

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
34th CLINICAL TRIALS AND TRANSLATIONAL RESEARCH
ADVISORY COMMITTEE (CTAC) MEETING**

**Summary of Meeting
November 1, 2017**

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

CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE
Summary of Meeting
November 1, 2017

The 34th meeting of the Clinical Trials and Translational Research Advisory Committee (CTAC) of the National Cancer Institute (NCI) was on Wednesday, November 1, 2017, at 8:30 a.m. The CTAC chair, Dr. Nancy E. Davidson, presided.¹ The meeting was adjourned at 12:35 p.m.

Chair

Nancy E. Davidson

CTAC Members

David F. Arons (absent)
Susan M. Blaney
Walter J. Curran, Jr.
David M. Gershenson (absent)
Paul A. Godley
Anne-Marie R. Langevin (absent)
Michael L. LeBlanc
Patrick J. Loehrer, Sr.
David A. Mankoff
Neal J. Meropol
Edith P. Mitchell
Nikhil C. Munshi (by telephone)
Augusto C. Ochoa
Roman Perez-Soler
Gloria M. Petersen
Steven T. Rosen
Dan Theodorescu
Louis M. Weiner

Ad Hoc Members

Debra L. Barton
Janet Ellen Dancey
Timothy J. Eberlein
Howard J. Fingert
Lynn M. Matrisian (absent)

Ex Officio Members

William L. 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
Anthony Kerlavage, NCI
Richard Pazdur, U.S. Food and Drug
Administration

Executive Secretary

Sheila A. Prindiville, NCI

Presenters

Henry Ciolino, PhD, Director, Office of Cancer Centers, Office of the Director, NCI
Nancy E. Davidson, MD, Senior Vice President, Director, and Full Member, Clinical Research Division,
Fred Hutchinson Cancer Research Center
Andrea Denicoff, RN, MS, ANP, Nurse Consultant, Cancer Therapy Evaluation Program, Division of
Cancer Treatment and Diagnosis, NCI
James H. Doroshow, MD, Deputy Director, Clinical and Translational Research, Director, Division of
Cancer Treatment and Diagnosis, NCI
Lori Henderson, PhD, Program Director, Clinical Trials Branch, Cancer Imaging Program, NCI
Grant D. Huang, MPH, PhD, Acting Director, Cooperative Studies Program, Office of Research &
Development, U.S. Department of Veterans Affairs
Michael J. Kelley, MD, National Program Director for Oncology, Veterans Health Administration, U.S.
Department of Veterans Affairs
Warren Kibbe, PhD, Professor, Biostatistics and Informatics, Division Chief, Translational Biomedical
Informatics, Chief Data Officer, Duke Cancer Institute

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

Douglas R. Lowy, MD, Deputy Director, NCI

Worta McCaskill-Stevens, MD, MS, Chief, Community Oncology and Prevention Trials Research Group,
Division of Cancer Prevention, NCI

Sheila A. Prindiville, MD, MPH, Director, Coordinating Center for Clinical Trials, Office of the Director,
NCI

Gisele Sarosy, MD, Medical Officer, Coordinating Center for Clinical Trials, Office of the Director, NCI

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 34th meeting of CTAC to order and welcomed participants to the meeting.

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>.

Motion. A motion to accept the minutes of the 33rd CTAC meeting held on July 12, 2017, was approved.

Dr. Davidson introduced Norman “Ned” Sharpless, MD, the new NCI director. Dr. Sharpless said that he was excited to take on this new role. He was spending his initial time at NCI in listening mode, attending meetings like this one to learn more about NCI. He has already discovered that NCI is doing diverse and excellent work. The mission of CTAC is particularly important to Dr. Sharpless. As a former cancer center director, he is familiar with the challenges of clinical trials organizations, and he knows that oncology clinical trials have changed dramatically over the last decade. Keeping up with these changes is challenging for NCI, and Dr. Sharpless looked forward to learning more about NCI’s clinical trials. Finally, Dr. Sharpless thanked CTAC members for serving on this council, which involves a great deal of time.

II. The Clinical Trials Informatics Working Group Report

Henry Ciolino, PhD

Warren Kibbe, PhD

Gisele Sarosy, MD

Louis Weiner, MD

Dr. Sarosy provided background on the Clinical Trials Reporting Program (CTRP; <https://www.cancer.gov/about-nci/organization/ccct/ctrp>), a comprehensive database of information on all NCI-supported interventional clinical trials. It supports registration and results reporting to ClinicalTrials.gov in compliance with National Institutes of Health policies and the Food and Drug Administration Amendments Act. CTRP allows NCI to oversee its entire clinical trials portfolio. Dr. Sarosy described CTRP’s features, content, and workflow.

Dr. Weiner explained that the Clinical Trials Informatics Work Group (CTIWG) was formed to advise NCI on the implementation of its clinical trials informatics initiatives, including ways to use CTRP effectively. Dr. Kibbe described the process that CTIWG used to develop its recommendations, which he and Dr. Weiner then summarized.

Dr. Ciolino pointed out that one of the CTIWG recommendations is to replace the site-generated Data Table 4 with a CTRP-generated table in Cancer Center Support Grant renewal applications. Data Table 4 is a summary of all clinical research protocols open during a recent 12-month period. With site-generated tables (1 for each of 62 cancer centers), it is impossible for NCI to conduct a meaningful

analysis of its entire portfolio of clinical trials because of issues related to inconsistent interpretation of definitions, multisite accrual reporting, and accrual to screening trials. The CTIWG report addressed these issues. The report can be found at <https://deainfo.nci.nih.gov/advisory/ctac/1117/1-CTIWGreport.pdf>.

Questions and Discussion

As a CTIWG member, Dr. LeBlanc reported that the group had a robust discussion about the tradeoffs between the value of the additional information from CTRP and the impact of the recommendations on cancer centers. Dr. Curran, another CTIWG member, was pleased with the clarity of the recommendations and their sensitivity to the burden of additional requirements on cancer centers. Dr. Davidson reported that Dr. Matrisian, a CTIWG and CTAC member who was unable to attend the current meeting, supported the recommendations from her perspective as an advocate.

Dr. Doroshov said that if NCI implements these recommendations, the NCI staff and every cancer center will have a much better idea of what is occurring in clinical trials on a national level. Cancer centers have adapted their reporting processes to allow real-time reporting, which is very valuable.

Portfolio Analyses. Dr. Dancy described the report as a “great step forward” that clearly addresses NCI’s need to monitor clinical trials. She asked whether CTRP will be used to identify duplicative studies, which would be useful for prioritizing clinical trials. Dr. Kibbe replied that the report does address this issue. As searching CTRP becomes easier, investigators will be able to identify ongoing trials that overlap with a planned study. The investigators can then decide whether to join those trials if they are multicenter studies or learn whom to contact to determine whether the trials are truly duplicative.

Dr. Prindiville explained that reports on all ongoing clinical trials in each disease within and outside the NCI clinical trial networks would help NCI’s scientific steering committees prioritize clinical trials. Until reporting tools are developed to support portfolio analyses, NCI staff can help with these analyses.

Data Privacy. Dr. Kibbe explained that CTIWG had an extensive debate about data privacy concerns. Some cancer centers, especially those in competitive markets, might be reluctant to make their data public and available to competitors, who might use those data for nonscientific purposes. CTIWG concluded that the best approach is to make the information as transparent as possible so that it is accessible to patients, advocates, and community physicians. CTRP has an enormous amount of data that could be used for important research by NCI or interested investigators. However, CTIWG consistently drew the line at protecting individual research participant privacy. For example, if ZIP codes were publicly available, some clever individuals might be able to determine which participants were being treated for a specific type of cancer.

Dr. Mitchell said that ZIP code data could be useful because, based on a plethora of evidence, they are related to cancer outcomes. Dr. Weiner explained that releasing ZIP code data was discussed extensively and that the recommendations do call for the release of aggregate data on the ZIP codes of the institutions that provide the treatment. However, the ZIP code data that are most relevant are those for patients’ homes. ZIP codes from less densely populated areas could allow patients to be inadvertently identified, so the CTIWG recommended releasing only aggregate ZIP code data.

Dr. Kibbe added that CTIWG recommended that NCI develop a process by which individual researchers can request patient-level data, but these data should not be available to the public. ZIP code

data can be used to determine the reach of a specific cancer center and the differences in cancer center catchment areas, and this information can help centers extend their reach into diverse populations.

Dr. Weiner said that CTRP should support the ability to determine outcomes or trial participation differences among ZIP codes, but if these data were available to the public, NCI might not be able to fully protect the privacy of individuals. Dr. Loehrer said that if asked, many patients would probably want their ZIP codes to be made public. He suggested that NCI survey patients to find out their thoughts about sharing these data. Dr. Weiner said that CTIWG's main concern was protecting participant privacy.

CTRP Searches. Dr. Doroshov asked for CTAC's feedback on whether NCI should develop a search tool that might be more relevant to researchers than the tools commonly available to the public. This development would take a considerable amount of work. Dr. Kibbe reported that he was involved in a similar activity through the Cancer Moonshot but that this tool is not as sophisticated as it will be in the future.

Dr. Meropol said that the availability of an application programming interface feed and augmentation of structured data would allow cancer centers to match potential participants to trials. Several cancer centers are already developing such applications, as are some commercial entities. Increasing the amount of structured data against which to match patients would be a huge opportunity and could leverage public-private partnerships.

Biomarkers. Dr. Mankoff was pleased that CTIWG called for continuing to structure biomarker eligibility criteria for clinical trial searching. An increasing number of institutions are acquiring and analyzing biomarkers, and knowing whom to ask for these data will be helpful. He asked whether CTIWG considered imaging biomarkers, given that many trials will not only have imaging entry criteria but also imaging response data. Currently, it is difficult to know who has these datasets. Dr. Sarosy replied that imaging trials are included in CTRP and that the database has information on how outcomes are evaluated. Plans are in place to capture data on imaging studies in a systematic, standardized fashion.

Dr. Barton pointed out that observational studies that collect biomarker data longitudinally are important. Dr. Weiner said that one concern is that biomarkers are not always well structured and can be idiosyncratic and exploratory, so CTIWG was somewhat reluctant to include data on these types of biomarkers in CTRP unless they were part of a trial's eligibility criteria. Dr. Sarosy added that CTRP will capture biomarkers used for treatment assignment or stratification in interventional trials (which could require follow-up with the study team) and for observational studies will include biomarkers as specified in the protocol without asking for more information.

Precision Medicine Screening. Dr. Petersen said that the requirement for separate reporting for precision medicine screening will illustrate the large amount of work required to identify eligible patients for such trials. At a recent ECOG-ACRIN Cancer Research Group meeting, patients and advocates were concerned that patients who spend a substantial amount of time signing the consent forms and providing samples for the Molecular Analysis for Therapy Choice (MATCH) trial but are not eligible for a MATCH study arm want their specimens and information to be available for analyses. They said that this process is not really screening but rather part of trial accrual.

Dr. Weiner said that CTIWG's recommendations address this issue to some extent. It is important to collect information on the number of individuals who have provided consent to undergo an interventional procedure, such as a biopsy or computed tomography scan. The next step is for NCI to

develop a vocabulary for this process so that all cancer centers and study sites can report this activity consistently. Dr. Kibbe agreed that patients face some risk and burden during the screening process and that this activity should be reflected in the accrual data.

Dr. Loehrer noted that patients considered for MATCH who are not eligible would probably like to know whether they might be eligible for other NCI studies. Providing this information to patients is one way to pay them back for their effort to sign up for MATCH.

Observational Studies. Dr. Petersen commented that many cancer centers are not reporting community-based studies that do not involve patients with cancer—or any patients—treated at the institution. She asked whether CTIWG will develop guidelines on the types of observational studies that need to be reported in CTRP.

Dr. Kibbe replied that cancer centers have a fair amount of latitude to decide which studies to report and that they should report all studies in CTRP that they would include in Data Table 4. Dr. Weiner said that as long as observational studies, even those that do not involve interventions, are scientific, they are a cancer center activity. Information on these studies will therefore be useful for NCI portfolio analyses and to help the larger community understand what cancer centers do.

Dr. Petersen suggested that NCI provide clear guidance on which observational studies to report in CTRP instead of leaving this decision to the discretion of cancer centers, and Dr. Barton agreed. Dr. Ciolino said that all cancer centers are likely to want to report their observational studies and that they will need to do so in a separate Data Table 4 or in CTRP so that reviewers can assess their population science programs.

Timeline. Dr. Davidson characterized the timeline for making the transition from Data Table 4 to CTRP as “brisk.” According to the report, noncompeting renewal applications should already be using CTRP to report these data, and NCI’s Cancer Centers Program must determine whether the plan is feasible.

Motion: A motion to accept the CTIWG report carried.

III. Reducing Trial Barriers: Broadening Eligibility Criteria, Improving Informed Consent Language, and Providing National Coverage Analyses for NCI Network Trials

Andrea Denicoff, RN, MS, ANP

Broadening Eligibility Criteria for Clinical Trials. The American Society of Clinical Oncology and Friends of Cancer Research recently issued joint recommendations (published in four papers in the *Journal of Clinical Oncology*, <https://www.asco.org/advocacy-policy/asco-in-action/asco-and-friends-cancer-research-release-comprehensive>) for broadening eligibility criteria to include patients with certain health conditions (such as HIV infection and brain metastases) and children and adolescents. Some NCI National Clinical Trials Network (NCTN) and NCI Community Oncology Program (NCORP) trials are already incorporating these broadened eligibility trials, and discussions about how to do so for Experimental Therapeutics Clinical Trials Network studies are underway.

Revised Informed Consent Language. NCI recently published a revised informed consent template (https://ctep.cancer.gov/protocoldevelopment/informed_consent.htm) that addresses the January

2017 revisions to the Common Rule (<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/finalized-revisions-common-rule/index.html>) released by the Office for Human Research Protections of the Department of Health and Human Services. In addition to complying with the new Common Rule requirements, the revised template has more information on trials involving genomic testing along with examples, clarification of the “Costs” and “Exams, Tests, and Procedures” sections to address billing and insurance coverage, improved readability to facilitate patient understanding, and changes in formatting to enhance ease of use. Protocols initially approved by an NCI central institutional review board on or after January 19, 2018, will be required to use the revised informed consent template.

National Coverage Analyses of NCI Network Trials. A national coverage analysis (NCA) is a review of all tests, procedures, and interventions associated with a clinical trial to determine which ones are billable to a third-party payer. NCI’s Cancer Trials Support Unit (CTSU) is pilot-testing NCAs in NCI network trials, and NCI consulted the Centers for Medicare & Medicaid Services about developing this pilot. NCAs developed by the CTSU will use National Coverage Determinations as defined by Medicare as the basis for coverage analysis development. The goals are to decrease the burden of trial budgeting and billing; prevent patients from being billed for tests or services that they expect to have covered by insurance, Medicare, or the study; and prevent billing for research tests (see information on Medicare’s clinical trial policies at <https://www.cms.gov/Medicare/Coverage/ClinicalTrialPolicies/index.html>).

Questions and Discussion

Expanded Eligibility Criteria. Dr. Pazdur reported that the Food and Drug Administration (FDA) believes that broadening eligibility criteria for clinical trials is important, because trial populations need to reflect the patients who will ultimately undergo the treatments being studied. FDA has been working on this issue since before the American Society of Clinical Oncology and Friends of Cancer Research initiative began. The agency is working with sponsors to consider whether their eligibility criteria have a rationale or were simply taken from a previous protocol.

One concern of sponsors is that if trials enter patients who have certain health conditions, a competitor that does not include such patients might show that its intervention is more effective. FDA has identified different ways of addressing this concern. For example, certain statistical techniques can be used to exclude patients from the primary analysis of efficacy and safety, and analyses can focus on subgroups of patients who might have a higher risk of developing toxicities.

Dr. Meropol stated that several real-world datasets are available to inform the choice of eligibility criteria for specific clinical trials and that use of these databases will be important as new eligibility criteria evolve. These real-world data can help sponsors avoid excluding patients who could benefit from an intervention and increase the generalizability of results.

Dr. Fingert said that a challenge with expanded eligibility criteria is the example of frail older patients who may need an alternative to another computed tomography scan. This could be considered a deviation and render the trial invalid. Although this possibility can be addressed, it needs to be considered prospectively.

Revised Informed Consent Language. Dr. Rosen pointed out that patients rarely read informed consent forms. He suggested that, in addition to the detailed consent forms that studies must use for legal purposes, very short summaries be created that explain the trial in lay language. Dr. Mitchell agreed and

asked whether NCI considered ways to simplify and shorten the consent form so that patients would read it.

Ms. Denicoff replied that several studies have shown that page length does not affect patient willingness to join a study. She noted Dr. Meropol's published results from a randomized controlled trial showing that patients who viewed an explanatory video before the informed consent process were better prepared for the clinical trial decision-making process. Consent forms must comply with numerous federal regulations that make the documents long. Ms. Denicoff agreed with comments that describing trials in lay language is extremely important and that the informed consent form is only part of the informed consent process, which also involves ongoing discussions with the patient.

Dr. Rosen agreed with Ms. Denicoff that informed consent is a process and that the form is only part of that process. Only the patient's physician or other health care provider truly understands the therapeutic options for a given patient, and that person has a responsibility to help patients understand their options.

Dr. Dancey asked whether a Spanish translation of the new informed consent template is available. Ms. Denicoff said that NCI does not translate the informed consent template into Spanish, but the specific consent forms for all large trials are translated into Spanish.

National Coverage Analyses of NCI Network Trials. Dr. Loehrer said that as the payment system moves toward bundled payments, pressure to minimize the amount of testing will increase. Ms. Denicoff agreed that this issue will be challenging for cancer centers.

Dr. Dancey asked whether the results of the NCAs will be fed back into the protocol before it is finalized. Ms. Denicoff said that in the pilot, the analyses were initially conducted at the end of protocol development, but NCI quickly learned that NCAs needed to be developed in parallel. Now the analyses start early, at the first protocol submission.

Dr. Curran asked whether the coverage analyses could be used to create a set of standards that might offer greater clarity for payers in future clinical trials. Ms. Denicoff said that this is happening. One challenge is that often there are no clinical guidelines for some rare tumors, but sites want a peer-reviewed document that they can use to identify standard treatments for negotiations with payers. As the CTSU works to develop the NCAs for these trials, it needs assistance from investigators to identify key publications that provide a rationale for a given treatment. The national coverage analyses cite peer-reviewed literature so that cancer centers and community sites have this evidence to support their billing practices and use this evidence if they need to answer questions from payers.

IV. NCI's Implementation of the National Institutes of Health Clinical Trials Stewardship Policies

Lori A. Henderson, PhD

National Institutes of Health (NIH) Stewardship Policies. In 2016, NIH announced the first series of reforms and initiatives to improve the oversight, quality and efficiency of NIH-funded clinical trials focused on a variety of key points along the "lifespan" of a clinical trial. NIH has modified existing policies and created new ones that govern research involving human participants and their participation in clinical trials. These policies include a requirement for applicants to submit the new Public Health Service (PHS) Human Subjects and Clinical Trials Information form starting on January 25, 2018 (NOT-OD-17-

062), and that a single institutional review board of record be established for multisite studies that include human subjects (NIH-OD-16-094). For applications containing clinical trials, NIH requires training in good clinical practice for all NIH-funded investigators and staff who conduct, oversee, or manage clinical trials (NOT-OD-148). Any application containing a clinical trial must be submitted to a funding opportunity announcement (FOA) that accepts clinical trials (NOT-OD-16-147); a new review criterion, the study timeline, has been added to these FOAs for the review of applications. NIH has also expanded its requirements for registration and results reporting in ClinicalTrials.gov (NOT-OD-16-149).

NCI Stewardship Activities. NCI is not participating in the NIH parent R01 and R21 FOAs that require clinical trials. Instead, NCI has created an FOA requiring clinical trials for Division of Cancer Treatment and Diagnosis studies and a second FOA for Division of Cancer Prevention and Division of Cancer Control and Population Sciences studies. NCI is beta-testing tools that use risk classification of trial characteristics and clinical trial management plans during reviews of progress reports for NCI-funded trials. The NCI Office of Communication and Public Liaison has developed a standardized email as well as a website on cancer.gov to inform the research community of the changes in NCI's clinical trials stewardship policies.

Questions and Discussion

Dr. Fingert asked about efforts to coordinate the activities that Dr. Henderson described with international initiatives engaged in similar work. One example is the effort of the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use to revise its clinical guidance. In addition, the Multi-Regional Clinical Trials Center is doing work similar to NIH's, but on a global level. Dr. Henderson was not aware of NIH participation in these types of forums, but she will recommend that the NIH Clinical Trials Operation Work Group consider Dr. Fingert's suggestion.

Dr. Mankoff requested clarification on the new NCI FOA for clinical trials. Dr. Henderson explained that NCI is about to release a parent R01 FOA that requires clinical trials and that other NIH Institutes and Centers have their own FOAs that require or allow clinical trials. NIH is producing only two parent R01 FOAs, one that requires clinical trials and one that does not permit them. NCI is not participating in the NIH R01 FOA that requires clinical trials.

Dr. Blaney said that some of the fields in the PHS Human Subjects and Clinical Trials Information form duplicate the information in CTRP and ClinicalTrials.gov. She asked about efforts to link these fields so that sites do not have to enter the same information multiple times. Dr. Henderson said that the databases are linked and that sites will need to enter the information only once. Dr. Sarosy confirmed that the elements required under the new policy and those that must be entered into CTRP and ClinicalTrials.gov are the same and that all the systems use the same definitions. Efforts to minimize the need for duplicative data entry are underway.

In response to a question about the new review criteria from Dr. Petersen, Dr. Henderson explained that NOT-OD-17-118 provides examples of the questions that reviewers use for each category. Dr. Petersen wondered why reviewers need to assess study timelines. Dr. Henderson said that this is part of the review of clinical trial feasibility. Educational materials on how to interpret the review questions are being developed for reviewers.

V. NCI Community Oncology Research Program (NCORP) Renewal

Worta McCaskill-Stevens, MD, MS

NCORP is a national NCI-supported network, launched in 2014, that brings cancer treatment, imaging, symptom control, and prevention clinical trials and cancer care delivery research to people in their communities. NCI requires external evaluation of large-scale infrastructure grants, such as NCORP, before each funding opportunity renewal. The NCORP External Evaluation Working Group was formed in the spring and issued its report in September (<https://deainfo.nci.nih.gov/advisory/ctac/1117/2-NCORPreport.pdf>).

The working group recommended that NCI reissue NCORP, noting its important scientific and clinical contributions. The working group offered feedback and recommendations for the program as a whole, as well as for NCORP's infrastructure, study development and accrual, collaborations, and cancer care delivery research. After summarizing these recommendations, Dr. McCaskill-Stevens described NCI's response.

Questions and Discussion

NCORP Strengths. Dr. Loehrer, a member of the NCORP External Evaluation Committee, explained that NCORP grew out of the NCI Community Clinical Oncology Program and the NCI Community Cancer Centers Program. He noted that the relationship between these programs and cancer centers was sometimes competitive. NCORP sites now account for 25 percent to 30 percent of NCI NCTN treatment trial accrual, and the types of patients accrued through these sites are different from those accrued at academic medical centers. As a result, cancer centers and NCORP now have a more synergistic relationship. Dr. Loehrer recommended that NCI develop a map showing the locations of NCI-Designated Cancer Centers as well as NCORP Community Sites, Minority/Underserved Community Sites, and Research Bases to demonstrate that NCI-funded studies are available across the country.

Dr. Munshi, another member of the evaluation committee, listed numerous strengths of NCORP:

- Ninety percent of patients with cancer are treated in the community, and NCORP brings these real-world patients into clinical trials, making these trials more meaningful.
- NCORP's role does not overlap with that of NCTN, because the two programs conduct different types of trials, showing that NCORP is clearly needed.
- NCTN trials would have more difficulty accruing participants without NCORP.
- NCORP brings almost 4,000 community oncologists into research, and those physicians use what they have learned from this experience in their practices.
- NCORP provides access to novel interventions in communities that are not well served by cancer centers.

These and other strengths identified in the review make NCORP indispensable and an important partner for the NCTN.

Dr. Lowy noted that the many publications that have resulted from NCORP research are another testament to its value. Furthermore, many NCORP trials are changing practice. He recommended that NCI develop a written "elevator speech" on the value of NCORP. He also commented that he would like the NCORP sites and the NCTN Lead Academic Participating Sites to see themselves as part of the same system. He recommended encouraging these sites to enroll patients into NCORP trials.

Community Oncologists. Dr. Ochoa commented that NCORP has renewed interest among community oncologists in participating in clinical research, especially studies involving genomics. In turn, they are developing innovative approaches to community-based clinical trials, such as telehealth and cancer control studies. He agreed with Dr. Munshi that NCORP is essential.

Dr. Barton said that, in her experience, community oncologists who participate in clinical trials tend to be early adopters of the clinical trial findings, and that data showing that this is the case would be useful. Furthermore, she has been involved in the development of guidelines in which NCORP research was part of the evidence base; NCI should consider reporting that information to support the importance of NCORP. Another area that NCORP might address as part of cancer care delivery is the translation of clinical guidelines into practice.

Role of Insurance Companies in CCDR. Dr. Perez-Soler asked about engagement of insurance company CEOs in NCORP trials in addition to hospital CEOs. Kathleen Castro, RN, MS, a nurse consultant in the Office of the Associate Director of the Healthcare Delivery Research Program in NCI's Division of Cancer Control and Population Sciences, explained that the insurance market is evolving too rapidly to make companies' participation in NCORP trials feasible now, but NCI might consider including insurance company CEOs in NCORP trials in the future.

Specialization of Research Bases. Dr. Mankoff asked, for the benefit of someone reviewing the new research base applications, whether the new request for applications could encourage the research bases to specialize in some but not all NCORP goals. Dr. McCaskill-Stevens explained that research bases do not need to address all the NCORP priorities. Some research bases, for example, focus on screening and surveillance, and others work only on cancer control. NCI can clarify that NCORP research bases should focus on their areas of expertise and not try to address every NCORP priority.

Dr. Godley congratulated Dr. McCaskill-Stevens on her presentation and thanked her for her stewardship of such an important, diverse, and complex clinical research resource.

VI. NCI and Department of Veterans Affairs Interagency Group to Accelerate Trials Enrollment (NAVIGATE)

Sheila A. Prindiville, MD, MPH

Grant D. Huang, MPH, PhD

Michael J. Kelley, MD

Dr. Prindiville described NAVIGATE, which will facilitate veterans' enrollment into NCI-funded clinical trials. Although VA Medical Centers (VAMCs) have been involved in NCI trials, participation has declined in the last decade. Including more VA patients in NCTN and NCORP clinical trials will not only advance the health of the VA population but also help NCI's national clinical trials system complete trials more rapidly.

Specifically, NAVIGATE will provide infrastructure funding to eight to 10 VA sites to enroll VA patients in NCTN and NCORP clinical trials. Anticipated benefits include increased access for veterans with cancer to promising new treatments, accelerated accrual to NCI-supported clinical trials, participation of minority populations within the VA in NCI-supported clinical trials, VA clinical investigator participation in NCI's scientific steering committees, increased VA clinical investigator participation in clinical cancer research, and an enhanced leadership role for the VA in cancer care and clinical research.

Dr. Kelley explained that NAVIGATE is, in part, the result of Cancer Moonshot discussions that highlighted ways to increase interagency cooperation, as well as recommendations from CTAC in response to a presentation he had given about VA clinical trials in July 2016. Dr. Huang reported that NAVIGATE will not only increase veterans' participation in cancer clinical trials but also increase clinical trial efficiency at the agency through central coordination.

Questions and Discussion

Dr. Lowy said that the collaboration between NCI and the VA to systematically address various bureaucratic issues has been remarkable, and he expressed appreciation for VA's efforts in these discussions. He hoped that NAVIGATE will be a harbinger of more to come.

State-of-the-Art Treatments for VA Patients. Dr. Rosen wondered whether veterans have access to the latest treatments, most of which are only available through clinical trials. Dr. Kelley said that veterans have access to the most up-to-date treatments—all standard treatments available outside VA are also available to VA patients. If VA does not offer a treatment at its facilities, it can be available at a non-VA institution.

Kaiser Model. Dr. Rosen suggested that VA consider replicating the Kaiser model in southern California, where Kaiser covers all treatment costs of patients participating in clinical trials at another institution. Dr. Kelley explained that VA has used a similar approach to Kaiser's to enroll patients in clinical trials outside VA, but this approach is not universal. VA has been considering whether to broaden this approach and, if so, how.

Patients with Comorbidities in Cancer Clinical Trials. Dr. Fingert stated that NAVIGATE might make possible more trials that include patients with comorbidities, such as frail older adults. He gave an example of a phase II myeloma trial in frail elderly patients across the VA system that answered questions about their experience with that treatment. He also wondered whether adherence rates might be different in veterans than in the general population, noting that adherence is a major issue, especially for oral drugs taken on an outpatient basis.

Dr. Kelley replied that more VA patients have comorbidities than people in the general population. He added that veterans tend to be altruistic and are often willing to volunteer for clinical trials. Furthermore, the VA uses several novel approaches to deliver care at a distance that can track patient compliance, but he did not know whether adherence rates are higher in veterans.

Dr. Munshi has had a long association with the VA and agreed that studies of this population are important for providing appropriate care. The comorbidities of patients in the VA are a strength for NCI clinical trials. The VA also provides a unique population, including patients from underrepresented minority groups, to answer important questions. He also acknowledged the quality and experience of VA clinical investigators. Dr. Munshi predicted that NAVIGATE will fill an important gap and help the VA become a great partner for NCI.

Dr. Huang agreed that the high comorbidity rates in VA patients are a strength and that these comorbidities could inform the designs of NCI trials. Furthermore, VA has conducted clinical trials for decades and can use this experience to help NCI make its trials more efficient at VA sites, which is one of the aims of NAVIGATE. One challenge for clinical trials at the VA is that sites do not always learn from

each other's experiences with clinical trials, so the VA is trying to centralize coordination among its clinical trials more effectively.

Relationships Between VAMCs and Academic Medical Centers. Dr. Mitchell reported that the VAMCs have agreements with 130 medical schools around the country. She asked whether these affiliations might be leveraged to support cancer clinical trials and whether the eight to 10 VAMCs that will be funded through NAVIGATE have affiliations with medical schools that have an NCI-Designated Cancer Center. Dr. Kelley noted that most VAMCs are affiliated with an academic medical center in some way. Dr. Huang said that these affiliations are a strength and that the NAVIGATE team has discussed how to incorporate these affiliations into the program. The eight to 10 VAMCs have not been selected yet, but sites that apply are likely to highlight their affiliations with academic centers. Dr. Lowy added that NAVIGATE will accept applications from all VAMCs, not just those affiliated with an NCI-Designated Cancer Center. All applications will be judged by peer review, and the best ones will be selected.

Drivers of Successful Accrual. Dr. Theodorescu asked about the drivers of successful versus less successful accrual to clinical trials in the VA and the reasons why VA participation in NCI clinical trials has declined in recent years. Dr. Huang replied that the VA is collecting these data but has not analyzed them yet. The experience levels of VA clinical trials personnel can affect accrual. For example, an investigator who came to the VA from an academic center might not know how to navigate the VA system or be familiar with VA policies. VA's Cooperative Studies Program is therefore forming local and national networks of clinical trials personnel so that those with less experience can learn from their more experienced peers.

Dr. Kelley said that the VA has identified several barriers to accrual, such as the long time required to obtain institutional review board approval to open a trial at a VA facility. A small number of VA sites are successfully accruing patients to clinical trials, and discussions with investigators at these sites would identify the factors in their successes. Successful accrual in the VA requires individuals who work full time at a VA site and have some financial resources and support from facility and possibly regional leaders. Dr. Prindiville explained that NAVIGATE will provide an opportunity to systematically collect data on barriers to and drivers of successful accrual to cancer clinical trials in VA.

Ms. Denicoff participated in an interagency agreement between NCI and VA 20 years ago, and the reason it was effective was that VA leaders wanted it to work. However, when the VA leadership changed, this collaboration was no longer a priority. This experience demonstrates the importance of support from the top leaders at VA. Dr. Kelley commented that VA leaders are very supportive of this effort.

VII. NCI Deputy Director's Update

Doug Lowy, MD

New NCI Director. Dr. Lowy announced the appointment of Norman "Ned" Sharpless, MD, as the new NCI director.

Appropriations. As both houses of Congress have recognized, the Cancer Moonshot's \$300 million budget is supposed to augment, not replace, NCI's annual appropriation. Most of the research discussed at this meeting is covered by the annual appropriation, not the Cancer Moonshot. A concern is that the Cancer Moonshot has received a great deal attention, but less attention has been paid to research

carried out with the annual appropriation. The research supported by the annual appropriation includes training, investigator-initiated research, and the Precision Medicine Initiative for Oncology (which includes MATCH and the RAS Initiative).

A continuing resolution that includes separate funding for the Cancer Moonshot is in place through December. NCI received its fiscal year (FY) 2017 funding in May, relatively late in the fiscal year. NCI hopes that decisions about the full FY 2018 appropriation will be made by the end of December. The House's version of the appropriations bill called for a \$1.1 billion increase for the National Institutes of Health including an \$82 million increase for NCI and \$300 million for the Cancer Moonshot. The Senate's version included a \$2 billion increase for NIH, of which NCI would receive \$169 million more than in FY 2017, as well as \$300 million for the Cancer Moonshot.

Cancer Moonshot. NCI has worked hard with CTAC's help to implement the recommendations for the Cancer Moonshot from the Blue Ribbon Panel. Several FY 2018 Moonshot requests for applications will be issued soon, and a full list is available on the Cancer Moonshot website (<https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative>).

NCI has initiated the Cancer Immune Monitoring and Analysis Centers (CIMACs) and the Cancer Immunologic Data Common, which are part of the Cancer Moonshot and will develop molecular signatures that define immune response categories to correlate with the clinical outcomes of immunotherapy in cancer. The CIMACs are cooperative agreements with four extramural medical centers and will leverage resources available at the Frederick National Laboratory for Cancer Research. A public-private partnership involving 11 pharmaceutical companies recently announced plans to provide increased support for the CIMAC network and related precompetitive immunotherapy research.

International Collaborations. The International Cancer Proteome Consortium met in September, and former Vice President Joe Biden was the keynote speaker. More countries plan to join the consortium, which will make more genomic and proteomic datasets available to the public through the Clinical Proteomic Tumor Analysis Consortium to advance cancer care. The consortium has already made data available on oral squamous cell, breast, and ovarian cancer.

VIII. Ongoing and New Business

Dr. Davidson recognized Dr. Blaney, who is leaving CTAC, for her advice to NCI and CTAC, especially related to pediatric oncology clinical trials.

Dr. Prindiville reported that the National Institutes of Health (NIH) Clinical Center released a Request for Information on Enhancing the Utilization of the NIH Clinical Center (NOT-OD-007) and that responses will be accepted until November 24, 2017. Dr. Dahut explained that the Clinical Center provides a unique resource for inpatient treatment that does not require third-party billing or face other barriers that are common in extramural facilities. He asked CTAC members to share this notice with their colleagues. In particular, NIH would like to identify research ideas that have not been thought of before, types of research that are difficult to conduct at local institutions, and ways to expand partnerships with external faculty members. Dr. Rosen suggested using the Clinical Center for research on chimeric antigen receptor T-cell therapy.

Dr. Dahut also said that the Cancer Moonshot is funding the NCI Rare Tumors Initiative. This program will gather data on patients across the country with rare tumors, especially brain tumors and rare

pediatric tumors. It will use NIH resources to accelerate the understanding of these tumors, including bringing patients and outside investigators to the Clinical Center and facilitating treatment throughout the country.

Dr. Weiner noted that the appointment of Ethan Dmitrovsky, MD, as the new director of the Frederick National Laboratory for Cancer Research might provide an opportunity for CTAC to discuss ways to leverage the laboratory's resources for clinical research at a future meeting. Dr. Curran suggested a presentation on the role of NCI's Quantitative Imaging Network in the NCI clinical trials enterprise. Dr. Prindiville reported that over the next year, CTAC might hold some of its meetings at NCI's Shady Grove facility while the meeting space in Building 31 on the NIH campus is renovated.

IX. Adjournment

Nancy E. Davidson, MD

There being no further business, the 34th meeting of CTAC was adjourned at 12:35 p.m. on Wednesday, November 1, 2017.

Appendix

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

CHAIR

Nancy E. Davidson, MD 2018
Senior Vice President, Director, and Full Member
Clinical Research Division
Fred Hutchinson Cancer Research Center
President & Executive Director
Seattle Cancer Care Alliance
Head, Division of Medical Oncology
Department of Medicine
University of Washington
Seattle, WA

MEMBERS

David F. Arons, JD (NCRA) 2018 Chief Executive Officer National Brain Tumor Society Watertown, MA	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
Susan M. Blaney, MD 2017 Vice President for Clinical and Translational Research and Vice Chair for Research Department of Pediatrics Baylor College of Medicine Texas Children's Hospital Texas Medical Center Houston, TX	Paul A. Godley, MD, PhD, MPP 2021 Vice Dean for Diversity and Inclusion and Dickson Distinguished Professor of Medicine, Hematology/Oncology Lineberger Comprehensive Cancer Center University of North Carolina School of Medicine Chapel Hill, NC
Walter J. Curran, Jr., MD, PhD 2019 Executive Director Winship Cancer Institute of Emory University Atlanta, Georgia	Anne-Marie R. Langevin, MD 2021 Greehey Distinguished Chair in Pediatric Oncology Department of Pediatrics Hematology/Oncology University of Texas Health Science Center San Antonio, TX

Michael L. LeBlanc, PhD Member Fred Hutchinson Cancer Research Center Research Professor Department of Biostatistics University of Washington Seattle, WA	2019	Roman Perez-Soler, MD (BSC) Chairman Department of Oncology Montefiore Medical Center Deputy Director Albert Einstein Cancer Center Director Division of Medical Oncology Albert Einstein College of Medicine Bronx, NY	2020
Patrick J. Loehrer, Sr., MD Director Melvin and Bren Simon Cancer Center Associate Dean for Cancer Research Indiana University School of Medicine Indianapolis, IN	2020	Gloria M. Petersen, PhD Deputy Director Mayo Clinic Cancer Center Professor of Epidemiology Department of Health Sciences Research Mayo Clinic College of Medicine & Science Rochester, MN	2020
David A. Mankoff, MD, PhD Gerd Muehllehner Professor of Radiology and Chief of Nuclear Medicine and Clinical Molecular Imaging Perelman School of Medicine University of Pennsylvania Philadelphia, PA	2019	Steven T. Rosen, MD Provost, Chief Scientific Officer, and Director Comprehensive Cancer Center and Beckman Research Institute Irell & Manella Cancer Center Director's Distinguished Chair Comprehensive Cancer Center City of Hope Duarte, CA	2021
Edith P. Mitchell, MD, FACP Associate Director for Diversity and Minority Programs Sidney Kimmel Comprehensive Cancer Center Clinical Professor of Medicine and Medical Oncology Thomas Jefferson University Philadelphia, PA	2018	Dan Theodorescu, MD, PhD Professor and Director Department of Pharmacology and Urology University of Colorado Comprehensive Cancer Center Aurora, CO	2020
Nikhil C. Munshi, MD Associate Director Jerome Lipper Multiple Myeloma Center Dana-Farber Cancer Institute Professor of Medicine Harvard Medical School Boston, MA	2018	Louis M. Weiner, MD (BSC) Director Lombardi Comprehensive Cancer Center Francis L. and Charlotte G. Gragnani Chair Department of Oncology Georgetown University Medical Center Washington, DC	2018
Augusto C. Ochoa, MD Director Stanley S. Scott Cancer Center Professor Department of Pediatrics Louisiana State University Health Sciences Center New Orleans, LA	2018		

Ex Officio Members

William L. Dahut, MD

Scientific Director of Clinical Research
Center for Cancer Research
National Cancer Institute
National Institutes of Health
Bethesda, MD

James H. Doroshow, MD

Deputy Director
Clinical and Translational Research
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Michael J. Kelley, MD, FACP

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National Institutes of Health
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Richard Pazdur, MD, FACP

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U.S. Food and Drug Administration
Silver Spring, MD

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Director, Canadian Cancer Trials Group
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Department of Surgery
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Howard J. Fingert, MD, FACP 2020

Senior Medical Director
Oncology Clinical Research
Millennium: The Takeda Oncology Company
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Chief Research Officer
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Neal J. Meropol, MD 2021

Vice President of Research Oncology
Flatiron Health
New York, New York

Executive Secretary

Sheila A. Prindiville, MD, MPH

Director

Coordinating Center for Clinical Trials

Office of the Director

National Cancer Institute

National Institutes of Health

Bethesda, MD