

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
30th CLINICAL TRIALS AND TRANSLATIONAL RESEARCH
ADVISORY COMMITTEE (CTAC) MEETING**

**Summary of Meeting
July 13, 2016**

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

CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE
BETHESDA, MD
Summary of Meeting
July 13, 2016

The 30th meeting of the Clinical Trials and Translational Research Advisory Committee (CTAC) of the National Cancer Institute (NCI) was held on Wednesday, July 13, at 8:00 a.m. in Conference Room 10, C Wing, Sixth Floor, Building 31, on the National Institutes of Health main campus in Bethesda, Maryland. The CTAC chair, Dr. Nancy E. Davidson, presided.¹ The meeting was adjourned at 2:48 p.m.

Chair

Nancy E. Davidson

CTAC Members

David F. Arons (absent)
Susan M. Blaney
Kevin J. Cullen
Walter J. Curran
Gwendolyn A. Fyfe*
David M. Gershenson
Michael L. LeBlanc
Patrick J. Loehrer, Sr. (absent)
David A. Mankoff
Lynn M. Matrisian*
Mary S. McCabe
Edith P. Mitchell
Nikhil C. Munshi
Augusto C. Ochoa
Gloria M. Petersen
George W. Sledge, Jr.
Chris H. Takimoto (absent)
Miguel A. Villalona-Calero
George J. Weiner
Louis M. Weiner

*Pending appointment

Presenters

Jeffrey S. Abrams, MD, Associate Director, Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis, NCI
Nancy E. Davidson, MD, Director, University of Pittsburgh Cancer Institute, University of Pittsburgh
James H. Doroshow, MD, Deputy Director for Clinical and Translational Research, NCI
M. K. Holohan, JD, Director, Office of Government and Congressional Relations, NCI
Michael J. Kelley, MD, National Program Director for Oncology, Veterans Health Administration, Department of Veterans Affairs
Warren A. Kibbe, PhD, Director, Center for Biomedical Informatics and Information Technology, NCI

Ex Officio Members

William Dahut, NCI
James H. Doroshow, NCI
Paulette S. Gray, NCI
Rosemarie Hakim, Centers for Medicare & Medicaid Services
Michael J. Kelley, U.S. Department of Veterans Affairs (VA)
Warren A. Kibbe, NCI
Richard Pazdur, U.S. Food and Drug Administration (absent)

Executive Secretary

Sheila A. Prindiville, NCI

¹A roster of CTAC members and their affiliations is included as an appendix.

Douglas R. Lowy, MD, Acting Director, NCI

Barbara Mroczkowski, PhD, Special Assistant to the Director, Office of the Director, NCI

Charles M. Rudin, Chief, Thoracic Oncology Service; Co-Director, Fiona and Stanley Druckenmiller
Center for Lung Cancer Research; Sylvia Kay Hassenfeld Chair in Lung Cancer Research, Memorial
Sloan Kettering Cancer Center

Louis M. Weiner, MD, Director, Lombardi Comprehensive Cancer Center; Francis L. and Charlotte G.
Gagnani Chair, Department of Oncology, Georgetown University Medical Center

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I. Call to Order and Opening Remarks

Nancy E. Davidson, MD

Dr. Davidson called the 30th meeting of CTAC to order and welcomed participants to the meeting. She introduced a new ad hoc CTAC member, Dr. Lynn M. Matrisian, and two new *ex officio* members from NCI, Dr. Warren Kibbe and Dr. William Dahut.

Dr. Davidson reviewed the confidentiality and conflict-of-interest practices required of CTAC members during their deliberations. She invited members of the public to send written comments on issues discussed during the meeting to Dr. Prindiville within 10 days of the meeting. National Institutes of Health Events Management was videocasting the meeting, and the videocast would be available for viewing following the meeting at <http://videocast.nih.gov>.

Dr. Davidson asked CTAC members to put the dates for upcoming CTAC meetings on their calendars.

Motion. A motion to accept the minutes of the 29th CTAC meeting held on March 9, 2016, was approved unanimously.

II. NCI Acting Director's Update

Douglas R. Lowy, MD

James H. Doroshow, MD

NCI's Fiscal Year (FY) 2016 Budget. Dr. Lowy reported that NCI received a \$265 million (5 percent) increase in its budget for FY 2016. Most of the additional funds are being allocated to:

- The President's Precision Medicine Initiative in Oncology (PMI-O)
- Investigator-initiated research
- Cancer center support grants
- Overhead/inflation costs

Between FY 2013 and FY 2015, NCI increased its funding for type 1 and type 2 (new and competing, respectively) awards by 25 percent. NCI expects to spend somewhat more on type 1 and 2 awards in FY 2016 than in FY 2015. NCI also increased the base grant sizes for 21 of 69 cancer centers. Over the next 5 years, an additional \$30 million will be available for competing P30 programs.

Positive Outlook for Cancer Research. Opportunities exist to accelerate progress in virtually all areas of cancer research, especially in treatment. Maximizing progress will require support for research on:

- Prevention
- How to reduce cancer mortality overall and for specific cancers
- Implementation and dissemination of what we know improves cancer health
- How to reduce disparities in cancer incidence and mortality in populations with low socioeconomic status, underrepresented minorities, and rural populations

Another priority is attracting and retaining high-quality young investigators.

Vice President's Cancer Moonshot. President Obama announced this initiative during his state of the union speech in January 2016. The initiative's purpose is to accelerate progress against cancer, including in prevention and screening. Vice President Biden is especially keen to break down silos and increase cooperation among government agencies, academic institutions, and the private sector.

The Cancer Moonshot Federal Task Force, comprised of agency heads (including National Institutes of Health Director Dr. Francis Collins and Dr. Lowy) and cabinet members, has been established. The task force will foster interactions among agencies and increase the involvement of various federal agencies in cancer research.

A Blue Ribbon Panel of experts has been established as a working group of the National Cancer Advisory Board. The panel's 28 members will identify major scientific opportunities that are poised to be accelerated by additional emphasis and funding. The panel will also identify major scientific and regulatory hurdles and suggest mechanisms to address research gaps, key technology development, and impediments to progress. The panel will develop a preliminary report with recommendations from its seven working groups for submission to the National Cancer Advisory Board by August 2016. NCI will then prepare funding opportunity announcement concepts, with application receipt dates from January to March 2017. After reviewing the applications, NCI will make the awards in the summer of 2017.

NCI had been planning a re-competition for the Frederick National Laboratory contract in FY 2017. However, because of the Frederick National Laboratory's potentially important role in the Moonshot, NCI has decided to delay the new award until 2018, when the current contract ends.

Where We Need to Go. Dr. Lowy listed the following priorities for NCI:

- Increase the fundamental understanding of cancer, its causes, and its pathogenesis
- Improve prevention, screening, and treatment to continue to decrease cancer mortality rates, including for cancers in which progress has been limited
- Redouble efforts to understand and overcome cancer health disparities
- Take full advantage of the opportunity to accelerate progress by working together on a wide range of projects, from the most basic to the most applied

NCI Molecular Analysis for Therapy Choice (NCI-MATCH). Dr. Doroshow began by acknowledging the ECOG-ACRIN staff who manage the MATCH trial; the hundreds of clinicians, pharmacologists, and tumor biologists who contributed their expertise to designing the study arms; and the NCI National Clinical Trials Network and Community Oncology Research Program sites that provided patient tumor samples. He explained that after opening in August 2015 with 10 treatment arms, NCI-MATCH closed to new accrual temporarily for a planned interim analysis in November 2015. The trial reopened on May 31, 2016, with 24 treatment arms.

The interim analysis showed that 795 patients were screened during the trial's first 3 months at an accrual rate not seen before. The 192 active sites screened approximately 100 patients per week, instead of the originally expected 50 per week. In addition, two thirds of patients were from community sites, and 87 percent of tumors met quality control criteria. NCI is using the interim analysis results to change the protocol by, for example, providing more resources to sequencing centers to support higher throughput of samples.

With the increased funding for PMI-O, NCI had the resources needed to increase the number of patients screened from 3,000 to 5,000 patients in NCI-MATCH, which makes it possible to increase the number of study arms (24 currently, with 8 to 10 more in development). Another important change to the protocol is to allow patients with rare mutations detected at non-MATCH sites to participate once their mutation is confirmed. Thanks to the new funding, NCI will be able to conduct a detailed molecular analysis on approximately 1,000 patients including whole exome sequencing and RNA sequencing.

Experimental Therapeutics Clinical Trials Network (ETCTN) Revision. This recent competition was part of a revision of NCI's approach to early-phase clinical trials in the ETCTN. Approximately 2 years ago, NCI decided to integrate the ETCTN's phase 1 grant program and phase 2 contract program. The 11 UM1 phase 1 grantees can receive supplements through cooperative agreements for phase 2 programs. This revision makes it easy to move from very early trials to large phase 2 studies with correlative science or marker development.

Most phase 1 studies in the ETCTN are now multisite, so they can accrue much more rapidly. This is important, because many of the studies have narrow entry requirements that require ascertainment of molecular information. To increase access to patients, NCI is now funding accrual by 15 cancer centers that did not receive a phase 1 grant or a phase 2 supplement. This change makes it possible to open ETCTN trials across the entire cancer center network. Almost all NCI-designated cancer centers with clinical capabilities are now active in the ETCTN.

NCI Drug Formulary. Pharmaceutical and biotechnology companies will donate drugs to the new NCI Drug Formulary. Researchers will obtain compounds from this preapproved "formulary" list and test them for new purposes or in new combinations. This approach will eliminate the need for separate negotiations with each company for each research project. NCI has pledge letters covering approximately 30 drugs from about 10 companies. In early 2017, a website will list the available compounds and the studies of interest to the companies. Dr. Lowy noted that the notion of the formulary had first come up only a few months earlier. The Vice President's call for doing things differently helped NCI make rapid progress with the formulary.

Questions and Discussion

Dr. Gershenson asked about interim results for NCI-MATCH. Dr. Doroshow replied that the initial match rate was about 8 to 10 percent, but it is too soon to have any therapeutic efficacy data on patients who have been matched.

Dr. Gershenson asked whether the Moonshot is restricted to U.S. sites and investigators. Dr. Lowy explained that the Moonshot can support international research.

Dr. Sledge asked whether the 8 to 10 percent match rate reflects a paucity of drugs in the pipeline or biological reality. Dr. Doroshow explained that the match rate has increased to 25 percent with the addition of certain drugs and depends on the frequency of mutations. With more arms, it will be more likely to find eligible patients.

Dr. Sledge asked whether there is a biology-based ceiling on the match rate. Dr. Abrams explained that with the addition of approximately 10 arms, the match rate might increase to approximately 30 percent.

Dr. Davidson asked about the impact of the increase in the NCI budget on the R01 grant payline. Dr. Lowy said that the success rate for R01 grant applications is not likely to change because the number of applications increased substantially between FY 2015 and FY 2016.

Dr. Davidson asked about NCI's role in the PMI cohort and whether any PMI-O funding will be used to support the cohort. Dr. Lowy replied that in addition to the oncology component that he had described, the PMI will create a cohort of 1 million people. The cohort studies do not currently include cancer-related interventions or prevention strategies. The cohort has its own budget of \$130 million, which is separate from the \$70 million for the oncology component of the PMI.

Dr. Munshi asked what will happen after NCI-MATCH ends in a year. Dr. Doroshov said that no decisions have been made about follow-up initiatives.

Dr. Ochoa asked about minority representation in NCI-MATCH. Dr. Lowy replied that 8 to 10 percent of participants are African American and that the study also includes Native Americans.

III. Legislative Update

M. K. Holohan, JD

National Institutes of Health (NIH) Fiscal Year (FY) 2016 appropriation. In FY 2016, the NIH appropriation increase (\$2 billion, including a \$265 million increase for NCI) was the biggest in 12 years. Two versions of an NIH authorizing bill currently under consideration by the House of Representatives and the Senate would provide mandatory funding for NIH that would be separate from annual appropriations. However, these bills are on hold until the sponsors find ways to offset these costs.

FY 2017 Budget Request for NIH. The President requested \$82.8 billion for the Department of Health and Human Services discretionary programs, a reduction of \$658 million from FY 2016. This budget would cut \$1 billion in discretionary funding from the NIH budget but would add \$1.8 billion in mandatory funding and includes \$680 million for the Vice President's Cancer Moonshot. Because of concerns about the national debt, proposals to increase mandatory funding in general have little support.

The Senate appropriations committee passed an appropriations bill on June 9 that included a \$2 billion increase for NIH and a \$216 million increase for NCI. The House of Representatives version includes a \$1.25 billion increase for NIH and a \$124.9 million increase for NCI. (The House Appropriations Committee ultimately approved the FY 2017 Labor, Health and Human Services, Education, and Related Agencies appropriations bill, including the \$1.25 billion increase for NIH, on July 14). These bills do not include funding specifically for the Vice President's Cancer Moonshot, although the appropriators have indicated that they would consider a specific allocation after the Cancer Moonshot Federal Task Force report has been issued. It is important to note that the President's budget request did not ask the appropriators to fund the Cancer Moonshot. To the contrary, the budget request specified a \$1 billion cut to the NIH budget while simultaneously requesting a \$1.8 billion increase in mandatory funds, from which the Cancer Moonshot would be supported.

Congress, which was about to leave for a recess until September 6, was likely to pass a continuing resolution in September 2016 to keep the government funded. After the November elections, Congress will return for a lame duck session and take up negotiations on an appropriations bill for FY 2017, which might be one large omnibus bill for all 12 spending bills or a combination of smaller "minibuses" that would combine a few spending bills together. If they cannot reach an agreement for

FY 2017 spending, Congress might extend the continuing resolution into March until the new administration takes office, or they could pass a full year continuing resolution that would maintain funding for all agencies at the FY 2016 level.

Zika Virus Funding. The House and Senate each passed their own bills to address the Zika virus, with smaller budgets than the \$1.9 billion that the President requested. The two bodies did not reach an agreement on funding to combat Zika before their summer recess.

Election. All House seats and one third of Senate seats will be up for election in November 2016. NIH and cancer research are bipartisan priorities, but the effects of the election on NIH and NCI cannot be predicted.

Interactions with Congress. NCI provides education and technical assistance to members of Congress and their staffs as often as possible. NCI also gives briefings and submits a professional judgment bypass budget every year. Dr. Lowy and Dr. Davidson recently gave a briefing on cancer research, including the importance of basic research, to a standing-room-only crowd that included 60 congressional staff members.

Appropriators, authorizers, and their staff members like to hear from constituents, including grantees and cancer center directors, about cancer research. Briefings on Capitol Hill provide an opportunity to help congressional staff members understand how the research advances that they hear about are supported by NCI.

Questions and Discussion

Dr. Davidson asked whether Ms. Holohan's office is keeping track of the components of the political party platforms that pertain to biomedical research. Ms. Holohan replied that NCI has no official relationship with the party platforms.

Dr. Munshi asked whether or not funding for the Vice President's Cancer Moonshot was included in the FY 2017 budget. Ms. Holohan explained that the President proposed cutting discretionary funding but increasing mandatory funding for NIH; appropriator support for this approach is lacking. NIH and NCI might not receive funding in the manner in which it was requested in the President's budget, but Congress is likely to be receptive to the Blue Ribbon Panel recommendations for the Cancer Moonshot.

Dr. Cullen asked about the timing of NCI's bypass budget and whether this document can address funding for the Cancer Moonshot. Ms. Holohan explained that NCI was expected to deliver the bypass budget in September 2016. Dr. Lowy added that the bypass budget will be for FY 2018 and will include the Cancer Moonshot.

Dr. Davidson said that this is an important year for researchers and their professional societies to educate Congress about the importance of cancer research.

IV. Recognition Ceremony

James H. Doroshow, MD

Douglas R. Lowy, MD

Cancer Clinical Investigator Team Leadership Awardees

Dr. Doroshow explained that the Cancer Clinical Investigator Team Leadership Awards recognize outstanding mid-level clinical investigators at NCI-Designated Cancer Centers whose participation in NCI-funded collaborative clinical trials promotes a culture of clinical research. The awards also encourage the retention of clinical investigators in academic research careers. The clinical oncologists who receive these awards, which provide \$60,000 per year for 2 years, must devote at least 15 percent of their effort to the activities associated with the award. The 2016 awardees are:

- Rahul Aggarwal, MD, Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco
- Jamie Bakkum-Gamez, MD, Mayo Clinic Cancer Center
- Catherine Diefenbach, MD, Laura and Isaac Perlmutter Cancer Center, New York University Langone Medical Center
- Noah Hahn, MD, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University
- Erin Hofstatter, MD, Yale Cancer Center, Yale School of Medicine
- Kevin Kelly, MD, PhD, Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California
- Sarah Leary, MD, MS, Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium
- Frederick Locke, MD, H. Lee Moffitt Cancer Center & Research Institute
- Rachel Miller, MD, Markey Cancer Center, UK HealthCare, University of Kentucky
- Taofeek Owonikoko, MD, PhD, Winship Cancer Institute, Emory University
- Geoffrey Oxnard, MD, Dana-Farber/Harvard Cancer Center, Dana-Farber Cancer Institute
- Dale Shepard, MD, PhD, Case Comprehensive Cancer Center, Case Western Reserve University
- Theresa Werner, MD, Huntsman Cancer Institute, University of Utah Health Care

Recognition of Retiring CTAC Members

Drs. Lowy and Doroshow thanked the retiring CTAC members—Dr. Cullen, Ms. McCabe, Dr. Sledge, Dr. Villalona-Calero, Dr. George J. Weiner, and Dr. Takimoto—for their service. Each retiring member has served NCI in many ways beyond their roles in CTAC. All have contributed a great deal of time and input that have improved NCI's efforts on behalf of patients.

V. Chemical Biology Consortium

Barbara Mroczkowski, PhD

The Chemical Biology Consortium (CBC) is the discovery engine of the NCI Experimental Therapeutics (NExT) program and represents NCI's venture into early-phase drug discovery. NCI created the CBC in 2009 to fill the chemistry void at the National Institutes of Health (NIH) at that time. The consortium was modeled on the NIH Molecular Libraries Program, but unlike that program, it works to advance therapeutics in addition to generating chemical probes. The CBC and NExT focus on projects that are unlikely to be pursued by industry.

The CBC pilot phase began in 11 centers in late 2009 and ended in early 2016. The favorable results of an extramural review of the pilot phase led to a request for proposals for dedicated and specialized centers to participate in the next phase. As a result of the recently completed competition, the consortium has now expanded to 23 centers. The CBC has the expertise and capabilities needed to support all drug development activities and is heavily invested in a team science approach.

The benefits of partnership with the CBC include significant in-kind support to move hit and lead molecules toward becoming clinical candidates, collaboration with industry-seasoned scientists, and access to enabling resources and cutting-edge technologies. The CBC also offers diverse, well-curated compound libraries with more than 5 million small molecules and quantitative high-throughput screening that lets projects identify weak hits that could become potent leads. Dr. Mroczkowski highlighted a number of ongoing projects, including one on inhibitors of Mcl-1 (a myeloid leukemia cell differentiation protein), lactate dehydrogenase, and isocitrate dehydrogenase 1.

An analysis of factors contributing to the closure of NExT projects showed that more than 80 percent of late-discovery studies (those requesting resources to enable investigational new drug applications) closed due to reproducibility issues. Without progression of the CBC early discovery projects, NExT would have had only one project in the late-discovery phase.

Questions and Discussion

Dr. Mankoff asked whether NCI had considered including diagnostic molecules, such as imaging probes, in the CBC. Dr. Mroczkowski replied that the CBC does have some imaging probe studies, and all of the imaging projects in the CBC to date have advanced to phase 2 clinical trials.

Dr. Munshi inquired about the acceptance rate for CBC applications. Dr. Mroczkowski replied that NExT accepts approximately 15 percent of applications each cycle. These applications span the pipeline to include pharmaceutical agents, imaging modalities, early discovery, and target validation.

In response to a question from Dr. Fyfe about judging the success of the CBC, Dr. Mroczkowski said that pharmaceutical companies often license products and then put them on the shelf. The purpose of the CBC is to conduct proof-of-concept studies to find out whether the compounds have utility in the clinic. If a compound generates evidence of efficacy in phase 1/2 trials, it might move on to commercialization.

Dr. Mroczkowski answered a question from Dr. Ochoa about repurposing drugs by saying that the CBC does support studies to repurpose drugs. Investigators can apply for this support through NExT or the NIH Therapeutics for Rare and Neglected Diseases program.

Dr. Petersen asked whether NCI will improve the ability to stop project development at an early stage when appropriate. Dr. Mroczkowski said that fewer and fewer late-discovery projects are entering the NCI portfolio, because NCI uses new approaches to educate applicants about its expectations and establish milestones to obtain a “quick read” on each project’s progress. She added that the government needs to support early discovery, even with its limited funds, because very few clinical candidates show efficacy and are worth pursuing by the private sector.

Dr. Davidson asked about the endpoints NCI will use to determine success when the current projects end. Dr. Mroczkowski explained that progression to proof-of-concept clinical trials will indicate

success, and one such study is under way. Another marker of success is publications. Dr. Fyfe suggested that giving a license to someone else who can take the compound through the next steps would be another indicator of success. Dr. Mroczkowski explained that NCI would like to move these compounds into the clinic itself. Dr. Doroshov added that NIH has a unique ability to conduct first-in-human trials at a very modest cost.

VI. Clinical Trials and Opportunities for Collaboration at the Department of Veterans Affairs

Michael J. Kelley, MD

Background. Approximately 22 million Americans are veterans. Of these, 9 percent are female and 22 percent are minority. Approximately 9 million veterans are enrolled in the Veterans Health Administration (VHA), which has 144 hospitals and 1,203 outpatient sites. Approximately 50,000 patients are diagnosed with cancer in the VA every year. The VA has a mature, well-integrated electronic health record system that captures data in a central location.

Quality of Care in the VA. Quality of care in the VA is almost always similar to or higher than outside the VA. For example, colorectal cancer is diagnosed at earlier stages in the VA, and rates of curative-intent surgery for colon cancer are higher. A 2001 study showed that the VA system offers cancer care that is generally similar to or better than the cancer care offered to fee-for-service Medicare beneficiaries. However, the adoption of some expensive new technologies can be slower inside than outside the VA.

VA National Precision Oncology Platform (POP). The VA developed POP before the Vice President's Cancer Moonshot was announced. POP established turnkey processes for molecular profiling in the VA's system in a way that reduces costs and increases uniformity. The program also offers a molecular oncology consultation service for clinicians and makes new drugs available to patients through research partnerships. Patient data on the outcomes of these activities are aggregated for learning and research purposes. The POP goals are to:

- Define and disseminate precision oncology best practices
- Provide standardized, high-quality care
- Use program data to understand cost and effectiveness, generate knowledge of what does and does not work, and provide opportunities for clinical trial participation
- Realize economies of scale for laboratory and drug costs

Molecular profiles have value only if a drug corresponds to that particular defect in a patient's tumor. Moreover, the targeted therapies need to reach patients who have been profiled. The large patient populations in the VHA enable a complete view of the full landscape of patient profiles. Many profiles have substantial numbers, which can speed up learning and make it possible to find patients in the VHA with the appropriate profile for any clinical trial.

The POP also offers opportunities for traditional research because of the VA's ability to open intramural and sponsored clinical trials nationally to enable broad patient access. The VA Cooperative Studies Program and the VA Central Institutional Review Board (CIRB) provide structure, and VA clinicians and external stakeholders offer intellectual capital. Patients can be matched to clinical trials at the point of care through the VA's data repository. Furthermore, the VA offers rapid clinical trial

enrollment because of its size, its cost-effective participation, its infrastructure and programs, and its potential for collaboration with the Vice President's Cancer Moonshot.

Features of the VA that can appeal to sponsors and partners include the application of analytics to the VA's data repository to predict patient outcomes based on experience. The VA's molecular tumor board obtains information from electronic medical records that providers, tumor boards, researchers, and program sponsors can use for decision support, practice guidelines refinement, determination of POP effectiveness, and publication if the knowledge is generalizable. Rapid learning opportunities at the VA include the Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) Network, of which NCI is a member.

Clinical Trials in the VA. In 2001–2003, participation rates in NCI Cancer Therapy Evaluation Program trials in the VA system were lower (0.37 percent) than the national rate for males (0.74 percent). However, the enrollment rate among VA facilities with women was substantially higher (2.7 percent) than the national rate (1.8 percent).

Very few VA facilities have significant clinical trial activity according to ClinicalTrials.gov, and much more could be done. In June 2015, NCI and the VA signed a memorandum of agreement to use the NCI CIRB as an institutional review board (IRB) of record. Four VA sites have since added this IRB, and two more are doing so. A few VA sites have opened NCI precision medicine studies (NCI Molecular Analysis for Therapy Choice [NCI-MATCH] trial, Lung Cancer Master Protocol [Lung-MAP], and Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials [ALCHEMIST]). Moreover, VA facilities have opened 49 other NCI-sponsored trials. SWOG's Hope Foundation provided grants to five VA sites to enroll patients on SWOG trials.

The VA has a complex procedure to obtain regulatory approval for a clinical trial. The process includes a pre-review (approval by a privacy officer and an information security officer) followed by the IRB review, research and development committee review, and a signature from the associate chief of staff for research. The amount of time required to complete these processes varies by facility. In 2001–2011, the mean VA IRB review time was 131 days. Only 10 percent made it in 60 days or less, which is the industry standard.

In the future, the VA needs to maximize the use of VA and NCI CIRBs, regardless of the study sponsor. Until recently, the VA CIRB considered only VA-sponsored studies. Now, the VA CIRB is accepting pharmaceutical company-sponsored studies. Clinical trials should be prioritized by disease-based steering committees, much like NCTN trials are. Going forward, the VA needs to leverage its clinical studies program support and partner with others, including NCI, industry, and nonprofit foundations.

Questions and Discussion

Dr. George J. Weiner commented on the regulatory burden involved in opening a clinical trial at a VA facility, including the requirement for investigators to undergo special training. He asked whether the training and experience of NCI-supported investigators could be taken into account to streamline the VA's approval process for investigator-initiated trials. Dr. Kelley responded that all investigators conducting studies in VA facilities must be trained in ethics, good clinical practice, and other issues. He offered to discuss Dr. George J. Weiner's experience with him in greater detail later.

Dr. Sledge commented that most VA facilities are affiliated with academic medical centers, where the proportions of patients enrolled in clinical trials are higher than the national averages. Instead of comparing VA enrollment rates to national rates, it makes more sense to compare VA enrollment rates to those at academic medical centers. VA facilities that are on the same campus as academic medical centers and have the same faculty members have much lower rates of opening clinical trials than the academic medical centers. Dr. Kelley's response was that Dr. Sledge's point is well taken, but VA patients are somewhat different from those in academic medical centers. For example, VA patients tend to have lower socioeconomic status. Regardless of these differences, the goal should be to increase accrual in VA facilities.

Dr. Gershenson wondered about VA women enrolled in clinical trials. Dr. Kelley explained that approximately 7 to 9 percent of VA patients are women, but only 3 percent of patients with cancer are women, partly because women enrolled in the VA tend to be younger than enrolled men. He did not know the proportion of women with cancer enrolled in clinical trials at the VA, but it might be lower than the national rate because, for example, breast cancer trials are uncommon in the VA.

Dr. Mankoff inquired about the VA's plans to reinvigorate clinical trials in VA facilities. Dr. Kelley said that the model of care in the VA is closer to that of a community practice than an academic medical center. Furthermore, VA facilities tend not to have many patients with a given disease, lowering the efficiency of any trial in this setting. The way to increase the efficiency of clinical trials in the VA is to pool these patients together and use the CIRB.

Dr. Cullen commented that about a decade ago, the VA was responsible for a significant proportion of accruals in his institution's trials. Today, the VA accrues virtually no patients to trials. He asked about numbers of accruals 10 years ago and now. Dr. Kelley reported that he does not have these data, but a survey is under way to collect this information.

In response to a question from Dr. LeBlanc about the VA CIRB, Dr. Kelley said that the CIRB is used extensively for VA-sponsored trials, but the VA sponsors very few cancer trials. One of the VA facilities that has opened 20 clinical trials is in Kansas City, where the hospital director provided support for two clinical research associates, staff needed to complete the paperwork required to make clinical trials possible in VA facilities.

Dr. George J. Weiner said that the integrated VA/academic medical center model that existed 15 to 20 years ago worked well. Since then, the administrative burden for academic medical centers to enroll VA patients in clinical trials has increased so much that centers no longer try to open studies at VA facilities. He asked about the possibility of returning to the earlier model. Dr. Kelley said that the regulatory requirements to approve trials in the VA are unlikely to change. Once the VA's regulatory processes are understood, trials can be opened in VA facilities. However, academic medical centers must provide extra resources to do the paperwork required to open studies.

Dr. Mitchell said that patients often live far from VA facilities and do not come in regularly. Clinical trials require an infrastructure that provides compensation to patients for the costs involved in traveling to the hospital for clinical trial-related procedures. Dr. Kelley said that the VA does reimburse patients for travel expenses depending on their VA eligibility and travel distance. Discussions are ongoing about increasing reimbursements for patients undergoing cancer treatment. In addition, the VA has an extensive and well-developed telehealth network that can allow patients to receive their care close to home.

Dr. Louis M. Weiner said that part of the challenge with enrolling VA patients in clinical trials is a difference in cultures; changing a culture usually requires a top-down approach. He asked about the attitudes of VA leaders in ensuring that veterans have access to cutting-edge treatments through clinical trials. Dr. Kelley explained that many people at VA headquarters and at each VA facility contribute to decisions that affect the facility's culture. They decide, for example, whether to hire oncologists with clinical trial experience, which is necessary for on-site clinical trials. Barriers to clinical trials at one VA facility might not exist at another facility. For example, one VA facility might have academic oncologists but no support for trials, whereas another might have support for trials but no academic oncologists. The issue is not only culture but also resources.

Dr. Louis M. Weiner said that CTAC has an opportunity to create a call to action and that we owe our veterans opportunities to enroll in clinical trials. This call to action is particularly timely in the era of the Vice President's Cancer Moonshot. Dr. Kelley reported that the VA leaders did fund POP, which includes clinical trials. The question is how to disseminate this attitude into the field.

Dr. Dahut asked whether the VA has enough physicians who want to do clinical trials. Dr. Kelley explained that a few VHA facilities have very sophisticated faculty members with clinical trial experience as well as some disease-specific clinics. The academic model of clinical trials works well in these facilities. Other facilities have only one oncologist. The VA needs to establish a central office at a more sophisticated VA facility and collect data centrally while delivering care locally. Dr. Kelley believes that such a model is possible.

Dr. Munshi said that some challenges to enrolling VA patients in clinical trials are that patients are older, many are on multiple medications, and they often have several comorbidities. However, the VA has a huge patient population that could be used to answer some veteran-specific questions. The VA also has an outstanding information system that can identify patients throughout the VA network who might be eligible for a trial. The VA offers great opportunities that could be leveraged through resources that could come from collaboration with NCI. Dr. Kelley agreed that such a model can work and that now is the time for it.

Dr. Munshi asked about the Million Veteran Program. Dr. Kelley explained that this program is enrolling patients for genetic analysis. Almost half a million veterans have enrolled to date, and genotypic information is available on many of them. One Million Veterans Program project focuses on cancer. Dr. Munshi pointed out that the Million Veterans Program tissue samples collected for genomic analysis could be used for cancer diagnosis, and these patients might participate in a next-generation NCI-MATCH trial.

Dr. Davidson asked how CTAC could help the VA expand its participation in cancer clinical trials. Dr. Kelley said that simply having this discussion was helpful and that an ongoing discussion is planned between NCI and the VA about how to make NCI-sponsored trials a priority in VA facilities and how to enroll VA patients in these trials. VA leaders also need to talk to each other about the structure the system needs to support clinical trials. POP gives priority to providing access to new drugs, which the VA could do through NCI.

VII. Immuno-Oncology and Precision Medicine Initiatives

Jeffrey S. Abrams, MD

Cancer Immunotherapy Trials Network

The Division of Cancer Treatment and Diagnosis Cancer Immunotherapy Workshop in January 2016 brought together thought leaders to discuss opportunities and gaps in cancer immunology/immunotherapy and how NCI should facilitate further development in this field. Participants recommended clinical trials rich in “translation” along with biomarkers and a database. In response to the experts’ recommendations, NCI has developed funding opportunity announcements for adoptive cell therapy trials.

Furthermore, NCI is reissuing the Cancer Immunotherapy Trials Network (CITN). The previous round of funding supported early-phase, multisite trials at 32 sites. Some of these studies have completed their enrollment and are starting to generate results. One successful CITN trial showed that 68 percent of patients with advanced Merkel cell carcinoma responded to treatment with the programmed cell death protein 1 inhibitor pembrolizumab.

The reasons to renew the CITN include its access to immunologic agents not in the Division of Cancer Treatment and Diagnosis portfolio. Furthermore, 40 percent of CITN sites are not part of the Experimental Therapeutics Clinical Trials Network (ETCTN), so the CITN gives NCI access to a wider pool of qualified immunotherapists. The CITN trials are translationally rich, which has allowed NCI to quickly take advantage of clinical opportunities in immunotherapy.

An external panel reviewed the CITN and recommended renewing it. However, the panel suggested that NCI integrate the CITN into existing ETCTN processes for data management and regulatory support to avoid paying for additional infrastructure. The panel also recommended limiting the number of members to the best 20 sites and separating the immunomonitoring core from the CITN through a separate request for applications. This core could then provide immunomonitoring support to all NCI-sponsored networks and consortia. NCI plans to implement these recommendations.

The new CITN sites will develop combinations of immunotherapies with other immunomodulatory agents, targeted agents, or chemotherapies. The total budget is \$1.5 million per year, which will allow the network to enroll 120 patients per year at an average cost of \$6,000 per patient.

Immunotherapy Monitoring

NCI is considering issuing requests for applications for Cancer Immune Monitoring and Analysis Centers (CIMACs) and a Cancer Immunological Data Commons (CIDC). Although immunotherapy has remarkable activity in a variety of cancers, only a minority of patients benefit from this treatment, with typical response rates of 20 to 30 percent. Optimizing patient outcomes will require combination therapies to overcome resistance and biomarkers (especially predictive biomarkers to identify the right treatment for each patient). Research on biomarkers is needed to predict benefits and toxicities of drugs, support target modulation and rational design of combination therapies, assess responses to therapy and monitor patients, and select doses. The CIMACs and CIDC would:

- Determine which assay and instruments are most appropriate for the biomarker question
- Perform assays through designated laboratories in the CIMACs

- Establish and manage a database for immune and tumor profiling data from NCI-sponsored clinical trials
- Perform within- and cross-trial analysis
- Prepare for the next phase of biomarker development when a trial identifies candidate markers.

Centralizing the data from these small trials will make it possible to draw conclusions from multiple trials about immune responses.

NCI would establish up to three CIMACs. The CIMACs would partner with one or more NCI clinical trials networks to conduct correlative studies and provide immunoprofiling analyses for specimens from NCI-supported clinical trials. Each CIMAC would conduct biomarker studies for a group of clinical trial sites, provide multidisciplinary experts to carry out immune profiling and analyses, and offer computational biology and biostatistics resources. In some cases, NCI-supported R01 or P01 clinical trials would have an opportunity to work with a CIMAC.

The CIDC would be responsible for quality and harmonization across CIMACs. A bioinformatics core would collect and store the data from CIMAC studies, facilitate standardization of immunologic data collected by the CIMACs and best practices, develop information resources and share data to promote secondary analyses by other investigators, and collaborate with other data centers when possible. A laboratory coordinating committee would coordinate the network and optimize resources. The annual budget would be \$6.5 million for the three CIMACs and \$1 million for the CIDC. This would support immune parameter analyses on about 360 patients per year at a cost of approximately \$8,000 per patient.

Questions and Discussion

CITN. Dr. Louis M. Weiner suggested that the CITN serve as an idea generator and hypothesis tester that could help National Clinical Trial Network (NCTN) sites do high-risk or hypothesis-generating studies that are not easily done through the pharmaceutical industry. He asked whether the plans call for including prevention vaccines in the CITN. Dr. Abrams agreed with Dr. Louis M. Weiner's suggestions, adding that the CITN will do important early studies with many correlatives. However, it is a small network that conducts only a small proportion of NCI immunotherapy trials.

CIMACs. In response to a question from Dr. Davidson about the key concerns with the CIMACs, Dr. Abrams explained that the Board of Scientific Advisors (BSA), which also reviewed this concept, wanted NCI to better describe how the NCI clinical trials would partner with the CIMAC laboratories. Furthermore, the BSA noted that it is difficult to draw conclusions about predictive markers from small early-phase studies. NCI agrees, but the CIMAC trials would develop candidate markers to be tested in other studies. In addition, these studies could provide information about immunomodulation and guidance on optimal ways to combine different agents.

Dr. Louis M. Weiner said that the Vice President's Cancer Moonshot's immunology and prevention panel is likely to be interested in the types of analyses to be conducted by the CIMACs. However, the Cancer Moonshot panel might be concerned about the modest size of the clinical research enterprise to be supported through the CIMACs. In addition to collaborating with other clinical networks, NCI might leverage the unique perspectives of the immunotherapy community and create a cancer immune atlas. He recommended that NCI integrate biospecimen procurement from clinical trials and develop an adequate pathology infrastructure. Dr. Abrams said that one reason for creating a data commons was to learn from integrating all of the trial data.

Dr. Ochoa said that 360 patients per year is a small number given the interest in immunotherapy. He wondered whether the CIMACs can do the proposed sequencing and asked about the logistics of sending samples quickly to a centralized location. For these reasons, three CIMACs might not be enough. Furthermore, the CIMACs should use standardized flow cytometry measures. Dr. Abrams said that NCI does plan to take advantage of existing resources where possible and that he agreed that 360 patients a year is a starting point. The plan was to start with a manageable number of CIMACs and perhaps increase the number if the first activities are successful.

Dr. Curran said that it will be critical to determine how the CIMACs would support NCTN trials and other trials in cancer centers, where immunotherapy will become a core business in the next few years. Cancer centers do not need a standalone immunotherapy program for this purpose. NCTN and ETCTN investigators should discuss how the CIMACs can support their research.

Dr. George J. Weiner said that given the concerns about reproducibility, using centralized laboratories to do these challenging assays makes a great deal of sense. He asked about opportunities for trials that are not part of NCI's trials networks to work with the CIMACs. Dr. Abrams explained that important trials that are not part of an NCI clinical trials network and that lack resources for immune monitoring could request permission from the laboratory coordinating committee to use the network capabilities. He added that once the CIMACs develop expertise, they could serve as reference laboratories. At the January 2016 meeting, industry representatives said that NCI could add value to immunotherapy development in this area.

Dr. Mitchell commented that cancer centers have resources that could speed up the work of the CIMACs and help them expand their capacity. She also thought that NCI Community Oncology Research Program and NCTN institutions would love to participate in the proposed program. Bringing more institutions into the initiative, especially those associated with NCI, would boost an already outstanding infrastructure and program.

Dr. Mankoff asked whether the studies will assess markers that can be used with imaging modalities to distinguish between progression and response. Dr. Abrams said that the January 2016 meeting included some good suggestions for imaging biomarkers, and he would like to include those modalities in clinical trials if they mature a bit.

Dr. Fyfe inquired about the relationship of the immune assays to patient benefit and the extent of intra-patient consistency as opposed to reproducibility in different laboratories. She advocated for including fewer assays and making sure that they are modulated by drugs. Three hundred and sixty patients might be too many if the markers' ability to predict a given outcome is unknown. Dr. Abrams explained that not every assay will be done on every patient. The reason why the number of patients is small is to understand immunomodulation and find potential predictive models. The studies will generate hypotheses, and much larger randomized trials will be required to move to the next phase. To ensure that the assays are reproducible, they will be implemented in a centralized facility.

Dr. Blaney advocated for integrating the CIMACs with the NCTN and NCI Community Oncology Research Program from the beginning. Dr. Abrams said that early-phase trials must be handed off to later-phase trials in clinical trial networks to conduct more definitive trials. This would be an early step in the process.

Dr. Doroshow said that 360 patients might be just enough to keep three CIMACs going. However, NCI might need six or more CIMACs to address the obvious need. The cost to provide the resources for 360 patients is \$7.5 million per year because these activities are expensive. This initial investment would help NCI determine what to do once it is ready to invest in studies in many more patients. The CIMACs would be part of a pilot program that would show how to apply appropriate standard operating procedures in multiple laboratories. To really serve the clinical trials community in this area will require scaling up this activity significantly.

VIII. Progress in Small-Cell Lung Cancer Research Working Group Report

Charles M. Rudin, MD

Small-cell lung cancer (SCLC) is one of the leading causes of cancer mortality in the United States, with a survival rate of 7 percent. Most patients present with advanced-stage disease and a prognosis of less than 1 year. Treatments for this disease have not changed substantially in the last 30 years.

In the Recalcitrant Cancer Research Act of 2012, Congress charged NCI to develop scientific frameworks for research programs in pancreatic cancer and SCLC. NCI created internal action planning groups to track progress in each disease site, and CTAC created working groups to develop scientific frameworks for the two diseases and monitor progress in these frameworks (essentially how NCI is responding to the frameworks by funding initiatives in this area).

Dr. Rudin reviewed the accomplishments within each initiative in the SCLC scientific framework as well as the Progress in SCLC Working Group's conclusions and recommendations for each initiative. The initiatives are:

1. Better Research Tools for the Study of SCLC
2. Comprehensive Genomic Profiling of SCLC
3. New Diagnostic Approaches for SCLC
4. Therapeutic Development Efforts
5. Mechanisms Underlying Both High Rate of Initial Response and Rapid Emergence of Drug and Radiation Resistance

In general, implementation of each of the five initiatives is on target, although it is too early to assess their scientific progress.

The working group will probably report back to CTAC in 2018. It will revise the scientific framework in 2018–2019 and evaluate the effectiveness of framework activities in 2020.

Questions and Discussion

Dr. Matrisian asked how the working group plans to measure NCI's progress in each initiative. Congress will want to see advances in survival, new therapies, and new diagnostic approaches. Dr. Rudin said that the working group is seeking real progress for patients and will measure this progress based on clinical outcomes. Other metrics might be NCI funding for SCLC research, numbers of SCLC investigators, new treatments under development, and new targets with translational importance. By 2020, it should be possible to produce these kinds of data. Dr. Prindiville added that the Recalcitrant Cancer Research Act of 2012 requires NCI to examine, in 2020, the effectiveness of using a scientific framework

to direct research. The pancreatic cancer and SCLC working groups will probably use some of the same measures to assess effectiveness.

Dr. Petersen asked whether the genomic profiling initiative described in the working group's report is complementary to the efforts of The Cancer Genome Atlas (TCGA). Dr. Rudin explained that TCGA does not include SCLC, so the working group decided to do a comprehensive analysis of the SCLC genome. Thus, this effort is complementary to the activities of TCGA. He added that sequencing efforts to date have mostly used fresh frozen tissue from surgically resected pulmonary nodules that turned out, on review, to have SCLC. These samples therefore represent very early-stage disease and not the more typically advanced presentation. More research is needed on metastatic SCLC.

Dr. Petersen asked why NCI is focusing on SCLC and not lung cancer in general. Dr. Rudin explained that NCI was charged with addressing SCLC in the Recalcitrant Cancer Research Act of 2012. Although better early-detection strategies are needed for cancer in general, SCLC is particularly problematic, because it is usually metastatic at oncogenic transformation; no precursor lesions for SCLC have been identified. Although the National Lung Cancer Screening Trial found that annual computed tomography screening reduced lung cancer and overall mortality, it had no effect on SCLC mortality.

Ms. McCabe asked about expanding the number of investigators interested in SCLC research. Dr. Rudin said this is very important, because no "big hits" have been made in SCLC research for a very long time—perhaps 40 years. But the field is primed for more big hits now. The funding opportunity announcements arising from the scientific framework will attract new investigators to this field. Pharmaceutical industry sponsors are also showing more interest in this field, and this interest is likely to trickle down to investigators.

A motion carried to accept the report of the Progress in SCLC Working Group.

IX. Clinical Trials Strategic Assessment Working Group and National Clinical Trials Network Request for Applications Evaluation Working Group

Jeffrey S. Abrams, MD

Clinical Trials Strategic Assessment Working Group Update

The Clinical Trials Strategic Assessment (CTSA) Working Group, which has not yet been constituted, has been charged with the following activities associated with the National Clinical Trials Network (NCTN) groups and NCI Community Oncology Research Program (NCORP) research bases:

- Assess the strategic clinical trial priorities established by the Scientific Steering Committees (SSCs) in 2015
- Assess the process for establishing the strategic clinical trial priorities
- Assess the quality and objectivity of the individual strategic clinical portfolio assessments conducted by the SSCs
- Perform a cross-portfolio assessment.

NCI asked each SSC to develop a few well-defined strategic priorities for trials under their purview to ensure that the NCTN and NCORP clinical trial investments address the most important and promising clinical questions. Each SSC completed this process.

In November 2015, CTAC agreed with the NCI recommendation to include assessments of the strategic clinical trial priorities and the priority-setting process in the CTSA Working Group (WG) charge. NCI would like the working group to consider whether this process needs any refinements. Proposed CTSA Working Group activities related to strategic priorities are to:

- Review priorities, their categorization, and NCI's operational definition of a strategic clinical trial priority
- Review feedback from NCI medical officers, SSC chairs, and NCTN group and NCORP research base representatives on the priorities, their categorization, and the priority-setting process
- Develop recommendations for refining the process and possibly the operational definition of a strategic clinical trial priority for future rounds of priority setting
- Report to CTAC on assessments of the current priorities, the operational definition of a strategic clinical trial priority, the priority-setting process, and recommendations for future priority setting.

CTAC had recommended that each SSC conduct a self-assessment of the individual trials within its portfolio. The CTSA WG will perform a high-level assessment of the overall strength of the NCTN/NCORP clinical trial portfolio based on the quality of the individual trials within the portfolio and whether the trial portfolio as a whole addresses the most important clinical questions under the purview of each SSC. It will then assess the overall strength of the NCTN/NCORP clinical trials across portfolios.

Formation of the CTSA WG was delayed while the Breast Cancer and Gynecologic Cancer SSCs conducted pilot assessments. Dr. Abrams summarized the lessons learned from these pilot assessments. They were both valuable and feasible, and they should be conducted every 4 to 5 years at an in-person meeting. Assessment should include all trials open, approved, disapproved, or closed since the last assessment and not be limited only to trials approved since the last assessment. Accrual performance should be an ongoing activity, independent of the self-assessment process.

The proposed timeline calls for the CTSA Working Group to begin assessing the strategic clinical trial priorities and priority-setting process approximately between October 2016 and March 2017. In July 2017, the CTSA Working Group will present its first report to CTAC.

Questions and Discussion

Dr. George J. Weiner commented that the SSCs might not want to establish strategic priorities every year, but they should be required to look at their priorities every year and determine whether they need to change these priorities, because many changes can happen in 5 years. Dr. Abrams agreed with Dr. Weiner and said that the SSCs would look at their priorities yearly but would complete the self-assessments every 4 to 5 years.

Dr. Munshi suggested that the SSCs report on their responses to the recommendations from CTAC's NCTN Working Group, which made an interim report in 2013 and its final report in 2014. Dr. Prindiville explained that NCI has not formally analyzed the SSC responses to the recommendations, but such a review would be a reasonable component of the next SSC self-assessment.

Dr. Gershenson pointed out that the SSCs do not have a good sense of the other SSCs' best practices. Sharing the CTAC working group assessments with all of the SSCs would help all SSCs.

Dr. Fyfe suggested that the SSC self-assessments consider outcomes in different categories of clinical trials (such as randomized phase 2 trials). These outcomes might include how many trials were completed and whether they resulted in publications in top journals, for example. The goal would be to learn what kinds of trials succeed and fail and to plan future trials accordingly. A second recommendation from Dr. Fyfe was for the cross-portfolio assessments to compare the strategic insights of the SSCs. Dr. Abrams explained that NCI monitors trial implementation and accrual and then shares the results with the SSCs.

Dr. Curran emphasized the need to include the NCTN group leadership in the assessment process. He encouraged an assessment of the strategic priorities in the SSCs and how their alignment with concepts or a lack thereof affects the function of the entire network. Dr. Prindiville agreed that the NCTN group chairs should be included in the process.

Dr. Sledge suggested that the assessment of the SSC priorities should take place a year or so before the NCTN group renewals because their results would be helpful to the study sections that review these applications.

Dr. Dahut commented that the SSCs do not always consider whether the concepts they are reviewing address their strategic priorities. Dr. Abrams said the strategic priorities are new, and NCI needs to talk to the SSC chairs about integrating their strategic priorities into their concept reviews. SSCs may approve concepts that do not address a strategic priority, but they need to justify these decisions.

Dr. Mankoff suggested sharing the insights from the initial self-assessments with the SSCs that are too new to have completed a strategic self-assessment, such as the Clinical Imaging Steering Committee.

Dr. Davidson asked how CTAC should respond when it receives the cross-portfolio assessments and final strategic portfolio assessment report in November 2018. Dr. Abrams responded that in the NCTN Working Group Reports in 2013 and 2014, which were accepted by CTAC, some disease areas were doing very well, taking advantage of the clinical opportunities in that disease and doing very interesting trials, and some diseases were not, and that sometime afterward changes in some of the NCTN group disease committees occurred.

Dr. Sledge suggested that CTAC include SSC efforts to implement the recommendations of the NCTN Working Group in future grant reviews. Dr. Prindiville added that NCI plans to make the self-assessments an ongoing process, and the reports should be issued in the middle of each funding cycle. The purpose is not to assess each group but, rather, to evaluate the network as a whole, which will help NCI make midcourse corrections for the NCTN.

Dr. Blaney asked about the use of the annual reports from each group in the assessments. Dr. Abrams responded that NCI reviews the reports to ensure that the grant requirements are being met. However, the questions that NCI considers in this process are different from those asked during the strategic prioritization and assessment process.

NCTN Request for Applications Renewal Evaluation Working Group

Dr. Abrams explained that NCI needs an external evaluation of the NCTN as part of the process for developing the NCTN request for applications (RFA) renewal. This group will assess the NCTN's

scientific contributions since the new NCTN awards were issued in March 2014 and will develop recommendations for enhancing the science and functioning of the NCTN. Because of the large investment in the NCTN, NCI recommends that this external review be conducted under CTAC's auspices. NCI would like to convene the NCTN RFA Renewal Evaluation Working Group in the fall of 2016. Its members will include CTAC members, cancer center directors, biostatisticians, and patient advocates. The committee will hold deliberations in the fall of 2016 and report on its findings to CTAC in March 2017.

Questions and Discussion

A motion carried to form the NCTN RFA Renewal Evaluation Working Group.

X. Clinical Trials Informatics Working Group Update

Louis M. Weiner, MD

Warren Kibbe, PhD

Clinical Trials Informatics Working Group

Dr. Louis Weiner explained that CTAC formed the Clinical Trials Informatics Working Group (CTIWG) in the spring of 2016 to provide extramural expertise and advice on implementing clinical trial informatics initiatives. The working group's initial focus is on NCI's Clinical Trials Reporting Program (CTRP), a comprehensive registry of interventional cancer trials supported by NCI. The CTIWG plans to form subgroups focused on:

- Enhancing the usability and accessibility of CTRP data for patients, treating physicians, and the public
- Enhancing the value of CTRP data for the cancer research community
- Using CTRP data as the source for Cancer Center Support Grant (CCSG) clinical trials reporting (i.e., the CCSG data tables)

The CTIWG will hold an in-person meeting on November 9, 2016, to discuss the types of information available in CTRP and how to enhance and provide access to that information by the broader research community.

NCI Clinical Trials Informatics

Dr. Kibbe described the Genomic Data Commons, a unified knowledge base that promotes sharing of genomic and clinical data between researchers and facilitates precision medicine in oncology. This resource contains standardized data from approximately 14,500 patients derived from several NCI programs. The Genomic Data Commons became publicly available following an announcement by Vice President Biden at the American Society of Clinical Oncology (ASCO) annual meeting on June 6, 2016.

The Genomic Data Commons is an important start, but additional types of data need to be deposited into a central resource and made available to the cancer research community. Ultimately, researchers need to learn from the experience of every single cancer patient. Currently, the Surveillance, Epidemiology, and End Results (SEER) program is NCI's primary mechanism for this type of learning. However, there is a long lag time between each patient visit and the availability of their data in SEER.

Vice President Biden asked NCI to engage the Presidential Innovation Fellows to improve access to information about NCI's clinical trials. The new clinical trials application programming interface (API), developed by the Presidential Innovation Fellows, makes a subset of trial registration information from CTRP accessible to third-party innovators for building new digital tools tailored to the clinical trial search needs of their users, much like weather data are made available from the National Oceanic and Atmospheric Administration.

Other changes to enhance access to clinical trials include the @NCICancerTrials Twitter feed, which features announcements of new trials with hashtags that patients and advocates can use to find trials. NCI also plans changes to enhance the ability to search for clinical trials on Cancer.gov.

Other initiatives announced or discussed at the Vice President's Cancer Moonshot Summit include:

- The NCI-Pharma & Biotech Drug Formulary, to make agents available to the cancer clinical trials community
- The Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) initiative, a partnership among NCI, the Department of Defense, and the Department of Veterans Affairs
- A partnership between NCI, the Department of Energy (DOE), and GlaxoSmithKline to apply advanced supercomputing capabilities to the analysis of drug development data
- The National Institutes of Health Public-Private Partnership for Accelerating Cancer Therapies, a collaboration with 12 biopharmaceutical companies to harness high-performance computing and biological data to accelerate the drug discovery process
- A partnership between NCI and DOE to incorporate computational science into cancer research using the DOE supercomputer

Finally, NCI is collecting ideas on its website (cancerresearchideas.cancer.gov) from patients, caregivers, advocates, health professionals, and technical partners on how to make information on NCI-supported clinical trials more accessible to these stakeholders.

Questions and Discussion

CTIWG. Dr. Louis M. Weiner asked for feedback on whether the CTIWG is asking the right questions and has identified the right subgroups. Subgroup 1 will focus on ways to enhance the usability of the CTRP data for patients, treating physicians, and the public. Subgroup 2 will address how to share this information with the cancer research community in a way that allows researchers to learn from one another and determine what research is being done and what that research shows. Subgroup 3 will discuss practical issues related to cancer center support grant activities. Although there is some overlap among these topics, they need to be considered separately.

Dr. Matrisian said that subgroup 1 is the right way to start. A concern, however, is that the public will want advice on which clinical trials to join and not just descriptions of existing clinical trials. There is a tension between wanting the basic information and wanting someone to evaluate that information for each patient. Dr. Louis M. Weiner said that subgroup 1 could discuss ways to narrow down the possibilities to a handful of trials for a patient to consider and tools that the public could use to prioritize trials.

Dr. Davidson pointed out that the CTIWG needs to address the needs of two constituencies: patients and physicians. She asked how to narrow down the choices for the busy oncologist. Dr. Louis M.

Weiner said that it would be great if NCI could offer a service that provides this kind of information, but this would require a great deal of effort.

Dr. George J. Weiner suggested that a fourth group be added to focus on how the data can be utilized. Dr. Kibbe responded that subgroups 1 and 2 will examine how patients, physicians, and the research community find value in CTRP data. Dr. Louis M. Weiner said that the first hour of the CTIWG meeting on November 9, 2016, will focus on what kinds of data are available in CTRP and what kinds of information can be extracted from the database. Dr. Kibbe invited CTAC members to join one of the CTIWG subgroups.

Dr. Mankoff asked whether subgroup 3 will consider National Clinical Trial Network (NCTN) group trials. Dr. Kibbe explained that information about NCTN trials is submitted to CTRP from the Cancer Therapy Evaluation Program.

Dr. Petersen asked for clarification on the activities of subgroup 1, because investigators are already mandated to enter clinical trial data into ClinicalTrials.gov and many organizations have patient-friendly search tools to find clinical trials. Dr. Kibbe explained that cancer centers and NCI have invested a great deal of effort in making sure that the data submitted by the centers to CTRP are accurate, well structured, and up to date. NCI would like to share this well-curated and up-to-date information about all NCI-supported clinical trials with the community. Cancer centers, advocacy groups, and others will be able to use the API to make understandable information on NCI-supported clinical trials available to their constituencies. ClinicalTrials.gov has a different mandate, and the clinical trial abstracts in ClinicalTrials.gov are not always easy for patients to understand and use. Dr. Villalona-Calero noted that it is useful to have information specifically tailored to patients or physicians.

Dr. Davidson concluded from this discussion that the three proposed subgroups are appropriate. She asked what will happen after the CTIWG's meeting on November 9. Dr. Louis M. Weiner said that the subgroups will start creating action plans at the meeting, and the working group might be ready to submit a formal report to CTAC in July 2017.

NCI Clinical Trial Informatics. Dr. Blaney asked about data analytics on use of CTRP. Dr. Kibbe explained that CTRP is not publicly accessible at this time. Cancer centers submit data into this repository, and NCI makes data from CTRP available at Cancer.gov. Dr. Blaney asked for usage statistics for CTRP data once they are uploaded to Cancer.gov. Dr. Kibbe said that these data are available, but he has not reviewed them recently. Dr. Blaney pointed out that many research groups and sites spend a great deal of effort submitting their data, and a concern is that people will analyze these data and draw incorrect conclusions.

Dr. George J. Weiner asked whether Dr. Kibbe has spoken to the Patient-Centered Outcomes Research Institute (PCORI) about allowing the public to view data from the types of clinical trials that NCI conducts and PCORI's pragmatic trials in the same way. Dr. Kibbe has spoken to PCORI staff members. Dr. Louis M. Weiner said that the vast majority of clinical trials in CTRP are therapeutic, not pragmatic, and he suggested not trying to develop an integrated approach to viewing data from clinical and pragmatic trials. However, learning about PCORI's perspectives on the public's use of its data might inform NCI's thinking.

Dr. Mankoff commented that physicians and patients will use the new interface, and this could provide opportunities to educate these stakeholders about the benefits of clinical trials through media

companies. Dr. Kibbe said that every time someone visits Cancer.gov, NCI has an opportunity to educate that person. NCI still needs to determine what types of advice it should give and how to work with the advocacy community to make sure that this advice is relevant to patients. This issue is not currently in the purview of the CTIWG. Dr. Louis M. Weiner said that before giving patients advice, NCI should determine how best to give them information. A concern is that patients will want to know about aspects of clinical trials that they might misinterpret. For example, patients might be concerned about toxicities in clinical trials and not realize that these toxicities stop once the dose is adjusted.

CTRP includes information on many patients in investigator-initiated trials that are not part of the NCTN or any other grant-supported networks. The CTIWG needs to help NCI assess the potential value of these data along with their accrual rates and other factors.

Dr. Louis M. Weiner said that a challenge is to not try to do too much too quickly. The first step is to determine whether it is possible to collect data, which data need to be collected, and how to collect those data. It is important to avoid imposing an unfunded mandate on cancer centers. Dr. Prindiville said that CTAC had discussed examining the clinical trial activity of the cancer centers and began by asking the CTIWG to determine what information should be available in CTRP. Another group might then examine the types of clinical trials taking place at cancer centers.

Dr. Matrisian warned against allowing the perfect to be the enemy of the good. A great deal of information exists, but much of it is not accessible. Physicians planning a trial do not need details on the accrual rates of potentially duplicate clinical trials; they need to know that a similar trial already exists and how to contact the principal investigator. There are some easy things that could be done. NCI could educate the public about the differences between phase I and phase III trials and make abstracts from clinical trials easy to find. These types of issues are much less sensitive, and addressing these needs would be a major step forward.

Dr. Cullen said that the goal is to provide more transparent information to health care providers, patients, and the community. Doing so is very expensive, and NCI has invested an enormous amount of time and effort in developing CTRP. NCI probably cannot afford the time and resources required to make the CTRP data accessible to health care providers and patients in addition to all of the other uses that might be desired. Dr. Louis M. Weiner agreed. He suggested that when the subgroups craft their recommendations, they estimate the amount of labor and other costs required to implement these recommendations, helping NCI determine which recommendations are achievable based on cost.

Dr. Villalona-Calero asked whether the data submitted by cancer centers are overdue. Dr. Kibbe explained that at the Cancer Moonshot Summit, Vice President Biden expressed concern about the timeliness of information in ClinicalTrials.gov. Dr. Louis M. Weiner noted that accuracy is sometimes a problem. Dr. Davidson pointed out that the problem is not limited to cancer trials.

XI. Ongoing and New Business

Nancy E. Davidson, MD

Dr. Prindiville listed some potential agenda items for a future CTAC meeting:

- An evaluation plan for the Experimental Therapeutics Clinical Trials Network and activities of the Investigational Drugs Steering Committee
- Precision medicine trials and how to facilitate enrollment

- The NCI–American Association for Cancer Research Task Force Cancer Patient Tobacco Use Assessment Questionnaire
- The U.S. Food and Drug Administration Oncology Center of Excellence
- Collaborations between NCI and the Department of Veterans Affairs
- An analysis of the reporting of cancer clinical trial results in ClinicalTrials.gov

Dr. Mitchell suggested that a future agenda item be research on cancer mortality rates in minority populations, which are increasing. Dr. Doroshow suggested that the November 2, 2016, CTAC meeting feature the recommendations for the Vice President’s Cancer Moonshot.

Appendix

**National Institutes of Health
National Cancer Institute
Clinical Trials and Translational Research Advisory Committee**

CHAIR

Nancy E. Davidson, MD **2018**
Director
University of Pittsburgh Cancer Institute
University of Pittsburgh
Pittsburgh, PA

MEMBERS

David F. Arons, JD (NCRA) **2016**
Director of Public Policy
National Brain Tumor Society
Watertown, MA

Susan M. Blaney, MD **2019**
Vice President for Clinical and Translational
 Research
Vice Chair for Research
Department of Pediatrics
Baylor College of Medicine
Texas Children’s Hospital
Houston, TX

Kevin J. Cullen, MD (NCAB) **2016**
Director
Marlene and Stewart Greenebaum Cancer Center
University of Maryland
Baltimore, MD

Walter J. Curran, MD, PhD **2019**
Professor and Chairman
Department of Radiation Oncology
Emory University School of Medicine
Atlanta, GA

Gwendolyn A. Fyfe, MD* **2020**
Independent Contractor
San Francisco, CA

David M. Gershenson, MD **2020**
Professor of Gynecology
Department of Gynecologic Oncology and
 Reproductive Medicine
Division of Surgery
University of Texas MD Anderson Cancer Center
Houston, TX

Michael L. LeBlanc, PhD **2019**
Member
Fred Hutchinson Cancer Research Center
Research Professor
Department of Biostatistics
University of Washington
Seattle, WA

Patrick J. Loehrer, Sr., MD **2020**
Director
Melvin and Bren Simon Cancer Center
Associate Dean for Cancer Research
Indiana University School of Medicine
Indianapolis, IN

David A. Mankoff, MD, PhD **2019**
Gerd Muehllehner Professor of Radiology
Division Chief, Nuclear Medicine and Clinical
 Molecular Imaging
Perelman School of Medicine
University of Pennsylvania
Philadelphia, PA

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|---|-------------|---|-------------|
| Lynn M. Matrisian, PhD, MBA* Chief Research Officer Pancreatic Cancer Action Network Washington, DC | 2019 | Mary S. McCabe, RN Director Cancer Survivorship Initiative Memorial Sloan Kettering Cancer Center New York, NY | 2016 |
| Edith P. Mitchell, MD Clinical Professor of Medicine and Medical Oncology Program Leader, Gastrointestinal Oncology Sidney Kimmel Cancer Center Thomas Jefferson University Philadelphia, PA | 2016 | George W. Sledge, Jr., MD Chief Division of Medicine–Oncology Stanford University School of Medicine Palo Alto, CA | 2016 |
| Nikhil C. Munshi, MD Associate Director Jerome Lipper Multiple Myeloma Center Dana-Farber Cancer Institute Professor of Medicine Harvard Medical School Boston, MA | 2016 | Chris H. Takimoto, MD, PhD Chief Medical Officer Forty Seven, Inc. Palo Alto, CA | 2016 |
| Augusto C. Ochoa, MD Director Stanley S. Scott Cancer Center Professor Department of Pediatrics Louisiana State University Health Sciences Center New Orleans, LA | 2018 | Miguel A. Villalona-Calero, MD Deputy Director and Chief Scientific Officer Miami Cancer Institute Baptist Health South Florida Coral Gables, FL | 2016 |
| Gloria M. Petersen, PhD Professor of Epidemiology Department of Education Administration Mayo Clinic College of Medicine Rochester, MN | 2019 | George J. Weiner, MD C.E. Block Chair of Cancer Research Professor, Department of Internal Medicine Director, Holden Comprehensive Cancer Center University of Iowa Iowa City, IA | 2016 |
| | | Louis M. Weiner, MD (BSC) Director Lombardi Comprehensive Cancer Center Francis L. and Charlotte G. Gagnani Chair Department of Oncology Georgetown University Medical Center Washington, DC | 2017 |

*Pending appointment

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Rosemarie Hakim, PhD, MS

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Sheila A. Prindiville, MD, MPH

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Rockville, MD