Researchers grappling with if, how changes made to trials during the pandemic should continue

During the COVID-19 pandemic, oncology trials have rapidly undergone a series of substantial changes to adapt to a fluid situation and prevent clinical research from coming to a complete halt. Now, researchers are grappling with if and how changes to trials—many of which had long been discussed in the oncology community—should remain in place after the pandemic. They are also considering lessons learned from COVID-19 research that could be applied to cancer research.

“One needs to understand just how far we’ve gone in how short a time … these are changes that might have taken a decade or more [to implement] in the absence of the pandemic,” noted James Doroshow, MD, director of the Division of Cancer Treatment and Diagnostics at the NCI, during a panel discussion at the second session of the American Association for Cancer Research Annual Meeting 2021, held virtually May 17–21. “There are real silver linings.”

A major shift has been the decentralization of oncology trials, which involves conducting aspects of trials remotely or at local sites rather than at a centralized location—a change supported by an FDA guidance (https://www.fda.gov/media/136238/download). NCI surveys conducted early in the pandemic and again 5 to 6 months later revealed helpful modifications in this realm, including electronic consent for trials, mailing oral investigational agents to trial participants, offering scans and blood draws at local sites, and routine use of telemedicine. Also beneficial: remote auditing of trials and allowing investigators to skip reporting low-grade adverse events unlikely to affect safety. “I think it’s very clear that most, if not all, of those things that we changed need to continue,” Doroshow said.

During the COVID-19 pandemic, “people were forced to make changes. They had to interpret regulations, they had to proceed in a way that they felt was best,” said Noolie Gregory of Syneos Health. Sponsors are now considering if and how they should continue those changes, she added, decisions that need to be supported by robust case studies.

Similarly, researchers will need to evaluate whether alterations made to trials during the pandemic affect efficacy endpoints and statistical analyses, said Sundeep Agrawal, MD, of the FDA. “I think a one-size-fits-all approach will be difficult,” he added. “We do obviously want to make sure that we’re maintaining the trial and data integrity.”

These changes bring a key question to the fore: What data are necessary to collect, and what information is nice to have but not essential? “The cost of doing trials today is so extraordinary that the whole system is under severe pressure,” Doroshow said. “Every data bit that you collect that you don’t need costs money, and it’s wasted money.”

Moreover, nonessential data collection often translates into more appointments and procedures for patients, creating an extra burden and potential barrier to trial participation, noted Jill Feldman of the patient advocacy group EGFR Resisters. The NCI is currently planning randomized trials that gather different types of data to investigate this question further.

The FDA’s Nicole Gormley, MD, also noted that “there are definitely lessons from the experience with COVID clinical trials that could be applied and carried forward” in oncology. COVID-19 vaccine trials not only raised awareness about the importance of clinical trials, but also enrolled a greater proportion of African American and Hispanic individuals than typical oncology trials.

“Increasing representation is possible,” Gormley said. In oncology, this means that sponsors and investigators should consider disease-specific disparities when planning trials and repeatedly evaluate eligibility criteria to expand the pool of potential participants. They could also choose sites that attract diverse patients, an effort that may be aided by continuing decentralized trials. Additional steps include developing diversity study plans and appointing diversity study officers, as well as working with community leaders and clinicians to raise awareness and promote participation.

Gathering real-world data also became essential during COVID-19, offering a template for how such data might be better used in cancer research. “COVID has had a catalytic role for real-world data, largely because of the need for rapid knowledge,” said Donna Rivera, PharmD, of the FDA. In fact, several databases quickly launched, including the COVID-19 and Cancer Consortium and the Thoracic Cancer International COVID-19 Collaboration.

In oncology, “I think real-world data can play a complementary role for therapeutic development,” Rivera said. For example, real-world data could point researchers to drugs that might be repurposed or provide preliminary evidence of drug activity that could be validated in clinical trials. Real-world data may also offer insight into subsets of patients not included or insufficiently represented in trials. “This conversation is not around a dichotomy of either/or, but really how can real-world data increase knowledge and evidence in a more rapid fashion when needed in combination with trials?” Rivera said.

The biggest lesson of the pandemic, however, is that a great deal can be accomplished through urgent, large-scale collaboration. “We saw as a society across the world that actually it didn’t matter your country; it didn’t matter your product. It was about how we collectively work together to tackle this challenge ahead of us,” Gregory said.

“The unprecedented level of scientific collaboration [has] been essential,” Rivera agreed. “I think we’ve learned what’s possible.” —Catherine Caruso
# CANCER DISCOVERY

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