ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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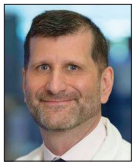
The National Cancer Institute's Clinical Trials Innovation Unit



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H&O What is the National Cancer Institute's (NCI's) Clinical Trials Innovation Unit (CTIU), why was it established, and what are its goals?

MJM The CTIU is a multiagency forum for the NCI, the US Food and Drug Administration (FDA), and the extramural cancer community to advance clinical care and promote equitable participation in clinical trials through innovative approaches in science, trials design, and operational efficiencies for a few high-priority clinical research studies. The CTIU is part of NCI's comprehensive strategy to systemically improve our clinical trials system over time. It is multipronged, with the CTIU representing one aspect of various initiatives undertaken by the NCI.

The term innovation in this context encompasses a wide range of applications within which the CTIU operates. This includes innovative interventions, biomarker development, data extraction methods, collaborations, and ways of conducting clinical trials. The key focus is on expediting and streamlining the process through creative solutions.

H&O Can you give us a breakdown of what the CTIU has been up to since it launched in February 2023?

SP We have been making significant strides since the launch. Initially, we spent time developing foundational documents, outlining roles, clarifying goals, and specifying the types of studies and projects appropriate for the CTIU. In May, we decided to initially pilot the process within the NCI's National Clinical Trials Network (NCTN). We issued a call for short proposals, and by mid-June, we received up to 4 short, 1- to 2-page ideas from each NCTN group. The CTIU members, particularly the NCTN group chairs within the CTIU, promptly worked to prioritize these short proposals and identify those for further consideration. We are hoping that by early fall, we will have identified a proposal that will be selected for development into a clinical trial.

MJM We deliberately designed the process to be streamlined and easy for both the investigators submitting proposals and the CTIU members who evaluated them. Once proposals were selected, they were then invited to submit more detailed, expanded proposals based on their initial ideas. In cases where ideas seemed mutually complementary, we recommended collaboration. These comprehensive proposals underwent further evaluation, and those deemed particularly promising received broader scientific input. We aimed for a process that was quick and efficient, striving to minimize unnecessary burdens for all involved, but also garnering the required expertise for development.

For future rounds, we are hoping to broaden beyond the NCTN to get a wider reservoir of ideas for the CTIU. Dr Prindiville and I, along with the rest of the CTIU, are currently working on the best approach to achieve this.

SP In addition to proposal selection, this collaborative effort provides a forum for discussions of general clinical trial design and operational issues among the NCTN Group Chairs, NCI, and FDA. For example, one area that we have discussed is improving access to specimens from clinical trials for correlative science. This group has recognized some challenges in this area, and we believe the CTIU could play a role in addressing them. Therefore, besides proposal selection, we also are actively working on problem-solving across our clinical trials system.

H&O How will a multistakeholder approach contribute to CTIU's overall success?

MJM Although a wide variety of stakeholders are either members of or contributors to CTIU, they all align around a similar understanding of the current state of play of clinical trials. Whether you are looking at it from the perspective of the NCI, investigators, patients, or the FDA, it is evident that clinical trials are plagued by complexity, high costs, burdensome designs, unnecessary data collection, slow activation, and delays in results reaching those patients and providers who need them. These burdens have also hampered access across the enterprise for both patients and providers. Bringing together these stakeholders who share this common view allows for the development of mutually beneficial solutions that focus on simplification, innovation, and problem-solving.

Each stakeholder approaches these solutions from a different perspective. The FDA approaches these issues from a regulatory standpoint, investigators approach them from the design and conduct of trials, patients provide input on how trials are conducted and how they affect their lives, and the NCI plays a crucial role in shepherding clinical trials through the NCTN system and running that infrastructure. Having all these perspectives at the table for collaborative problem-solving is the most effective way to identify, test, and implement solutions.

A key benefit of this approach is the involvement of all stakeholders early in the development of a proposal. Early involvement allows for early guidance up front, minimizing the potential for missteps along the way.

H&O What are the interactions like between the CTIU and other agencies?

MJM There is no set limit on who we can collaborate with. Although our initial round focused primarily on the NCTN, future rounds will include collaborators from across academia, industry, other agencies, additional networks, and cancer research foundations, such as the American Society of Clinical Oncology and the American Cancer Society. We are enthusiastic about fostering these types of collaborations, especially those that venture into innovative territory, potentially breaking new ground in ways that have not been explored before.

> Our patient advocates . . . play a role in the selection of proposals by the CTIU, providing invaluable insights into what is both feasible and effective from the perspective of patients.

H&O What are some of the major challenges in the current clinical trials landscape that the CTIU seeks to address?

SP The current state of affairs is such that some trials can be complex and expensive, contain burdensome designs, and collect data in excess of what is necessary. It can sometimes take quite a long time to get them activated, leading to delays in getting results to patients and providers as well as inequitable access to studies.

In general, we know that this model is not sustainable over time. This is where the CTIU comes in, as part of the broader strategic efforts by the NCI to enhance and streamline its clinical trials system. If we are going to transform how clinical trials are conducted, we need a way to identify and test new, higher-risk approaches to understand what works, without disrupting clinical trials already underway. To do this, the CTIU will select a few high-priority studies that could test innovative study designs and operational procedures, and then work with partners necessary to carry them forward through the NCTN.

H&O Can you describe the domains for which you have received clinical trial proposals?

MJM One category of proposals that we are considering includes interventional therapeutic trials. Many of these have a specific focus on a pragmatic design, specifically

focusing on standard-of-care therapies and broader populations. The emphasis here is on increasing access and equity and simplifying studies.

Another area of keen interest to us is biomarker qualification. We have received a couple of proposals regarding biomarkers that we hope will accelerate drug approvals if they are appropriately qualified for such use.

As Dr Prindiville mentioned, we are also serving as a platform for addressing challenging issues that arise among cooperative groups, particularly in terms of shared resources and collaborative problem-solving.

H&O How will the CTIU ensure that clinical trials are inclusive and accessible to a diverse group of patients?

SP As Dr Morris alluded to earlier, one area of interest is to identify trials that are streamlined and pragmatic. These are trials that we hope will improve access and inclusivity for patients. The CTIU also adheres to all the National Institutes of Health clinical trials inclusion policies to ensure that women and underrepresented populations are appropriately included in all clinical research, depending on the specific scientific question under investigation.

Additionally, the NCI has taken several other steps to promote inclusion and access. Firstly, we have adopted the ASCO-Friends of Cancer Research broadened eligibility criteria. This philosophy emphasizes the importance of making trial eligibility as inclusive as possible, avoiding unnecessary patient exclusions. Secondly, the NCI has recently launched the Connecting Underrepresented Populations to Clinical Trials, or CUSP2CT, program. This initiative aims to assess strategies for reaching out and educating underrepresented populations, with the primary objective of increasing referrals for studies conducted through our networks. This not only allows us to explore innovative ideas and trial designs but also grants us the opportunity to leverage the various programs already established within the NCI clinical trials system.

H&O What role does the community play in shaping the future of cancer clinical trials through the CTIU?

SP The community, including our scientific and advocacy partners, plays an extremely important role. These are the individuals we rely on to propose ideas and insights, letting us know what needs to change, or highlighting important research questions that may not be easily addressed within our current system. Through facilitation and cross-agency partnerships, these ideas can potentially lead to the testing of new scientific or operational approaches within the NCI's network.

Our patient advocates are a critical component of all NCI research endeavors. They play a role in the selection of proposals by the CTIU, providing invaluable insights into what is both feasible and effective from the perspective of patients. In essence, it is the collective involvement of all the stakeholders in the community that contributes to the selection and launch of trials through the CTIU.

Additional Affiliations

Dr Morris is on the faculty of Memorial Sloan Kettering Cancer Center, where he heads the Prostate Cancer Section and is a member and attending on the Genitourinary Oncology Service.

Disclosures

Dr Prindiville has no conflicts of interest to report. Dr Morris is an uncompensated advisor to Bayer and Novartis; a paid advisor to AstraZeneca, Lantheus, Daiichi Sankyo, Convergent Therapeutics, Pfizer, ITM Isotope Technologies, Clarity Pharmaceuticals, Blue Earth Diagnostics, POINT Biopharma, Telix, and Z-Alpha; and has received institutional research funding from Bayer, Corcept, Roche, Janssen, Celgene, Novartis, and Astellas.

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