DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
55TH CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE MEETING

Summary of Meeting
November 6, 2024

NCI Shady Grove, Conference Room TE406/408/410
9609 Medical Center Drive
Rockville, MD 20850

CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE

Summary of Meeting

November 6, 2024

The 55th meeting of the Clinical Trials and Translational Research Advisory Committee (CTAC) of the National Cancer Institute (NCI) was convened Wednesday, November 6, 2024, at 8:30 a.m. The CTAC chair, Dr. Julie M. Vose, presided.[1] The meeting was adjourned at 2:50 p.m.

Chair

Julie M. Vose

CTAC Members

Nilofer S. Azad
Smita Bhatia (virtual)
Charles D. Blanke (virtual)
Adam P. Dicker (virtual)
Gary C. Doolittle
Ernest T. Hawk
Ken Kobayashi (virtual)
Seth P. Lerner
Sumithra J. Mandrekar
Robert S. Mannel (absent)
Ruben A. Mesa (virtual)
Carolyn Y. Muller
Raymond U. Osarogiagbon
Raphael E. Pollock (absent)
Suresh S. Ramalingam
Victor M. Santana
Patricia A. Spears
George Wilding (virtual)

Ex Officio Members

Michael J. Kelley, US Department of Veterans Affairs
Richard Pazdur, US Food and Drug Administration (FDA) (absent)

Designated Federal Official

Sheila A. Prindiville, NCI

Presenters

LeeAnn Bailey, M.B.B.S., Ph.D., M.S., Branch Director, Community Outreach, Research and Engagement Branch, Center to Reduce Cancer Health Disparities, NCI
Brandy Heckman-Stoddard, Ph.D., M.P.H., Acting Chief, Community Oncology and Prevention Trials, Division of Cancer Prevention (DCP), NCI
M.K. Holohan, J.D., Director, Office of Government and Congressional Relations, Center of External Affairs, NCI

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

S. Percy Ivy, M.D., Associate Branch Chief, Investigational Drug Branch, Program Director, Experimental Therapeutics Clinical Trials Network, Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis (DCTD), NCI

Wolf Lindwasser, Ph.D., Deputy Director, Coordinating Center for Clinical Trials (CCCT), Office of the Director (OD), NCI

Lori Minasian, M.D., FACP, Deputy Director, DCP, NCI

Meg Mooney, M.D., M.S., Associate Director, CTEP, DCTD, NCI

Sheila A. Prindiville, M.D., M.P.H., Director, CCCT, OD, NCI

W. Kimryn Rathmell, M.D., Ph.D., Director, NCI

Julie M. Vose, M.D., Neumann M. and Mildred E. Harris Professor, Chief, Division of Hematology/Oncology, Department of Internal Medicine, University of Nebraska Medical Center

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I. Call to Order and Opening Remarks

Julie M. Vose, M.D.

Dr. Vose called the 55th CTAC meeting to order at 8:30 a.m. She welcomed Julie Schneider, Ph.D., Associate Director for Research Strategy and Partnerships, Oncology Center of Excellence, US Food and Drug Administration (FDA), who attended as the FDA representative.

Dr. Vose 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 (NIH) Events Management provided a VideoCast of the meeting. The VideoCast recording is available for viewing at https://videocast.nih.gov/watch=54127.

Motion. A motion to accept the minutes of the 53rd CTAC meeting, held on March 13, 2024, was approved.

II. NCI Director's Update

W. Kimryn Rathmell, M.D., Ph.D.

Dr. Rathmell welcomed CTAC members and thanked them for committing their time to assisting NCI in fulfilling its mission of advancing cures for cancer. She went on to present an overview of recent events and staff changes, provide budget updates, and highlight research and program accomplishments.

Recent News. Over the past months, Dr. Rathmell has prioritized efforts to understand issues related to cancer research in settings beyond academic centers. During visits to NCI Community Oncology Research Program (NCORP) sites, she learned about challenges of gaining the trust of transient multilingual populations in the Bronx and delivering care in rural Kansas. She attended the Iowa Cancer Summit and toured local sites across the state, where a network is being established to provide optimal care to patients who cannot travel to major academic medical centers; this is a burning issue in a state with a steeply rising cancer incidence. Visits to academic centers offered opportunities to engage with students, trainees, and postdoctoral researchers and urged them to consider a cancer research career. On the global front, NCI and the World Health Organization (WHO) renewed their collaboration to strengthen global cancer control, with NCI continuing its role as a WHO Collaborating Centre. NCI leadership also met with contingents from Australia and Japan to discuss shared interests.

White House Office of Management and Budget (OMB) examiners visited NIH to learn about Cancer Moonshot projects. The Deputy Secretary of Health and Human Services (HHS) visited NCI Frederick to review efforts to eliminate HPV-driven tumors and rare tumors; the White House OMB team also joined this visit.

NCI Senior Leadership Updates. Since the March 2024 CTAC meeting, several NCI senior leaders have retired: Dr. Henry Ciolino, Director, Office of Cancer Centers (OCC); Dr. Tony Kerlavage, Director, Center for Biomedical Informatics and Information Technology (CBIIT); Ms. Donna Siegle, Deputy Director for Management/Executive Officer; and Dr. Tom Misteli, Director, Center for Cancer Research (CCR). Dr. Krysztof Ptak is now Acting Director of OCC; Dr. Jill Barnholtz-Sloan is now Acting Director of CBIIT; Ms. Amber Lowery is now Deputy Director for Management/Executive Officer; Drs. James Gulley and Carol Thiele are now Acting Co-Directors for CCR. There have also been several additions to NCI's senior leadership team in inaugural positions: Dr. Warren Kibbe is Deputy Director for Data Science and Strategy; Mr. Peter Garrett is Director for Center for External Affairs; and Dr. Kristin Komschlies is Associate Director for NCI Frederick.

In September, NCI hosted a scientific symposium to honor Dr. Steven A. Rosenberg for his 50 years of pioneering research at NCI. Dr. Stephen J. Chanock, Director of the NCI Division of Cancer Epidemiology and Genetics, was elected to the National Academy of Medicine.

An NCI leadership retreat was held in July to identify areas of focus for which NCI can demonstrate output and value to the public. Key themes included trust/trustworthiness, rising incidence of early onset cancers, survivorship, cancer biology, immunology, prevention, data science, training, artificial intelligence (AI), obesity, and vaccines.

Budget. The NCI fiscal year (FY) 2026 Annual Plan and Professional Judgment Budget Proposal highlights the following scientific opportunities: tackling emergence of early-onset cancers in young adults; approaching cancer as a disease that affects the whole body; alleviating financial toxicity for cancer survivors and caregivers; and expanding the use of cancer-targeting vaccines.

In FY23, NCI requested $7.766 billion and received $7.3 billion. In FY24, NCI requested $9.988 billion and received $7.22 billion, which represented a $120 million increase to the base but an overall decrease of $96 million. For FY25, NCI requested $11.466 billion. The President's budget proposal includes $9.287 billion for NCI.

Budget increases have not kept pace with inflation, making it difficult to invest in new programs or broadly expand how clinical research is conducted in communities. Another factor influencing NCI spending decisions is an increased number of R01 and R37 applications, which have seen approximately a 15% increase in the first two funding cycles of FY25 compared with FY24 and FY23.

The current Continuing Resolution (CR) expires on December 20, 2024. Until a budget is passed, NCI's interim grant funding policy assumes a flat budget with noncompeting grants funded at 90% of the committed level. Interim paylines for R21 exploratory research grants are set at the 7th percentile; R01s for established and new investigators at the 9th percentile; and R01s for early-stage investigators at the 15th percentile.

Research and Program Highlights. A recent study found that the cost of cancer screening is less than the annual cost of treatment in the first 12 months after diagnosis. Another large clinical trial showed that immunotherapy after surgery helps people with high-risk bladder cancer live cancer-free longer.

Key initiatives aimed at modernizing clinical trials include myeloMATCH and Pragmatica-Lung. Launched in October 2024, the precision medicine trial MyeloMATCH will test treatments for myeloid cancers, rolling out new substudies over time. Pragmatica-Lung's streamlined model eliminates many barriers to study access; the study was launched in April 2023, and enrollment completion is expected by the end of 2025. New streamlined National Clinical Trials Network (NCTN) data collection standards developed under the auspices of the CTAC Streaming Clinical Trials Working Group will go into effect beginning January 1, 2025.

The National Cancer Plan focuses on accelerating cancer care delivery with goals to maximize data utility, eliminate inequities, optimize the workforce, and engage every person. NCI's clinical research priorities include expanding access to clinical studies and developing strategies for testing new clinical research models and their integration with care delivery, as well as preparing for the rapid onslaught of drugs, devices, and strategies in transforming cancer care delivery.

Dr. Rathmell asked CTAC members for their guidance on content, direction, and deliverables to accomplish these clinical research priorities as well as their support as champions for the transformation and modernization of clinical trials across the country.

Questions and Discussion

Dr. Ramalingam asked about plans to simplify the process for investigators to access biosamples for preliminary research. Dr. Rathmell responded that this topic has arisen with repositories, and NCI is on the cusp of clarifying availability and opportunities to use biosamples to advance science.

Ms. Spears expressed enthusiasm for engaging every person in implementation of the National Cancer Plan and the new NCI Center for External Affairs. She encouraged increased inclusion of the patient community within NCORP, NCTN, and cancer centers. Dr. Rathmell agreed that opportunities for coordinated bidirectional communication between the patient and research communities are tremendous.

Dr. Dicker asked what NCI component oversees or engages in validation of AI classifiers, radiomics, etc., to ensure data quality similar to the Clinical Laboratory Improvement Amendments program. Dr. Kibbe responded that NCI must work closely with FDA on validation of AI tools. The NCI AI working group is charged with identifying where AI is being used and how to validate it. Most of the AI tools that FDA approves are tied to imaging analysis.

Dr. Azad commented on the need for greater NCI engagement with private industry to improve access to exciting new agents. Dr. Vose agreed, noting that NCI timelines can be a barrier to collaborations with industry.

Dr. Muller expressed interest in addressing challenges with private partnerships and engaging community health systems owned by private equity groups in research and clinical trials. Dr. Rathmell briefly shared the concerns a nurse in Spencer, Iowa expressed about her ability to follow through if she offered clinical trials to her patients. This conversation highlighted the need to address concerns of community health providers as well as the importance of being adaptable and flexible to meet their needs.

III. Legislative Update

M.K. Holohan, J.D.

FY25 Appropriations. The federal government is operating under a CR for FY25, which maintains funding for federal agencies at FY24 levels through December 20, 2024. It is unclear whether the lame-duck 118th Congress will complete FY25 appropriations before the 119th Congress convenes on January 3, 2025. Furthermore, the federal debt limit suspension ends on January 2, which will necessitate congressional action addressing the debt limit within the first few months of 2025.

A review of NCI's FY24 appropriations highlighted an overall $96 million decrease in total funding to NCI compared with FY23 due to the conclusion of the 7-year mandatory funding stream for the Cancer Moonshot provided by the 21st Century Cures Act, even though congressional appropriators provided a $120 million increase for the NCI base budget. The overall decrease is a concern for many congressional members who are committed to cancer research and want to see the trajectory of increased investment continue.

In June 2024, the House Energy and Commerce Committee (E&C), the authorizing committee for NIH, proposed consolidation of 27 Institutes and Centers (ICs) to 15 and recommended a commission to review NIH. NCI was not included on the list of ICs for consolidation. Periodic reform proposals at the time of reauthorization are not unexpected; NIH reform bills were put forth in 2006 and 2016, and the 21st Century Cures Act introduced changes to NIH structure and reporting policies.

Although the E&C proposal was not formally introduced as legislation, the House Labor-HHS appropriations subcommittee incorporated the restructuring proposal into its FY25 spending bill. The bill proposed a flat funding level for NIH as a whole but included a $651 million increase for NCI. The bill also would cut $1 billion from the Advanced Research Projects Agency for Health (ARPA-H). In contrast, the FY25 Senate NIH spending bill does not address NIH restructuring and proposes a $2.05 billion increase for NIH, which includes a $266 million increase for NCI and flat funding for ARPA-H.

Congressional Calendar. The lame-duck session begins on November 12. Following a Thanksgiving recess, the session continues through the third week of December. Members-elect will arrive in Washington for orientation during the second week of November.

Engagement. Ms. Holohan emphasized the importance of cancer research community engagement with Congress to highlight the value of cancer research. She described the May 2024 Senate Appropriations hearing on the NIH budget, the first hearing in which Dr. Rathmell participated, along with Dr. Monica Bertagnolli and others.

Questions and Discussion

Dr. Blanke asked if there were any messages academic representatives should bring when visiting the Hill on Advocacy Day. Ms. Holohan highlighted the importance of telling patients' stories, which are meaningful to all members of Congress, regardless of party affiliation. She noted that cancer researchers and patients can effectively demonstrate how investment in cancer research leads to results for patients and highlight the importance of training the oncology workforce.

IV. Strategic Planning Working Group Implementation Report

Dr. Julie Vose, MD

The CTAC Strategic Planning Working Group (SPWG) 2020 report included 15 recommendations aligning with NCI's strategic vision for clinical trials for 2030 and beyond, focusing on the development of flexible, faster, simpler, less expensive, high-impact clinical trials that seamlessly integrate with clinical practice.

In 2024, NCI reconstituted the SPWG to review the implementation status of the 2020 strategic plan initiatives, determine whether additional SPWG recommendations should be pursued at this time, and identify new initiatives for consideration. The SPWG met in July 2024 and provided additional input in September 2024 to assess recommendations not yet implemented and to consider a new SPWG initiative.

Dr. Vose summarized the SPWG assessment of the three 2020 SPWG recommendations that have not yet been implemented: use of external control arms, modernizing the informed consent process, and refining the audit process.

Use of External Control Arms

2020 SPWG Recommendation: Investigate whether and in what situations data from previously completed clinical trials or contemporaneous clinical practice sources could be used as "synthetic" control arms without jeopardizing trial validity.

2024 SPWG Assessment: There is extramural interest in the potential value of external control arms to facilitate accrual and reduce costs, especially for trials in rare diseases. Some statisticians remain skeptical of the feasibility of external control arms. The SPWG recommended NCI convene an expert group to rigorously assess feasibility of using external control arms and identify clinical trial scenarios for which their use would be appropriate.

Modernize the Informed Consent Process

2020 SPWG Recommendation: Modernize the informed consent process by moving toward risk-based, modularized, dynamic consent forms and procedures.

2024 SPWG Assessment: Extensive regulatory requirements limit NCI freedom to change the informed consent process. The Cancer Therapy Evaluation Program (CTEP) should continue its efforts to improve the informed consent template while staying within regulatory constraints and monitor external efforts to improve communication with trial participants (e.g., videos, AI-based tools) to identify approaches appropriate for adoption by CTEP and/or NCTN groups.

Refine the Audit Process

2020 SPWG Recommendation: Redesign the audit process to audit only data elements essential for determining safety, efficacy, and regulatory compliance.

2024 SPWG Assessment: Audit burden remains an important concern, and there is a continuing need to improve standardization and coordination of audit timing and frequency across NCTN. The SPWG recommended that a retrospective analysis of past audit results be conducted to help identify areas where changes to the audit process could most effectively reduce burden. Revisions to the audit process should be implemented in a way that enhances process improvement and the collaborative educational aspects of the audit process.

Clinical Trial Activation Timelines

The SPWG also considered a proposed new initiative to assess clinical trial activation timelines. Implementation of standard timeline recommendations from the 2010 CTAC Operational Efficiency Working Group led to reduced duration of both median and outlier trial activation steps. However, timeline performance is perceived to have deteriorated in recent years due to impacts from the COVID-19 pandemic, clinical trial staffing challenges, increased trial complexity, institutional and practice payment issues, and industry delays in supplying agents.

2024 SPWG Assessment: The SWPG recommended that an updated analysis of NCTN clinical trial activation timeline performance be conducted. The analysis should document which timeline components and milestones are under control of NCI, NCTN groups, cancer centers, and other NCI clinical trial network participants, and pharmaceutical companies; assess outliers as well as median values; and investigate the causes of observed bottlenecks.

In September 2024, the SPWG provided input on the urgency of implementing the remaining 2020 SPWG recommendations that have not yet been pursued.

Community Outreach

2020 SPWG Recommendation: Increase interest in NCI clinical trial participation among community oncologists and health care institution leaders.

2024 SPWG Assessment: Outreach to community oncologists was deemed of greater urgency than outreach to leaders of health care institutions; however, both were ranked of high importance for implementation. Challenges include low per-case funding and a lack of necessary infrastructure.

Workforce Training

2020 SPWG Recommendation: Develop clinical trials training programs for community oncologists, oncology trainees, and local providers.

2024 SPWG Assessment: Training for the clinical trial workforce was deemed highly urgent, but funding remains a challenge.

Statistician Involvement

2020 SPWG Recommendation: Involve statisticians earlier in protocol design for correlative, early phase, and cancer center-led studies.

2024 SPWG Assessment: SPWG members considered this recommendation less urgent compared with the recommendations for workforce training and community outreach. Barriers include lack of financial resources to support statistician involvement, limited statistician availability, and challenges related to expanding the clinical trial statistician workforce due to poor alignment of trial support activities with incentive structure for academic careers.

Mobile/Remote Device

2020 SPWG Recommendation: Use mobile/remote devices for NCI clinical trial data collection.

2024 SPWG Assessment: This recommendation was judged to be the least urgent of the remaining SPWG recommendations. Challenges include the need to develop data standards and address analytic implications, data integration, and security issues. Application in the clinical trial context imposes incremental training requirements. Other concerns include equitable access to these devices and rapidly evolving technology that makes implementation a moving target.

In summary, the SPWG assigned the highest urgency to two initiatives: (1) workforce training, including community oncologists, oncology residents and fellows, and physicians and staff who provide ancillary support and (2) outreach to encourage community oncologist participation in clinical trials. The SPWG assigned lesser urgency to (1) outreach to institutional leaders; (2) early involvement of statisticians in protocol design for correlative, early-phase, and cancer center-led studies; and (3) use of mobile/remote devices for NCI clinical trial data collection.

Motion. A motion to accept the Strategic Planning Working Group report was approved.

V. Recognition Ceremony

Wolf Lindwasser, Ph.D.
W. Kimryn Rathmell, M.D., Ph.D.

Early Career Cancer Clinical Investigator Awards (ECIA). Dr. Lindwasser announced this year's ECIA awardees. The award recognizes and supports outstanding early career clinical investigators at NCI-Designated Cancer Centers who demonstrate a commitment to becoming academic clinical researchers and to supporting the NCI-funded clinical trials enterprise. These competitive awards promote retention of early career investigators who initiate a career path focused on interventional cancer clinical trials and academic clinical research. The 2024 ECIA recipients are:

- Nusayba Bagegni, M.D., Siteman Cancer Center
- Manali Bhave, M.D., Winship Cancer Institute
- Stephanie Dixon, M.D., M.P.H., St. Jude Children's Research Hospital Comprehensive Cancer Center
- Deborah Doroshow, M.D., Ph.D., Tisch Cancer Institute
- Mridula George, M.D., Cancer Institute of New Jersey
- Laila Gharzai, M.D., Robert H. Lurie Comprehensive Cancer Center
- Neda Hashemi, M.D., University of New Mexico Comprehensive Cancer Center
- Benjamin Herzberg, M.D., Herbert Irving Comprehensive Cancer Center

- Ryan Hughes, M.D., Atrium Health Wake Forest Baptist Comprehensive Cancer Center
- Zin Myint, M.D., University of Kentucky Markey Cancer Center

Retiring CTAC Members. Dr. Rathmell recognized outgoing CTAC members—Drs. Charles Blanke, Edward Chu, Adam Dicker, Ernest Hawk, and Sumithra Mandrekar—for their service on CTAC.

VI. Patient Access: Modernizing Informed Consent

Meg Mooney, M.D., M.S.

Informed consent documents (ICDs) can be challenging as they require finding a balance between fulfilling all regulatory requirements and being clear, concise, and understandable. Dr. Mooney traced the history of NCI's ICD development from the original template developed in the 1990s through major revisions in 2013 and 2017 as well as minor updates launched in 2018, with each revision being informed by broad stakeholder input.

The primary audience for the ICD template includes researchers and research staff who write and edit informed consent documents. The current template includes instructions to ICD authors, required text, and example text that can be adapted for a specific trial. Patients and caregivers considering participation in a trial are the primary audience for trial-specific ICDs, which are authored from the ICD template.

Modernizing the informed consent process requires moving toward risk-based, modularized, dynamic forms and procedures. In doing so, informed consent must still conform with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use E6(4) Good Clinical Practice, 21 Code of Federal Regulations (CFR) 50 (covering FDA-regulated trials), and 45 CFR 46 (Common Rule). The revised Common Rule sections on consent for biospecimen collection and potential future use along with NCI's emphasis on data sharing for clinical data and specimens present new research opportunities. However, conveying this information clearly and concisely to patients in order to obtain their consent can be challenging.

One of the primary aspects of the revised Common Rule, which makes it more modular, is the requirement of a key information section (2–3 pages) that provides a succinct overview of the trial for discussion with patients. Patients interested in participating after reviewing the key information section can continue with the full consent discussion.

The NCI Central Institutional Review Board (CIRB) processes allow for sites to add their local context. Additions related to local contact information, state and local laws, and institutional policy related to research are allowed per NCI CIRB guidelines. The only permissible deletion from local boilerplate language is reproductive language for faith-based institutions. Under the NCI CIRB, remote consent is an option that any site can elect to use. The NCI CIRB also approves trial-specific patient educational materials to supplement the consent discussion. For items that do not fall under the IRB mandate, lead organizations can provide trial-specific resources to assist site staff in facilitating discussions.

The HHS Office of Human Research Protections (OHRP) and FDA jointly issued draft guidance on "Key Information and Facilitating Understanding in Informed Consent" on March 1, 2024. The proposed guidance and an FDA proposed rule would harmonize FDA and Common Rule consent requirements and offer suggestions on approaches to the key information section. As an example, one approach is to present the key information section in ICDs in a visual format along with written text with the goal of succinctly communicating an overview of the clinical trial.

NCI oversees and periodically revises the NCI ICD template. The current revision effort enables response to changing science and research opportunities and incorporates input from a wide range of stakeholders to improve clarity. The latest revision includes reducing the length of the key information section, streamlining content most relevant to patients, improving usability by moving example text from the main template to a separate document, and streamlining information related to risks of standard of care. The changes have shortened the template from 51 pages to fewer than 25. Placing the example text in a separate document also allows for easier updates with more relevant examples as science and trial designs evolve, without requiring changes to the entire template.

Dr. Mooney outlined specific changes to the key information section designed to further streamline and emphasize modularity of the ICD, which include consolidating information to improve clarity and using textboxes to clearly delineate the start and end of the key information section. Because the template is intended for hundreds of trials conducted across thousands of sites, minimal formatting is needed for sites when they add local context. A potential change being considered would streamline references to standard of care commercial agent risks. This approach was recently used in the Pragmatica-Lung trial where only the most common and serious risks for standard of care were listed in the ICD with the expectation that a more detailed and lengthy discussion about the specific treatment regimen would occur outside of the ICD.

Dr. Mooney went on to summarize the challenges to improving the informed consent process. Required elements are drawn from federal regulations and must be adequately addressed at time of consent. Although FDA and OHRP released draft guidance with recommendations for the key information section, all required language must still be provided elsewhere in the consent. Unfortunately, complex trials—especially those that involve additional correlative research and multiple optional studies—require longer, more complex consent documents.

Dr. Mooney asked CTAC members for feedback on proposed changes, particularly any issues to consider when revising the standard of care risk list tables.

Questions and Discussion

Ms. Spears applauded modularization of the ICD and expanding the key information section to serve as a protocol summary. She noted that patients often do not understand the difference between what is being done as part of standard of care versus what is being done as part of the study. Presenting the study-specific side effects would help patients understand the differences.

Dr. Vose commented on the value of including a flow diagram for the study in the shortened consent form, noting that this is helpful to review with patients during the consent process. Dr. Santana strongly agreed and recalled a patient who returned for a visit 10 years later, bringing a diagram Dr. Santana had drawn during a previous appointment.

Dr. Ramalingam asked about translation of the ICD for those who are not proficient in English. Dr. Mooney noted that all ICDs are translated into Spanish, but capacity and funding to translate the entire ICD for specific studies into multiple languages is lacking, however, the ICD "Short Form Consent Document" is available in multiple languages but does not contain study-specific language. It was suggested to look into translating portions of the ICD that often seldom change into multiple languages.

Dr. Kobayashi noted that a tear-out section with a calendar explaining what the patient needs to do each day is highly practical. He noted the challenges of obtaining consent from patients with visual or physical limitations and other disabilities and encouraged addressing these to ensure proper consent is obtained.

Dr. Mandrekar commented on the importance of helping patients understand the trial they are being asked to participate in as well as what they are being asked to provide. Some of the consents for specimen collection, for example, are complicated and contradictory, making it difficult to know what samples can and cannot be utilized for future research. Dr. Mooney responded that CTEP is considering ways to streamline the biospecimen section. Dr. Mandrekar pointed out that rates of withdrawal on trials may be related to the way in which the studies are presented to patients. Dr. Mooney said that people withdraw for many reasons, noting that participants can withdraw at any time for any reason, but she acknowledged it would be beneficial to understand this better. Groups sometimes ask for additional information about the reason for withdrawing. However, these questions are optional for patients to answer.

Dr. Santana noted that the NCI CIRB reviews hundreds of consents, and most comments are related to the informed consent. A review of NCI CIRB comments could provide a wealth of information to inform the ICD revision. Dr. Mooney responded that the NCI CIRB is providing feedback on the revisions under consideration, which has proven helpful in reducing the amount of back and forth between the NCI CIRB and the study team.

Dr. Rathmell offered kudos to Dr. Mooney and her team for accepting the challenge of balancing regulatory requirements and meeting the needs of patients who are signing consent during a difficult time in their lives.

VII. Electronic Collection of Patient-Reported Outcomes in NCI-Sponsored Clinical Trials

Lori Minasian, M.D., FACP

Patient-reported outcomes (PRO) include any item reported by patients such as quality of life tools, symptoms scales, patient diaries, and PRO-Common Terminology Criteria for Adverse Events. Dr. Minasian outlined the value of PRO data and summarized efforts to improve the feasibility and usability of PRO data in NCI clinical trials. Incorporating PROs into study designs can help researchers identify safe, effective interventions to treat, prevent, and control cancer. It can also improve researchers' ability to identify tolerable regimens; understand the patient experience; and enhance clinicians' ability to communicate with patients about the anticipated therapeutic trajectory from the patient perspective.

Including PROs in NCI trials will require improving operational efficiency for PRO collection; that is, streamlining data collection, improving data quality, and facilitating analysis through integration of PROs into the existing electronic data capture system. Typically, patients are happy to provide their perspective, especially when they know that the information will be used.

Historically, PRO data collection was conducted via paper booklets that research staff transcribed into case report forms. Some groups have also used telephone collection. Current industry standard is electronic data capture. Three of the four adult NCTN groups use some form of electronic PRO (ePRO) collection. An NCI pilot project in 2016–2020 tested the Medidata ePRO tool, which improved data quality but created challenges for sites and patients. The pilot demonstrated that accommodating multiple modalities is critical for increasing patient participation.

Lessons learned from the pilot informed the decision to proceed with an ePRO platform integrated into the Cancer Trials Support Unit (CTSU), which coordinates all aspects of NCI clinical trials systems and provides standardized, integrated support services across networks. Extramural clinical trial investigators perform their work through CTSU, which improves efficiency and eliminates redundant processes. CTSU facilitates all the regulatory requirements and is working to ensure compliance with the Clinical Data Interchange Standards Consortium (CDISC) while CDISC is identifying data standards for PROs.

The current CTSU ePRO task order is designed to identify, configure, and pilot an ePRO platform for possible future use by NCI. The stakeholder-driven process is led by a multicenter organization working group, which includes members from NCTN and NCORP research bases to define, clarify, and prioritize workflows. Additionally, a working group made up of site and patient representatives provides input on streamlining the user experience, increasing patient satisfaction, and strategizing on ways to maximize adoption of ePRO.

Dr. Minasian described the ePRO platform evaluation and selection process, which identified 25 potential platforms that were narrowed down to 5 and the eventual selection of OpenClinica. This platform received the top evaluation score, provided the most robust responses to the Request for Proposal, and was the most responsive of the final vendor candidates.

OpenClinica features and benefits include synchronization to a Rave-based study calendar that accommodates treatment or study delays and schedule changes; flexibility to accommodate unique PRO needs of individual studies; access to item libraries and form templates; support for non-English-speaking participants; protocol-specific notifications and scheduled reminders; ePRO completion monitoring across participants, sites, and trials; and robust reporting capabilities by user type. Benefits to sites include the use of existing NCI credentials for access; automatic notifications to patients; reporting capabilities; and technical support. For participants, OpenClinica offers link-based access (no passwords); does not require downloading an app; can be accessed from a smartphone, tablet, or personal computer; and enables saving responses for later completion.

Next steps for the CTSU task order include integration with NCI systems, system configuration, re-engaging working groups, and development of training and evaluation plans. Beginning in early 2025, the pilot phase will include up to eight studies that will be evaluated for functionality, usability, acceptability, and adoption. Funding for OpenClinica will be on a study-by-study basis. Studies selected for the pilot should emphasize collection of PROs; that is, PROs would be a primary, coprimary, or key secondary endpoint.

Dr. Minasian shared examples of studies that collected PROs and the value they contributed. PROs can provide complementary information when captured rigorously. Electronic capture of PROs can help with the rigorous collection of PROs but must be feasible for use by patients.

Questions and Discussion

Dr. Mandrekar asked how OpenClinica is different from earlier electronic platforms that did not work well. Dr. Minasian noted that, in the earlier pilot, they learned that some patients did not want to provide PROs electronically. Therefore, determining the extent to which paper forms will still be needed is critical. Patients can leave questions unanswered on paper forms, and OpenClinica offers the ability to leave questions blank as well. For example, options such as “not applicable” or “prefer not to answer” can be included. Dr. Mandrekar also asked if OpenClinica will allow patients to enter information while they are still in the clinic instead of when they get home. Dr. Minasian responded that the platform can help facilitate the collection of PRO data around clinic visits while also defining a time window for completing the PRO instrument (e.g., 24–48 hours after the clinic visit).

Dr. Osarogiagbon asked whether Dr. Minasian anticipates that PRO collection will become standard in clinical trials. Dr. Minasian acknowledged the push and pull between incorporating PROs versus streamlining data collection. The decision to collect PROs should be linked to their relevance to the study as well as the types of PRO data being collected.

Dr. Bhatia wondered whether using electronic mechanisms might leave certain patients behind, and she asked about participation rates across populations. Dr. Minasian responded that the previous pilot included people of different ages and demographic characteristics. It remains to be seen whether OpenClinica will be streamlined enough to measure demographic differences in patient willingness to use the platform.

Dr. Minasian noted that she hopes to include an example study from the Children's Oncology Group, where the challenge will be having PROs designed for the right age groups. She also hopes to include a study that will collect PROs from both patients and caregivers.

Dr. Dicker asked whether any of the Clinical Trials Innovation Unit trials might be included in the pilot. Dr. Minasian replied that they are considering which trials will be best for the pilot, but short-term studies will be optimal.

Ms. Spears expressed concern about a lack of different modalities for people who prefer a verbal option and those with disabilities. She also asked whether OpenClinica will simplify data analysis. Dr. Minasian responded that, if the pilot is successful, the platform would be available for studies that prioritize PROs and integrate their analysis into study results. She noted that it will be important to return completed PRO results to patients.

Dr. Ramalingam offered appreciation for collecting only PROs that add value rather than those that simply increase burden. He favored directing NCI clinical trials to collect only hypothesis-driven PROs.

Dr. Blanke commented that the PROs being collected should be important not only to the investigator but also to the patient. Dr. Minasian noted that patients may have different perspectives than clinicians about adverse events (AEs). Therefore, determining if integration of the patient perspective into the interpretation of the study results is critical in deciding whether to incorporate PROs into the study. For example, patients have reported that they would accept a short high-grade AE over a chronic low-grade AE that interferes with their function every day for the rest of their lives.

Dr. Muller pointed out that PROs are only effective when they are completed and completed longitudinally. She asked whether OpenClinica can push positive messaging that supports retention in the study. Dr. Minasian indicated that this can be done by the platform and is something worth considering for the pilot.

Dr. Wilding noted that OpenClinica's expense had been mentioned several times and asked where the funding is coming from. Dr. Minasian explained that the pilot will be implemented through CTSU, which is funded by NCI.

Dr. Hawk asked whether the tool could collect patient perspectives related to financial toxicity. Dr. Minasian noted that the platform can be used to collect any information from the patient.

Dr. Philip Castle, Ph.D., M.P.H., Director, NCI Division of Cancer Prevention (DCP), NCI, emphasized the importance of this work as NCI moves toward precision medicine and approaches to symptom management. When appropriate to collect these data, it should be done rigorously and comprehensively. There are 19 million cancer survivors now, and the number will grow exponentially over the next few years.

Ms. Spears pointed out that financial toxicity questions are often rejected in the study design process. She recently conducted a survey of patients asking whether they would participate in a study if surveys were included; patients said this would not affect their decision to enroll. Dr. Minasian agreed and plans to consider the possibility of incorporating these kinds of questions in the pilot.

Dr. Bhatia commented on the importance of having someone available on the study team who can act immediately if a response indicates that a participant wants to end his or her life. Dr. Minasian noted that clinical site staff will be able to see patient responses and respond accordingly. Additionally, the platform can trigger an alert if a participant responded in a particular way. She will check to ensure that this is a feature that can be implemented.

VIII. Connecting Patient Populations to Clinical Trials

LeeAnn Bailey, M.B.B.S., Ph.D., M.S.

Multiple barriers at different levels—site, provider, and patient—prevent individuals from being referred to clinical trials. Site-level barriers include limited outreach as well as a lack of standard screening processes, referrals from community sites, leadership, and resources. Barriers at the provider level include lack of awareness of available trials, limited time to discuss trials, discomfort with trial communication, and potential biases. Patient-level barriers include fear or distrust of research, inconvenience, financial burden, and lack of awareness and understanding of trials. Addressing these barriers must occur simultaneously at all levels when considering how to engage and establish trust with patients in order to encourage participation and to have an impact on referral and future clinical trial recruitment.

Strategies to increase participation in clinical trials include prioritizing community-engaged research, establishing metrics and evaluating impact, building academic and community partnerships, and promoting bidirectional communication and shared decision-making.

The purpose of the Connecting Patient Populations to Clinical Trials (CUSP2CT) initiative is to develop, adapt, implement, and evaluate multilevel and culturally tailored outreach and education interventions with the primary goal of increasing referrals to NCI-supported clinical trials. The CUSP2CT network has defined a clinical trial referral as communication behavior or an action conducted by an individual (e.g., healthcare provider, clinical coordinator, lay health worker, patient caregiver) to link a potential participant to a clinical trial. CUSP2CT enhances clinical trial participation through integrated partnerships of health care professionals and collaborators. Partners include community health educators (CHEs), lay health advisors (LHAs), clinical trial coordinators, and referring primary care physicians, oncologists, and other providers. CUSP2CT aims to accomplish this work through enhancements to existing NCI clinical trial programs such as the NCTN, NCORP, and the Experimental Therapeutics Clinical Trials Network (ETCTN), as well as community outreach and engagement (COE) cores embedded within P30 comprehensive cancer centers.

The CUSP2CT program aligns with the patient access recommendation from the 2020 CTAC SPWG report of identifying and piloting tactics that have high potential to improve patient recruitment and retention. The CUSP2CT network aims to implement its strategies with flexibility and cultural humility.

The CUSP2CT network comprises a U24-supported data, evaluation, and coordinating center (DECC) that connects and coordinates the four grantee sites (U01s). The U24 DECC at Mayo Clinic provides project management expertise for CUSP2CT network activities, including data management and analysis. The DECC has established three active working groups to support program activities: Working Group 1 - Data Collection, Management, Statistical Analyses, Sharing and Research Dissemination; Working Group 2 - Program Evaluation; and Working Group 3 - Learning Collaborative. The DECC is working with U01 sites to establish common data elements to support consistency, reproducibility, data sharing, quality, and accuracy.

Dr. Bailey listed the four U01 grantees and described the work being done at their sites. The ECOG-ACRIN cancer research group is developing a clinical trial support tool that serves as a clinical research literacy tool for patients and a resource guide for patients and provider navigators. The University of Florida is utilizing artificial intelligence to implement a virtual community health educator. Moffitt Cancer Center is leveraging a variety of digital strategies to promote outreach within the community of health educators and patient navigators. The Ohio State University is implementing an accrual enhancement protocol to enhance engagement with various patient populations. These grantees are focused on scalable, portable interventions. Each U01 grantee is expected to leverage existing partnerships and foster new partnerships with community-based organizations to collaborate in tandem with CHEs/LHAs; leverage existing partnerships and foster new partnerships with referring providers to enhance the identification of potential referrals to clinical trials; identify available and appropriate clinical trials that have a strong potential for positively impacting variations in cancer health outcomes; establish baseline data regarding community member awareness and knowledge of clinical trials and provider referrals of patients to clinical trials; and implement and evaluate novel multilevel interventions to enhance representation in NCI-supported clinical trials.

Now entering the program's third year, the network has focused on engagement of community advisory members, developing tailored communication with multichannel approaches, gathering qualitative data, and implementing feedback mechanisms that enable real-time actions or adjustments.

Community participation was prominent during the CUSP2CT's second annual meeting, where strong relationships between the principal investigators, community representatives, and the greater population were evident. Participants discussed recommended strategies for engagement and connectedness, including building relationships with community members, offering fair compensation, public outreach, sharing testimonials and encouraging storytelling, training community leaders, hosting community events, and disseminating community reports. Decision-making strategies discussed included ensuring there are representative voices, encouraging bidirectional communication, and ensuring the community is involved in study design.

Dr. Bailey summarized key accomplishments of the program, which include the data collection and analysis currently underway, development of network infrastructure, engaging community members as active participants, the development of seven constructs for measurement, and operationalizing the definition of clinical trial referral. Next steps will focus on establishing and measuring the common data elements as well as ensuring continued engagement of community members and that interventions are implemented with fidelity. Program evaluation is ongoing.

CTAC members were asked to consider and provide feedback on the following questions:

- How can CUSP2CT better engage with CTAC and leverage their expertise going forward?
- How responsive is the CUSP2CT program to the CTAC SPWG patient access recommendations?
- What steps can be taken to ensure sustainability of these efforts to preserve impact for years to come?

Questions and Discussion

Ms. Spears asked how the program had tapped into the COE cores at the P30 comprehensive cancer centers. Dr. Bailey noted that different administrative supplements are available to the P30s to support this type of work; for CUSP2CT, they reached out directly to the COE to ask what was in place. The CUSP2CT geographic span goes beyond the P30 centers.

Dr. Hawk commented on insurability status and household income barriers to trial participation and suggested collecting data to understand the underlying social determinants of health more deeply. Dr. Vose agreed that distance to cancer centers is a barrier in rural areas, as well as insurance financial issues. Dr. Bailey noted that rural populations are included in the populations of interest to the program.

Dr. Santana asked how the program can increase understanding of referrals from private oncology practices to community practices that may or may not have access to clinical trials. Dr. Bailey responded that the intervention can be at a systematic or provider level. PIs can coordinate with the providers involved in the network with regard to specific clinical trials. A more comprehensive approach is something that could be considered for the future.

Dr. Osarogiagbon commented that it is not too early to start planning for scaling up this work. Dr. Bailey replied that data collected, lessons learned, and commonalities across sites will inform scalability.

Dr. Lerner remarked on the number of cancer centers with clinic systems serving various patient populations and said they seem like low-hanging fruit for recruitment into clinical trials. He asked how opportunities could be created for those systems. Dr. Bailey described the program's focus on engaging federally qualified health centers and changing the perception that clinical trials are a luxury.

IX. NCI Community Oncology Research Program Update

Brandy Heckman-Stoddard, Ph.D., M.P.H.

NCORP has a long history, starting with the Community Clinical Oncology Program and Minority-Based Community Clinical Oncology Program in the early 1980s and the NCI Community Cancer Centers Program launched in 2007. These programs were brought together in 2014 to form NCORP, which included cancer care delivery research (CCDR) as part of its mission. The first NCORP funding cycle ran from 2014 to 2019. The second funding cycle was given a one-year extension and will run through 2025.

NCORP aims to enroll patients in treatment and advanced imaging clinical trials that are developed in the NCTN through the Division of Cancer Treatment and Diagnosis; support the inclusion of health-related quality of life correlative studies in NCTN treatment trials; engage large and diverse patient populations receiving care in a variety of community oncology settings in studies focused on cancer control, prevention, and care delivery; and generate a broadly applicable evidence base that contributes to improved patient outcomes and reduction in cancer disparities.

The current NCORP infrastructure includes seven research bases (including five NCTN cooperative groups as well as Wake Forest and University of Rochester Cancer Center), 31 community sites, and 14 minority/underserved (M/U) sites. Centralized functions included in the program are the CIRB; CTSU; common data management systems; Biomarker, Imaging, and Quality of Life Studies Funding Program; biobanks; and the Imaging and Radiation Oncology Core. Each NCORP includes a multitude of affiliate sites; for example, the Montana NCORP has affiliates and subaffiliates across Idaho, Montana, Oregon, and Wyoming. Because each site is made up of diverse health systems and site structures, flexibility is critical during protocol development.

A new funding opportunity, the NCI Worta McCaskill-Stevens Career Development Award for Community Oncology and Prevention Research (PAR-24-153), was announced in April 2024. This K12 award supports training of clinical scientists in community cancer prevention, screening, intervention, control, and treatment research.

The NCORP network has grown significantly in the last five years. Since 2019, the number of nonphysician investigators involved in NCORP has more than quadrupled (418%), largely due to allowing advanced practice providers to enroll patients in clinical trials and enabling such providers to write prescriptions for clinical trials. The number of affiliate and subaffiliate sites participating in CCDR trials has increased by 59%.

NCTN and NCORP are linked by community sites that accrue to NCI clinical trials. NCORP is managed by the NCI DCP and the NCI Division of Cancer Control and Population Sciences and focuses on cancer control, quality of life, cancer prevention and screening, and cancer care delivery trials. NCTN is managed by CTEP and focuses on late-phase treatment trials and primary advanced imaging trials. NCORP treatment trial accrual from 2019 to 2023 has been stable. Accrual for quality-of-life trials has increased steadily, and accrual for cancer prevention and control studies has more than doubled. Overall and minority accrual within NCORP has also been stable and is excellent among M/U sites.

NCORP study development occurs via one of two paths. Investigators can work with a research base working group to develop a concept that can then be submitted for research base approval and subsequent review by a steering committee within the NCI Coordinating Center for Clinical Trials. If approved, the concept will go on to protocol development and funding through the network. NCORP trials can also be externally funded. For these studies, investigators also work with research base working groups to develop a concept. Once support for a grant submission is obtained from the research base, NCI approval is needed to proceed with grant submission. If funded, the study comes to NCI as a protocol within 90 days. Externally funded studies comprise about 25% of the NCORP portfolio.

In 2015, the NCI Symptom Management and Quality of Life Steering Committee set strategic priorities that continue to drive the science that NCORP is doing today. First-tier high priority areas include cognitive impairment, neurotoxicity, cardiovascular toxicity, fatigue, and cancer-specific pain. Second-tier high priority areas include sleep disorders, bone health toxicity, metabolic toxicity, and psychological distress. Examples of NCORP symptom management trials include studies of memantine for neurocognitive protection; electrical nerve stimulation for chemotherapy-induced neuropathy; use of duloxetine for prevention of oxaliplatin-induced chemotherapy-induced neuropathy; pharmacological reversal of ventricular remodeling in childhood cancer survivors at risk for heart failure; and an evaluation of carvedilol in prevention of cardiac toxicity. In addition, results of an NCORP study recently presented at the 2024 American Society of Clinical Oncology Quality of Care Symposium showed that both olanzapine and prochlorperazine significantly reduced refractory nausea.

The NCORP prevention portfolio includes standard prevention trials, precision prevention trials, and prevention delivery trials. Examples of NCORP prevention studies include the use of metformin for breast cancer prevention, the use of eflornithine and sulindac to prevent recurrence of adenomas and second primary cancers, the preventive effect of denosumab on breast cancer in *BRCA1* carriers, a comparison of interventions to reduce ovarian cancer risk among *BRCA1* carriers, and a cluster randomized control trial (RCT) of patient and provider decision support for breast cancer chemoprevention.

Recommendations from CTAC regarding the Tomosynthesis Mammographic Imaging Screening Trial (TMIST) led to the development of DCP screening trial requirements focusing on study design, recruitment planning, and accrual milestones and monitoring. TMIST, one of two large active NCORP screening trials, is randomizing participants to 2D digital or 3D tomosynthesis mammography. The other active NCORP screening trial is the Five- or Ten-Year Colonoscopy for 1–2 Non-Advanced Adenomatous Polyps study (FORTE), which is comparing 5- or 10-year colonoscopy for 1-2 nonadvanced adenomatous polyps to help determine whether certain individuals can wait for a follow-up colonoscopy after a routine screening colonoscopy.

Over the past 10 years, the NCORP cancer care delivery portfolio has produced 30 protocols, accrued more than 12,000 patients and more than 2,000 nonpatients to studies that enrolled at 839 practices, with minority accrual similar to overall NCORP studies at 23.4%. An example of an NCORP cancer care delivery study is a cluster RCT comparing standard practice with an educationally enhanced genomic tumor board intervention to increase evidence-based, genome-informed therapy.

NCORP is a prime program that takes trials into the community and maximizes data utility. Each NCORP site is working to optimize its workforce in unique ways. NCORP is a community-academic partnership and a trans-NCI collaboration with the goal of improved clinical practice and patient care in the community. NCORP focuses on the importance of quality of life, incorporating the patient experience, and developing interventions to reduce the risk of cancer and improve the cancer experience.

Questions and Discussion

Dr. Osarogiagbon noted the importance of scaling up NCORP as a way to increase access and high-quality care in rural settings.

Ms. Spears expressed a desire for NCORP to conduct more treatment trials. A large proportion of accrual to recent trials occurred at the community level. She encouraged better integration with NCTN and increased community engagement. Dr. Heckman-Stoddard responded that some timelines in treatment trials do not work well in the community; for example, obtaining an MRI within 10 or 15 days following biopsy may not be feasible in the community setting. Therefore, expanding timelines and increasing flexibility in treatment protocols may enable community sites to accrue more patients to treatment trials. Dr. Vose agreed that such timelines do not work well for many sites.

Dr. Dicker asked about NCORP concept approval timelines. Dr. Heckman-Stoddard noted that data review would be necessary to more closely analyze the steps in the approval process that can cause long delays.

Dr. Lerner remarked that about 20% of accruals at his institution come through NCORP. They plan to engage an NCORP co-investigator in concept development on every trial moving forward with the aim of reducing or eliminating barriers to accrual in community centers. Dr. Heckman-Stoddard responded that she pushes research bases for this type of authentic community engagement—listening to community investigators and ensuring their advice is reflected in the protocols.

Dr. Lerner added that his responsibilities include educating members of the SWOG Cancer Research Network cancer care and cancer control committees about NCORP opportunities. Trials that require external funding are challenging for investigators on these committees. Dr. Heckman-Stoddard reported recent success obtaining funding through NIH and external sources for trials through the network. This was as a result of a new process where a DCP team meets with the study team and the research base to review their study timeline and budget to ensure successful integration with the network.

Dr. Hawk commented on the challenge of accruing patients without cancer into prevention trials that involve other specialists and asked if NCORP had addressed this issue. Dr. Heckman-Stoddard noted that the NCORP cancer care delivery landscape survey was expanded to include survivorship care and cancer control but has not included prevention. However, a new iteration of the survey is being planned to improve understanding of how NCORP sites connect to all aspects of the landscape to inform efficient planning of prevention trials moving forward.

Dr. Hawk encouraged collection of information on household income, insurance status, and geography. Dr. Heckman-Stoddard replied that household income is not collected but insurance status is collected. This topic has been raised during discussions about enrolling Medicaid patients into clinical trials. The analysis will be expanded to show how NCORP can enhance enrollment of those patient populations into trials. She pointed out a DCP screening study that collects data such as household income from all patients who have been screened for NCORP trials, providing a potentially rich source of data that could give insights into why patients do not enroll in clinical trials. This screening study has enrolled 55,000 patients to date.

Dr. Hawk asked how the prevention and screening portfolio will be managed alongside the new Cancer Screening Research Network (CSRN). Dr. Castle responded that the portfolios are meant to be complementary and that the CSRN will not include agent development. Dr. Heckman-Stoddard added that there is a possibility of collaborative accrual between NCORP and CSRN. Dr. Castle went on to add that the data infrastructure is the same across both networks.

X. Experimental Therapeutics Clinical Trials Network Program Overview

S. Percy Ivy, M.D.

Since its formation in 2013, the ETCTN has evolved into a team-based clinical trials network that is collaborative and inclusive. The transformation of the ETCTN into its current state required strengthening good clinical practice standards in clinical trial operations; developing and implementing a new, centralized infrastructure; incorporating team science into the drug development process; developing a collaborative process involving the extramural community; and adding scientific rigor to the incorporation of biomarkers into clinical trials.

The ETCTN program comprises eight lead academic organizations (LAOs), two reference pharmacokinetic (PK)/pharmacodynamic (PD) laboratories, specialized teams, the ETCTN Tumor Bank (EET), and the National Clinical Laboratory Network (NCLN). The NCLN helps with molecular characterization, sequencing, assays and assay development, and immunotherapy biomarkers, which eliminates lab-to-lab variability. All assays are performed in a Clinical Laboratory Improvement Amendment certified environment and are acceptable for use in a clinical trial where integral biomarkers are used in selecting patients to go on study. In the last year, an independent and central ETCTN data safety and monitoring board was developed. ETCTN participating sites are broadly distributed throughout the United States with the exception of the Northwest. A site at Oregon Health & Science University has recently been added. The ETCTN program continually seeks to identify other high-quality cancer centers to participate in the network.

Dr. Ivy gave an overview of the ETCTN timeline, including outlining activities that occurred in the first two funding periods. From 2013 to 2015, the network was first developed by implementing centralized services, promoting involvement of early career investigators, developing drug development project teams, and creating a biobank where all ETCTN specimens could be sent. Specimens sent to the central biorepository could then be forwarded to the respective ETCTN PK/PD reference laboratories. One of the goals of the ETCTN was for all studies to be biomarker-driven. Therefore, an interventional radiology team was developed in 2019 to determine which patients are suitable for biopsy because in some instances more than one biopsy may be needed. The second funding period, from 2020 to 2026, included the development of the CATCH-UP.2020 program as well as equity-focused clinical trial investigator (E-FCI) teams. During the COVID-19 pandemic, R01 grants were set up to address drug resistance and sensitivity, which ultimately evolved into the Acquired Resistance to Therapy Network, which is a network that works to identify targets and pathways as well as potential drug interventions of interest for use in the ETCTN.

Several goals were set for the 2014–2020 funding period that were successfully accomplished. The goals focused on research, development, and improvement of cancer treatments; biomarker- and cancer biology-driven studies using patient-derived specimens; and career enhancement for early career investigators.

An opportunity for early career development highlighted by Dr. Ivy is participation on an ETCTN drug development project team. These are temporary teams put together to design ETCTN trials, made up of a cancer biologist, an expert in translational and biomarker work, and a clinician to write and conduct the trial. Notably, 85% to 90% of project teams are headed by an early career investigator. At the conclusion of the project development process, the project team makes a presentation to NCI's Investigational Drug Steering Committee (IDSC). If a project is approved by the IDSC, it will move on for further development. Another example of early career development is the development of disease-focused clinical investigators. Early career investigators are paired with mentors working in disease-defined clinics to chair disease-focused webinars, which are geared to enhance investigator collaborations for the conduct of ETCTN studies.

Goals for the 2020–2026 funding period focused on competing more effectively for patients; improving biopsy specimen quality; and enhancing the use of validated biomarker assays with assistance from the NCLN.

With funds from a congressional budget line item, ETCTN awarded one-year supplements to eight NCI Cancer Centers (centers not participating in the ETCTN) to enhance accrual of underserved/underrepresented patient populations (UUPPs) to ETCTN trials. CATCH-UP.2020 grantees were challenged to accrue at least 24 patients and have at least 50% of enrollees be from UUPPs, and they were given one year to complete accrual. Supplement recipients activated 111 trials within the first 2 months; overall, 571 patients were screened and 373 were enrolled, 51% of whom were from UUPPs.

Dr. Ivy noted that each CATCH-UP site employed a unique approach. Best practices for identifying UUPP patients included having motivated investigators, working through community oncology outreach offices, using patient navigators and community immersion techniques, offering telemedicine, and performing genomic data screening. Building on these best practices and lessons learned from successful CATCH-UP site accrual, ETCTN established four E-FCI teams. The highest accruing CATCH-UP centers were incorporated into LAOs as affiliated organizations to help LAOs address UUPP recruitment. Additional E-FCIs were established in LAOs that did not absorb a CATCH-UP site.

Dr. Ivy highlighted ETCTN accrual by race and ethnicity. Non-White and/or Hispanic/Latino accrual increased from 19.4% in the first funding period to 22.6% in the second funding period. ETCTN interventional accrual by year and trial phase showed slow growth in project period 1 (2014–2020), reaching a peak (1,076) in grant year 5, followed by vacillating levels through grant year 7. For project period 2 (2020–2024), overall ETCTN interventional accrual saw an increase through the first quarter of 2021, despite the COVID-19 pandemic, before dropping significantly through the second quarter of 2022, and then gradually climbing back toward pre-pandemic numbers.

ETCTN has been successful at combining experimental investigational agents with other investigational agents or standard-of-care therapies. Between 2001 and 2011, a total of 118 investigational agent combination trials were conducted. In the most recent two funding periods, 170 ETCTN phase 1, phase 2, and phase 1/2 novel combination studies were conducted. Biomarker analysis for the 109 ETCTN trials using the EET are in varying stages of completion. There are 47 trials still accruing patients and collecting specimens.

An overview of ETCTN accomplishments included the development of new agents (e.g., molecular, immune-oncology, first-in-human combinations); increased participation of early career investigators in the ETCTN (from 27 investigators participating in 26% of protocols to 40 investigators participating in 45% of protocols); uniform usage of technically and clinically validated fit-for-purpose biomarker assays; uniform categorization of biomarker types used in early clinical trials (i.e., integral, integrated, and exploratory); determination of optional versus mandatory biopsy performance based on biomarker type; and improved general metrics.

Questions and Discussion

Dr. Santana asked whether the variation in accrual numbers is linked to trial complexity. Dr. Ivy replied that the early-phase trials are biomarker-driven and complex trials by nature. An analysis has not been completed, but there is a possibility that accrual can be affected by trial complexity.

Dr. Kobayashi applauded the opportunities for young investigators to learn research practice as well as drug development, a specialized skill. Dr. Ivy noted that the early career investigators work at academic organizations within ETCTN and generally only use NCI Investigational New Drug agents. Entry of investigators from outside of the network is rare, although not impossible.

Dr. Kobayashi commented that early-phase trials are much more complicated than phase 3 trials in terms of demands and ability to understand requirements of the trial. He commented that patients with physical or cognitive disabilities are rarely included in clinical trials; expanding approaches to enrolling them could bring huge benefits to many. Dr. Ivy agreed that this was an excellent suggestion and noted challenges in reaching those patients.

Dr. Dicker asked about inclusion of imaging in the datasets. Dr. Ivy responded that some include imaging, and some do not. Generally, imaging is not prospectively collected. However, when developing radiopharmaceutical agents as cancer therapies that require dosimetry, those images are collected and centrally evaluated.

Dr. Azad asked about the process for targeting drugs and drug classes, given that some classes have many options, and some of the "hot" drugs are not available. Dr. Ivy replied that IDSC members team with an NCI investigator to search for agents in specific categories such as DNA damage repair. Regular meetings are held to remain informed and aware of agents as early as possible and to approach companies to potentially codevelop their agent with NCI. Investigators are encouraged to draw attention to companies with which they are collaborating to discuss potential NCI partnerships.

XI. Ongoing and New Business

Julie M. Vose, M.D.
Sheila A. Prindiville, M.D., M.P.H.

Dr. Prindiville encouraged members to submit agenda topics for the next CTAC meeting scheduled for March 12, 2025, and noted the meeting will likely be virtual.

XII. Adjourn

Julie M. Vose, M.D.

There being no further business, the 55th meeting of CTAC was adjourned at 2:50 p.m. on Wednesday, November 6, 2024.

Date Julie M. Vose, M.D., Chair

Date Sheila A. Prindiville, M.D., M.P.H., Executive Secretary

Appendix

October 2024

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute
Clinical Trials and Translational Research Advisory Committee

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