ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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The FDA's Patient-Focused Drug Development Initiative

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H&O What is patient-focused drug development (PFDD)?

PK Essentially, PFDD is taking the patient into account throughout the entire drug development process. There are many things that could be considered PFDD, but it starts at the earliest stage of drug development by asking patients what is most important to them regarding their disease and treatment. Trial conduct can be more patient-focused, through the rigorous collection of symptom and functional data and with the use of digital health technology. In addition, the number of patients enrolled in clinical trials can be increased by expanding eligibility criteria and permitting enrollment through local institutions. PFDD should lead to better communication of the risks and benefits of a new treatment, so that patients can make the most informed decision based not only on factors such as the treatment's effects on the tumor, the impact on overall survival, and clinician-reported side effects, but also on information drawn from rigorously collected symptom and functional data.

H&O What are the goals of the FDA's PFDD program?

VB Our 3 main goals are to (1) actively engage with patients and advocacy groups, (2) foster research into the measurement of the patient experience in cancer clinical trials, and (3) generate science-based recommendations for regulatory policy to include the patient experience in cancer drug development. We accomplish these goals using public workshops, publishing articles, interacting with patients and advocacy groups, participating in regulatory policy development, and advising industry sponsors.

H&O What kinds of resources does the PFDD program offer?

VB Our program provides consultation to the US Food and Drug Administration (FDA) review divisions across centers regarding the measurement and analysis of symptoms and function in cancer trials. We are also very active in engaging patients and the drug development community to provide a regulatory perspective and to advance trial designs that can be more efficient and less burdensome to patients, such as decentralized trials and those that incorporate digital health technologies.

One new public resource is Project Patient Voice, a novel web-based platform to communicate patient-reported symptomatic side effects to health care providers and patients. This is a publicly available website (accessible at https://www.fda.gov/about-fda/oncology-center-excellence/project-patient-voice). We are working to expand this website to include patient-reported symptoms and side effect data from cancer clinical trials voluntarily provided by industry sponsors. The website allows patients and their healthcare providers to access symptom and

side effect data provided by patient-reported outcome (PRO) assessments in clinical trials. These data can serve as unique complementary information to the standard safety data found in the FDA prescription drug label. Project Patient Voice has the added benefit of reporting preexisting symptoms and information about symptoms over time, providing week-to-week snapshots of each symptom. This allows novel insights into the patient experience. For instance, we can present levels of nausea throughout the trial in the subgroup of patients without nausea before treatment started.

H&O How does the PFDD program engage with patient groups?

PK Interacting with patients with cancer is one of the most rewarding parts of our work, and our highest priority. One example is a workshop we hosted called Partners in Progress, which is a resource for new and experienced patient advocates alike to learn more about current initiatives and activities at the Oncology Center of Excellence (OCE). Equally as important, these workshops are a great way for patient advocates to share their experiences, and to network with each other and the FDA staff. The PFDD group (and the OCE as a whole) regularly interacts with patients at workshops, advisory committees, and listening sessions, such as a series called "Conversations on Cancer" hosted by the OCE. It is important that patients inform our science and our policy. We have had significant patient feedback for efforts such as Project Patient Voice.

H&O How does the PFDD program collaborate with other divisions at the FDA?

VB The PFDD program works very closely with the oncology review divisions and collaborates across all of the FDA centers. The day-to-day work of the PFDD program is to provide bespoke, actionable advice to drug sponsors about patient-focused issues for oncology trials. The PFDD program also reviews and analyzes clinical outcome assessment data on symptoms and function that are submitted with product applications. At the same time, the PFDD program works with other divisions and centers outside of oncology to align on guidance development and research.

H&O Does the PFDD program work with practicing clinicians or clinical trial investigators?

PK Both Dr Bhatnagar and I are medical oncologists, and members of the clinical community are an important group of collaborators in our work. For instance, Project Patient Voice is intended to be a tool for practicing clinicians to assist them when discussing side effects of a treatment. In addition, clinical trial investigators and practicing clinicians have been a valuable resource for our program to learn more about the logistics of how best to assess patient symptoms and function in the settings of clinical care and clinical trials. Another emerging area is decentralizing trials, or moving some or all of the trial conduct closer to where patients live. Decentralized trials could decrease the burden of trial participation for patients, and we are interested in helping to facilitate these efforts, which will entail working with the broader health care delivery system. The lines between clinical trials and clinical care are blurring, and we anticipate more engagement with academic and community clinicians to advance many of our efforts.

H&O Are there examples of how the PFDD program has impacted the development of a drug?

VB One clear example is the increased use of PRO symptom and function data in regulatory reviews and product labeling. Since the program's inception, there have been 11 products whose FDA labels include information on patient experience. In each case, the PFDD program has been instrumental in analyzing PROs and working with the FDA divisions on the best way to communicate symptom and function data in labeling. For example, the product label for crizotinib (Xalkori, Pfizer) provides important patient-reported information about the duration and timing of treatment-related visual disturbance. There are also examples in which efficacy was supported by symptom and function data, such as with ibrutinib (Imbruvica, Pharmacyclics/Janssen) for graft-vs-host disease and ruxolitinib (Jakafi, Incyte) for myelodysplastic syndrome. In addition to product labeling, more symptom and function data are now being presented at Oncology Drug Advisory Committee meetings. Our team helps to analyze and interpret these data to inform the FDA presentation on the overall risks and benefits of a treatment. These examples are the tip of the iceberg, and we anticipate that symptom and function data will increasingly be used to support tumor and survival data, and to distinguish a new drug from an increasing number of available therapies.

H&O Do you have any recommendations on how trial investigators or practicing clinicians can measure PROs?

VB Trial investigators and practicing clinicians measuring PROs should know that patients have expressed to us

a desire to know what PRO data will be collected, why these data are important, and what these data will be used for. Providing this information to patients at the outset of treatment (or a clinical trial) will invariably improve the quality of the PRO data. Patients should also be informed about whether their health care team will be monitoring and responding to patient-reported symptoms in real time. There are logistical complexities to incorporating PROs into the workflow, and we recommend that clinicians new to the use of PRO data seek advice from others with a track record of successful deployment. For clinical trials intended for FDA submission, our team routinely provides detailed recommendations based on the specific trial context.

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H&O Could you share some insights gained through the PFDD program?

PK This program puts us in contact with patients and advocacy groups more than most, and I would say that working with patients keeps you humble. All too often, those of us involved in caring for or developing treatments for patients with cancer think we know what patients want. But when you reach out and ask patients, you may not get the answer you expected. Clinicians throughout the drug development scientific community are experts in disease pathophysiology, clinical trial design, and regulatory policy. Patients are experts in living with the disease and knowing what is important to them. By ensuring a continuous dialogue, we can have the best chance to develop safe and effective treatments that provide a benefit that is meaningful to patients. We can and should meet this goal in the most efficient and least burdensome manner possible. We are continually learning from patients, academics, international regulatory counterparts, and other governmental colleagues, and this collaborative aspect of our program is very rewarding.

H&O Does the PFDD program have any ongoing or upcoming initiatives you would like to discuss?

VB After a successful Clinical Outcomes Assessment in Cancer Clinical Trials (COA-CCT) public workshop held in 2020 (recordings available at https://www.fda.gov/drugs/news-events-human-drugs/fda-asco-public-workshop-2020-clinical-outcome-assessments-cancer-clinical-trials-fifth-annual), we are planning for the Sixth Annual COA-CCT workshop, to be held in July 2021. We will provide a retrospective look at the past workshops, and discuss ways that our experience with symptomatic adverse events can inform research questions and analytical methods for assessment of physical functioning in patients with cancer.

Disclosure

Drs Kluetz and Bhatnagar have no real or apparent conflicts of interest to report.

Suggested Readings

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