Opportunities to Improve Dose-Finding and Optimization for Rare Disease Drug Development

Public Virtual Workshop

Tuesday, October 29, 2024

10:00 am - 3:30 pm ET

Background

There are over 10,000 known rare diseases worldwide with an estimated 30 million individuals in the United States with these conditions.[1] Only a small percentage of rare diseases have an approved treatment, leaving significant unmet treatment needs for many patients impacted by rare diseases. Conduct of clinical trials intended for rare disease populations often faces challenges such as: small population size, disease heterogeneity, and absence of established endpoints to support regulatory approval among others. These challenges impact the design and strategies employed throughout the drug development process, including key early-stage activities like dose-finding and optimization that inform later steps of the drug development process.

The purpose of a dose-finding study is to evaluate the efficacy and safety of a range of doses to ultimately determine the optimal therapeutic dosage. However, the challenges associated with rare disease drug development impact conventional dose-finding and optimization approaches. This includes challenges such as heterogeneity in clinical manifestations, age of onset, disease severity, and prognosis, complicate establishment of safe and efficacious dosing regimens. Because of these complexities, conventional dose-finding and optimization approaches applied in drug development for common diseases are often not pursued, and further advancements are necessary to promote more precise and patient-centric methodologies for dose selection and optimization.

The Duke-Margolis Institute for Health Policy, under a cooperative agreement with the U.S. Food and Drug Administration, is convening a one-day public virtual workshop on effective strategies for dose-finding and optimization in rare diseases including: considerations for pediatric populations, opportunities to enhance early-phase trial design, and potential applications for real-world data.

[1] https://www.fda.gov/patients/rare-diseases-fda

Agenda

10:00 AM **Opening Remarks**

10:05 AM **Introduction to Dose-Finding and Optimization in Rare Disease Drug Development**

Objective: A high-level introductory presentation on the major challenges for dose-finding and optimization in rare disease drug development.

Presentation

10:15 AM **Session 1: Patient and Clinical Perspectives on Dose-Finding and Optimization in Rare Disease Drug Development**

Objective: Patients and clinicians will discuss their experiences participating in clinical trials, such as going to the clinic and medication administration routes. Panelists will emphasize the importance of efficient dose-finding and optimization approaches for rare disease drug development and discuss the challenges and opportunities for enhancement.

Panelist Remarks

Moderated Panel Discussion and Q&A

11:00 AM **Session 2: Early-Phase Clinical Trial Design to Support Dose-Finding and Optimization**

Objective: Panelists will discuss the role of nonclinical models in informing early phase trial design. Panelists will also discuss novel statistical methodologies and trial approaches to support dose-finding and optimization in early phase trials for small and heterogenous populations.

Presentations

Moderated Panel Discussion and Q&A

12:00 PM **Break**

12:20 PM **Session 3: Integrating Sensitive Endpoints in Early-Phase Trials**

Objective: Panelists will discuss best practices and considerations when selecting appropriate clinical outcome assessments that are also meaningful to patients, with a focus on strategies for integrating sensitive endpoints in early phase trials.

Presentations

Moderated Panel Discussion and Q&A

1:20 PM **Session 4: Real-World Data Considerations for Dose-Finding and Optimization**

Objective: Experts will discuss opportunities to enhance data used for dose-finding and optimization in the post-marketing setting. The discussion will include the challenges and limitations to pre-market data collection to support the use of real-world data in evaluating use of alternate dosages in the post-marketing setting.

Panelist Remarks

Moderated Panel Discussion and Q&A

2:05 PM **Break**

2:20 PM **Session 5: Defining and Optimizing Doses for Pediatric Populations**

Objective: In this closing session, panelists will reflect on the topics discussed throughout the day. Panelists will tie together the threads through a pediatric rare disease case-study, and by discussing dose optimization efforts based on special considerations such as drug types, safety event management, administration, and data collection. Finally, they will discuss near-term next steps for applying such approaches.

Presentation

Moderated Panel Discussion and Q&A

3:20 PM **Closing Remarks**

3:30 PM **Adjournment**

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