Duke | Robert J. Margolis, MD Center for Health Policy

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

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