Statistical Issues Think Tank II

19 November, 2014

Bethesda North Marriott Hotel & Conference Center
5701 Marinelli Rd, Bethesda, MD 20852
Bethesda, Maryland 20852 USA

Meeting Goal: To provide an update on the current status of statistical methodologies for the design and analysis of antibacterial drugs, to discuss ongoing challenges in the development and adoption of innovative methods, and to generate strategies to propel antibacterial drug development forward.

Meeting Agenda
Wednesday November 19, 2014
9:00 AM-4:00 PM

8:00-9:00 AM **Registration/ Breakfast**

9:00-9:20 AM **Welcome and Opening Remarks: Lisa LaVange, PhD**
Director, Office of Biostatistics, OTS/CDER/FDA
Session goal: Understand the objectives for this meeting and summarize the discussion and advances since the first CTTI statistical issues think tank in August 2012.

Session 1 **Current status of drug development and ongoing challenges**
9:20-10:20 AM **Session Chair: Dionne Price, PhD**
Director, Division of Biometrics IV, Office of Biostatistics, OTS/CDER/FDA

Session goal: To understand the status of antibacterial drug development and the ongoing challenges in the design and analysis of antibacterial drug products

Presentations

Joseph Toerner, MD, MPH (10 min)
Office of Antimicrobial Products/CDER/FDA
Brief Summary of Regulatory Standards and Guidances

Dan Rubin, PhD (15 min)
Mathematical Statistician, Office of Biostatistics, OTS/CDER/FDA
Summary of the Unmet Need Guidance and Statistical Challenges

Seong Jang, PhD (15 min)
Reviewer, Office of Clinical Pharmacology, OTS/CDER/FDA
Application of Pharmacokinetics/Pharmacodynamics in New Anti-Infective Drug Development: Current Challenges and Future Perspectives

Aaron Dane (15 min)
Biometrics & Information Science, Infection TA Head, AstraZeneca
Statistical Considerations for a Tiered Approach to Antibiotic Drug Development

Questions and Answers on presentations

10:20-10:30 AM **Break**

10:30-12:00 PM **Moderated Discussion**

Discussion questions:

1. What concerns exist regarding incorporating preclinical evidence into the analysis of confirmatory trial results? What analyses techniques might be appropriate for incorporation of preclinical data?

2. Is there a role for single arm trials in evaluating anti-infective drugs? If not, what are viable alternatives to single arm trials? Discuss possible strategies aimed at leveraging external data in development programs in potentially limited populations.

3. Discuss considerations involved in using a master clinical trial protocol to evaluate new anti-infective drugs.

12:00-1:00 PM **Lunch**

Session 2 **Current research and additional opportunities for the future**
1:00-2:15 PM

Session Chair: Dionne Price, PhD

Session goal: To review current methodological research and to generate strategic research ideas for the future

Presentations

Erica Brittain, PhD (15 min)
Deputy Branch Chief, Biostatistics Research Branch, NIAID/NIH I
Discordant MIC Analysis: Testing for Superiority Within a Non-inferiority Trial

Thamban Valappil, PhD
Mathematical Statistician, Division of Biometrics IV, Office of Biostatistics, OTS/CDER/FDA
and
Mohamed Huque, PhD (15 min)
Senior Stat AdvisorOffice of Biostatistics, OTS, CDER, FDA
Hierarchical Nested Trial Design (HNTD) for New Antibacterial Drugs in Patients with Emerging Bacterial Resistance

Scott Evans, Ph.D, MS. (15 min)
Senior Research Scientist, Harvard University
RADAR

Margaret Gamalo-Siebers, PhD (25 min)
FDA
Proposals for the Analysis of Antibacterial Drug Trials

Questions and answers on presentations

2:15-2:30 PM **Break**

2:30-3:45 PM **Moderated Discussion**

Discussion topics:

1. Discuss the advantages and disadvantages of Bayesian approaches to design and analysis, and how a prior distribution would be chosen to analyze a confirmatory trial of an anti-infective drug. What would be some of the challenges and how might they be overcome?

2. Discuss evaluation of drugs posited to have similar efficacy profile to existing drugs but a superior safety profile. When can efficacy and toxicity measures be combined into a composite or ordinal endpoint to test for superiority, and when should a non-inferiority trial be conducted?

3. What are potential analysis strategies for a single trial enrolling subjects with infections at different body sites?

4. What additional opportunities exist for statistical innovation in anti-infective trials?

3:45-4:00 PM **Next steps and adjourn**