com/categories/documents.

Arguments over earmarking funds for specific diseases have been a part of the cancer funding process for at least two decades. However, no group has ever tried to bypass the NIH peer review system while keeping the money within HHS.

Why didn't PanCAN try to take pancreatic cancer research outside NCI, to the Department of Defense? At DOD, such research programs are rigorously reviewed.

Fleshman said the idea of building a program within DOD was discarded to allow maximum collaboration with institutions receiving NCI funding.

"Unlike many other cancers, the only federal institute that is truly looking at pancreatic cancer in any real way is the NIH and the NCI," she said.

At NIH, the institutes set their own spending priorities.

If the bill passes, pancreatic cancer would become the largest earmarked cancer program within the federal government. With $177.6 million a year to spend, it would overtake the DOD breast cancer program, which received $120 million during fiscal 2012. According to PanCAN, pancreatic cancer currently receives approximately $99 million a year from NCI.

The fundamental question is whether scientists have the leads that would make it possible to put additional funds to good use.

"The notion that there are only a few leads on the etiology of pancreatic cancer is erroneous," Fleshman said. "Over the past decade, scientists have gained a much better understanding of pancreatic cancer and

what makes it unique biologically.

"For instance, scientists now know that there is a dense microenvironment that surrounds the pancreatic cancer tumor and that understanding this microenvironment will help aid in drug delivery. Further, scientists now know about the genetics of pancreatic cancer, including the genes that need to be targeted, like the KRAS gene. KRAS is present in 90 percent of pancreatic cancer cases. Additionally, there is a genetically engineered mouse model for pancreatic cancer that allows scientists to test drugs. Scientists believe that these mice mimic how the test drugs would react in humans.

"And due to increased efforts of the NCI and private foundations, there are a growing number of scientists—senior and junior—focusing on pancreatic cancer. This was perhaps best evidenced by the first ever American Association of Cancer Research special conference for pancreatic cancer, which occurred a month ago. The conference had 450 attendees and was considered a great success.

"However, there is still more progress that needs to be made. One area that is particularly problematic is the number of researchers. While there is a growing field of researchers dedicated to pancreatic cancer, it is still very small compared to the amount that we need to truly make progress. For example, the number of training grants and significant grants of $500,000 or more, which sustain laboratories, are generally much less than those funded for the other leading cancer killers. There aren't enough scientists in the field directly related to the resources available."

While this information has been discovered—mostly as a result of NCI funding—hardly any of it is ready to be translated into clinical advances, critics say.

David Tuveson, a pancreatic cancer researcher, said the federal government has the potential to advance pancreatic cancer research if it proclaims that clinical trials are the standard of care for the disease and if it funds a large number of proof of concept studies.

"I am not advocating bypassing peer review; I never would advocate that," said Tuveson, a professor at the Cold Spring Harbor Laboratory and co-chair of a recent PanCAN-AACR meeting on pancreatic cancer research. "I am advocating increased concentration by regulatory agencies and by funding bodies on pancreas cancer."

Tuveson was not involved in work on the PanCAN bill and was not familiar with its provisions, he said.

"We have to be an evidence-based effort, and I would not advocate loosening peer review," Tuveson said. "I would advocate increasing the spending on hypothesis-driven research conducted in the clinic and in the laboratory for pancreas cancer patients.

"If NCI is willing to fund proof of concept trials that physician scientists direct, where they can determine in small and very organized clinical studies, then I would support continuing the process," Tuveson said.

"If they are going to continue to ignore this serious need we have in the field, then we have to find an alternative funding arrangement. They have to do it in the clinical realm. If they take it back from CTEP, take it back from PhRMA, they are not going to do it properly, if they are going to allow the academics drive that discovery process, then I would remain a full supporter of the peer review system we have now.

Tuveson, who recently came to Cold Spring Harbor from Cancer Research UK and Cambridge Research Institute, said the U.S. government should sponsor innovative clinical trials, "where we have multiple companies giving their drugs and you are able to test them in combination, just like during the HIV days, when arm-twisting by activists and a little intervention by the government allowed combination trials to get off the ground.

It's possible to move research forward faster, Tuveson said.

"The trials that I want are ones that are science-driven proof of concept—prove your principle—in patients, and those are not trials supported by the private sector, by and large, not supported by our government, by and large," Tuveson said. "We are not funding the essential first step in the fight against this disease."

Bill to Create Two SPOREs

Under the pancreatic cancer legislation, $733 million will be allocated over five years for the creation of the coordinating committee, which will develop a plan to review pancreatic cancer grant applications—including grants awarded through NCI—and to enlist additional review personnel.

The committee will supervise the budget for an additional incubator pilot project as well as two Specialized Programs of Research Excellence, which would be designed to focus solely on pancreatic cancer research.

This aspect of the proposal is particularly noteworthy at a time when NCI officials are talking about cutting SPOREs as part of reprogramming the institute's resources.

Besides the $733 million earmarked for the main initiative, the bill authorizes:

• $107.5 million for two SPOREs focusing solely on pancreatic cancer research. The secretary may choose to designate one or more satellite centers that augment the work of a previously designated SPORE.

• $26.3 million for a new incubator project, allowing the HHS secretary to award five-year grants to research institutions for use in pancreatic cancer research. Recipients of these grants will be encouraged to use the funds for research activities that may serve as a "springboard" for the receipt of other grants, including SPOREs grants, from the NIH.

• $10.5 million for a primary care provider education program, which the secretary will develop in consultation with NIH, CDC and patient advocates. Accredited continuing medical education programs and activities may be included as the secretary deems appropriate.

• $10.5 million for the development of a communication toolkit for patients and families, which requires NCI and CDC directors to work with patient advocacy organizations such as PanCAN to focus on specific pancreatic cancer issues.

"We hope to be included in that discussion as well," Fleshman said. "The Pancreatic Cancer Action Network has a good relationship with NCI, so we would welcome the opportunity to work closely with them as they implement the bill."

Collaboration With AACR

In a related development, PanCAN has been working closely with AACR in designing an agenda for accelerating progress against pancreatic cancer.

The two organizations held a meeting on the "progress and challenges" in pancreatic cancer at Lake Tahoe June 18-21, forming a joint Scientific Review Committee. The meeting's co-chairs included Daniel Von Hoff, of Translational Genomics Research Institute, Dafna Bar-Sagi, of New York University School of Medicine, Chi Van Dang, director of the University of Pennsylvania Cancer Center, and Cold Spring Harbor's Tuveson.

The review committee formed by PanCAN and AACR "will oversee a new grant opportunity that provides a 1-3 year grant of $1,000,000 to an existing, multi-institutional, clinical or translational research project within the pancreatic cancer research community," said AACR CEO Margaret Foti in a recent letter to a scientist who agreed to serve on the committee.

The text of Foti's letter follows:

The current grant review and selection process is as follows: Letters of Intent (LOI) will be accepted between late August and early October. Once all submitted LOIs are reviewed by AACR staff for eligibility and compliance, committee members are directed to access proposal CENTRAL to view the LOIs and select those most suitable to review based on their scientific knowledge.

Committee members must also indicate whether any LOI constitutes a conflict of interest. Each LOI will be assigned to at least 3 committee member reviewers that will have approximately three weeks to complete their critiques. Once the LOI reviews are completed, AACR staff will compile the scores and comments, and provide the results to the committee.

A conference call with the committee will then be held to select the applicants worthy of proceeding to the full application phase (25% of the LOIs). We anticipate this call to be held in late November/early December. Once all full applications are received, the application review period will begin in January of 2013. A second teleconference will then be held in February to select the finalists as well as primary and alternate grantees.

For the remainder of your two-year term, based on confirmation from the award supporter, this grant may be launched once more with the review and selection process occurring between October 2013 and February 2014. Throughout this time, AACR's Scientific Review and Grants Administration staff will provide full support and guidance to both you and the committee.

Please note that committee members may be called upon in the future to review selected grantees' annual and final progress reports and possibly to provide feedback to the grantees on his/her project. Also, selection committee members are prohibited from applying for or participating on any applications for this grant throughout the course of their term.

The Text of the Bill

The House and Senate versions of the bill, H.R.733 and S.362, are identical.

The text follows:

More than 43,000 Americans were expected to be diagnosed with pancreatic cancer in 2010, and over 36,800 were expected to die from the disease. The incidence among African Americans is 40 to 50 percent higher than other ethnic groups.

Pancreatic cancer is one of the few cancers for which survival has not improved substantially over the past 40 years. As a result, in 2003, pancreatic cancer

surpassed prostate cancer as the 4th leading cause of cancer-related death in the United States.

Seventy-five percent of pancreatic cancer patients die within the first 12 months of the diagnosis. The five-year survival rate is only 6 percent.

Scientific understanding of pancreatic cancer—its etiology, pathogenesis, detection, and treatment—lags far behind that of most other forms of cancer. In fact, pancreatic cancer is the only one of the top ten cancer killers in the United States that still has a five-year survival rate in the single digits.

In 2001, the National Cancer Institute developed 'Pancreatic Cancer: An Agenda for Action.' As of 2010, only five of the report's 39 recommendations have been implemented because of a lack of funding, focus, and commitment. In the meantime, pancreatic cancer deaths have continued to increase. Further, according to the 'Cancer Trends Progress Report–2009/2010 Update,' death rates for pancreatic cancer are increasing while death rates for all cancers combined, including the four most common cancers (prostate, breast, lung, and colorectal), continue to decline.

Pancreatic cancer research funding constitutes 2 percent of the National Cancer Institute's Federal research funding, a figure far too low given the severity of the disease, its mortality rate, and how little is known about how to arrest the disease.

Of the more than 6,200 research grants awarded in fiscal year 2009 by the National Cancer Institute, only 272 (approximately 4 percent) were categorized by the Institute as at least 50 percent relevant to pancreatic cancer research.

The future supply of scientists entering this field of study is in serious jeopardy. Training grant (F, K, and T awards) funding in pancreatic cancer decreased by 15 percent from 2008 to 2009, a decline larger than that experienced by any of the other leading cancers. Pancreatic cancer trainees were awarded between 2.4- and 6.5-fold less grant money in 2009 than young researchers studying the other four top cancer killers.

In 2007, the Scientific Advisory Board of the Pancreatic Cancer Action Network reviewed the current state of the science and the Federal Government's efforts on pancreatic cancer research and prepared 'The National Plan to Advance Pancreatic Cancer Research' to identify the highest research priorities, scientific infrastructure needs, and workforce training requirements that are needed to provide the answers that pancreatic cancer patients and their families and loved ones so desperately need.

PANCREATIC CANCER INITIATIVE

ESTABLISHMENT– The Secretary shall establish and implement a Pancreatic Cancer Initiative to assist in coordinating activities to address the high mortality rate associated with pancreatic cancer. Such Initiative shall focus on–

(A) advancing research on the causes, diagnosis, and treatment of pancreatic cancer with the goal of increasing the five-year survival rate;

(B) promoting a cadre of new investigators in the field of pancreatic cancer research; and

(C) increasing physician and public awareness of pancreatic cancer.

CONSULTATION– In carrying out this subsection, the Secretary shall consult with the Director of the National Institutes of Health, the Director of the National Cancer Institute, the Director of the Centers for Disease Control and Prevention, and the Interdisciplinary Pancreatic Cancer Coordinating Committee established under subsection (b).

(b) Interdisciplinary Pancreatic Cancer Coordinating Committee–

ESTABLISHMENT– Not later than 60 days after the date of the enactment of this section, the Secretary, in consultation with the Director of the National Institutes of Health, shall establish a committee to be known as the Interdisciplinary Pancreatic Cancer Coordinating Committee (in this subsection referred to as the "Committee").

The members of the Committee shall be appointed by the Secretary, in consultation with the Director of the National Institutes of Health, and shall consist of 13 individuals as follows:

• Nine experts in pancreatic cancer research, who are each a full professor at a major academic research institution and who have each received multiple grants from the National Cancer Institute or other entities of the National Institutes of Health with a primary focus on pancreatic cancer research.

• Two new principal investigators in pancreatic cancer, who are each an assistant-level professor in a major academic research institution and who have each received at least one grant from the National Cancer Institute or another entity of the National Institutes of Health with a primary focus in pancreatic cancer research.

• One pancreatic cancer advocate.

• The Director of the National Cancer Institute (or the Director's designee).

The Secretary shall designate the Chair of the Committee from among its members.

Not later than 30 days after the establishment of the Committee, the Secretary shall publish the names of the Chair and members of the Committee on the Website of the Department of Health and Human Services.

The members of the Committee shall each be appointed for a three-year term and, at the end of each such term, may be reappointed.

A vacancy on the Committee shall be filled by the Secretary in the same manner in which the original appointment was made.

The Committee shall:

• provide advice on overall research objectives and benchmarks for pancreatic cancer research;

• develop not later than six months after the Committee's establishment and update not less than every five years thereafter a strategic plan for the conduct and support of pancreatic cancer research and awareness during the upcoming five-year period; and

• conduct evaluations and make recommendations to the Secretary, the Director of the National Institutes of Health, and the Director of the National Cancer Institute regarding the prioritization and award of National Institutes of Health research grants relating to pancreatic cancer.

STRATEGIC PLAN

The Committee shall develop not later than six months of the Committee's establishment and update not less than every five years thereafter a strategic plan for the conduct and support of pancreatic cancer research and awareness during the upcoming fiscal five-year period.

The Committee shall:

• submit to the Secretary each strategic plan for the upcoming five-year period; and

• publish each such plan on the Website of the Department of Health and Human Services within 30 days after the date of submitting the plan to the Secretary.

Each strategic plan shall include:

• recommended budgetary requirements for pancreatic cancer research, including research grants awarded through the National Cancer Institute, funding for Specialized Programs of Research Excellence (SPORE) that are focused on pancreatic cancer, and funding for the portion of the cancer research incubator pilot project established by section 409J(a) that is focused on pancreatic cancer;

• recommendations on the coordination of extramural and intramural pancreatic cancer research initiatives and possibilities for partnerships among the national research institutes, including the National Cancer Institute, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Environmental Health Sciences, the National Center for Complementary and Alternative Medicine, and the National Center on Minority Health and Health Disparities;

• recommendations for improving physician and public education about pancreatic cancer;

• recommendations for increasing the number of scientists with doctorate degrees and clinician-scientists specializing in pancreatic cancer research; and

• guidelines for information gathered by pancreatic cancer patient registries and tissue banks to ensure uniformity and accessibility to the research community.

PRIORITIZATION AND AWARD OF NIH RESEARCH GRANTS

IN GENERAL– The Committee shall conduct evaluations and make recommendations as needed to the Secretary, the Director of the National Institutes of Health, and the Director of the National Cancer Institute regarding the prioritization and award of National Institutes of Health research grants relating to pancreatic cancer.

PEER REVIEW COMMITTEE: The Committee may appoint a peer review committee to assist in the evaluation of pancreatic cancer grant applications to ensure that such applications are reviewed by individuals with the appropriate expertise.

EVALUATION: In evaluating pancreatic cancer grant applications, the Committee shall emphasize grants that achieve at least one of the following goals:

The grant is determined to be predominantly relevant to pancreatic cancer research and has a primary focus on at least one of the following areas:

• Basic research to advance the understanding of the biology of pancreatic cancer, its natural history, and the genetic and environmental factors that contribute to its development.

• Research on more precise diagnostic methods and screening to detect pancreatic cancer in earlier stages.

• Advanced innovative clinical trials testing targeted therapeutics and novel agents that will extend

the survival of pancreatic cancer patients and improve their quality of life.

The grant will increase the number of new pancreatic cancer investigators.

The grant will meet identified needs, criteria, or specific research goals set forth in the strategic plan.

RECOMMENDATIONS: The Committee shall make recommendations for exception funding for grant applications that–

• are predominantly relevant to pancreatic cancer; and

• score within 10 points of the payline.

Physician Awareness

PROGRAM– The Secretary, in consultation with the Director of the National Institutes of Health, the Director of the Centers for Disease Control and Prevention, and relevant patient advocate and physician organizations, shall develop a primary care provider education program on pancreatic cancer. The Secretary may include in such program accredited continuing medical education and such other activities as the Secretary determines appropriate.

DEFINITION– The term "relevant patient advocate and physician organization" means a nationwide organization that–

• provides evidence-based disease information to the public in a case management style;

• directly funds research in an unbiased manner by working collaboratively with health professionals at a variety of institutions and using a peer-reviewed process;

• advocates public policy outcomes that reflect the needs of patients; and

• provides information to patients, families, and health professionals at the community level.

Communication Tool Kit

The Director of the National Cancer Institute and the Director of the Centers for Disease Control and Prevention, working collaboratively with patient advocate organizations, shall develop a communication tool kit for patients and their families that focuses on specific pancreatic cancer issues related to patient choices and patient care.

Report to Congress

Not later than one year after the date of the enactment of this section, and annually thereafter, the Secretary shall submit a report to the Congress identifying the steps taken to implement the Pancreatic Cancer Initiative. The report shall include–

• an assessment of the progress in improving outcomes and reducing mortality rates for those diagnosed with pancreatic cancer;

• an explanation of how recommendations of the Interdisciplinary Pancreatic Cancer Coordinating Committee in the strategic plan developed for the preceding year have been implemented;

• a summary of the recommendations that were made by the Interdisciplinary Pancreatic Cancer Coordinating Committee for grant funding, including exception funding, the number of such recommendations that were met, and the reasons why any recommendations were not met;

• a breakdown of research grant award amounts by the National Institutes of Health during the past year that are deemed relevant to pancreatic cancer research along with a quantifiable measure as to the relevancy of the grants to pancreatic cancer;

• the number of such grants awarded to new principal investigators in pancreatic cancer and

• a summary of progress and deficiencies that were noted in pancreatic cancer research during the preceding year.

Authorization of Appropriations–

There are authorized to be appropriated–

• to carry out subsection [Pancreatic Cancer Initiative] (a), $140,000,000 for each of fiscal years 2012 through 2014, $154,000,000 for fiscal year 2015, and $159,000,000 for fiscal year 2016;

• to carry out subsection [Physician Awareness] (c), $2,000,000 for each of fiscal years 2012 through 2014, $2,225,000 for fiscal year 2015, and $2,300,000 for fiscal year 2016; and

• to carry out subsection [Communication Tool Kit] (d), $2,000,000 for each of fiscal years 2012 through 2014, $2,225,000 for fiscal year 2015, and $2,300,000 for fiscal year 2016.

NATIONAL INSTITUTES OF HEALTH RESEARCH

Part B of title IV of the Public Health Service Act (42 U.S.C. 284 et seq.) is amended by adding at the end the following:

CANCER RESEARCH.

(a) Cancer Research Incubator Pilot Project–

GRANTS–

IN GENERAL– The Secretary may award grants to research institutions for use in developing innovative compounds or technologies for the prevention, early detection, or treatment of those cancers with five-year survival rates of less than 50 percent.

RELATION TO OTHER NIH GRANTS– Subject to subparagraph (A), the Secretary shall encourage each recipient of a grant under this section to use the grant for research activities that may serve as a springboard for the receipt of other grants, including Specialized Programs of Research Excellence (SPORE) grants, from the National Institutes of Health and its national research institutes.

GRANT PERIOD– The period of a grant under this section shall be five years.

FOCUS– During the initial five fiscal years of carrying out this section, the Secretary shall focus on awarding grants for use in developing innovative compounds or technologies for the prevention, early detection, or treatment of pancreatic cancer.

REPORT– Not later than five years after the date of the enactment of this section, the Secretary shall submit a report to the Congress evaluating the program under this section and making recommendations for expansion of the program to other cancers.

AUTHORIZATION OF APPROPRIATIONS– To carry out this subsection, there are authorized to be appropriated $5,000,000 for each of fiscal years 2012 through 2014, $5,500,000 for fiscal year 2015, and $5,750,000 for fiscal year 2016.

Centers of Excellence

DESIGNATION– The Secretary may designate two additional Specialized Programs of Research Excellence (SPOREs) focusing solely on pancreatic cancer research. In carrying out this paragraph, the Secretary may choose to designate 1 or more satellite centers that augment the work of a previously designated Specialized Program of Research Excellence.

AUTHORIZATION OF APPROPRIATIONS–

To carry out this subsection, there are authorized to be appropriated $20,000,000 for fiscal year 2012, $20,750,000 for fiscal year 2013, $21,500,000 for fiscal year 2014, $22,250,000 for fiscal year 2015, and $23,000,000 for fiscal year 2016.

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Conversation with The Cancer Letter

Fleshman: No Shortage of Leads In Pancreatic Cancer Research

(Continued from page 1)

Fleshman discussed the pancreatic cancer legislation with reporter Matthew Ong in an e-mail exchange:

MO: I've read the text of the bill. How did it come about?

JF: From our perspective, there were a number of factors that led to the creation of the Pancreatic Cancer Research & Education Act. The incidence and deaths for pancreatic cancer were on the rise at a time when overall cancer incidence and deaths were declining, as they are now.

At the same time, there was heightened media attention on the disease with Carnegie Mellon professor Dr. Randy Pausch gaining fame after delivering his Last Lecture while dying of pancreatic cancer, in addition to the high profile diagnosis and subsequent death of actor Patrick Swayze. Realizing the need to start a new national discussion on finally making progress in pancreatic cancer, our Scientific Advisory Board issued a report on what federal resources would be necessary to move the needle on pancreatic cancer research and spur true progress towards increased survival for the disease.

MO: What are PanCAN's contributions to this bill? How large of a role does PanCAN play in the development of this measure?

JF: The Pancreatic Cancer Action Network has provided technical assistance to the bill sponsors.

MO: If the bill passes, from PanCAN's perspective, how effective do you think the measure will be in progressing pancreatic cancer research?

JF: There hasn't been significant progress in pancreatic cancer survival rates to date, so it makes sense to be looking for new approaches that can be added to what NCI is already doing.

A disease as deadly as pancreatic cancer, with a five-year relative survival rate in the single digits and for which there are no early detection tools or effective treatment options, needs a long-term comprehensive strategic plan.

MO: How much does the bill allocate for the entire initiative? What do you think of this amount of authorized funds?

JF: We strongly believe that pancreatic cancer research needs more federal resources. Pancreatic cancer is the fourth leading cause of cancer death and

the five-year relative survival rate is just 6 percent. Taking into account current funding, the bill authorizes $393 million over five years, which is an average of approximately $78 million per year.

MO: How much of an involvement will PanCAN have in the discourse if this legislation passes? Will PanCAN, in any way, benefit from the appropriation of NIH money for the new initiatives?

JF: The Pancreatic Cancer Action Network has a good relationship with the NCI, so we would welcome the opportunity to work closely with them as they implement the bill. The legislation also calls on the NIH and CDC Directors to work with patient advocacy and physician organizations to develop a communications tool kit for patients and their families, so we would hope to be involved in that discussion as well.

The Pancreatic Cancer Action Network does not currently receive any federal funds, and the passage of this bill would not change that.

MO: Your website lists NCI's small budget for pancreatic cancer research as one of the reasons for the lack of the development of early detection tools or effective treatment. Why do you think NCI allocates so few of its dollars towards pancreatic cancer research?

JF: This question would be better suited for the NCI.

MO: Since there are so few leads on the etiology of pancreatic cancer, do you think that the allocation of a large amount of money for research in this area is justified? Basically, is the money, in this case and at this point in time, worth investing in an area where there are few leads to pursue, and when there are many other cancer research priorities in the field?

JF: The notion that there are only a few leads on the etiology of pancreatic cancer is erroneous. Over the past decade, scientists have gained a much better understanding of pancreatic cancer and what makes it unique biologically.

For instance, scientists now know that there is a dense microenvironment that surrounds the pancreatic cancer tumor and that understanding this microenvironment will help aid in drug delivery. Further, scientists now know about the genetics of pancreatic cancer, including the genes that need to be targeted like the KRAS gene. KRAS is present in 90 percent of pancreatic cancer cases.

Additionally, there is a genetically engineered mouse model for pancreatic cancer that allows scientists to test drugs. Scientists believe that these mice mimic how the test drugs would react in humans.

And due to increased efforts of the NCI and private foundations, there are a growing number of scientists—senior and junior—focusing on pancreatic cancer. This was perhaps best evidenced by the first ever AACR special conference for pancreatic cancer, which occurred a month ago. The conference had 450 attendees and was considered a great success.

However, there is still more progress that needs to be made. One area that is particularly problematic is the number of researchers. While there is a growing field of researchers dedicated to pancreatic cancer, it is still very small compared to the amount that we need to truly make progress. For example, the number of training grants and significant grants of $500,000 or more, which sustain laboratories, are generally much less than those funded for the other leading cancer killers. There aren't enough scientists in the field directly related to the resources available.

MO: Instead of being the sole authority in the peer review process, NIH and NCI seem to be merely constituents in this bill instead of being the governing force—any comments? Why do you think the bill was designed as such?

JF: The Pancreatic Cancer Action Network reads the bill as creating a committee that provides recommendations to the NCI Director, but does not change the NCI's peer review process.

We have also proposed to the bill sponsors that they add more NCI staff to the coordinating committee.

MO: The bill seeks to use NIH and NCI funds as an allocation for this initiative but doesn't allow NIH full governance of the processes. Why do you think that is? Why do you think the funds are drawn from NIH and NCI instead of say, Department of Defense, whose peer review process has been used before to bypass NIH?

JF: Unlike many other cancers, the only federal institute that is truly looking at pancreatic cancer in any real way is the NIH and the NCI. There is very little Department of Defense funding that is even available to pancreatic cancer research, so it makes sense that any pancreatic cancer research program would be based at the NIH and the NCI.

Also, given that pancreatic cancer is a specifically tough cancer to research, it may make sense to keep this program within the NCI realm as it will allow for maximum collaboration within the world's preeminent cancer research institution and other institutions receiving NCI funding.

MO: It seems like the bill aims to shift the

power of awarding research project grants to the HHS secretary, something that's usually within NIH's and NCI's domain. Do you have any comments; why do you think that is?

JF: Our understanding is that authorizations are often written to the HHS secretary as a way to convey how important a priority the subject is. But as a practical matter, the responsibility is subsequently delegated to the NIH or NCI director as the law is implemented.

MO: Ultimately, what exactly do you hope this bill will achieve? Can you specify PanCAN's expectations?

JF: The Pancreatic Cancer Action Network hopes that the bill will lead to the creation of a national long-term strategic research plan for one of our nation's leading cancer killers, so that we can finally see some true progress in the five-year relative survival rate. We believe this legislation will finally give pancreatic cancer patients the hope that they deserve.

MO: Any other thoughts, concerns, or messages you would like to get across?

JF: The NCI and the NIH are both doing significant work that is making a significant difference in cancer research, including pancreatic cancer.

However, the statistics for pancreatic cancer are still dismal. The five-year relative survival rate is in the single digits, while the overall five-year relative survival rate for cancer in general is 67 percent. In this aspect, pancreatic cancer stands apart from most other major cancers.

We believe that investigator-initiated research can help and we also believe that the NCI's process has worked for a lot of cancers. This bill is not about changing the NCI grant system, rather it is about taking a closer look at a major cancer killer for which there are currently no early detection tools or effective treatment methods and creating a national strategic plan to spend our resources in the best way to move the field forward.

FDA Approvals

FDA Approves Zaltrap Regimen For Metastatic Colorectal Cancer

FDA approved Zaltrap (ziv-aflibercept) for use in combination with a FOLFIRI (folinic acid, fluorouracil and irinotecan) chemotherapy regimen to treat adults with metastatic colorectal cancer. Zaltrap is an angiogenesis inhibitor.

It is intended for patients whose tumors are resistant to or progressed after an oxaliplatin-containing chemotherapy regimen.

Zaltrap's safety and effectiveness was evaluated in a randomized clinical study of 1,226 patients with metastatic colorectal cancer whose cancer grew while receiving oxaliplatin-based combination chemotherapy, or whose cancer was removed by surgery but returned within six months after receiving oxaliplatin-based combination chemotherapy for adjuvant treatment.

The study was designed to measure overall survival. Patients who were assigned to receive the Zaltrap plus FOLFIRI combination lived an average of 13.5 months compared to an average of 12 months for those receiving FOLFIRI plus placebo.

A reduction in tumor size occurred in 20 percent of patients receiving the Zaltrap plus FOLFIRI combination versus 11 percent for those receiving FOLFIRI plus placebo.

In addition, the clinical trial demonstrated an improvement in progression-free survival. The progression-free survival for patients receiving the Zaltrap plus FOLFIRI combination was 6.9 months compared with 4.7 months for those receiving FOLFIRI plus placebo.

Zaltrap is being approved with a warning from FDA alerting patients and health care professionals that the drug can cause severe and sometimes fatal bleeding, including gastrointestinal bleeding, and the development of holes in the gastrointestinal tract. Zaltrap can also make it more difficult for wounds to heal.

The most common side effects observed in patients receiving Zaltrap plus FOLFIRI were decreased white blood cell count, diarrhea, mouth ulcers, fatigue, high blood pressure, increased amount of protein in the urine, weight loss, decreased appetite, abdominal pain, and headache.

Zaltrap is manufactured by Sanofi S.A.