FDA and Its Role in Drug Development

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Presenter's disclosure of conflicts of interest is found at the end of this article.

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Abstract

JADPRO Live 2020 was honored to have Dr. Richard Pazdur, the Director of the Oncology Center of Excellence at the FDA, discuss recent changes to oncology drug development and the approval process, the roles of the advanced practitioner in the execution of clinical trials, and changes that have taken place as a result of the COVID-19 pandemic.

As the first U.S. Food & Drug Administration (FDA) Inter-Center Institute, the Oncology Center of Excellence (OCE) fosters a unified interaction between the three FDA centers: the Center for Biologics Evaluation and Research (CBER); the Center for Drug Evaluation and Research (CDER); and the Center for Devices and Radiological Health (CDRH).

During JADPRO Live Virtual 2020, Richard Pazdur, MD, Director of the OCE, described the role of the OCE as well as recent changes to the oncology drug development and approval process. Dr. Pazdur also discussed the role of the advanced practitioner in the execution of clinical trials and the impact of the COVID-19 pandemic on drug development.

ONCOLOGY DRUG DEVELOPMENT

According to Dr. Pazdur, oncology differs from other therapeutic areas regulated by the FDA due to the large public interest and the need to expedite drugs. Compared with other drugs, there's also different risk tolerance for side effects, and there's an active advocacy community. Furthermore, said Dr. Pazdur, nearly half of all drugs designated "breakthrough therapies" by the FDA are in oncology.

"We're also moving into innovative indications for drugs, including biomarker-defined populations," he added. "Hence, the need to create the OCE at the FDA."

The FDA is involved throughout the drug development continuum from the earliest phase, development, to drug approval and post-marketing. In early-phase development, drug safety and activity are examined, while in the later stages, the question becomes whether a drug provides "meaningful benefit," said Dr. Pazdur.

In the United States, there are two pathways for drug approval: regular and accelerated. Given the rapid pace of innovation in oncology, said Dr. Pazdur, the OCE has also piloted multiple programs to explore more efficient review process-

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es. The Real-Time Oncology Review program, for example, begins a dialogue with the sponsor and receives data before an application is actually submitted to the FDA in order to take earlier actions on oncology products.

"This is particularly important because many of these drugs are breakthrough therapies that offer substantial improvements to patients with cancer, so there is some urgency to review and approve these drugs in a timely basis," said Dr. Pazdur, who noted that 13 of 49 total approvals in 2019 came on the basis of the Real-Time Oncology Review.

"We're not cutting corners," he added. "We're simply moving the process up and reviewing drugs before the application is submitted."

ROLE OF ADVANCED PRACTITIONERS IN ONCOLOGY

Scientific advances over the past 10 to 15 years have enabled the development of cancer drugs aimed at specific mutations and pathways tailored to individual patients, and approximately 40% of all pharmaceutical activity in the United States is now in the area of oncology and malignant hematology. In order to keep up with the additional workload created by this "tremendous growth in oncology," the OCE employs advanced practitioners in a variety of settings, said Dr. Pazdur.

Many advanced practitioners are involved in the project management aspect of moving applications through the agency during the review process and even in the Investigational New Drug (IND) stage while preliminary studies are being conducted.

In addition, the OCE employs advanced practitioners as data scientists to interrogate applications regarding drug safety and efficacy as well as special population considerations. These data scientists also look at safety issues in the post-marketing setting after drugs are approved.

"This is an important part of what we do here at the FDA, both in the early and later phases of drug development," said Dr. Pazdur.

Advanced practitioners play a major role in the FDA's outreach program as well. A project at OCE called "Project Community" interacts with diverse communities that have not had traditional contacts with the agency to hear points of view outside the academic setting. This involves soliciting feedback from patient groups about the drug development process and earlier access to treatments, such as unapproved drugs.

"We're interested in bringing underserved and minority groups into the regulatory process here at the FDA," said Dr. Pazdur, who noted that a "considerable number" of advanced practitioners work in outreach.

Advanced practitioner involvement in outreach extends to international drug development too. With Project Orbis, OCE coordinates and reviews activities with Australia, Brazil, Canada, Singapore, Switzerland, and the United Kingdom to promote international collaboration of drug regulators. According to Dr. Pazdur, this collaborative process has allowed drug companies to submit applications where there may have been a time lag of 2 to 3 years, making subsequent drug development "much easier."

OCE INITIATIVES

Another OCE initiative, Project Facilitate, aims to provide personalized support to oncologists and health-care teams seeking unapproved drugs for patients with life-threatening diseases who may often have exhausted all other therapeutic options. Given the complicated nature of the regulatory process, said Dr. Pazdur, the purpose of this project is to "facilitate a somewhat difficult process for people who are not familiar with it and to help patients access investigational drugs."

Project Patient Voice incorporates patients in assessing the toxicities of drugs and has developed a pilot website that describes patient-reported longitudinal symptomatic adverse events. While most clinical trials have a physician or another health-care provider record adverse events, Patient Voice has actual patients provide this information directly.

"This is our attempt to get the patient voice out to the medical community and into product labeling rather than having a third-party description of their experience," said Dr. Pazdur.

The FDA also has a large educational initiative, and the OCE has piloted many programs that have been exemplary for the entire FDA, said Dr. Pazdur. Project Socrates is an umbrella project to unify these many educational efforts.

Finally, Project Renewal is a public health initiative that is updating labeling information for oncology products by evaluating relevant scientific evidence from published literature.

"We spend a lot of time at the FDA on drug labeling for new drugs before a drug comes out," said Dr. Pazdur. "With this initiative, however, we're paying special attention to drug labels that may not have been revised for many years."

FDA ONCOLOGY AND COVID-19

The OCE has maintained its commitment to patients with cancer during the pandemic, Dr. Pazdur said, starting with a series of listening sessions with patients and practitioners to understand how the pandemic has affected oncology care in the United States (Table 1).

"One of the most disturbing things we have heard during the pandemic is that patients with cancer feel they have been forgotten," said Dr. Pazdur. "We recognize that we must keep our aim on oncology by assessing and approving new drugs in a timely fashion."

Since the start of the pandemic on March 1 through the end of August 2020, FDA Oncology has approved 12 new molecular entities. In addition to these new drugs, a total of 33 new indications have been approved, including extensions of preexisting indications and new indications of already approved drugs.

"Much of the agency has invested its resources in addressing the COVID population, and rightly so, but at the Oncology Center of Excellence, we needed to focus our attention on the patients with cancer to make sure that they are not forgotten during this pandemic," said Dr. Pazdur.

Table 1. FDA Oncology and COVID-19

- Oncology reviews and approvals continue
- FDA guidances on clinical trials
- FDA supports efforts to decentralize clinical trials
- Longer dosing regimens approved
- Research collaborations on real-world evidence of patient outcomes
- OCE Listening Sessions with patients and practitioners

The OCE has also been active in writing guidance on clinical trials to support decentralization.

"We realize that many times patients cannot go back to major cancer centers," noted Dr. Pazdur. "Hence, some of the testing and provider visits can be conducted in communities that are nearer to patients' homes, and we have permitted that."

In addition, FDA Oncology has made a concerted effort to approve longer dosing regimens. Many regimens have been extended to allow patients to visit doctors less frequently to get drugs, to have these drugs administered at home, or to have intravenous drugs administered subcutaneously.

"This was done to limit patient interaction with providers and [minimize] potential infection risks to patients," said Dr. Pazdur.

Finally, FDA Oncology has developed research collaborations on real-world evidence to look at patient outcomes during the pandemic. ●

Disclosure

Dr. Pazdur had no conflicts of interest to disclose.