



TCL

THE CANCER LETTER

Inside information on cancer
research and drug development

Vol.

44

No.

16

APRIL 20, 2018

www.cancerletter.com

SHARPLESS ADDS \$100 MILLION TO NCI'S RPG POOL, R01S FOR YOUNG INVESTIGATORS BOOSTED BY 25%

NCI will bump up the budget for its Research Project Grant pool by \$100 million in 2018—the largest increase to the institute's RPG pool since 2003, NCI Director Norman "Ned" Sharpless said at the annual meeting of the American Association for Cancer Research in Chicago.

→ PAGE 3

PIANTADOSI LEAVES CEDARS-SINAI FOR ALLIANCE AND HARVARD

→ PAGE 12

IN BRIEF
SU2C FOCUSES ON PRECURSOR CONDITIONS IN MULTIPLE MYELOMA

→ PAGE 14

CLINICAL ROUNDUP
KEYTRUDA COMBINATION IMPROVED OS REGARDLESS OF PD-L1 EXPRESSION, INCLUDING PATIENTS WHO TESTED NEGATIVE FOR PD-L1

→ PAGE 17

DRUGS AND TARGETS
FDA APPROVES TAGRISSO FOR FRONT-LINE METASTATIC NSCLC WITH COMMON EGFR MUTATIONS

→ PAGE 19

In this issue

Editor & Publisher

Paul Goldberg

Reporter

Matthew Bin Han Ong

Designer

Jacqueline Ong

Illustrator

Katherine Goldberg

Web Developer

David Koh

Editorial Assistant

Claire Dietz

Editorial, Subscriptions and Customer Service

PO Box 9905 -
Washington, DC 20016

T 202-362-1809

F 202-379-1787

W www.cancerletter.com

Subscription \$555 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Other than "fair use" as specified by U.S. copyright law, none of the content of this publication may be reproduced, stored in a retrieval system, or transmitted in any form (electronic, photocopying, or facsimile) without prior written permission of the publisher. Violators risk criminal penalties and damages. Founded Dec. 21, 1973, by Jerry D. Boyd.

© Copyright 2018
The Cancer Letter Inc.
All rights reserved.

® The Cancer Letter is a
registered trademark.

COVER STORY

- 3** Sharpless adds \$100 million to NCI's RPG pool, RO1s for young investigators boosted by 25%

- 12** Piantadosi leaves Cedars-Sinai for Alliance and Harvard

IN BRIEF

- 14** SU2C focuses on precursor conditions in multiple myeloma

- 15** St. Baldrick's commits \$8 million to SU2C Pediatric Cancer Dream Team

- 16** Isabella Santos Foundation gives \$5 million for rare & solid tumor program at Levine Children's Hospital

- 16** MedStar Georgetown offers proton therapy with HYPERSCAN technology for adults and kids with cancer

- 16** Reprocell and Fox Chase to open biosample repository in India

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

- 17** Keytruda combination improved OS regardless of PD-L1 expression, including patients who tested negative for PD-L1

- 17** Keytruda reduced risk of recurrence or death by over 40% vs. placebo as adjuvant therapy in resected, high-risk stage III melanoma

- 18** SU2C researchers find treatment strategy for stage I-III NSCLC

DRUGS & TARGETS

- 19** FDA approves Tagrisso for front-line metastatic NSCLC with common EGFR mutations

- 19** FDA approves Opdivo and Yervoy for front-line advanced RCC

- 20** FDA approves Tavalisse for ITP

- 20** FDA issues guidance on investigational in vitro diagnostics in oncology trials

CTEP PROTOCOLS

- 20** NCI Trials for April

SHARPLESS ADDS \$100 MILLION TO NCI'S RPG POOL, RO1S FOR YOUNG INVESTIGATORS BOOSTED BY 25%

By Matthew Bin Han Ong

NCI will bump up the budget for its Research Project Grant pool by \$100 million in 2018—the largest increase to the institute's RPG pool since 2003, NCI Director Norman “Ned” Sharpless said at the annual meeting of the American Association for Cancer Research in Chicago.

“This is possible thanks to increases in the past three years in our congressionally appropriated budget,” Sharpless said in his first public speech as NCI director at the meeting April 16. “While this is not solely for basic science—there are lots of laudable clinical trials and health services research funded from the RPG pool—this is the most straightforward way to assure we continue to fund investigator-initiated basic science.”

An audio recording of Sharpless's talk, titled “NCI and the Cancer Community: Focusing on Patients Through Innovative Research,” is posted [here](#).

A week ago, in a Town Hall speech at NCI's Shady Grove campus, Sharpless

listed four key focus areas for the institute, and said he would be announcing the specifics of his administration's priorities at the AACR meeting (The Cancer Letter, [April 13](#)).

The institute received an additional \$275 million—on top of \$300 million in Cancer Moonshot funds—as a part of the \$3 billion raise to the NIH budget in FY18. Washington insiders attributed the unusual increase to steadfast congressional support for biomedical research, as well as advocacy by philanthropist Jed Manocherian (The Cancer Letter, [April 6](#)).

This year, NCI is also increasing the total number of first RO1s given to ear-

ly-stage investigators by at least 25 percent, Sharpless said.

“To also support the ESIs, we have created a new mechanism to support their first grant—the R37. Under this change, ESIs who receive an RO1 will be eligible to have their grant transitioned to an R37 award and, as a result, have the opportunity for extended funding for up to two years,” Sharpless said. “In other words, a five-year RO1 grant could become a seven-year R37 grant with minimal extra work.

“The R37 has ‘gone live’ and further info is available on the NCI website. We hope two years of extra funding will allow ESIs to focus on doing their best research and building their careers.”

In his speech, Sharpless recapped his priorities for NCI—growing the workforce, pursuing more basic science, using Big Data, and modernizing clinical trials.

“So, how to modernize clinical trials, given these new realities of cancer care? NCI can promote better design of clinical trials,” Sharpless said. “We have to get rid of unnecessary exclusion criteria and confusing consent forms. We need to adopt central IRBs. We need trials with innovative design, to find inactive agents quickly and thereby prioritize good drugs for further testing.”

A transcript of Sharpless's prepared remarks follows:

Ned Sharpless: As I join you here for the first time as NCI director, I feel it's appropriate to extend a word of appreciation on behalf of NCI. First, thank you to AACR and its 40,000 members from across the globe, many of whom are in the room today or are joining us online via the Facebook live stream, for your pioneering research and dedication to progress against cancer.

Thank you to the cancer research advocates for your informed voice that helps drive policy change. A big thank you to the members of Congress and the President who clearly appreciate the important work of NCI. With the recent passage and signing of this year's Omnibus spending bill we have seen 4 years of budget increases, including a terrific \$275M increase to the NCI budget in 2018, as well as continued full funding for the Cancer Moonshot.

And I'd be remiss if I didn't acknowledge my immediate predecessor, Dr. Doug Lowy, who paved the way for my tenure with his steady and professional leadership as NCI acting director over the past two years. I'm grateful that he continues to be a driving force at NCI.

Finally, and most importantly, thank you to the cancer survivors and patients. Your experiences are the ones that ultimately matter the most. You continue to lend vital inspiration and help shape how the research enterprise works to better prevent, diagnose, and treat cancer.

NCI is a large and complex organization with tremendous scale and capabilities. I show a few parts of NCI here. I was sworn in as NCI director in October of 2017. Given the scale of the job, I decided I would spend the first 6 months on the job on what I've been calling my “listening and learning tour.”

And I did exactly that, engaging with, listening to, and learning from the people across the cancer community including students, scientists, patients, advocates, federal employees, and former NCI directors. Although the official tour has ended, I have realized it should never really end, that is, I should keep listening and learning from these same groups throughout my tenure as NCI director.

Today, I'm pleased to share with you key insights I've taken away from this time and what I view as the critical focus areas for NCI. But let me first take a moment to share a bit about my personal experience with NCI and how I arrived there.

My first job as a scientist was at NIH nearly 30 years ago, between my second and third years of medical school. I took a year off to live on the NIH campus and work in an HIV lab as part of the NIH-Howard Hughes Medical Institute program. I loved that experience.

I'd been a math major in college and so this was the first time I'd actually done anything useful. I realized I loved basic investigation, keeping your own hours, studying a topic of your choosing, and poring over data you generat-

ed. After my year at NIH, I did return to medical school and then residency at Massachusetts General Hospital, followed by a medical oncology fellowship at Dana-Farber; But throughout my clinical training, I remained that sort of resident who would sneak away from his shift in the ER to go read the latest issue of *Cell* in the hospital library. I was that guy.

Returning to the lab after clinical work was hard, but I recall exactly why I did it. I felt back then that I was letting my patients down. I felt like our tools back in the late 1990s were inadequate for the cancers we faced.

Like so many of you, I have numerous patient stories about how I came to this realization, but will share one from a favorite patient who had breast cancer. A delightful 40-ish year-old woman, she had widely metastatic disease—what I suspect we would call, today, “triple negative disease.” But, back then, it was just “breast cancer.” She had lost all of her hair from the chemotherapy I gave her, but she remained positive and upbeat at all times.

During one visit, as it was becoming clear that the initial chemotherapy was no longer working, I had that “goals of therapy” conversation. She told me her main goal for therapy was not to get cured, because she knew was not going to happen, but rather to live long enough to see her 11-year-old daughter—the youngest of her three kids—graduate from high school. Just 6 more years, she asked. It did not seem like too much to ask. But I knew that wasn't going to happen, not given the limited options for therapy we had.

That was a hard day. That patient, and many others like her, taught me something: that as much as I enjoyed patient care and clinical oncology,

what we really needed were better ways to prevent and treat cancer.

And like many others, I figured that the largely empirical approach to finding good cancer treatments employed back then was not adequate. Instead, more effective therapy and prevention would only come from a better understanding of the biology of this disease. And, I realized I wanted to work on that.

So, I decided to become a mouse geneticist and molecular biologist in earnest, so I could find better ways of addressing cancer to help patients. I did that for many years and found, with great collaborators, interesting things about tumor suppressor genes and aging and circular RNA and novel therapeutics.

And along the way I got to train a lot of junior scientists and found I really liked that. And I got to turn some of our basic science ideas into commercializable intellectual property and found I liked that too. And then I became director of a cancer center charged with organizing the cancer research activities in basic, clinical, and population science of a large multidisciplinary center in a diverse and complex catchment area. And I liked that job a lot.

Then the White House called about this job and, well, so far so good!

Through all this, my resolve to prevent and treat cancer has only become stronger. I know that each of you also shares this passion. And I find this energizing, charging...this sense that all the brilliant people working together, we can get things done!

I would now like to turn to my vision for NCI. I have identified four key focus areas where I think NCI can be particularly important to the cancer

research enterprise. These are not new areas for NCI. However, I believe the time is ripe for a laser-sharp focus on these four areas, based on where we are today in terms of the developing science and technology, where the mass and heft of the NCI can play a unique role, and where NCI's resources, convening power, and leadership can act as catalysts.

Let me explain the overarching principles that guided my thinking to arrive at these four key areas.

The heterogeneity of cancer

First, cancer is not one disease but many diseases. Take lung cancer, for example. It started as just plain old lung cancer. Then we had non-small cell lung cancer. Then non-small cell lung adenocarcinoma, or RAS mutant non-small lung adenoCA, and RAS mutant non-small cell lung adenocarcinoma with low tumor mutational burden and PD-L1 expression. And each of these new levels of distinction is important in terms of clinical behavior, response to therapy, risk factors, etc.

So, what once was one disease—lung cancer—is now more than 100 clinically distinct entities. This same fragmentation has occurred in every major cancer and, what this means, is even a common cancer like lung cancer really comprises many far less common but highly relevant subtypes. And each of these clinical subentities occurs in a patient who is entirely unique. But features about each patient apart from their disease—their education, their beliefs, their socioeconomic status, etc.—are all critical to the success or failure of therapy too.

A second guiding principle in this effort is the realization that we owe it to patients to make progress against all

cancers—not just some of them—which is a real challenge since cancer is so heterogeneous. But we must work on all the difficult problems and intractable challenges in cancer research. We cannot work on just the easy cancers or the common ones or the best-understood ones. We have to work on all of them.

And a third guiding principle—this staggering heterogeneity of cancer and need to work on all types of cancer demands new approaches: new understanding of the molecular and cellular biology of the cancer, new ways of conducting clinical trials, scientists with different training, and new ways of harnessing data to learn from every patient.

So, those were the principles that shaped my thinking as I considered where NCI should focus priorities now.

Developing a diverse workforce

The first key focus area is about who is doing the science, the patient care, the work in cancer research, and how they are trained to do it. One of our most important jobs at NCI is to ensure a talented and innovative research workforce for the decades ahead. That means making sure that the best and the brightest don't get discouraged, that researchers continue to work to further science and fuel the discovery of new approaches and technology that will benefit patients.

NCI wants to strengthen and enhance opportunities at every career level from budding high school scientists, fellows and early stage investigators to seasoned researchers and staff scientists. We do this by providing funding for training at all stages of the career path. But more than funding, we must focus also on



Workforce Training & Development

#CancerTraining

- Ensure diversity and representation
- Encourage training of the right skills (Ks and Rs)
- Set aside R01 funding for early-stage investigators (ESIs)
- Method to Extend Research in Time (MERIT) – R37

NIH NATIONAL CANCER INSTITUTE

#NCIFuture 5

developing the right skills for today's cancer researcher. That means training people with the right expertise to match the heterogeneity of cancer. For example, it requires training in basic immunology, disparities research, prevention methodologies, and data science.

Here are a few examples of how our workforce development efforts must evolve. We must continue to press for a diverse workforce with regard to background, interest areas, ethnicity and gender. We must encourage the right skill set through dedicated funding of training grants and opportunities. For example, create additional slots on awards focused on patient oriented research (the K12), new research experiences (R25s), and other grant mechanisms that open new pathways to independence.

Although we are looking at ways to help cancer researchers at all stages, we have appreciated that there are particular problems for newly independent early-career investigators—what NCI calls early-stage investigators (ESIs). Congress, in particular, has asked NIH to pay particular attention to this group of scientists.

As many of you know, one of the biggest hurdles for ESIs is obtaining their first R01—the most common award for investigator-initiated grants. Given the strong support from Congress as demonstrated by the increase they provided to NCI's 2018 appropriation, we have been provided the resources to decrease this hurdle a bit. Specifically, I am directing our extramural funders to set aside in 2018 a significant amount of additional new funding to increase the total number of first R01s given to ESIs by at least 25 percent.

To also support the ESIs, we have created a new mechanism to support their first grant—the R37. Under this change, ESIs who receive an R01 will be eligible to have their grant transitioned to an R37 award and, as a result, have the opportunity for extended funding for up to two years. In other words, a five-year R01 grant could become a seven-year R37 grant with minimal extra work.

The R37 has “gone live” and further info is available on the NCI website. We hope two years of extra funding will allow ESIs to focus on doing their best research and building their careers.

So, to recap, we will not only train a diverse group of scientists and clinicians to ensure the expertise they need to be successful. We will especially target support for ESI investigators with more R01s this year and a lengthened initial period of funding.



Basic Science

#BasicResearch

- Increase support for investigator-initiated research
- Let PIs do more science and less paperwork
- Provide infrastructure (big data, Cryo-EM, etc.)

NIH NATIONAL CANCER INSTITUTE

#NCIFuture 8

Focusing on investigator-initiated discovery

A second key area for NCI focus is on the foundation, that is, renewing our commitment to basic science to increase understanding and drive novel approaches and technologies. It would not be fair to say that NCI has turned away from basic science in the recent past. Far from it. But there are some voices who feel we have done so well in a few cancer areas that this basic biological focus is no longer needed.

These people may argue for more and more spending to address a specific type of cancer, arguing the need in one tumor type is greater than others. And I understand this perspective. There can be a sense that the great ship of cancer research is

passing one by when progress is made in treating some cancers but not the ones you personally care most about. Watching the TV ads for highly effective therapies in lung cancer and melanoma can feel like a fist to the stomach if your loved one has pancreatic cancer or certain types of refractory pediatric brain cancer.

I understand this frustration, and the ferocious desire to see progress in all cancers. It is also important to note that NCI has a large investment in translational and disease-specific research, but we can't afford to bypass the basic science step. An apt quote that is often attributed to Abraham Lincoln goes, "Give me six hours to chop down a tree and I will spend the first four sharpening my axe." We must sharpen our axes and maintain a committed focus on fundamental science, because there is still very much about cancer that remains unknown.

While we have made tremendous progress in some cancers, we have to acknowledge that little or no progress has been made in other types. If you most want to see progress in one of these types of cancer, basic science provides hope.

Take, for example, NTRK inhibitors, which work against the fusion oncoproteins of the TRK kinases. These fusion events are very rare, but the kids and adults with cancers driven by these fusions have marvelous responses to NTRK inhibitors, as recently shown in *New England Journal of Medicine* and *Lancet Oncology* papers, with response rates exceeding 90 percent in one trial.

We should celebrate the success of these new agents, but we should also ask where did they come from, and how do we find more like them? The answer, in this case, comes from basic science studies in the 1980s at NCI,



Big Data

#BigData

- Support the linkage of existing datasets
- Maintain a data ecosystem
- Create common data standards
- Incentivize sharing and aggregation

NIH NATIONAL CANCER INSTITUTE

#NCIFuture 11

in fact, at what is now the national lab at Frederick, where Mariano Barbacid was trying to clone the “OncD” oncogene he had discovered, and it turned out to be this weird fusion protein containing the TRK kinase.

I doubt Dr. Barbacid expected to find a new treatment for childhood cancers at the time he did this, but that is what his work ultimately accomplished.

So, if we accept that we still really need basic science, how can NCI help? First, I believe a top-down approach is not the way to go here. Focus has to be on investigator-initiated discovery. NCI has some role to identify topics for specific focus, but once we have done that, we have to sit back and let the magic happen. One of the best ways to support investigator-initiated science is through the funding of Research Project Grants—the RPG pool. This pool funds the vast major-

ity of investigator-initiated awards—the RO1s I already mentioned and the even larger program project grants, such as PO1s.

In addition to the set-aside specifically for ESIs I already described, we will also put another \$100M into investigator-initiated science in 2018. This is the largest increase to the RPG pool since 2003 is possible thanks to increases in the past three years in our congressionally appropriated budget. While this is not solely for basic science—there are lots of laudable clinical trials and health services research funded from the RPG pool—this is the most straightforward way to assure we continue to fund investigator-initiated basic science.

We also need to minimize the administrative burden on scientists. We understand that the grant application and management process is grueling, and I also understand that

NIH bureaucracy is particularly challenging on young investigators. One initial step in the right direction has been longer, for example, seven-year award periods, such as the Outstanding Investigator Award and the R37 I mentioned earlier. These are steps that have already been taken, and we’re actively looking at other approaches.

“NCI can lead in standards setting”

Finally, we must help provide great scientific infrastructure to allow cutting-edge science. This includes things like the Cryo-EM facility at the Frederick National Laboratory for Cancer Research, the SEER registry and the Genomic Data Commons. We have several new initiatives underway in this area that I will discuss at a future date.

For the third key focus area, we must catalyze technologies, specifically data technology, to add speed and dimension to our work across the cancer enterprise. If you consider that more than 90 percent of all digital data created to date across all fields was produced in the last two years, you get the idea.

And this brings up the idea of a data lake. They sound so great, you imagine them peaceful and serene. But really, they don't work as you might imagine. I grew up in the South, and lakes are where you'd commit your old pickup truck. And they are a great place to hide a sea monster. My problem with the data lake concept is that they allow passive data sharing. Just upload your data in some unusable format, and you have complied with the data sharing policy. No one else without a PhD in computer science can use it.

We must move from passive data sharing to data aggregation—establishing linkage and interoperability of diverse, complex data sets to understand cancer care and provide real world evidence. For example, linking the genomic data with the path data with the radiology data with clinical data mined by machine learning from an EHR in a large number of patients, in a way that assures data privacy and security.

I would argue that almost no matter what your interest is in cancer research, data aggregation helps your research. Say you want to know the effects of diet or exercise on cancer risk. Or say you want to know why a certain cancer disparity in outcome exists. Or you want to know why some rare patients with melanoma still have good response to an old, and usually ineffective drug, like dacarbazine.

Such questions are almost intractable by traditional means. But all are addressed by large, annotated multimodal datasets.

So how are we going to harness Big Data? This is a place where we need to pay special attention to the workforce, attracting young data scientists into cancer research. We will focus on the linkage of many large datasets maintained by NCI to provide interoperability. There are several interesting efforts in this area that range from linking genomic data to clinical data in specific patient datasets. Toward that end, many different groups have begun contributing large datasets into the Cancer Research Data Commons.

This also includes efforts on much larger numbers of patients like novel methods of data linkage within the SEER registry. And we are working with partners, such as the DOE, who have novel capabilities, or FDA and CMS, who have rich datasets.

These data are supported by a developing NCI Cancer Data Ecosystem, which is being significantly amplified with significant new targeted funding from the Cancer Moonshot. This includes highly successful cloud resources for storage and computing.

NCI can lead in standards setting and we have efforts underway to solve the problems of unique identifiers, common ontologies, and a data thesaurus. We need to change our practices to reward and incentivize data sharing and aggregation, for example, by making aggregation possible by smart consenting and good trial design.

We have to do this because the costs of not having Big Data are too great.

“Trials done the old way are inefficient”

For the last area of key focus, we turn to the vexing problem of clinical trials. Clinical trials are the fundamental means whereby progress is made in cancer therapy and prevention, and we need clinical trials to work for the researchers, clinicians, and our patients. But, we have to admit that the performance of clinical trials has been deeply affected by the fact that cancer is so heterogeneous. Gone are the days when the cardiology paradigm of clinical trials reigned and when we enrolled hundreds of patients in a large phase III randomized study with slightly different treatment protocols.

Since there are so many types of cancer, this approach no longer works, and now we are in the era of precision oncology. But, this has caused some major problems. Enrollment is poor with approximately 5 percent of adult patients enrolled on a clinical trial, and one in five cancer clinical trials for adults is never completed because of accrual issues.

The endeavor is also incredibly expensive, which means many good ideas never get tested. And it means the costs of drug development are skyrocketing, and such costs get passed on to patients. While enrollment is better on pediatric cancer trials, it is clear pediatric oncology trials also have some problems.

There have been difficulties getting great new ideas tested in kids with cancer; pharma has come late to this. Pediatric trials also share the increasing cost issues. And the present system does not work for patients; they have trouble finding trials and having trouble getting access to trials.



Clinical Trials

#ClinicalTrials
#LearnFromEveryPatient

- Foster better and innovative trial designs
- Accrue patients in community settings
- Invest in NCI clinical trials network
- Learn from every patient

NIH NATIONAL CANCER INSTITUTE

#NCIFuture 14

So, how to modernize clinical trials, given these new realities of cancer care? NCI can promote better design of clinical trials. We have to get rid of unnecessary exclusion criteria and confusing consent forms. We need to adopt central IRBs. We need trials with innovative design, to find inactive agents quickly and thereby prioritize good drugs for further testing.

A great example of modern trial design is the NCI-MATCH trial. This precision oncology trial allocated patients to one of 30-plus arms of therapy based on somatic genetic testing. While the efficacy of agents tested in NCI-MATCH will be presented at a later date, this trial enrolled over 6,000 patients at 1,100 sites. This is the fastest-accruing trial in the history of NCI.

We are also employing this same approach through the Pediatric MATCH Trial. Working with the Children's Oncology Group, NCI has brought Pedi-

atric MATCH to 200 sites across the country with 8 arms currently open.

In adult oncology, 85 percent of patients are not treated at comprehensive cancer centers, and to boost enrollment, we need to accrue patients to clinical trials in the community setting. As NCI-MATCH has made it clear, it is possible to accrue patients to fairly complex trials in community settings. Many of the patients on NCI-MATCH were enrolled at sites within the NCI's Community Oncology Research Program or NCORP. NCORP comprises seven research bases and 46 community sites across the United States, 12 of which are situated to serve minority or underserved populations.

While industry funds more clinical trials than government agencies do, we will always need NCI to support certain kinds of large trials that don't work well in industry, such as complex

multimodality approaches including surgery, radiation oncology, etc. This is why I am eager to work with the National Clinical Trials Network, which represents NCI's major effort to conduct studies across many academic institutions. I look forward to working with the five clinical trials groups making up the NCTN to conduct trials more quickly and more effectively.

NCI has also created the Experimental Therapeutics Clinical Trials Network (ETCTN), a collaboration among the pharmaceutical industry, academic institutions, and individual investigators to conduct early-stage trials of innovative cancer treatment therapies in high-priority areas of unmet medical needs.

I am aware that the NCTN and related NCI networks have been under-supported. And I am committed to looking at the funding models and to search for additional per-patient

Key Focus Areas

WORKFORCE DEVELOPMENT

Support the cancer research enterprise by focusing on the workforce of cancer investigators

BASIC SCIENCE

Reaffirm our commitment to basic science to drive novel approaches and technologies

BIG DATA

Increase data aggregation and interpretation to speed our work across the cancer enterprise

CLINICAL TRIALS

Fully realize the power of clinical trials through innovative design, administration, and analyses

funding for NCI network trials in order to maintain critical NCI clinical trials networks.

Lastly, we have to admit that trials done the old way are inefficient. Rather than testing one specific variable in a trial, by aggregating data at greater scale, we can learn from every patient. This will require thinking about trials differently, seeing drug development through the lens of a health service researcher, and using the tools of Big Data and data aggregation, as I mentioned before.

So these are the four key focus areas for NCI while I am at the helm: Workforce development. Basic Science. Big Data. Clinical trials.

It should be clear that these four areas are highly related. For example, workforce development is a big issue for Big Data, which directly benefits clinical trials, and all of this is underpinned by

basic investigation. Also, let me assure you that focus on these areas does not mean that other areas not explicitly included here will be forgotten. NCI is responsible for the entire National Cancer Program, for research and progress that spans the entire research continuum. And we will remain committed to that mission.

As I see it, these are areas of particular opportunity where we need to focus now. In a moment, I'll continue the conversation with two esteemed colleagues here on stage. But let me finish as I began, by talking about patients.

I started today with the story of a patient that I cared for a long time ago, a patient for whom our therapies back then did not provide much hope. Memories of her and patients like her have provided my motivation. They keep the devastating effects of cancer at the forefront of my thinking. I

believe we can work together to lessen these awful burdens of cancer in our patients' lives. And to be sure, we have already made tremendous progress since those bad old days of limited options and a poor understanding of the biology of cancer.

I believe by applying focus in these areas now, we can further accelerate the pace of that progress. We need to honor every patient and realize that those we successfully treat as well as those we are unable to help all have experiences that are valuable for process against cancer.

We owe it to them to work together to see this potential realized.

Piantadosi leaves Cedars-Sinai for Alliance and Harvard

By Paul Goldberg

Steven Piantadosi is moving to Alliance, where he will serve as the associate group chair for strategic initiatives and innovation.



For a decade, Piantadosi served as director of Cedars-Sinai Samuel Oschin Comprehensive Cancer Institute. He stepped down from that position in August, 2017, to head the newly established Cedars-Sinai Clinical Trials Design Research Center (The Cancer Letter, [July 17, 2017](#)).

Piantadosi's move to the Alliance headquarters in Boston was presaged by his joining the group's external advisory boards.

"This meeting generated so many exciting ideas, we asked Steven to consider working with us as a collaborator," said Monica Bertagnolli, chair of the Alliance. "Pretty soon, the research teams at Brigham and Women's, Dana Farber, and the Harvard School of Public Health all joined in to convince Steven to join us full time in Boston."

Piantadosi's last day at Cedars-Sinai will be June 30. In Boston, he will work from the Alliance group chair's office in Boston, where he has recently accepted a position as a professor of surgery and biostatistics at Harvard Medical School. He will also join the Alliance Statistics and Data Management Program, working with the group statistician, Sumithra Mandrekar.

"Having Steven at Alliance is going to make it possible for us to tackle a new initiative to make clinical trials smarter, faster, and with less unnecessary expense," Bertagnolli said.

"A key part of my activity there will be collaborating with some very sharp MIT scientists on innovative clinical trial informatics. Other activities include research, collaboration, and teaching with colleagues at Partners. Brigham

“

Having Steven at Alliance is going to make it possible for us to tackle a new initiative to make clinical trials smarter, faster, and with less unnecessary expense.

”

– Monica Bertagnolli

and Women's Hospital offers me many ways to make an impact on the science of clinical trials, and consequently on the care of patients by working in the world's premier academic medical institutions."

In an email to The Cancer Letter, Piantadosi said the Alliance has selected the following areas for innovation:

- "Improve access of underrepresented populations in cancer clinical trials and related research—people over age 65, adolescents and young adults, underrepresented minorities, and participants for whom data collection is very difficult, such as those with rare tumors, or those living in rural locations. The strategy is to provide a data collection tool that can interface with any electronic health record, and replace cumbersome conventional clinical trials case report forms that are labor-intensive to complete. This approach is currently under initial testing at a number of Alliance sites.
- "Statistical modeling of treatment outcomes to identify patients who are outliers with respect to response to adjuvant therapy for solid tumors. Honing in on these exceptional cases provides a strategy to identify differences in biology. We can then target these cases to fully characterize them using comprehensive molecular analyses. This can be a much more efficient and less costly way of linking clinical behavior to molecular subtyping than analyzing all specimens available."

In a letter to his colleagues at Cedars-Sinai, Piantadosi wrote:

"Many opportunities presented themselves to me in the past nine months, including remaining here with a wide circle of collaborators nationally. But the scientific and

funding opportunities presented to me in Boston were too exciting to pass up (despite their annual snowfall totals).

"A key part of my activity there will be collaborating with some very sharp MIT scientists on clinical trial informatics. My other activities will include research, collaboration, and teaching with colleagues at Dana Farber and the Harvard T.H. Chan School of Public Health, in addition to the Brigham and Women's Hospital Center for Clinical Investigation.

"Both the current and incoming ASCO Presidents will be my close collaborators at Harvard, so cancer will remain my research and teaching focus. But I will also explore contributing to other disease areas, as has been an integral part of my career for 30 years.

"Brigham and Women's Hospital has about \$700M in annual research funding—the total funding in the Partners system is about \$1.6B yearly. Opportunities are endless. I will have many more chances to make an impact on the science of clinical trials, and consequently on the care of patients by working in several of the premier academic medical institutions in the world."

Mandrekar, Alliance statistician, who is based at Mayo Clinic, said Piantadosi will be focused full-time on developing new ideas and approaches.

"He will be able to coordinate efforts currently distributed across many Alliance disease committees and projects," Mandrekar said. "We are also particularly excited to have Steven as a mentor to train and inspire a new generation of clinical trial statisticians."

FOLLOW US ON LINKED-IN



[linkedin.com/
company/
The-Cancer-Letter](https://www.linkedin.com/company/The-Cancer-Letter)

NEVER MISS AN ISSUE!

Get e-mail alerts now.



[CLICK HERE](#)

or sign-up at:
[https://cancerletter.
com/mailling-list/](https://cancerletter.com/mailling-list/)

IN BRIEF



SU2C focuses on precursor conditions in multiple myeloma

Stand Up To Cancer announced a \$10 million award to a Stand Up To Cancer Dream Team focused on revolutionizing the treatment of multiple myeloma through early detection of precursor conditions before they turn into full-blown disease.

The SU2C Multiple Myeloma Dream Team will be led by Irene Ghobrial, associate professor of medicine at Dana-Farber Cancer Institute and co-director of the Center for the Prevention of Progression of Blood Cancers at DFCI, with Ivan Borrello, associate professor of oncology at Johns Hopkins University School of Medicine and director of the Cell Therapy and GMP Biologics Core at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, as co-leader.



Irene Ghobrial



Ivan Borrello

The announcement of the new SU2C Multiple Myeloma Dream Team was made at an event during the 2018 Annual Meeting of the American Association for Cancer Research, SU2C's Scientific Partner. The Dream Team is the 23rd announced by SU2C since its inception in 2008 and the first SU2C Dream Team devoted entirely to a hematologic malignancy.

The project will involve what is believed to be the first large-scale population survey in the United States for precursor conditions of multiple myeloma, specifically monoclonal gammopathy of undetermined significance or smoldering multiple myeloma.

Blood samples from approximately 50,000 people, recruited largely through social media, will be analyzed to find what is expected to be about 3,000 with the precursor conditions, which cause no symptoms and are usually detected only when a physician orders a blood test for another reason.

Because it is unclear how to tell whether someone with MGUS or SMM will

progress to full-blown multiple myeloma, the research team will follow those with the precursor conditions and will use the samples to discover biomarkers that will help predict those with a high risk of progressing. The team will also work to develop treatments for high-risk SMM and multiple myeloma.

The target population for the survey includes people with first-degree relatives who have had multiple myeloma, and African-Americans, since African-Americans are three times more likely than whites to develop the precursor conditions and tend to develop them at an earlier age.

Websites will allow people who have the specified characteristics to sign up for the survey, provide their consent, and obtain a sample kit which their doctors can use to draw blood samples and send the samples to the research team.

In addition to Ghobrial and Borrello, the Dream Team will include:



- **Joseph Mikhael**, associate professor of medicine, Mayo Clinic Arizona;



- **Timothy Rebbeck**, professor of epidemiology, DFCI;



- **Jeremiah Johnson**, associate professor of chemistry, MIT;



- **Lorelei Ann Mucci**, associate professor of epidemiology, Harvard T.H. Chan School of Public Health;



- **Gad Getz**, director of cancer genome computational analysis, Broad Institute; and



- **Viktor A. Adalsteinsson**, group leader, Blood Biopsy Team, Broad Institute.

Serving as patient advocates on the Dream Team are Cheryl Boyce, executive director emeritus of the Ohio Commission on Minority Health, and Jenny Ahlstrom, president and founder of the Myeloma Crowd, a division of the Crowd Care Foundation. Both are multiple myeloma patients.

The hypothesis of this proposal is that early detection of MGUS/SMM in a high-risk population, along with a good understanding of the molecular and immune factors that lead to disease progression, will lead to effective strategies that intercept disease progression and improve survival.

The Dream Team proposes to conduct a screening study of individuals over the age of 45, who are at a high risk for having MGUS or SMM, such as African-Americans and individuals who have a first-degree relative that has been diagnosed with a plasma cell disorder. This study will be called the PROMISEstudy. IT will focus on these populations because they are two to three-fold more likely than others to have these precursor conditions.

The team expects to screen 50,000 individuals to obtain 3,000 MGUS/SMM cases to intensively study and follow over time as a cohort. The Dream Team will study this cohort in an effort to define biological characteristics that will help to identify which patients will benefit from particular therapies. These biological characteristics include inherited mutations, acquired mutations, and immune factors. The Dream Team will also identify lifestyle and demographic factors that contribute to disease progression, such as obesity and race.

The team will use this information to develop new therapeutics that that can be used to prevent MM from progressing. These include novel technologies of nanoparticles for better imaging of early disease and the first personalized neoantigen vaccine study for the population of patients screened.

St. Baldrick's commits \$8 million to SU2C Pediatric Cancer Dream Team



The work of the Stand Up to Cancer-St. Baldrick's Foundation Pediatric Cancer Dream Team, launched in 2013 to help develop new immunotherapy approaches to high-risk childhood cancers, will continue with a commitment of \$8 million from the St. Baldrick's Foundation, the world's largest private funder of childhood cancer research grants. To further the impact of this gift, the eight institutions that make up the consortium have committed matching dollars to a total of \$16 million.

Continuing as co-leaders of the newly charged St. Baldrick's-Stand Up to Cancer Pediatric Cancer Dream Team are John Maris, pediatric oncologist and holder of the Giulio D'Angio Chair in Neuroblastoma Research at Children's Hospital of Philadelphia, and Crystal Mackall, professor of pediatrics (hematology and oncology) at Stanford University and associate director of the Stanford Cancer Institute.

St. Baldrick's and Stand Up to Cancer initially provided the Dream Team, consisting of more than 150 researchers at eight institutions, with \$14.5 million over a four-year term beginning in 2013. The Dream Team worked to improve and expand immunotherapy in childhood cancers.

Isabella Santos Foundation gives \$5 million for rare & solid tumor program at Levine Children's Hospital



Atrium Health's Levine Children's Hospital announced a \$5 million charitable commitment from the Isabella Santos Foundation to establish The Isabella Santos Foundation Rare & Solid Tumor Program at Levine Children's Hospital. The program will oversee care for all solid tumors, rare tumors, metaiodobenzylguanidine therapy and all related clinical and scientific research at Levine Children's Hospital.

The team will be constructed over a period of five years, with the initial focus on hiring a medical director, who will be the Isabella Santos Foundation Endowed Chair in Rare & Solid Tumors. This program will serve nearly one-third of the 135 new cancer patients Levine Children's Hospital sees each year and will allow the hospital to expand their clinical trials.

This \$5 million gift comes on the heels of a \$1 million donation the Isabella Santos Foundation made in 2017 to

help build a MIBG suite at Levine Children's Hospital. The two-room MIBG suite, which will include a lead-lined patient room and an adjoining room for parents and caregivers, will provide targeted radiation to pediatric neuroblastoma patients and is slated to open in late 2018.

In 2007, Isabella Santos was diagnosed with neuroblastoma, a rare form of childhood cancer that affects approximately 750 children a year. During her five-year fight against cancer, Isabella received much of her care at Levine Children's Hospital. However, some of the clinical trials and advanced treatments she needed were only available out of state.

While the Santos family had the option of seeking treatment elsewhere, Erin Santos, Isabella's mother and co-founder and president of the Isabella Santos Foundation, knew many others who couldn't. With this gift, families will have access to the latest cancer treatments and expertise in Charlotte and this region.

Javier Oesterheld, the Jeff Gordon Children's Foundation Endowed Chair in Cancer & Blood Disorders and Specialty Medical Director at Levine Children's Hospital's Torrence E. Hemby, Jr. Pediatric Hematology, Oncology and Blood and Marrow Transplant Center, cared for Isabella and has spent his career specializing in neuroblastoma, with an emphasis on conducting clinical trials.

MedStar Georgetown offers proton therapy with HYPERSCAN technology for adults and kids with cancer

MedStar Georgetown University Hospital has opened a Proton Therapy Center.



MedStar Georgetown is the first and only proton center in the world to offer the Mevion S250i with HYPERSCAN technology, producing beams that are sharper than previous proton systems. Proton therapy with HYPERSCAN is also faster than other proton systems, benefiting patients whose treatment includes holding their breath.

Reprocell and Fox Chase to open biosample repository in India

Reprocell USA, a subsidiary of Japan's Reprocell Inc., and Fox Chase Ltd., one of the Fox Chase Cancer Center organizations, formed a joint venture to operate a multi-site bio-sample repository facility in India.

Initial operations are underway in Delhi with plans to expand to Hyderabad later this year. The facilities will add approximately 3,000 new bio-samples monthly. Collected specimens will be supported by annotations that include medical history, mutation data and detailed records of treatment protocols as well as outcomes.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP



Keytruda combination improved OS regardless of PD-L1 expression, including patients who tested negative for PD-L1

Merck announced results from KEYNOTE-189, a pivotal phase III trial evaluating Keytruda (pembrolizumab) in combination with pemetrexed (Alimta) and cisplatin or carboplatin for the first-line treatment of metastatic non-squamous non-small cell lung cancer.

Findings showed that the Keytruda-pemetrexed-platinum chemotherapy combination significantly improved overall survival (OS), reducing the risk of death by half compared with chemotherapy alone (HR=0.49 [95% CI, 0.38-0.64]; $p < 0.00001$). In pre-specified exploratory analyses, an OS benefit was observed regardless of PD-L1 expression in the three PD-L1 catego-

ries that were evaluated, including: patients whose tumors were negative for PD-L1 (HR=0.59 [95% CI, 0.38-0.92]); patients whose tumors had PD-L1 tumor proportion scores (TPS) of 1-49 percent (HR=0.55 [95% CI, 0.34-0.90]); and patients who had a TPS of greater than or equal to 50 percent (HR=0.42 [95% CI, 0.26-0.68]).

The addition of Keytruda to pemetrexed plus platinum chemotherapy also achieved a significant improvement in progression-free survival (PFS), with a reduction in the risk of progression or death of nearly half for patients in the Keytruda combination arm, compared with chemotherapy alone (HR=0.52 [95% CI, 0.43-0.64]; $p < 0.00001$). A PFS improvement in the Keytruda combination group was observed in patients whose tumors were negative for PD-L1 (HR=0.75 [95% CI, 0.53-1.05]); patients with a TPS of 1-49 percent (HR=0.55 [95% CI, 0.37-0.81]); and patients with a TPS greater than or equal to 50 percent (HR=0.36 [95% CI, 0.25-0.52]).

These results are being presented today in a plenary session at the American Association for Cancer Research Annual Meeting, with simultaneous publication in *The New England Journal of Medicine*.

“In this trial, Keytruda in combination with pemetrexed and platinum chemotherapy, compared with chemotherapy alone, prolonged overall survival and progression-free survival in patients with advanced nonsquamous non-small cell lung cancer regardless of PD-L1 expression,” said Leena Gandhi, director of thoracic medical oncology at NYU Langone’s Perlmutter Cancer Center and lead author of *The New En-*

gland Journal of Medicine paper. “There is good scientific rationale for combining Keytruda with pemetrexed and platinum chemotherapy, and these clinical data now suggest this combination as a new standard of care for the first-line treatment of these nonsquamous non-small cell lung cancer patients.”

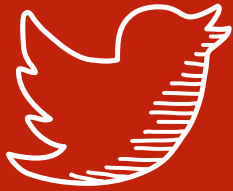
Keytruda reduced risk of recurrence or death by over 40% vs. placebo as adjuvant therapy in resected, high-risk stage III melanoma

Merck and the European Organisation for Research and Treatment of Cancer announced findings from the phase III EORTC1325/KEYNOTE-054 trial investigating Keytruda (pembrolizumab) as adjuvant therapy in resected, high-risk stage III melanoma.

Study results showed Keytruda significantly prolonged recurrence-free survival (RFS), reducing the risk of disease recurrence or death by 43 percent compared to placebo in the overall study population (HR=0.57 [98.4% CI, 0.43-0.74]; $p < 0.0001$).

For the primary endpoint of RFS in the overall study population, the one-year RFS rate was 75.4 percent (95% CI, 71.3-78.9) for Keytruda compared to 61.0 percent (95% CI, 56.5-65.1) for placebo. For the co-primary endpoint of RFS in patients whose tumors were considered PD-L1 positive, Keytruda demonstrated significantly prolonged

**FOLLOW US
ON
TWITTER**



@TheCancerLetter

**FOLLOW US
ON
FACEBOOK**



facebook.com/
TheCancerLetter

RFS compared to placebo (HR=0.54; 95% CI, 0.42-0.69; $p < 0.0001$). The safety profile of Keytruda was consistent with what has been seen in previous trials among patients with advanced melanoma.

These results are being presented today for the first time in the opening plenary session at the American Association for Cancer Research (AACR) Annual Meeting 2018 (Abstract #10526), with simultaneous publication in *The New England Journal of Medicine*.

“The EORTC is very pleased to have collaborated with Merck on this important study which showed a significant recurrence-free survival benefit across all stage III melanoma,” said Alexander Eggermont, study chair, director general at the Gustave Roussy Cancer Institute, professor of oncology, University of Paris-Saclay.

SU2C researchers find treatment strategy for stage I-III NSCLC

An immunotherapy administered prior to surgery is yielding outcomes in 45% of patients treated in this small study from researchers on the Stand Up to Cancer-Cancer Research Institute Cancer Immunology Dream Team, who is a scientific partner of Stand Up to Cancer, according to results presented at the American Association for Cancer Research Annual Meeting. It was published online in *The New England Journal of Medicine*.

Scientists at Johns Hopkins Bloomberg-Kimmel Institute for Cancer Immunotherapy and Memorial Sloan Kettering Cancer Center found that administering two doses of the Bristol-Myers Squibb anti-PD1 immunotherapy Opdivo (nivolumab) for several weeks prior to surgery was not only safe but 45 percent of the patients in the trial responded so well that there was little

evidence of the cancer remaining upon follow-up. In addition, the patients' immune systems also likely destroyed straggler tumor cells still circulating in the blood system, which can later take hold and lead to recurrence and metastasis.

This Dream Team's approach, designed to arrest disease progression within the microenvironment, expands the scope of SU2C's Cancer Interception research portfolio. SU2C is currently funding four Cancer Interception teams focusing on lung and pancreatic cancer.

In addition to the named Interception Teams, three additional SU2C-funded teams are engaged in interception-like approaches to treat multiple myeloma, colon cancer and ovarian cancer.

Historically, chemotherapy or chemoradiotherapy, is given to lung cancer patients to shrink a large, non-metastasized tumor, and in the past, immunotherapeutic agents have been administered after surgery with limited results.

SU2C-CRI Dream Team researchers hypothesized that leaving the tumor in place during initial treatment with immunotherapy would turn it into an “auto-vaccine” resulting in the activation of tumor-specific T cells that would then circulate through the body and find distant sites of micrometastases, thereby preventing relapse post-surgery which can happen to at least one-half of lung cancer patients who undergo surgery.

After a median follow-up of 12 months, three-quarters of the patients who underwent surgical resection were alive and recurrence-free. Recurrence-free survival at 18 months was 73 percent, and the median recurrence-free survival had not been reached at the time of data analysis. To date, only one patient has died of cancer recurrence after surgery. SU2C is cautious not to compare these outcomes with historical outcomes given that it was a small study.

DRUGS & TARGETS



FDA approves Tagrisso for front-line metastatic NSCLC with common EGFR mutations

FDA has approved Tagrisso (osimertinib) for the first-line treatment of patients with metastatic non-small cell lung cancer whose tumors have epidermal growth factor receptor exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.

The drug is sponsored by AstraZeneca Pharmaceuticals LP.

Approval was based on a multicenter, international, randomized, double-blind, active-controlled trial (FLAURA, NCT02296125) conducted in 556 patients with EGFR exon 19 deletion or exon 21 L858R mutation-positive, unresectable or metastatic NSCLC who had not received previous systemic treatment for advanced disease.

The trial results were presented at the European Society of Medical Oncology 2017 Congress and published in the *New England Journal of Medicine*.

Patients were randomized (1:1) to receive osimertinib 80 mg orally once daily or “standard-of-care” treatment of gefitinib 250 mg or erlotinib 150 mg orally once daily. Of those randomized to SOC, 20% received osimertinib as the next line of antineoplastic therapy.

The estimated median progression-free survival was 18.9 months (95% CI: 15.2, 21.4) in the osimertinib arm and 10.2 months (95% CI: 9.6, 11.1) in the SOC arm (hazard ratio 0.46 (95% CI: 0.37, 0.57), $p < 0.0001$). The confirmed overall response rate was 77% for the osimertinib arm and 69% for the SOC arm. The estimated median response durations for the osimertinib and SOC arms were 17.6 and 9.6 months, respectively. At the time of the primary PFS analysis, there were too few deaths to estimate or compare survival outcomes.

The recommended dose of osimertinib is 80mg orally once daily, with or without food.

In the US, Tagrisso is already approved for the 2nd-line treatment of patients with metastatic EGFRm NSCLC, whose disease has progressed on or after a 1st-line EGFR-TKI therapy and who have developed the secondary T790M mutation, as detected by an FDA-approved test.

In 2017, Tagrisso was granted Breakthrough Therapy and Priority Review designations by the FDA in the first-line treatment setting. Tagrisso is under regulatory review in the European Union and Japan for use in the 1st-line treatment setting with regulatory decisions anticipated in the second half of 2018.

Full prescribing information is available [here](#).

FDA approves Opdivo and Yervoy for front-line advanced RCC

FDA has granted approvals to nivolumab and ipilimumab (Opdivo and Yervoy, Bristol-Myers Squibb Co.) in combination for the treatment of intermediate or poor risk, previously untreated advanced renal cell carcinoma.

The approvals were based on Check-Mate 214 (NCT02231749), a randomized open-label trial. Patients with previously untreated advanced RCC received nivolumab (3 mg/kg) plus ipilimumab (1 mg/kg) every 3 weeks for 4 doses followed by nivolumab monotherapy (3 mg/kg) every 2 weeks, or sunitinib 50 mg daily for 4 weeks followed by 2 weeks off every cycle.

Efficacy was evaluated in intermediate or poor-risk patients ($n=847$). The trial demonstrated statistically significant improvements in overall survival and objective response rate for patients receiving the combination ($n=425$) compared with those receiving sunitinib ($n=422$).

Estimated median OS was not estimable in the combination arm compared with 25.9 months in the sunitinib arm (hazard ratio 0.63, 95% CI: 0.44, 0.89; $p < 0.0001$). The ORR was 41.6% (95% CI: 36.9, 46.5) for the combination versus 26.5% (95% CI: 22.4, 31) in the sunitinib arm ($p < 0.0001$). The efficacy of the combination in patients with previously untreated renal cell carcinoma with favorable-risk disease was not established.

The recommended schedule and dose for this combination is nivolumab, 3 mg/kg, followed by ipilimumab, 1 mg/kg, on the same day every 3 weeks for 4 doses, then nivolumab, 240 mg, every 2 weeks or 480 mg every 4 weeks.

Prescribing information for both nivolumab and ipilimumab have been updated with these results. Full prescribing information is available online: [Nivolumab PI](#) and [Ipilimumab PI](#).

FDA approves Tavalisse for ITP

FDA approved Tavalisse (fostamatinib disodium hexahydrate tablets) for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment.

The agent is sponsored by Rigel Pharmaceuticals Inc.

Approval was based on two identical, double-blind, placebo-controlled trials, FIT-1 (NCT02076399) and FIT-2 (NCT02076412) that enrolled a total of 150 patients with persistent or chronic ITP who had an insufficient response to previous treatment, which included corticosteroids, immunoglobulins, splenectomy, and/or a thrombopoietin receptor agonist.

Patients were randomized 2:1 to fostamatinib (100 mg orally twice daily) or placebo for 24 weeks. Dose could be escalated to 150 mg orally twice daily after one month.

Efficacy was based on stable platelet response (at least $50 \times 10^9/L$ on at least 4 of the 6 visits between Weeks 14 to 24). In FIT-1, stable platelet response was demonstrated in 18% (n=9) of patients receiving fostamatinib compared with 0% (n=0) of patients receiving placebo (p=0.03). In FIT-2, stable platelet response was seen in 16% (n=8) and 4% (n=1) of patients, respectively (p=0.26).

In the FIT-3 (NCT 02077192) extension study, a stable response was observed in 23% (n=10) of patients newly exposed to fostamatinib. Durable plate-

let responses were seen in the FIT-1, FIT-2 trials and the FIT-3 extension study.

The recommended dose initially is 100 mg administered orally twice daily. After a month, if platelet count has not increased to at least $50 \times 10^9/L$, increase dose to 150 mg twice a day.

Full prescribing information is available [here](#).

FDA issues guidance on investigational in vitro diagnostics in oncology trials

FDA has issued a draft guidance, "Investigational In Vitro Diagnostics in Oncology Trials: Streamlined Submission Process for Study Risk Determination," to describe for sponsors of certain oncology trials an optional streamlined submission process to determine whether use of an investigational in vitro diagnostic in a trial of investigational cancer drug or biological products is considered significant risk, non-significant risk, or exempt from further pre-market review.

This guidance, which is posted [here](#), will be open for public comment until June 15.

The draft guidance outlines criteria under which sponsors may include information about an investigational IVD in the Investigational New Drug application submission to the FDA center responsible for the therapeutic product (Center for Drug Evaluation and Research or Center for Biologics Evaluation and Research).

This would allow the pre-market information related to the investigational drug and the investigational IVD to be contained in a single IND application. Currently, separate applications are

required for the therapeutic product and the IVD.

Consolidating the information about the investigational drug and device into the same application enables more efficient review and assist in establishing the scientific relationship between the drug and the diagnostic used to select patients.

CDER or CBER would then coordinate with the FDA's Center for Devices and Radiological Health to determine whether use of the investigational IVD in the trial is considered significant risk, non-significant risk, or exempt.

CTEP PROTOCOLS



NCI Trials for April

The National Cancer Institute Cancer Therapy Evaluation Program approved the following clinical research studies last month.

For further information, contact the principal investigator listed.

Phase I - 10126

A Pilot Phase I Study of Atezolizumab (MPDL3280A) in Combination with

Immunogenic Chemotherapy (Gemcitabine-Oxaliplatin) and Rituximab for Transformed Diffuse Large B-Cell Lymphoma

City of Hope Comprehensive Cancer Center LAO
Herrera, Alex Francisco
(626) 256-4673 x 62405

Phase I - 10130

A Phase I Study of Single Agent Tazemetostat in Subjects with Advanced Solid Tumors and B-Cell Lymphomas with Hepatic Dysfunction

University Health Network Princess Margaret Cancer Center LAO
Renouf, Daniel John
(604) 877-6000

Phase I - 10131

A Phase I Study of AZD8186 in Combination with Docetaxel in Patients with PTEN Mutated or PIK3CB Mutated Advanced Solid Tumors, Potentially Amenable to Docetaxel

JHU Sidney Kimmel Comprehensive Cancer Center LAO
Smyth, Lillian Mary
(646) 888-4894

Phase II - 10129

A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) in IDH1 and IDH2 Mutant Advanced Solid Tumors

Yale University Cancer Center LAO
LoRusso, Patricia Mucci
(203) 785-5944

Phase II - EA2165

A Randomized Phase II Study of Nivolumab After Combined Modality Therapy (CMT) in High Risk Anal Cancer

ECOG-ACRIN Cancer Research Group
Rajdev, Lakshmi
(718) 405-8404

Phase II - S1701

A Randomized Phase II Trial of Carboplatin-Paclitaxel with or Without Ramucirumab in Patients with Unresectable Locally Advanced, Recurrent, or Metastatic Thymic Carcinoma

SWOG
Tsao, Anne S.
(713) 792-6363

Phase II - S1712

A Phase 2 Study of the PARP Inhibitor Olaparib (AZD2281) in IDH1 and IDH2 Mutant Advanced Solid Tumors

Yale University Cancer Center LAO
LoRusso, Patricia Mucci
(203) 785-5944

Phase II - 10129

A Randomized Phase II Study of Ruxolitinib (NSC-752295) in Combination with BCR-ABL Tyrosine Kinase Inhibitors in Chronic Myeloid Leukemia (CML) Patients with Molecular Evidence of Disease

SWOG
Sweet, Kendra
(813) 745-6841

Phase Other - AALL17B10-Q

DNA Methylation Stochasticity in Pediatric Acute Lymphoblastic Leukemia

Children's Oncology Group
Koldobskiy, Michael A.
(410) 614-5055

Phase Other - AALL17B9-Q

The Genetics of Relapsed and Refractory T-Acute Lymphoblastic Leukemia (T-ALL)

Children's Oncology Group
Ferrando, Adolfo A.
(212) 851-4611

REACH PEOPLE WHO MATTER IN ONCOLOGY

Advertise your meetings and recruitments in The Cancer Letter and The Clinical Cancer Letter

Find more information

HERE

or visit:
<http://cancerletter.com/advertise/>

INSTITUTIONAL PLANS

Allow everyone in your organization to read The Cancer Letter and The Clinical Cancer Letter.

Find subscription plans

HERE

or visit:
<http://cancerletter.com/subscribe/>