Duke | MARGOLIS CENTER *for* Health Policy

Measuring Clinical Benefit in Neonatal Randomized Clinical Trials: Challenges and Opportunities

March 23, 2023 • 9:00 AM – 4:30 PM
Hybrid Public Workshop: National Press Club, Washington D.C. and Virtual

Meeting Agenda

Objective: This meeting aims to promote discussion and collaboration between researchers, clinicians, industry, and regulators on efficacy endpoint considerations for neonatal randomized clinical trials, and to provide a forum for patients and families to share what clinical benefits they find important.

09:00 a.m. **Welcome and Introduction**
Morgan Romine, Duke-Margolis Center for Health Policy

09:10 a.m. **Opening Remarks**
Hilary Marston, U.S. Food & Drug Administration
Diana Bianchi, National Institute of Child Health and Human Development

09:30 a.m. **Session 1: Current Approaches to Measuring Efficacy in Neonatal Randomized Control Trials**
***Moderator*: Michele Walsh**, National Institute of Child Health and Human Development

This session will provide an overview of currently utilized approaches to measuring clinical benefit in neonatal randomized controlled trials (RCTs), highlighting differences between efficacy measurement to support regulatory approval versus clinical practice change. Presenters will discuss strategies and considerations related to endpoint selection and clinical outcome measurement in neonatal RCTs.

Presentations

- **Gerri Baer**, U.S. Food & Drug Administration
- **Barbara Schmidt**, McMaster University & University of Pennsylvania
- **Kristi Watterberg**, University of New Mexico

Q & A

10:30 a.m. **Session 2: Challenges in Measuring Efficacy for Neonatal Conditions with Unmet Clinical Needs**
***Moderator*: An Massaro**, U.S. Food & Drug Administration

This session will focus on the challenges and considerations for developing core outcome sets for neonatal research and choosing appropriate primary endpoints for regulated trials. During this session, speakers will review potential efficacy endpoints related to key neonatal conditions, such as bronchopulmonary dysplasia (BPD), neonatal seizures, neonatal opioid withdrawal syndrome (NOWS), and pain. The speakers will discuss best practices and key solutions for generating high-quality evidence for these conditions with high unmet clinical needs.

Presentations

- **Kanecia Zimmerman**, Duke University School of Medicine
- **Erik Jensen**, Children's Hospital of Pennsylvania
- **Janet Soul**, Boston Children's Hospital
- **Martin Offringa**, University of Toronto

Discussion Questions:

- What challenges exist in measuring efficacy and selecting endpoints for neonatal RCTs? How have these challenges impacted meaningful evidence generation?
- What are the best approaches for developing core outcome sets for key neonatal conditions and how can core outcome sets be used in demonstrating efficacy?
- What are the best approaches for justifying proposed efficacy endpoints for a neonatal trial?

Panel Discussion

12:00 p.m. **Break for Lunch**

1:00 p.m. **Session 3: Key Considerations for Endpoint Selection for Neonatal Conditions**
***Moderator*: Monica Lemmon**, Duke University School of Medicine

In this session, panelists will discuss endpoint types and key aspects of selection for neonatal conditions, including the timing of outcome measurement and the interpretability, reliability, and validity of measured endpoints. In addition, panelists will consider how feasibility with respect to timing, costs, and other burdens may impact endpoint selection. Session panelists will also consider the clinical importance of endpoints to various stakeholders, including patients and families.

Panelist Remarks

- **Keith Barrington**, Sainte Justine University Health Center
- **Ashley Darcy-Mahoney**, George Washington University School of Nursing & Pediatrix
- **JaNeen Cross,** Howard University
- **Deb Discenza**, PreemieWorld
- **Betsy Pilon**, Hope for HIE
- **Daniel Fuentes**, Chiesi USA, Inc.
- **Naomi Knoble**, U.S. Food & Drug Administration

Discussion Questions:

- What does each stakeholder believe are the most important factors to consider for measuring efficacy?
- When designing a clinical trial, how can investigators/sponsors determine the degree of improvement that would be clinically meaningful?
- How can study investigators/sponsors balance feasibility and meaningfulness when selecting outcome measures?

Panel Discussion

2:30 p.m. **Session 4: Novel Approaches to Measure Clinical Benefit in Neonatal Clinical Trials**
***Moderator*: Matthew Laughon**, UNC Health

This forward-looking session will focus on new approaches to measuring clinical benefit in neonatal RCTs, such as defining a global rank score (GRS), EHR/technology-based clinical outcome assessment tools, and data-driven surrogate or intermediate endpoints. In addition, speakers will focus on considerations related to balancing efficacy with potential or known safety concerns and challenges with using new approaches to neonatal trial conduct.

Presentations

- **Genny Taylor**, UNC Health
- **Kevin Hill**, Duke University Medical Center
- **Claudia Pedroza**, The University of Texas Health Science Center at Houston

Panelist Remarks

- **Dionna Green**, U.S. Food & Drug Administration
- **Kanwaljit Singh**, Critical Path Institute
- **Susan McCune**, PPD Clinical Research Business, Thermo Fisher Scientific

Discussion Questions:

- What new approaches are investigators considering for measuring clinical benefit in neonatal RCTs?
- What are the best approaches for validating an innovative measure of clinical benefit?
- How can innovative efficacy endpoints be efficiently incorporated into neonatal clinical trials?

Panel Discussion

4:00 p.m. **Fireside Chat**
***Moderator*: An Massaro**, U.S. Food & Drug Administration

Session moderators will summarize the key takeaways from their sessions and discuss next steps and how to improve clinical benefit measurement in neonatal randomized clinical trials in the future.

- **Michele Walsh**, National Institute of Child Health and Human Development
- **Monica Lemmon**, Duke University School of Medicine
- **Matthew Laughon**, UNC Health

4:25 p.m. **Closing Remarks and Meeting Adjournment**
Morgan Romine, Duke-Margolis Center for Health Policy

4:30 p.m. **Adjourn**

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