Public Workshop: Oncology Clinical Trials in the Presence of Non-Proportional Hazards
The National Press Club • Washington, DC
February 5, 2018

9:00 a.m. Welcome and Introductions
Mark McClellan, Duke-Margolis Center for Health Policy

9:10 a.m. FDA Opening Remarks
Gideon Blumenthal, U.S. Food and Drug Administration

9:20 a.m. Session I: Perspectives on Potential Limitations of Statistical Plans Based on Assumption of Proportional Hazards Over Time
Moderator: Mark McClellan

Objective: Provide an overview of FDA’s experience with current statistical methods and discuss observed challenges with the use of these methods. Highlight industry experience with current statistical methods and outline objectives of the cross-pharma working group.

Presentation: Overview of Current Statistical Methods, Case Examples, and Observed Challenges
- Rajeshwari Sridhara, U.S. Food and Drug Administration

Presentation: Overview of Industry Experience and Cross-Pharma Working Groups’ Objectives
- Renee Iacona, AstraZeneca and Tai-Tsang Chen, Bristol-Myers Squib

Reactants:
- Marc Theoret, U.S. Food and Drug Administration

Audience Q&A (15 min)

10:20 a.m. Break

10:30 a.m. Session II: Analysis Methods and Simulations: Addressing Non-Proportional Hazards
Moderator: Mark McClellan

Objective: Discuss, review, and provide feedback on the proposed alternative statistical tests for addressing non-proportional hazards, and identify outstanding issues regarding their potential use.

Presentation: Hypothesis Testing and Estimation
- Satrajit Roychoudhury, Pfizer

Presentation: Simulations and Assumptions
- Tianle Hu, Lilly
Panelists:
  - David Harrington, Harvard University
  - Kunthel By, U.S. Food and Drug Administration
  - Gideon Blumenthal, U.S. Food and Drug Administration

Panel Discussion (30-35 min)

12:00 p.m.    Lunch

1:00 p.m.    Session III: Retrospective Application of Novel Analysis Methods in Completed Trials
  Moderator: Mark McClellan

Objective: Discuss, review, and provide feedback on the application of the proposed combination test in clinical trials compared to commonly applied methods, and highlight remaining issues regarding its potential use and implementation.

Presentation: Delayed Effect and Long-Term Remission Case Study
  • Bo Huang, Pfizer

Presentation: Delayed Effect and Long-Term Remission Case Study
  • Kay Tatsuoka, Bristol-Myers Squib

Presentation: Diminishing Treatment Effect Case Study
  • Larry Leon, Genentech

Presentation: Crossing Survival Curves: IPASS Case Study
  • Pralay Mukhopadhyay, AstraZeneca

Presentation:
  • Xin Gao, U.S. Food and Drug Administration

Panelists:
  • Lijun Zhang, U.S. Food and Drug Administration
  • Eric Rubin, Merck
  • Susan Halabi, Duke University
  • Robert Brown, Syneos Health

Panel Discussion (15-20 min)

2:30 p.m.    Break

2:40 p.m.    Session IV: Considerations for Improving Future Trial Designs
  Moderator: Mark McClellan

Objective: Discuss, review, and provide feedback on proposed strategies for future trial designs, and examine any outstanding issues that may inhibit implementation.

Presentation: Sample Size Calculation, Timing of Analysis, Interims, Follow-up
  • Keaven Anderson, Merck
Panelists:
- Kun He, U.S. Food and Drug Administration
- Mary Redman, Fred Hutch Cancer Center
- Elad Sharon, NCI
- Cyrus Mehta, Cytel

Panel Discussion (25-30 min)

3:45 p.m.  Session V: Implications for the Broader Stakeholder Community
Moderators: Rajeshwari Sridhara and Mark McClellan

Objective: Reflect on the day’s discussion, revisit any statistical concerns that emerged, discuss key implications of the proposed statistical changes for a variety of stakeholders, identify any areas for future evaluation and research, and discuss a path forward for a new statistical paradigm.

Panelists:
- Samuel Wagner, Bristol-Myers Squib
- Tai-Tsang Chen, Bristol-Myers Squib
- Marc Theoret, U.S. Food and Drug Administration
- Francesco Pignatti, European Medicines Agency
- Andrea Ferris, Lungevity

Panel Discussion (10 min)
Audience Q&A (10 min)

4:30 p.m.  Closing Remarks
Mark McClellan, Duke-Margolis Center for Health Policy

Funding for this workshop was made possible in part by a cooperative agreement from the U.S. Food and Drug Administration Center for Drug Evaluation and Research. The views expressed in written workshop materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsements by the U.S. Government.