DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
41st CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE (CTAC) MEETING

Summary of Meeting
March 12, 2020

Webinar

CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE
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The 41st meeting of the Clinical Trials and Translational Research Advisory Committee (CTAC) of the National Cancer Institute (NCI) was on Thursday, March 12, 2020, at 11:01 a.m. The CTAC chair, Dr. Loehrer, presided.[1] The meeting was adjourned at 12:30 p.m.

Chair
Patrick J. Loehrer, Sr.

CTAC Members
Debra L. Barton
Janet Ellen Dancey
Nancy E. Davidson
Timothy J. Eberlein
David M. Gershenson
Anne-Marie R. Langevin
Lynn M. Matrisian (absent)
Neal J. Meropol
Augusto C. Ochoa
Roman Perez-Soler
Gloria M. Petersen
Steven T. Rosen
Dan Theodorescu

Ex Officio Members
William L. Dahut, NCI (absent)
James H. Doroshow, NCI
Paulette S. Gray, NCI
Michael J. Kelley, U.S. Department of Veterans Affairs
Anthony Kerlavage, NCI
Julie Schneider, U.S. Food and Drug Administration (alternate for Richard Pazdur)
Xiufen Sui, Centers for Medicare & Medicaid Services

Executive Secretary
Sheila A. Prindiville, NCI

Presenters
Janet Ellen Dancey, MD, FRCPC, Professor, Department of Oncology, Queen's University; Director, Canadian Cancer Trials Group
James H. Doroshow, MD, Deputy Director, Clinical and Translational Research; Director, Division of Cancer Treatment and Diagnosis, NCI
Patrick J. Loehrer, Sr., MD, Director, Indiana University Melvin and Bren Simon Cancer Center; Associate Dean for Cancer Research, Indiana University School of Medicine
Sheila A. Prindiville, MD, MPH, Director, Coordinating Center for Clinical Trials, Office of the Director, NCI
Norman E. Sharpless, MD, Director, NCI

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

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Thursday, March 12, 2020

I. Call to Order and Opening Remarks

Patrick J. Loehrer, Sr., MD

Dr. Loehrer called the 41st meeting of CTAC to order and welcomed participants. He then introduced Dr. Sui, the new ex officio CTAC member from the Centers for Medicare & Medicaid Services. He also introduced Dr. Schneider, who was representing the U.S. Food and Drug Administration in place of Richard Pazdur, MD, at this meeting.

Dr. Loehrer reviewed the confidentiality and conflict-of-interest practices required of CTAC members during their deliberations. He 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 (NIH) Events Management videocast the meeting, and the videocast became available for viewing at https://videocast.nih.gov/watch=35615 after the meeting.

Dr. Loehrer announced upcoming CTAC meetings on July 15 and November 4, 2020. He also listed the dates for CTAC meetings in 2021 and 2022.

II. NCI Director's Update

Norman E. Sharpless, MD

NCI Planning for the COVID-19 Outbreak. NCI has the important responsibility of working to rid the American public of cancer suffering. Continuing its operations to serve this responsibility is a top priority for NCI and the American public. NCI's leaders have therefore been planning how to maintain the institute's activities if the COVID-19 outbreak continues to cause operational challenges for NCI, including supporting external clinical trials and providing extramural grants. The institute will also maintain its intramural research to the extent possible.

Progress Against Cancer. NCI has recently released the *Annual Report to the Nation on the Status of Cancer,* which shows a continued trend of decreasing mortality rates for patients that dates back to the early 1990s. Between 2013 and 2017, mortality rates for all cancer sites declined, and progress was particularly rapid for melanoma and non–small-cell lung cancer. The declines in death rates occurred in every racial, ethnic, and age group. These advances reflect decades of painstaking basic science research and the translation of these findings through clinical trials to patients.

Lung cancer kills more Americans than breast, colon, and prostate cancer combined, so major progress in lung cancer has a large impact on national cancer statistics. Modeling by NCI's Cancer Intervention and Surveillance Modeling Network shows that if the expected decline in the use of combustible cigarettes occurs, lung cancer mortality rates will decline substantially in women and men over the next two decades. According to the modeling, these improvements will occur even without enhanced tobacco control, increased use of computed tomography screening, or better therapies.

Lung cancer mortality rates are decreasing more quickly than lung cancer incidence rates. One explanation could be that patients are receiving better treatment in the form of new therapies, such as immune checkpoint inhibitors, or better chemotherapy, surgery, and radiation. The fact that survival in patients with non–small-cell lung cancer, but not in patients with small-cell lung cancer, has improved over the past 15 years is consistent with therapeutic progress against this disease.

NCI Budget. The Cancer Moonshot will add $1.8 billion to NCI's budget over 7 years. NCI received $300 million in both 2017 and 2018 and then $400 million in 2019. In 2020 and the remaining 3 years, NCI will receive $200 million a year. NCI had advance notice that the annual funding amount would decrease and was able to prepare for this change.

The Childhood Cancer Data Initiative, which the president announced during his State of the Union address in 2019, is beginning in Fiscal Year (FY) 2020. This radical initiative will collect data on every child with cancer in the United States to better understand therapies and long-term toxicities. A new working group is developing a plan for the initiative.

In February 2020, the president issued his FY 2021 budget. Dr. Sharpless had recently attended a hearing of the House Appropriations Committee to discuss the president's budget and NCI's needs. Eventually, Congress will reconcile and finalize its appropriation legislation and will send it to the president for his signature. Congress continues to express strong bipartisan support for the National Institutes of Health (NIH).

In its 2020 budget, Congress showed awareness that the NCI paylines had become very low because of a massive influx of new applications, especially for the research project grant (RPG) pool. Congress therefore directed NCI to spend an additional $212 million to increase the success rate for competing grants and another $212 million for continuing grants. With this funding, NCI expects to increase R01 paylines from 8 percent to 10 percent and to fully fund noncompeting renewals of RPG grants (in contrast with 97 percent of these grant amounts in 2019).

Many important NCI activities, including the National Clinical Trials Network, cancer centers, Specialized Programs of Research Excellence, and training programs, are not part of the RPG pool. NCI has tried to maintain at least flat funding for all of these activities, and the institute has made a commitment in recent years to increase resources for clinical trials.

Leadership Updates. Oliver Bogler, PhD, recently became the director of NCI's Center for Cancer Training. Satish Gopal, MD, MPH, is the new director of NCI's Center for Global Health. NCI is working to fill the director's positions for the Division of Cancer Prevention and the Division of Cancer Biology.

CTAC Working Group Updates. Since CTAC accepted the report of the Glioblastoma Working Group on July 17, 2019, NCI has developed a concept to enhance glioblastoma therapies that incorporates some of the recommendations from the working group report. This concept will be presented to the NCI Board of Scientific Advisors.

The July 15, 2020, CTAC meeting is expected to include a report from the Radiation Oncology Working Group.

Clinical Trial Results Reporting. The Food and Drug Administration Amendments Act of 2007 required the reporting of clinical trial results to ClinicalTrials.gov. The Food and Drug Administration finalized its rule on clinical trials reporting in 2016, and NIH subsequently announced its policy in 2017. Noncompliance by institutions with these policies could result in fines as well as withholding of federal funds.

According to some recent external analyses, rates of compliance with the reporting requirements for academic institutions and NCI are less than optimal. NCI recently conducted its own analysis, which showed that rates of overdue reporting of results to ClinicalTrials.gov (i.e., results reported more than a year after the primary completion date) for clinical trials sponsored by NCI declined sharply between January 1, 2011, and January 1, 2020. To date, 98 percent of NCI-sponsored clinical trials covered by these policies have results posted on ClinicalTrials.gov. The real challenge, however, has been ensuring that results are reported on time (i.e., within 1 year after the end of primary data collection for each trial). NCI is working to improve the timeliness of results reporting for its clinical trials.

Undisclosed Support. Undisclosed payments from or arrangements with industry can lead to the perception of biased research. Such payments to NCI-supported investigators are a concern when they come from industry or from foreign funders, including foreign governments. NIH has made clear to investigators for decades that it expects its funded investigators to report all of the funding received that is relevant to their grant at the time their grant is filed.

NCI is working with academic and other institutions to ensure that they understand and comply with its policies related to disclosure of support. Collaboration with industry and with foreign scientists is important, but this collaboration must be transparent and comply with the law. NCI is collaborating with large professional societies (including the American Association for Cancer Research and the American Society of Clinical Oncology) to develop a voluntary database that will make conflict-of-interest reporting less burdensome and more uniform.

Questions and Discussion

Dr. Loehrer asked about the implications of the COVID-19 outbreak on NCI's workforce, budget, grant reviews, and grant funding. Dr. Sharpless said that the outbreak creates significant operational challenges for NCI, and the institute is working closely with NIH to proactively address these challenges. NCI has established a task force that discusses such issues as teleworking policies, animal care, and access to campus. The safety of NCI's workforce and contractors is a top priority.

Dr. Sharpless is optimistic about NCI's ability to administer grants during the COVID-19 outbreak, even in challenging circumstances. He anticipated that the institute would continue its normal disbursement of funds to extramural grantees, even if the situation at NIH worsens. NCI is working with the American Society of Clinical Oncology and other national associations to identify advice that can be provided to patients with cancer who are undergoing therapy during the COVID-19 outbreak.

Finally, NCI is considering how to handle any effects of the pandemic on clinical trials, such as barriers for patients to receive treatment. Dr. Doroshow reported that NCI plans to issue guidance in the near future on the flexibility needed for clinical trials conducted by the NCI Community Oncology Research Program, the National Clinical Trials Network, and the Experimental Therapeutics Clinical Trials Network. The plans will include ways to prevent problems with adverse event reporting and clinical trial audits.

Dr. Loehrer suggested that NCI consider allowing patients to receive treatment in their own communities while enrolled in clinical trials. Dr. Doroshow said that the new guidance will address this issue. Dr. Sharpless added that patient safety is NCI's top priority. NCI's guidance is an attempt to

mitigate the potential exposure to the novel coronavirus if patients enrolled in clinical trials continue to travel to receive treatment, while allowing good auditing and clinical trial practice.

III. Quantitative Imaging Network Working Group Report

Janet Ellen Dancey, MD, FRCPC

Quantitative imaging in clinical trials involves the extraction of measurable information from medical images to assess the status or change in healthy or diseased tissue. The NCI Quantitative Imaging Network (QIN) currently supports 20 teams that collaborate on the development and validation of tools and methods to measure or predict responses to cancer therapies in clinical trials.

QIN Clinical Decision Tools. The QIN tool catalog has 67 clinical decision tools, including 13 that have achieved QIN benchmarks for further clinical development. Six National Clinical Trials Network (NCTN) clinical trials are evaluating four of these benchmarked tools, typically for an exploratory objective.

One of the four benchmarked tools being evaluated in clinical trials is the Solid Tumor Segmentation tool, developed at Columbia University. This tool segments solid tumors to obtain tumor volume and contour data for validation of new quantitative imaging biomarkers. Three clinical trials are assessing this tool as part of an exploratory objective.

Another tool being evaluated in clinical trials (one that is underway and one that has not yet started) is the Auto-PERCIST (PET Response Criteria in Solid Tumors) tool, which analyzes fluorodeoxyglucose positron emission tomography images. This tool, developed at Johns Hopkins University and Washington University, will provide clinical decision support, image quantitation, image segmentation, image visualization, and response assessment.

Challenges. A considerable gap remains between tool development and translation of tools to the clinical community. Key questions are whether the QIN tools offer results that are useful to oncologists and whether these tools fit into clinical workflows without causing disruptions.

QIN Working Group. NCI formed the CTAC QIN Working Group after a presentation at the July 2018 CTAC meeting on the challenges faced by the QIN program in validating and demonstrating QIN tool utility in clinical trials. The working group, which Dr. Dancey chairs, includes current and former CTAC members, representatives of NCI's Cancer Imaging Program, and external experts.

The working group's mission is to advise NCI on strategies for enhancing the integration of quantitative imaging tools into clinical trials. The working group's deliverable is a report with recommendations outlining strategic approaches to develop and integrate quantitative imaging tools into NCTN clinical trials.

The working group has now completed its draft recommendations, which are as follows:

1. Form a pipeline oversight committee with NCTN, the Imaging and Radiology Core (IROC), and QIN leadership, as well as NCI program staff, to assess advanced QIN tools for NCTN clinical trial validation
2. Provide opportunities for QIN and NCTN scientific leadership engagement

3. Promote and incentivize QIN tool development and readiness for NCTN deployment
4. Ensure that imaging scientists, clinical radiologists, and clinical trialists have clarity about the use of QIN tools in clinical trials and the assessment of realistic endpoints
5. Ensure that NCTN sites are ready to open trials that include QIN tools
6. Support image data banking and sharing, with accompanying metadata from NCTN trials, in an archive such as The Cancer Imaging Archive (TCIA)

Questions and Discussion

Dr. Loehrer suggested that instead of encouraging imaging experts to develop imaging tools that they would like to have tested in clinical trials, NCI should issue funding announcements for the development of tools that address provocative imaging questions identified by clinicians. Dr. Dancey said that the working group tried to capture this idea in Recommendation 1, but there might be other ways to enhance communications between the imaging development and clinical communities.

Walter Curran, MD, Executive Director of the Winship Cancer Institute of Emory University, is also a working group member. He explained that the working group's recommendations are designed to bridge the cultural divide between imaging and clinical trial investigators, which is probably the most significant barrier to the translation of the QIN tools.

Dr. Theodorescu suggested that NCI host a meeting of leaders in clinical and imaging research to evaluate the QIN tools and narrow them down to a smaller set. Many of these tools are likely to overlap with one another, and NCI might benefit from input on which tools offer the greatest value propositions and could be implemented quickly in clinical trials. This approach might be more effective than trying to test all of the QIN tools and would allow the select set of tools to move forward more rapidly.

Dr. Schneider asked whether the working group learned about the use of QIN tools in any trials not supported by NCI. Dr. Dancey explained that the QIN Working Group did learn about some clinical trials testing the QIN tools that are not part of the NCTN. However, the group focused on the 13 tools that are clinically ready and are being investigated in NCTN trials. For this reason, the working group heard presentations from investigators about the successes and challenges of NCTN trials using the QIN tools.

Dr. Barton described the cultural divide between trialists from academic centers and community centers. She asked whether community center trialists would be involved in validation or other aspects of the assessments of the QIN tools. Giving community center trialists a voice is important. Dr. Barton also asked about the cost-effectiveness and cost–benefit ratios of the QIN tools.

Dr. Dancey explained that the working group described ways to overcome the various cultural differences in its recommendations. For example, the first recommendation calls for bringing together representatives of the QIN, IROC, and NCTN to determine which QIN tools could be particularly valuable and appropriate for incorporation into NCTN trials. In addition, the working group recognized the importance of engaging community center trialists in imaging tool development because these tools must be adopted broadly at both academic and community centers. The working group addressed this need in its recommendation to develop fit-for-purpose criteria for QIN tools (part of Recommendation 1) as well as in Recommendation 5, which calls for enabling sites to use the QIN tools appropriately in clinical trials. Questions about cost-effectiveness and cost utility can and should be embedded into

clinical trials. Clinical utility means not only that a tool is useful but also that its impact is valuable and the tool is affordable.

QIN Working Group member Michael Knopp, MD, PhD, Vice Chair of Research and Director of the Wright Center of Innovation in Biomedical Imaging at the Ohio State University, pointed out that quantitative imaging tools could reduce the duplication of imaging and help clinicians use imaging more effectively and efficiently. The data these tools collect from images can offer quantitative answers to disease-management questions. The collaboration among the QIN program, NCTN, IROC, and TCIA offers a major opportunity to exploit the benefits of big data, analytics, and personalized medicine. The working group's report points out that NCI has the needed infrastructure, tools, and capabilities in place to accelerate progress by giving the tool developers access to the infrastructure of the NCTN and TCIA.

Dr. Doroshow asked whether the working group identified incentives that NCI should offer to facilitate broader implementation of the QIN tools. Dr. Dancey said that NCI should encourage NCTN leaders to engage investigators in evaluating the tools in clinical trials and in providing data on the results. The best incentive is to include imaging and support for imaging as an integral or integrated biomarker in NCTN trials. If NCI offers funding for imaging studies within clinical trials, investigators are likely to design their trials to incorporate the QIN tools.

Dr. Knopp noted that two QIN tools can be used to collect more information from standard-of-care imaging. The QIN program's imaging add-ons, analytics of standard-of-care imaging, and support for the central collection of imaging data will be important incentives.

Dr. Loehrer said that conducting clinical trials in the NCTN has been a labor of love for medical and pediatric oncologists. Radiologists have been less involved in clinical trials, although their participation is increasing. Because quantitative imaging tools are not always included in clinical trial designs, nonmedical oncologists might need support.

Dr. Perez-Soler asked why only a small fraction of the 67 QIN tools have been benchmarked and whether industry is conducting research on quantitative imaging. Dr. Dancey said that the QIN pipeline includes many tools at different stages of development. To date, 13 tools have reached the stage of eligibility for incorporation into NCTN trials. Robert J. Nordstrom, PhD, Acting Chief, NCI Imaging Technology Development Branch, explained that some QIN teams include not only clinicians and imaging scientists but also industry representatives.

Motion. A motion to accept the report of the QIN Working Group, with the modifications recommended during this discussion, passed.

IV. Ongoing and New Business

Patrick J. Loehrer, Sr., MD
Sheila A. Prindiville, MD, MPH

Dr. Prindiville reported that CTAC's Ad Hoc Working Group on Glioblastoma has completed its final report, which CTAC approved in July 2019. NCI is implementing the recommendations in this report, and an update on the institute's progress is planned for the July 2020 CTAC meeting.

The CTAC Ad Hoc Working Group on Radiation Oncology has held an in-person meeting and should be ready to present its draft recommendations to CTAC at the July 2020 meeting.

CTAC formed the Strategic Planning Working Group in November 2019. Dr. Loehrer and Dr. Doroshow have been reviewing the input from CTAC members on the activities of this working group. Subgroups of the working group will meet virtually over the next several months to further refine the recommendations discussed in November.

Dr. Loehrer reported that the Strategic Planning Working Group meeting on November 6, 2019, was very engaging, and the group's report will help shape CTAC's activities over the next 5 years. Dr. Doroshow emphasized the importance of the role of subgroup leaders in moving the process forward.

Dr. Loehrer announced that the next CTAC meeting will be on July 15, 2020. He encouraged CTAC members and members of the public listening to the meeting to send CTAC meeting agenda items to Dr. Prindiville.

V. Adjourn

Patrick J. Loehrer, Sr., MD

There being no further business, the 41st meeting of CTAC was adjourned at 12:30 p.m. on Thursday, March 12, 2020.

November 16, 2020

Date Patrick J. Loehrer, Sr., MD, Chair

Sheila A. Prindiville -S Digitally signed by Sheila A. Prindiville -S Date: 2020.11.16 11:35:48 -05'00'

Date Sheila A. Prindiville, MD, MPH, Executive Secretary

Appendix

February 2020

NATIONAL INSTITUTES OF HEALTH
National Cancer Institute
Clinical Trials and Translational Research Advisory Committee

CHAIR

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Associate Dean for Cancer Research
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