DEPARTMENT OF HEALTH AND HUMAN SERVICES
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NATIONAL CANCER INSTITUTE
18th CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE MEETING

Summary of Meeting
November 30, 2012

Building 31 C, Conference Room 10
National Institutes of Health
Bethesda, Maryland

CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE
BETHESDA, MARYLAND
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The 18th meeting of the Clinical Trials and Translational Research Advisory Committee (CTAC) of the National Cancer Institute (NCI) was convened on Friday, November 30, 2012, at 9:00 a.m. in Conference Room 10, C-Wing, 6th floor, Building 31 on the National Institutes of Health (NIH) main campus in Bethesda, MD. The CTAC Chair, Dr. James L. Abbruzzese, Chairman, Department of Gastrointestinal Medical Oncology, The University of Texas M.D. Anderson Cancer Center, presided. The meeting was adjourned at 2:47 p.m.

Chair
James L. Abbruzzese

CTAC Members
Peter C. Adamson
Susan G. Arbuck
Monica M. Bertagnolli (absent)
Susan G. Braun
Curt Civin
Kenneth H. Cowan (absent)
Kevin J. Cullen
Nancy E. Davidson
Olivera J. Finn (absent)
J. Phillip Kuebler
Scott M. Lippman
Mary S. McCabe
Edith P. Mitchell
Nikhil Munshi
Lisa A. Newman (absent)
Nancy Roach
Daniel J. Sargent
Mitchell D. Schnall (absent)
Peter G. Shields
George W. Sledge, Jr.
Chris Takimoto
Joel E. Tepper
Gillian M. Thomas (absent)
Frank M. Torti (absent)
Miguel A. Villalona-Calero
George J. Weiner

***Ex Officio* Members**
James H. Doroshow, NCI
Paulette S. Gray, NCI
Rosemarie Hakim, CMS (absent)
Lee Helman, NCI (absent)
Michael J. Kelley, VA (absent)
Richard Pazdur, FDA (absent)
Alan Rabson, NCI (absent)
Chuck Shih, CMS (substitute for Rosemarie Hakim)

Executive Secretary
Sheila A. Prindiville, NCI

TABLE OF CONTENTS

FRIDAY, NOVEMBER 30, 2012

I. CALL TO ORDER AND OPENING REMARKS—DR. JAMES L. ABBRUZZESE

Dr. Abbruzzese called the 18th meeting of the CTAC to order and then introduced new CTAC members in attendance for the first time. Dr. Abbruzzese reviewed the confidentiality and conflict-of-interest practices required of Committee members during their deliberations. He asked CTAC members to review their signed conflict-of-interest statements and submit them to Dr. Sheila A. Prindiville, Director, Coordinating Center for Clinical Trials (CCCT), NCI. Members of the public were invited to submit written comments related to items discussed during the meeting to Dr. Prindiville within 10 days of the meeting. Any written statements by members of the public will be given careful consideration and attention.

Dr. Abbruzzese reminded members that the meeting was being videocast by NIH Events Management and that the videocast would be available for review following the meeting at: http://videocast.nih.gov/. He also noted that the meeting agenda had a change; the discussion of the proposed CTAC Program Planning Group would take place during the lunch break.

II. NCI UPDATE—DR. JAMES H. DOROSHOW

Dr. James Doroshow, Deputy Director, Clinical and Translational Research, NCI, gave an update on grant funding patterns and programmatic activities at NCI.

Data were presented on the success of investigator-initiated grants in fiscal year (FY) 2011 and FY2012. Beginning in FY2011, NCI adopted a new approach to the selection of grant applications for funding that set a zone within which nearly all applications are selected for funding. In both 2011 and 2012, that zone extended to the 7th percentile. Beyond that point, all applications are considered, resulting in a final success rate of 15 percent in 2011. For R01 applications in both FY2011 and FY2012, the number of grants funded decreased in direct proportion to the percentile ranking. Nevertheless, a substantial number of grants ranked beyond the 7th percentile were successful. The success rate for R01 applications in FY2012 is the same as the success rate for FY2011. Similar to the R01 applications, the number of R21 applications funded in FY2011 and FY2012 was dependent on the percentile ranking. In FY2011, 30 percent of R21 grants funded had rankings beyond the 7th percentile. Dr. Doroshow explained the difference between new investigators and early-stage investigators. Early-stage investigators are individuals within 10 years of completion of their training who have not had a previous grant. New investigators are individuals who have never received an R01 or R21 grant at any point in their careers. NCI is committed to ensuring that the overall success rate for new and early investigators approximates that for established investigators.

In September, the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP) conducted a review of the NCI Central Institutional Review Board (CIRB), the results of which will be finalized in December. Based on this review, NCI is changing the CIRB model to encompass not only Cooperative Group-related trials, but also early-stage trials. An additional adult CIRB will be added to review phase I and phase II trials. The new Early Phase Therapeutics Network will utilize this CIRB. The median length of time to go through CIRB approval has been reduced from 103 days in 2008-2009 to 17 days. This timeline reduction will make it possible for NCI to meet all of the Operational Efficiency Working Group (OEWG) guidelines and to facilitate use of the CIRB for all trials moving forward.

The NCI National Clinical Trials Network (NCTN) request for applications is due January 15, 2013. Review of those applications will take place in the spring and funding decisions will be released in the summer.

NCI held a Precision Medicine workshop in September at the request of Dr. Harold Varmus. The workshop was based on the 2011 Institute of Medicine (IOM) report *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease*. Precision medicine is the utilization of genomics and other molecular tools to develop a better approach to therapy. NCI has been developing plans to make precision medicine more broadly applicable across different areas of investigation.

A session at The Cancer Genome Atlas (TCGA) Second Annual Scientific Symposium held November 27-28, 2012, in Crystal City, Virginia, was devoted to bringing the tools of the TCGA to clinical practice and the development of clinical trials. NCI's Cancer Therapy Evaluation Program (CTEP) is partnering with the Cancer Centers, Cooperative Groups, and other groups conducting early-phase trials to identify patients who had an exceptional response to a therapy in trials that were discontinued due to otherwise low response rates for the trial as a whole. Studying those patients may allow NCI to identify and develop molecularly targeted therapies. NCI is also in early-stage discussions on a national study, the MATCH trial, that would be open at Cancer Centers, Community Clinical Oncology Programs (CCOPs), and other sites around the country to conduct a panel with mutational analyses of patients' samples to match appropriate drugs for treatment at NCI-designated clinical trials sites. One reason for the interest in doing this type of study is to understand the necessary informatics structure and the design of such studies, which will be emblematic of the future scientific direction.

NCI also recently held a workshop on data replication. The workshop focused on the issues of assessing the reproducibility of published scientific data. Dr. Doroshow shared examples in which data were not as robust as necessary, or were not reproducible, with important implications for downstream research. One of the issues discussed was the responsibility of journals in setting policies. There is a suggestion to write an NCI-related white paper on these topics of data reproducibility and necessary scientific rigor, including a possible checklist of good practices. However, Dr. Doroshow noted that this issue is difficult to address because at the same time that one wants scientists to follow practices to ensure that data are robust, one would not want to interfere with the inventiveness of scientists.

Dr. Doroshow concluded his presentation, referring to the issues of recalcitrant cancers and noting that CTAC has the right expertise to take on a variety of translational problems to inform NCI and help focus on the important translational research issues that should be addressed.

Questions and Discussion

Dr. Peter C. Adamson, Chair of the Children's Oncology Group and Chief of the Division of Clinical Pharmacology and Therapeutics, Children's Hospital of Philadelphia, University of Pennsylvania, asked whether NCI has data on the funding levels of R01 and R21 grants. Dr. Paulette Gray, Director, Division of Extramural Activities, NCI, said that funding data are available and can be provided, if requested. Dr. Adamson asked if the award amounts are being cut in order to maintain a 15 percent success rate. Dr. Gray stated that other than standard NIH and NCI cuts, funding dollars are not being cut substantially.

Dr. Miguel A. Villalona-Calero, Director, Division of Hematology and Oncology, The Ohio State University, asked about the funding patterns of grants such as T32s and K12s that do not receive percentile rankings. Dr. Gray responded that the funding of training grants has not changed drastically.

Dr. Adamson asked if there are any trends in the total numbers of applications funded over the past three to five years. Dr. Gray stated that the total number of grants funded has remained more or less flat over the past five years. Dr. Doroshow added that the total number of grants funded in FY2012 was close to 1,100, which was the same as for FY2011.

Dr. Nancy E. Davidson, Director, University of Pittsburgh Cancer Institute, asked whether the NCI leadership group continues to weigh in on grants as it has in recent years. Dr. Doroshow responded that NCI leadership spends a significant amount of time ensuring that the portfolio is balanced and programmatic issues are addressed.

Dr. Curt Civin, Director, Center for Stem Cell Biology and Regenerative Medicine, University of Maryland School of Medicine, inquired regarding the success rate for physician scientists. Dr. Gray responded that she can obtain those data.

Dr. Davidson asked how NCI's funding rates compare with those of other Institutes in FY2012. Dr. Gray said the success rate is comparable with those of other Institutes with similar portfolios, such as the National Heart, Lung, and Blood Institute (NHLBI).

Dr. Kevin J. Cullen, Director, University of Maryland Greenebaum Cancer Center, asked if funding data are available for P01 applications. Dr. Gray stated that she does not have those data at this time but can obtain that information.

Dr. Doroshow noted that the success rate for Specialized Programs of Research Excellence (SPORE) applications is 24 percent.

Dr. Abbruzzese asked whether details of the MATCH trial can be shared with CTAC early on for input and feedback. Dr. Doroshow confirmed that he will share those details once available.

Dr. Peter G. Shields, Deputy Director, Comprehensive Cancer Center, The Ohio State University Medical Center, asked how the additional funding for R01 phase I centers will be distributed. Dr. Doroshow said there likely will be more money available for a smaller number of Centers.

Ms. Nancy Roach, Consumer Advocate, C3: Colorectal Cancer Coalition, requested that NCI leadership think about the ethics of publishing data that are not reproducible. There are negative consequences to moving un-validated science forward.

Dr. Chris Takimoto, Johnson & Johnson, stated that data reproducibility is a major issue for the pharmaceutical industry, which tries to approach data with a high degree of skepticism, but the problem still exists. Dr. Abbruzzese requested that, as options are put forward to respond to the problem, there be a presentation to CTAC. Dr. Doroshow suggested that there be a mini-symposium or something similar, with speakers who were at the workshop as well as from the pharmaceutical industry.

Dr. Adamson asked whether there are any lessons to be learned from other areas of science. Dr. Doroshow said that this is an issue across NIH and across science. For example, the process for publishing studies in physics was discussed at the Data Replication workshop. In physics, an investigator posts his study on a website for online peer review before submitting it to a journal for publication.

III. LEGISLATIVE UPDATE— MS. SUSAN ERICKSON

Ms. Susan Erickson, Director, Office of Government and Congressional Relations, NCI, gave an update on legislative activities and reported on the status of appropriations.

Congressional Priorities. The priorities during the lame duck session—the session of Congress after the November election and before the new Congress commences—are organization of the Republican and Democratic caucuses, and ways to prevent sequestration. The new Congress convenes in January 2013. Leadership elections have taken place, and chairmen of committees are being appointed and new committee assignments are being made. The Budget Control Act of 2011 raised the debt ceiling but required significant deficit cuts over a 10-year period, which the bipartisan "Super Committee" failed to achieve in December 2011. The consequence, as laid out in the Budget Control Act, is sequestration, or across-the-board cuts, to bring the spending level down to what is required by the law (a $1.2 trillion savings over 10 years). Congress was given an additional year to come up with an alternative to avoid sequestration, which is due to occur the first week of January. Congress must either decide on targeted deficit cuts (as opposed to across-the-board cuts) or extend the deadline in order to prevent sequestration.

The immediate priorities of the new Congress will be to complete committee appointments and swear in new members. Sequestration will continue to be a threat if the deadline is extended. If sequestration does occur, there will be across-the-board cuts to nondefense discretionary programs (e.g., NCI) of about 8 percent. The government currently is operating under a Continuing Resolution (CR) that expires March 27, 2013. If the CR is allowed to expire, the government will shut down. It is anticipated that the new Congress will avoid a shutdown and fund the government by passing an Omnibus bill or a full-year CR, which would result in a flat budget for the rest of the fiscal year.

Legislation of Interest. The Recalcitrant Cancer Research Act (RCRA) originally was introduced as the Pancreatic Cancer Research and Education Act by Representative Anne Eshoo (D-CA), Representative Leonard Lance (R-NJ), and Senator Sheldon Whitehouse (D-RI) in February 2011 with strong bipartisan support. The Pancreatic Cancer Research Act would have required NCI to establish the Pancreatic Cancer Initiative and the Department of Health and Human Services (HHS) to establish the Interdisciplinary Pancreatic Cancer Coordinating Committee (with authority to make recommendations on prioritization and award of grants). Membership of the Committee would have included 11 pancreatic cancer research experts who have received NIH grants, the NCI Director, and 1 pancreatic cancer advocate. The bill authorized appropriations for pancreatic cancer research totaling $169 million. However, the bill has changed over time in response to feedback from HHS and NIH. In September 2012, the House Energy and Commerce Committee amended the Pancreatic Cancer Research and Education Act—the entire text was replaced and the title was changed to the Recalcitrant Cancer Research Act. The revised bill passed the House on September 19. Senator Tom Harkin introduced the bill in the Senate on September 20; the Senate has not yet voted on it.

The bill, as amended, would require NCI to develop a scientific framework to conduct and support research for "recalcitrant cancers," defined initially as cancers with a five-year survival rate of less than 20 percent and estimated to cause at least 30,000 deaths per year in the United States. Pancreatic cancer and a group of four types of lung cancer would qualify under this definition. For each recalcitrant cancer, NCI is directed to convene a working group of federal and nonfederal entities to provide expertise and assistance in developing the scientific framework. The framework must be submitted to Congress and made publicly available. On November 29, Senator Whitehouse proposed an amendment to the Defense Authorization Act to include the language from the Recalcitrant Cancer Research Act. The amendment was adopted but the Senate has not yet voted on the measure.

Questions and Discussion

Dr. Adamson asked Dr. Doroshow what impact sequestration will have on NCI, should it occur. Dr. Doroshow responded that the impact of sequestration on the Institute would be substantial. NCI's approach to the current fiscal year budget has been to operate as if there were a 30 percent cut. NCI cannot be in the position to spend money in the first quarter of the fiscal year that might not be available in the second quarter. Dr. Doroshow also noted that the pace of spending has slowed in anticipation of sequestration. Dr. Adamson asked what the impact would be on existing grants. Dr. Gray clarified that new competing type 2 grants would be impacted but existing grants that currently are being funded would not. NCI is not anticipating cutting funding to existing grants at this time.

IV. CANCER CLINICAL INVESTIGATOR TEAM LEADERSHIP AWARDS PROGRAM—DRS. JAMES H. DOROSHOW, ANTONIO C. WOLFF, SURESH S. RAMALINGAM, AND BRENDA J. WEIGEL

Dr. Doroshow described the NCI Cancer Clinical Investigator Team Leadership Award (CCITLA), which is designed to give mid-level Cancer Center clinicians protected time to carry out activities that enhance the clinical research culture of their Cancer Centers and to recognize their contributions for similar efforts carried out prior to receiving the award. The two-year awards provide $50,000 per year through supplements to P30 Cancer Center support grants. Investigators who have not reached the full professorial level and who have not received major NIH grants are nominated by their Cancer Center directors. NCI has funded between 10 and 12 new investigators per year in the four years of the program. Dr. Doroshow noted that the funds are not nearly as important as the recognition of what these individuals do for clinical research in their respective centers. He introduced three investigators who have received the CCITLA to report on the activities they have carried out with the Award, and explained that one purpose of the session is to get input from CTAC members on how to evaluate the usefulness of this mechanism.

Dr. Antonio C. Wolff, Professor of Oncology at The Johns Hopkins Kimmel Cancer Center, received his CCITLA in 2009. He became a tenured professor in 2011 following his two-year award. Dr. Wolff noted that the Award contributed to his ability to remain in academia instead of seeking better-paying but less-interesting positions in private practice or industry. He presented a timeline of his career, noting that the CCITLA has been part of a continuum of other awards (including three Komen awards), committee memberships, and collaborations with other investigators on a number of projects that have contributed to his growth as a physician and scientist. Dr. Wolff and his colleagues at the Kimmel Cancer Center have built a comprehensive infrastructure for breast cancer research. He also serves as Executive Officer of the Translational Breast Cancer Research Consortium, serves as associate editor for the *Journal of Clinical Oncology*, and has spent several years on the American Society for Clinical Oncology (ASCO) Guidelines Committee.

Dr. Suresh S. Ramalingam, Professor of Hematology and Medical Oncology at Emory University's Winship Cancer Institute, received his CCITLA in 2010. One of the specific aims of his work supported by the Award has been to enable the conduct of novel pilot studies in lung cancer. He also has focused on strengthening the Institute's clinical research program and Cooperative Group participation. The Award has resulted in institutional recognition within the University and expanded opportunities for collaboration. Dr. Ramalingam's professional development since receipt of the Award has included promotion to a professorship, appointment as Chair of the Eastern Cooperative Oncology Group-American College of Radiology Imaging Network (ECOG-ACRIN) Thoracic Committee, a

leadership role in the Drug Discovery and Development Therapeutics Program at the Winship Cancer Institute, a leadership role in clinical investigations for Emory's lung cancer P01 project, development of a Mastering Clinical Research training course, and the ability to serve as a mentor for fellowship trainees.

Dr. Brenda Weigel, Associate Professor, Pediatric Hematology and Oncology, Masonic Cancer Center (MCC), University of Minnesota Medical School, received her CCITLA in 2011. When she joined MCC, she brought a unique perspective on clinical trial participation based on her experience in developing and conducting early-phase and large front-line studies at the national level with the Children's Oncology Group along with her knowledge of large clinical Cooperative Group infrastructure and operating procedures. Soon after receiving the Award, Dr. Weigel was asked to lead the rewriting of the Data Safety Monitoring Plan for MCC and to assume medical directorship of the Clinical Trials Office (CTO). She is leading a restructuring of the CTO and is playing a major role in writing an application for the Cancer Center's funding renewal. The CCITLA has resulted in recognition by the academic health center and the University, of the importance of clinical translational science as a career path for promotion and advancement, as well as recognition of the Cooperative Group mechanism as a training resource for higher-level positions in cancer center leadership.

Questions and Discussion

Dr. Villalona-Calero asked whether NCI has funding to continue this award program. Dr. Doroshow replied that if there are no cuts to the budget, the program will have adequate support.

V. RECOGNITION CEREMONY—DRS. JAMES H. DOROSHOW AND JENNIFER HAYES

CCITLA Awardees. Dr. Jennifer Hayes, Program Director, Coordinating Center for Clinical Trials, presented awards to the 2011 and 2012 recipients of the **Clinical Cancer Investigator Team Leadership Award**. For more information, please see the tables below and the meeting information available at http://deainfo.nci.nih.gov/advisory/ctac/1112/index.htm.

Retiring CTAC Members. Dr. Doroshow recognized two retiring members of CTAC—Dr. Kenneth H. Cowan, Director, Eppley Cancer Center, University of Nebraska Medical Center, and Dr. Joel E. Tepper, Hector MacLean Distinguished Professor of Cancer Research, Department of Radiation Oncology, Lineberger Comprehensive Cancer Center, University of North Carolina. Dr. Doroshow thanked the members for their contributions to the CTAC and NCI.

2011 NCI Cancer Clinical Investigator Team Leadership Awardees

Nominee	*Institution*
Dr. Julie Bauman	University of New Mexico Cancer Center
Dr. Tanios Bekaii-Saab	The Ohio State University Comprehensive Cancer Center
Dr. Anthony El-Khoueiry	University of Southern California Norris Comprehensive Cancer Center
Dr. David Gerber	Harold C. Simmons Cancer Center, The University of Texas Southwestern Medical Center

Dr. Andrew Ko	UCSF Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco
Dr. Antonio Omuro	Memorial Sloan-Kettering Cancer Center
Dr. Chong-xian Pan	University of California, Davis Cancer Center
Dr. John Sarantopoulos	Cancer Therapy & Research Center, The University of Texas Health Science Center at San Antonio
Dr. Scott Schuetze	University of Michigan Comprehensive Cancer Center
Dr. Tait Shanafelt	Mayo Clinic
Dr. Brenda Weigel	Masonic Cancer Center, University of Minnesota

2012 NCI Cancer Clinical Investigator Team Leadership Awardees

Nominee	*Institution*
Dr. Lyudmila Bazhenova	University of California, San Diego Moores Cancer Center
Dr. Lisa Bomgaars	Baylor College of Medicine, Lester and Sue Smith Clinic at Texas Children's Cancer Center
Dr. Alberto Broniscer	St. Jude Children's Research Hospital
Dr. Daniel DeAngelo	Dana-Farber Cancer Institute
Dr. Konstantin Dragnev	Dartmouth-Hitchcock Norris Cotton Cancer Center
Dr. Shirish Gadgeel	Wayne State University Karmanos Cancer Institute
Dr. Shannon Puhalla	University of Pittsburgh Cancer Institute
Dr. Bart Lee Scott	Fred Hutchinson Cancer Research Center; University of Washington
Dr. B. Douglas Smith	Johns Hopkins University, Sidney Kimmel Comprehensive Cancer Center
Dr. Jonathan Strosberg	H. Lee Moffitt Cancer Center
Dr. Antoinette Tan	Cancer Institute of New Jersey/University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School
Dr. Jason Zell	University of California, Irvine Chao Family Comprehensive Cancer Center

VI. EVALUATION OF THE SPORE PROGRAM—DRS. TOBY T. HECHT, JUDITH A. HAUTALA, AND OREN GRAD

Dr. Toby Hecht, Associate Director, Translational Research Program, Division of Cancer Treatment and Diagnosis (DCTD), NCI, discussed the evaluation of the SPORE program. According to NCI policy, the SPORE program must be evaluated prior to the reissuance of the Program Announcement (PAR). The SPORE PAR was reissued in 2009 without an objective evaluation. An evaluation was not conducted due to the transition of the SPORE program from the Office of the Director into the DCTD in

2008. As a result of the reorganization, the program underwent major guidelines revisions. Guidelines were revised based on recommendations of the Guidelines Harmonization Working Group (GHWG) of CTAC and current fiscal realities. In 2011, DCTD established a contract with the Science and Technology Policy Institute (STPI) to conduct an extensive data capture and analysis of the SPORE program.

DCTD drafted a Scope of Work consisting of 11 questions. The questions were based on the program guidelines and focused on the unique features of the SPOREs as a translational research program as well as accomplishments that have had an impact on the practice of oncology. STPI was not asked to judge the SPORE program but to provide the data and analysis so that NCI leadership (and its advisory committees) could make the ultimate judgments. The Scope of Work included the following questions for analysis: (1) What specific concepts or scientific findings from SPORE research have had an impact on the practice of oncology? (2) How well have SPOREs been meeting the translational goal of reaching a human endpoint within the five-year funding period? (3) How well have basic and applied scientists worked together on the design and implementation of individual research projects? (4) How well have SPOREs collaborated with other SPOREs in their own organ sites or across organ sites, with other NCI networks (e.g., Cancer Centers and Cooperative Groups), with other government and nongovernment biomedical research mechanisms, or with industry to move important findings along the translational research pathway (with the ultimate goal of having an impact on medical practice)? (5) How well have SPOREs used the flexibility option to change research direction to have an immediate impact on improving cancer prevention, detection, diagnosis, and/or treatment? (6) How well have SPOREs fostered translational research careers? (7) How have SPOREs used the Developmental Research Program for pilot studies? (8) How well have the specialized resource cores supported the research projects? (9) Did the Biospecimen/Pathology Core provide materials for investigators outside the SPORE program? (10) How many clinical trials/studies were initiated and completed within SPOREs? (11) What have been the significant publications from SPOREs since 2004?

Dr. Hecht clarified that today's presentation is meant to provide information and that no vote or other action is required of the CTAC at this time. However, she requested comments and suggestions on the process and usefulness of the data. The full evaluation report for NCI leadership will be available later in the fiscal year.

Dr. Judith A. Hautala, Research Staff Member, STPI; presented the evaluation process. STPI used a sample set of 55 SPORE awards to conduct the analysis. These 55 awards were active at any time since 2004 and completed at least one five-year award cycle by 2011. The sample set had a fairly even distribution across the various organ sites. STPI obtained data for its analysis from applications and progress reports for the most recently completed five-year award cycle, an independent inquiry of major advances, and individual discussions with the SPORE principal investigators. Based on their analysis, STPI researchers came to five major conclusions. The first is that SPORE projects have a clear focus on early translation. Ninety-six percent of SPORE projects had a defined intervention or biomarker test development objective. Over 80 percent of intervention projects proposed late-stage development activities—either clinical trials or activities to develop or refine the modality, including the production of clinical grade material in anticipation of a clinical trial. In contrast, 90 percent of biomarker projects proposed to identify or confirm biomarkers, with much less activity in the areas of biomarker test development or in-human testing of biomarkers.

STPI's second major conclusion is that there are award-related constraints to translational progress in SPORE projects. The primary constraint is financial. SPORE projects total $200,000 to $400,000 per year, which is an insufficient amount to support most clinical trials. This constraint is even greater if clinical material must be prepared with SPORE funds. As a result, non-SPORE funding is required for most clinical trials and product manufacturing. This restricts projects to those that are attractive to industry, foundations, or other funders. Furthermore, obtaining external funding often delays

progress. The secondary award-related constraint is time. Five years is a very short amount of time for true "bench to bedside" conversion. The timeline favors projects that are already well advanced in development and may restrict the pursuit of innovative, high-risk ideas if subsequent award cycles cannot be used to conduct human testing.

The third conclusion is that the SPOREs have been successful in meeting a human endpoint, with 93 percent achieving that goal. Importantly, while the SPORE program requires that projects meet a human endpoint, a human endpoint can be defined simply as the use of primary human tumor specimens, mainly for biomarker studies. Thirty-six percent of SPORE projects have run clinical trials and 26 percent have run observational studies.

Conclusion four is that there are distinct niches for SPORE research. One niche is complex or risky development projects because the collaborative, multidisciplinary research environment of a SPORE encourages development of innovative ideas and approaches to difficult problems. Additionally, pilot projects under Developmental Research and Career Development programs provide "proof of concept" testing for new ideas. A second niche is creating a community of translational researchers in a disease. The SPORE program provides basic scientists an avenue for moving discoveries into the clinic and allows clinicians to test recent scientific advances. Developmental Research and Career Development Awards integrate new investigators into the network of research in a disease area. A third distinct niche is collaborative projects with industry.

STPI's final conclusion is that SPOREs have a key role in building capacity for translational research. Within host institutions, SPOREs build translational research core infrastructure (expertise, equipment, specimen services) around a specific disease, raise the profile of translational research and enhance its perceived value in the academic setting, and facilitate collaborations and outside funding. Within a disease area, the SPORE program creates a national community of researchers through meetings, conference calls, and research collaborations. Research collaborations, in particular, enable clinical trials, tissue sample collection, and epidemiology studies and catalyze the formation of consortia for the conduct of randomized early-phase trials.

Dr. Oren Grad, Research Consultant, STPI, highlighted major advances influenced by SPORE research. STPI identified 79 major advances from discussions with SPORE principal investigators and other senior investigators. Twenty-four of those advances have been accepted into clinical practice; 36 are in late-phase human testing; and 19 have broad clinical potential. NCI selected 14 of the 79 advances for further analysis, which includes identifying the discoveries and developmental steps underlying the advance and the role of SPORE-associated research in those discoveries and developmental steps. Dr. Grad presented four of these advances to CTAC.

Enzalutamide (MDV 3100) for Late-Stage Prostate Cancer. In 2004, Dr. Charles Sawyers, University of California, Los Angeles (UCLA, later Memorial Sloan-Kettering Cancer Center [MSKCC]), published three key findings elucidating the role of androgen receptors in prostate cancer. On the basis of these findings, Dr. Sawyers entered into a collaboration with a chemist at UCLA to generate a new family of androgen receptor antagonists that could be tested for therapeutic use. With the support of a SPORE Career Development Award, a UCLA postdoctoral fellow generated a novel analog, which eventually became lead candidate MDV 3100. A phase I/II clinical trial of MDV 3100 was carried out through the Department of Defense (DoD) Prostate Cancer Program Clinical Research Consortium with partial support from the MSKCC SPORE. MDV 3100 has been approved by the Food and Drug Administration (FDA) for metastatic castration-resistant prostate cancer. The MSKCC SPORE also supported preclinical development and a phase I trial of the further-refined androgen receptor antagonist ARN 509.

Chromosomal 1p/19q Deletion as an Oligodendroglioma Prognostic/Predictive Marker. Initially, groups at Massachusetts General Hospital (MGH) and in London, Ontario uncovered the empirical evidence that there is a strong association between tumor 1p/19q deletions and chemosensitivity, recurrence-free survival, and overall survival in an anaplastic oligodendroglioma case series. Dr. Robert Jenkins, Mayo Clinic, made additional key contributions to this line of research. He extended the initial finding to low-grade oligodendrogliomas and, with SPORE support, identified a whole-arm translocation as the likely mechanism for the combined deletion of 1p and 19q. A long-running Radiation Therapy Oncology Group (RTOG) trial, RTOG 9402, provided, in parallel, robust clinical evidence for the association between 1p/19q deletion and chemosensitivity and survival. Because of the accumulation of clinical evidence, the findings have been recognized within National Comprehensive Cancer Network (NCCN) guidelines as having useful predictive value.

Rindopepimut (CDX-110) Vaccine for EGFRvIII-expressing Glioblastoma. Drs. Albert Wong and Bert Vogelstein, Johns Hopkins, and Dr. Darrell Bigner, Duke University, elucidated the role of epidermal growth factor receptor (EGFR) amplification and genetic variance in human gliomas. The identification of EGFRvIII as the most common variant was built upon with the development of tumor-specific monoclonal antibodies against EGFRvIII. The efficacy of EGFRvIII peptide vaccination was also demonstrated in syngeneic tumor models. Subsequently, the Duke SPORE led the phase I and II clinical trials of the peptide vaccine. SPOREs at Duke, the University of California at San Francisco, and University of Alabama at Birmingham are participating in ongoing registration trials sponsored by Celldex in front-line and recurrent glioblastoma.

Sensitivity and Resistance to EGFR Tyrosine Kinase Inhibitors in Lung Cancer. In 2004, MGH, Dana-Farber Cancer Institute, and Memorial Sloan-Kettering and Washington University simultaneously reported the association of EGFR gene mutations with response to gefitinib and erlotinib. The Dana-Farber/Harvard Cancer Center SPORE supported the work of MGH and Dana-Farber. The same SPORE also supported Dana-Farber's work on the association of a secondary EGFR point mutation (T790M) with resistance to gefitinib and erlotinib. An extensive body of ongoing research is exploring genomic and other determinants of sensitivity and resistance to EGFR tyrosine kinase inhibitors. NCCN guidelines recommend EGFR mutation testing as standard clinical practice. There are several laboratory-developed EGFR mutant tests available as commercial or hospital laboratory services.

Dr. Hautala reported additional evaluation results on programmatic aspects of the SPORE program. STPI looked independently at the number of clinical trials associated with SPORE research projects. Almost 60 percent of intervention projects involved a clinical trial; 10 percent of biomarker projects, 20 percent of mechanism of action/tool development projects, and 17 percent of projects initiated via the flexibility option also involved clinical trials. Of these clinical trials, three have moved on to phase III studies. Two of the phase III trials are supported by Cooperative Groups and one is supported by industry. STPI also analyzed the number and type of SPORE external collaborations. There have been 1,022 documented collaborations, 45 percent of which have been active research collaborations and 41 percent of which have involved the receipt of research materials.

Additionally, STPI analyzed the success of all Career Development awardees supported by the 55 SPORE awards over the lifetime of the awards, which totals 786 Career Development awardees. STPI was able to find information on about 90 percent of those awardees. Of that subset, 38 percent have received subsequent NIH research funding; 39 percent have received promotions; 71 percent are authors on SPORE publications (45% with at least one first-authored publication); 14 percent are authors on 6 to 10 SPORE publications; and 15 percent are authors on over 15 publications. There are 25 Career Development awardees with over 30 SPORE publications.

STPI also evaluated the success of the 1,618 Developmental Research projects that were funded over the lifetime of the 55 SPORE awards. Of those projects, 136 have been promoted to SPORE research projects, representing about 20 percent of all research projects conducted over the lifetime of the SPORE awards. Four hundred nineteen projects, almost 30 percent, have received non-SPORE follow-on funding, including 248 NIH awards. Of the 55 SPORE award sample set, 51 percent have utilized the flexibility option to terminate and initiate projects. Thirteen percent of all research projects originally proposed by the 55 awards have been replaced with new projects. The flexibility option has been praised by SPORE principal investigators as an effective management tool that allows continued focus on the most promising translational opportunities and achievement of translational progress.

Questions and Discussion

Dr. Abbruzzese asked what the next steps are for NCI leadership in regard to the SPORE evaluation. Dr. Hecht responded that the full evaluation report will go to NCI leadership in a few months. They will decide whether the report should go to the Board of Scientific Advisors (BSA) and any changes or amendments to the program might happen at that point. She then asked for suggestions about how to put this kind of report into a better framework in order to best present the results. Dr. Doroshow added that they are interested in comments from CTAC members on what additional analyses are needed to understand where the program should go.

Dr. Adamson asked whether there will be an independent assessment of SPORE-supported clinical trials at the phase II level. Dr. Abbruzzese further defined this question by asking what percentage of studies among the 55 SPORE awards has progressed to larger phase II or phase III efforts. Dr. Hautala responded that STPI has information on what the phase II trials have been but did not collect data on the results of the trials. STPI could work with experts in the field to review the published phase II trials to determine whether the trial results were important or moved research forward. Dr. Hecht added that until 2008, SPOREs often were given supplements to conduct phase II trials. This was discontinued so that SPOREs could seamlessly hand off their concepts to another mechanism to conduct large phase II and randomized phase II trials.

Dr. Cullen suggested looking at trial accrual numbers, trial completion rates, why trials did not complete, and what trials have led to publications in order to conduct a complete evaluation of the core function of the SPORE program.

Dr. George J. Weiner, Director, Holden Comprehensive Cancer Center, asked whether correlative SPORE studies were included in the evaluation. Dr. Hautala said that correlative studies piggybacked on a trial done for another purpose were not counted as SPORE-supported clinical trials. Trials listed are those with a primary clinical endpoint, not a correlative endpoint.

Dr. Grad commented that it is important to not place too much emphasis on statistics about clinical trials associated with the SPORE program. STPI's charge was to document the activity of the SPORE program for NCI to make judgments on the program's scientific productivity. It is difficult to determine which clinical trials are SPORE-supported due to multiple streams of funding involved in trials. The SPORE evaluation helps elucidate the effectiveness of the SPORE mechanism. Dr. Abbruzzese responded that more than understanding how well the SPORE mechanism functions, he would like to understand the impact of the SPORE program in terms of human health. This is the key question for NCI leadership. Dr. Hautala stated that STPI has data available to begin a more in-depth analysis of SPORE-supported clinical trials if it is deemed important.

Dr. Nikhil C. Munshi, Associate Professor of Medicine, Hematologic Oncology Treatment Center, Dana-Farber Cancer Institute, commented that in evaluating the SPORE program, it is important to document the role of SPOREs in clinical outcomes when phase III trials are not SPORE funded. Early translational and correlative findings supported by the SPOREs can ultimately impact patient care, and that is what needs to be captured in order to really understand the impact.

Dr. Civin predicted that the BSA would look at the SPORE mechanism from the perspective of whether it is superior to a program-project-type mechanism or any other mechanism for accomplishing the aims.

Ms. Roach suggested that the evaluation also look at productive failure, and that it should be recognized and rewarded. She also commented that the advocates should be required to be part of the evaluation of what is working and what is not.

Dr. Takimoto commented that the definition of success used for the evaluation should not be exclusive. For example, a well-defined trial that does not produce favorable results is still a success because the study was well designed. He also asked if there are SPORE policies for interaction with industry. Dr. Hecht answered that the SPORE program encourages industry interactions but does not participate in that process.

Dr. George W. Sledge, Jr., Professor, Departments of Medicine and Pathology, Indiana University Cancer Center, commented that the real issue with evaluating the program is defining success. It is easy to count projects, but the real question is whether the SPOREs have had a major impact in a particular disease. He encouraged STPI to look at the impact of the SPORE program on a disease-by-disease basis.

Dr. Scott M. Lippman, Director, University of California, San Diego Moores Cancer Center, observed that the significant contributions of SPOREs are in the realm of preclinical discovery that may or may not ultimately have clinical impact but is the way to get high-risk/high-gain work.

Dr. Susan G. Arbuck, President, Susan G. Arbuck, M.D., LLC, suggested looking at whether there are any methodological lessons about trial design that could be used to enhance studies going forward.

Dr. Doroshow commented that the expertise of CTAC is exactly the expertise needed to help evaluate the SPORE program. It would be useful to have additional input from CTAC into the evaluation before going forward with it to the BSA.

VII. IMPACT OF THE IMPLEMENTATION OF THE OPERATIONAL EFFICIENCY WORKING GROUP (OEWG) REPORT ON THE CLINICAL TRIALS SYSTEM—DR. MARGARET M. MOONEY

Dr. Margaret M. Mooney, Chief, Clinical Investigations Branch, Cancer Therapy Evaluation Program, DCTD, NCI, provided an update on the implementation of recommendations of the Operational Efficiency Working Group (OEWG). Since 2010, all Cooperative Group treatment trials and CTEP early-phase trials have been monitored for adherence to OEWG's recommended absolute deadlines for the total period of trial development (i.e., from submission of a letter of intent (LOI/concept) to opening the trial to patient enrollment). Since January 2011, trials that do not meet those deadlines are being terminated. In April 2012, the deadline for phase III Cooperative Group trials was reduced from 730 to 540 days, and the deadline for early-phase studies was reduced from 540 to 450 days. The respective OEWG target timelines, 300 days and 240 days, have remained the same. Recommended target timelines also have been established for the different stages of development of a trial, including LOI/concept approval, protocol submission, and protocol approval and activation.

Project managers have been hired to track deadlines, and a secure website has been created to allow investigators, operations staff, and NCI to monitor timelines. Routine conference calls between NCI reviewers and external investigators have been instituted at key points in the review and development process to quickly resolve issues and decrease the need for multiple document revisions. Medical editors have been hired to compile and edit consensus reviews and insert applicable revisions directly into an unofficial copy of the protocol, saving investigators valuable time. Cooperative Groups and other organizations conducting trials have implemented similar processes.

Implementation of OEWG recommendations has resulted in a significant reduction in the number of protocol revisions. An increasing number of proposals are meeting targets for LOI/concept approval and protocol submission; less progress has been made in decreasing time for protocol approval and activation. Only two early-phase trials in the last 20 months have failed to go forward due to failure to meet the absolute deadline for trial activation. All phase III trials have been activated well below the original absolute deadline. The improvement rates for these types of trials, respectively, are 20 percent and 45 percent.

Questions and Discussion

Dr. Adamson asked whether the number of trials normalized each year has changed since implementation of the OEWG recommendations. Dr. Mooney said that there has not been a significant shift in those numbers in early-phase drug development trials, but for later-phase clinical trials, there has been a slight reduction in the number of phase III trials and an increase in phase II trials, particularly larger randomized phase II trials.

Dr. Takimoto asked for clarification of the definition of "trial activation." Dr. Mooney explained that a trial is said to be activated if it is available for patient enrollment at a minimum of one site.

Dr. J. Phillip Kuebler of Columbus Oncology Associates, Inc., asked whether reducing the number of protocols prior to activation is leading to increased protocol amendments after activation. Dr. Mooney stated that data will be available to address that question in the next six months to a year.

Dr. Villalona-Calero asked whether the LOI/concept approval milestone used in the analysis presented to CTAC is based on final approval or whether it could apply to an LOI/concept that is pending drug availability. Dr. Mooney said that it is based on full approval of the LOI/concept, but that she will need to confirm this. (The use of full approval as the milestone for this analysis was confirmed with CTEP/DCTD by Dr. Mooney after the presentation.)

Dr. Edith Mitchell, Director, Center for Elimination of Cancer Disparities, Kimmel Cancer Center at Jefferson, asked whether the OEWG implementation has resulted in improved trial accrual. Dr. Mooney said that, as with Dr. Kuebler's question, more data will need to be collected over time to determine whether there has been an effect on accrual. Dr. Villalona-Calero commented that accrual may be affected by other factors such as funding caps on the number of patients that can be enrolled.

Dr. Sledge asked whether the amount of time a concept spends waiting to be reviewed by a steering committee is taken into consideration in the OEWG timeline. Dr. Mooney replied that the start date for the timeline for concepts that undergo steering committee evaluation is the date on which the steering committee actually evaluates the concept.

VIII. PROPOSED CTAC PROGRAM PLANNING GROUP—DR. JAMES L. ABBRUZZESE

Dr. Abbruzzese led a discussion on how CTAC can function more effectively to help advise NCI. Drs. Abbruzzese and Prindiville proposed developing a working group of CTAC members to provide advice for the purpose of planning CTAC meetings and activities. The working group would establish priorities for presentations at CTAC meetings to maximize the informational value to members and determine how to make the meetings as effective as possible for the broad Committee (CTAC). The group would continually review emerging issues and assess CTAC's progress, achievements, and implementation of recommendations. The Program Planning Group would be a working group of CTAC with five or six individuals who would meet approximately three times per year, primarily via teleconference.

Dr. Davidson commented that she participates in CTAC meetings to advise as opposed to being informed. Adequate time should be allotted at meetings for CTAC members to give advice on topics of importance.

Dr. Tepper stated that during Committee meetings, too much time is spent on presentations and not enough time is spent analyzing and discussing. He suggested conducting videoconferences between the in-person meetings to present factual information that does not require discussion. An ongoing dialogue will provide the opportunity to develop and identify issues that warrant discussion in person. Dr. Lippman agreed with Dr. Tepper. If informational items could be shared with members prior to the in-person meetings, more time could be devoted to discussing the big issues and providing input before decisions are made rather than only hearing about these issues.

Dr. Gray noted that NCI is developing a secure website for the National Cancer Advisory Board (NCAB) to post presentations two to three days prior to Board meetings. This is something that could be done for CTAC. Ms. Roach stated that more access to the PowerPoint slides is needed. It would be helpful to be able to see the presentations prior to the meeting. Dr. Prindiville suggested that the real issue is having access to the necessary background information to set the stage for in-depth discussions.

Motion. A motion to establish the CTAC Program Planning Working Group was approved unanimously.

IX. CTAC WORKING GROUP AND SUBCOMMITTEE UPDATES—DRS. JAMES L. ABBRUZZESE AND GEORGE W. SLEDGE, JR.

Pancreatic Cancer Working Group: Scanning the Horizon for Focused Interventions Meeting. Dr. Abbruzzese provided background information on pancreatic cancer and gave an update on the recently formed Working Group. Pancreatic adenocarcinoma is a highly lethal tumor and is the fourth leading cause of cancer death. Cure for pancreatic cancer is rare and is seen only in surgically resected patients. About one-fifth of pancreatic cancer patients are candidates for surgical resection and, of those, only 3-4 percent will survive longer than five years. Pancreatic tumors are resistant to both chemotherapy and radiation. The mechanisms of resistance are diverse and not yet fully understood. Primary prevention is paramount to reduce the risk of this disease.

There are multiple risk factors for pancreatic cancer. Cigarette smoking is associated with pancreatic cancer in about 25 percent of patients. There is a strong association between type 2 diabetes and pancreatic cancer. Numerous studies have shown a relationship between obesity—particularly obesity that begins in the teens, twenties, and thirties—and development of pancreatic cancer. Genetic abnormalities also play a role in the development of the disease. There are pancreatic cancer families—numerous members within one family with the cancer—with a specific unknown abnormality. There are also inherited germ-line syndromes responsible for the disease; for example, families with *BRCA2* mutations are at very high risk of developing pancreatic cancer. Clinicians are seeing an increase in the number of patients with pancreatic cysts—another risk factor. Within the group of patients with cysts, there is a subset with mucinous cysts that are at high risk for developing invasive pancreatic cancer. Mucinous cystic neoplasm is seen mainly in women, and intrapancreatic mucinous neoplasm (IPMN) is seen most often in men.

Dr. Abbruzzese highlighted recent translational and clinical progress in pancreatic cancer. The initial histologic and molecular characterization of precursor lesions of pancreatic cancer is now known; these are early lesions that can be identified along the pancreatic duct. Initial descriptions of the mutational profile of pancreatic cancer also have been completed. In addition, researchers have developed genetically engineered mouse models (GEMMs) and patient-derived xenografts for pancreatic cancer. Further characterization of these models and validation of specific therapeutic interventions are still in progress. Researchers also have uncovered the importance of tumor-related stroma in the immunology of pancreatic cancer. Initial screening efforts have been implemented for patients at high risk of the disease. Clinicians also are beginning to understand the natural history of mucinous cystic neoplasms and are developing criteria for surgical resection. There is recognition that development of targeted agents will require understanding of pancreatic cancer cellular heterogeneity. Finally, there has been effective integration of currently available modalities (surgery, radiation, chemotherapy) for the treatment of pancreatic cancer.

The purpose of the CTAC Pancreatic Cancer Working Group is to develop strategies and recommendations that will advise NCI on ways to reduce the incidence and mortality rates of adenocarcinoma of the pancreas. The initial goal is to develop strategies to increase the extent of collaboration between centers studying pancreatic cancer. This may include increasing tissue acquisition in association with high-quality clinical data to facilitate greater genetic and biochemical characterization of the disease; assessing recent progress in the field; and scanning the horizon for future developments in medical science. Additional goals include developing recommendations to capitalize on new investment opportunities and providing advice on the NCI plan to implement recommendations.

The Pancreatic Cancer Working Group held an initial meeting, "Pancreatic Cancer: Scanning the Horizon for Focused Interventions," on October 23-24, 2012. Experts in all aspects of pancreatic cancer, from epidemiology to treatment, attended the meeting, which was organized around areas of greatest need in pancreatic cancer. These areas included identifying cohorts of individuals at high risk; screening patients deemed to be at high risk and identifying preinvasive pathologic precursors or very early cancer; and developing effective systemic therapies.

Despite being focused around these identified areas of need, the meeting touched upon many important issues in pancreatic cancer. Other provocative questions that were addressed include: Why does pancreatic cancer occur in some patients with no known risk factors or genetic abnormalities? Why do identical mutations (e.g., CDKN2A) result in pancreatic cancers in some patients and melanoma in others? Can aspirin and/or metformin prevent or control pancreatic cancer? Why do some patients with pancreatic cancer respond remarkably to treatment while most others do not?

The breakout sessions of the meeting were focused on epidemiology and risk assessment research; pathology, screening, and early detection research; and therapeutic research. In order to keep discussions productive, participants were asked to focus on developing precise near-term goals. Discussions were formulated around specific questions, such as: Are we in a position to test the clinical usefulness of available biomarkers to risk-stratify patients deemed at moderate risk based on clinical criteria (e.g., new-onset diabetes, obesity/metabolic syndrome, mucinous cystic neoplasms)? What can be done to improve screening of patients with high-risk germ-line mutations (e.g., *BRCA2*) or pancreatic mucinous cysts that are precursors to invasive pancreatic cancer? Can we specify efficacy criteria that should be generated during preclinical testing of a novel therapeutic before testing the agent in patients with advanced pancreatic cancer? Using available model systems, can we precisely identify the molecular or biochemical characteristics of the pancreatic cancer patient population likely to respond to the targeted intervention in the clinic?

Four high-level draft recommendations resulted from the meeting discussions. Two patient populations currently can be broadly defined that are at increased risk for pancreatic cancer—new-onset diabetics and patients with specific germ-line mutations, familial pancreatic cancer, or mucinous pancreatic cysts. Recommendations for these patient populations are to (1) develop a means to identify patients with new-onset diabetes who have early pancreatic cancer, and (2) develop screening methods to identify those patients with heritable pancreatic cancer (specific germ-line mutations) or mucinous pancreatic cysts who will progress to invasive pancreatic cancer and require (surgical) intervention. The remaining recommendations are to (3) develop strategies that neutralize the driver oncogene *KRAS*, which is almost uniformly mutated in pancreatic cancer, and (4) accelerate clinical and preclinical therapeutic approaches that target the immune and non-immune components in pancreatic cancer.

Questions and Discussion

Dr. Davidson suggested that if additional working groups emerge from the Pancreatic Cancer Working Group efforts, more diverse expertise should be included. Many of the individuals on the Pancreatic Cancer Working Group roster seem to be from the same institution.

Ms. Roach suggested developing a working group similar to the Pancreatic Cancer Working Group that is focused on metastatic cancers.

Ms. Susan G. Braun, Executive Director, Commonweal, asked whether preventive therapies are available for patients who are identified as being at high risk for pancreatic cancer by early detection

screening. Dr. Abbruzzese responded that if a high-risk lesion is identified early enough, surgery would be curative. However, there are many morbidities associated with surgery. The Working Group is focused on developing early intervention strategies that would eliminate the need for surgery in those cases.

NCI National Clinical Trials Network Working Group (NCTN WG). Dr. Sledge, Co-chair of the NCTN WG, Stanford University, provided an update on the NCTN Working Group, which is a working group of the NCI Clinical Trials Strategic Planning Subcommittee of CTAC. The Subcommittee advises NCI on the development of a fully integrated clinical trials system with a scope including NCTN Group trials and early-phase trials. The NCTN WG was developed to assess the strength and balance of the active NCTN clinical trials portfolio both within and across diseases. The WG will recommend new strategic priorities and directions for the NCTN Groups and NCI Scientific Steering Committees (SSCs), based on the current trial portfolio, evolving clinical needs, and emerging scientific opportunities. The Working Group is co-chaired by Dr. Sledge and Dr. Robert B. Diasio, Mayo Clinical Cancer Center. Twenty-eight extramural members serve on the WG and were selected from the following categories of stakeholders: Cooperative Group Chairs and statisticians, Community Clinical Oncology Program Principal Investigators, Cancer Control Research Base Principal Investigators, Cancer Center Directors, Steering Committee Chairs, advocates, translational scientists, and NCI leadership.

The NCTN Working Group held its first meeting on July 11, 2012, and discussed goals of the review of the NCTN clinical trials portfolio. The Group assessed the approach for evaluating disease-site-specific portfolios utilizing the colorectal clinical trials portfolio as a pilot. WG members received summaries of colorectal cancer trials prior to the meeting. At the meeting, one of the Gastrointestinal Cancer Steering Committee (GISC) Co-chairs and the NCI medical officer for colorectal cancer presented the colorectal cancer portfolio and overall disease strategy. Trials and concepts evaluated by the GISC were scored by the WG, and the scoring criteria were further refined. Based on this work, the Group concluded that the review of individual trials within a disease site is appropriate and feasible and that the WG meeting is an appropriate venue for conducting such a review and has the necessary expert judgment needed to evaluate the portfolio. WG members also identified a need for summary information on other major ongoing trials outside of NCTN (e.g., industry, international) in the disease area under review.

The WG's proposed criteria for evaluating portfolios focus on five clinical trial criteria: feasibility, clinical importance, scientific contribution, relative cost/resources, and appropriateness for the NCTN program. It was concluded that Group members should assign an overall score to each trial based on the scores on the individual criteria listed above. The scoring of trials will be applied for the review of multiple disease site portfolios (breast, gastrointestinal, genitourinary, and leukemia and lymphoma) at the December 2012 WG meeting. Group members will be assigned to disease-based subgroups to take the lead in the discussion of each disease area.

Questions and Discussion

Ms. Braun asked whether the NCTN WG considered accessibility as a criterion for trial evaluation given the changing demographics of the United States. Dr. Sledge responded that accessibility is a reasonable criterion to consider.

Dr. Davidson asked what other disease areas will be reviewed by the NCTN WG in 2013. Dr. Prindiville responded that the WG will review the remainder of the NCTN portfolio.

Dr. Abbruzzese asked how the recommendations/findings of the NCTN WG will be distributed to the Subcommittee and CTAC. Dr. Prindiville said that recommendations resulting from the December

review process will be collated and presented to the Subcommittee and CTAC so that they can be appropriately distributed to the groups actually conducting the research.

Dr. Mitchell asked whether the NCTN WG addressed the relationship between trial protocols and the overall landscape of colorectal cancer (e.g., the higher incidence of disease in African-American patients and the increasing incidence in younger patients). Dr. Sledge responded that the WG did not address specific population health disparities when reviewing the trials. Dr. Mitchell also asked if the WG discussed collaborations with other groups/organizations that are focusing on the same disease but in different ways. Dr. Sledge said that the WG asked NCI staff to provide information on trials outside of the NCI portfolio.

Ms. Roach suggested distributing the evaluation criteria developed for colorectal cancer out to the steering committees and task forces.

Dr. Adamson commented that in childhood cancer, the Children's Oncology Group is trying to assess trial outcomes versus the state of knowledge. The knowledge of the biology of disease is further advanced in some cancers, and it is in those cancers that clinical trial resources should be devoted. Other cancers may be commonly occurring diseases, but their biology is unknown; in those cases, resources should be devoted to early-phase research. In evaluating disease portfolios, the NCTN WG should consider whether the scientific knowledge is advanced enough to warrant a trial. Dr. Sledge added that the NCTN WG had a long discussion at its meeting on the lessons learned from pediatric clinical trials.

Dr. Lippman suggested investigating the disparities in accrual between pediatric and adult trials.

X. PROMOTING COLLABORATION AMONG NCI PROGRAMS SUPPORTING CLINICAL COMMUNITY ONCOLOGY AND OUTCOMES RESEARCH—DRS. WORTA MCCASKILL-STEVENS, RACHEL BALLARD-BARBASH AND STEVEN CLAUSER

NCI Community Oncology Research Program. Dr. Worta McCaskill-Stevens, Chief, Community Oncology and Preventive Trials Research Group, Division of Cancer Prevention, NCI, provided an update on development of the new NCI Community Oncology Research Program (NCORP), which derives in part from the realignment of the Community Clinical Oncology Program, Minority-Based CCOP (MB-CCOP), and NCI Community Cancer Centers Program (NCCCP). The NCORP will build on the strengths of these programs to create a community-based network with an integrated approach to conducting a wide range of clinical, cancer disparities, and cancer care delivery research (CCDR). Clinical trials will continue to be a core function; however, other types of studies will be used to address opportunities in health services, behavioral, dissemination, and outcomes research.

Two important goals of the NCORP are to expand clinical research into geographic areas where people previously have not had access to trials and to make the clinical research enterprise more responsive to changes in science, technology, and the health care system. The Program will build collaboratively on the combined strengths of a number of community-based organizations. A research portfolio will be designed to make participation possible at different levels for organizations with different sizes and capacities.

Baseline eligibility criteria for joining the Program include experience in clinical research and CCDR, access to study populations, and strong senior leadership and organizational support. Each core component will have its own set of specific eligibility criteria. Core components will include NCORP-

General and Minority and Underserved. Sites in the comprehensive group will be encouraged to serve as mentors to other sites. The research base will include Cooperative Groups currently being transformed into the NCTN, Cancer Centers, and organizations with research programs focused on care delivery and health disparities.

NCORP will be housed within the NCI Division of Cancer Prevention and will collaborate with the Division of Cancer Control and Population Sciences (DCCPS), the Division of Cancer Treatment and Diagnosis, and the Center to Reduce Cancer Health Disparities (CRCHD). External and internal advisory groups will be established. The U-10 mechanism will be used to support five-year Cooperative Agreements. For clinical trials, the organizational structure will be linked to the NCTN; for CCDR, three options for organizational structure are being considered: (1) CCDR integrated into each research base; (2) CCDR integrated into one research base; or (3) a dedicated CCDR research base.

The NCORP clinical trials research agenda will incorporate emerging science and novel trial designs into treatment, cancer control, prevention, and screening research. Expanded areas of focus will include overdiagnosis and underdiagnosis, post-treatment surveillance, and precancerous lesions. NCORP will seek to enhance accrual of racial/ethnic and underserved populations into clinical trials.

For CCDR, the research agenda will focus on the goals of ensuring that optimal evidence-based therapies and system supports are available in routine practice, building an evidence base for how clinical practices and organizational processes and policies improve patient outcomes, and building data capabilities to assess organizational approaches to improving cancer care for underserved populations, promote participation of underserved populations in clinical trials and CCDR, and incorporate specific disparities research questions into clinical trials and CCDR.

Current NCORP activities include analyzing programmatic requirements, collecting information on research capacities for CCDR at the site and research base levels, conducting an NCI research portfolio analysis on disparities research and CCDR, and developing baseline trial accrual requirements.

NCI will continue to engage stakeholders for comment through 2012. NCI plans to present the concept to the NCI BSA in June 2013. If all goes well, a Funding Opportunity Announcement will be released in the fall of 2013, with a goal of making awards in early 2014.

DCCPS Research Resources for Studying Cancer Care in the Community Setting.
Dr. Rachel Ballard-Barbash, Associate Director, Applied Research Program (ARP), DCCPS, NCI, reported that since the NCORP implementation began, many people have asked for a summary of what is already being done at NCI to build the capacity for research efforts and to examine cancer care in the community setting. She noted that the initial research in this area began at NCI nearly 25 years ago in the late 1980s.

The mission of the NCI ARP is to evaluate patterns and trends in cancer-associated health behaviors, practices, genetic susceptibilities, health services, economics, and outcomes, including patient-centered outcomes; monitor and evaluate these factors among the general population and specific populations in the United States; and determine their influence on patterns and trends in cancer incidence, morbidity, mortality, survival, cost, and patient-reported outcomes.

While much of DCCPS' surveillance efforts focus on data at the individual level, the Division also conducts research at the provider and care delivery system levels to understand how policies influence delivery of cancer care. Several studies and related databases have been created to support this research. The Patterns of Care/Quality of Care (POC/QOC) studies were initiated in 1987 in response to a mandate to collect more data on care delivery than is found in the Surveillance, Epidemiology and End

Results (SEER) registries. The SEER/Medicare database links SEER data to medical claims in the Medicare database to provide longitudinal data on health care utilization for Americans age 65 and older. The SEER-Medicare Health Outcomes Survey provides longitudinal data on patient-reported outcomes. The Medical Expenditure Panel Cancer Survivorship Survey addresses data gaps and endeavors to improve research resources for estimating cancer burden, including financial burden related to effects on employment, families, and caregivers.

Research initiatives and networks supported by DCCPS include the Breast Cancer Surveillance Consortium, the Population-based Research Optimizing Screening through Personalized Regimens program, the Cancer Care Outcomes Research and Surveillance Consortium, and the Cancer Research Network (CRN), which includes health care systems that have research programs.

The activities of DCCPS are integrated with a number of other NCI initiatives related to cancer care. There are ongoing discussions with CTEP about cancer treatment and control studies that could be conducted within the CRN. Several CRN sites are collaborating with Cancer Centers, and most CRN sites have helped recruit patients for Cooperative Groups. The CRN also is working with DCTD on the potential for developing a biospecimen inventory and linking specimen acquisition with clinical data. In making decisions about which treatments to study in the SEER POC/QOC studies, DCCPS has communicated with staff from across NCI and with investigators at the SEER sites. DCCPS research resources have been utilized extensively by Cancer Centers and Cooperative Groups. Experts involved in DCCPS community clinical care initiatives were consulted on the conceptual development of the CCDR component of the NCORP. Improved communication mechanisms have been initiated to support development of clinical research priorities. DCCPS is working with other NCI staff to share lessons learned about building standardized data capabilities to support CCDR and to study the effects of integrated and nonintegrated health systems on care delivery.

The NCORP is distinct from other CCDR efforts for several reasons. It focuses more on specialty providers and provider systems in communities often characterized by care fragmentation. It integrates CCDR with NCI-supported community-based clinical trials to improve accrual and dissemination of findings. It also includes a focus on access to care and disparities in care beyond what is being done through health care systems or insured care.

Dr. Steven Clauser, Chief, Outcomes Research Branch, ARP, DCCPS, NCI, stressed the importance of the NCORP in understanding issues that affect improvement of the clinical trials process. Accrual, for example, is usually more difficult in the community setting than in the academic setting. Efforts to build registries of genomic data in academic centers could be replicated in communities. NCORP will be useful in achieving adequate sample size for many studies that require multisite, practice-based research designs. The Program also provides an opportunity to help community-based organizations gain the expertise in data collection and analysis needed to address questions about cancer care delivery.

Questions and Discussion

Ms. Mary McCabe, Director, Cancer Survivorship Program, Memorial Sloan-Kettering Cancer Center, commented that this reorganization is very timely as oncologists are aligning themselves with community hospitals in anticipation of changes brought about by the Affordable Care Act.

Dr. Weiner asked whether plans for the NCORP include efforts to identify and encourage synergistic interactions between academic centers and community-based organizations. Dr. McCaskill-

XI. ADJOURNMENT—DR. JAMES L. ABBRUZZESE

There being no further business, the 18th meeting of the CTAC was adjourned at 2:47 p.m. on Friday, November 30, 2012.