Duke | MARGOLIS CENTER *for* Health Policy

Evaluating the Pressor Effects of Drugs & Ambulatory Blood Pressure Monitoring Studies

Conference Center at 1777 F Street NW • Washington, DC
February 4th, 2019

The Duke-Margolis Center for Health Policy, in collaboration with the U.S. Food & Drug Administration (FDA), is convening experts in blood pressure research and ambulatory blood pressure monitoring measurement from the regulatory, academic, and drug development communities to discuss the premarketing assessment of a drug's effect on blood pressure. Following a recently published draft guidance, "Assessment of Pressor Effects of Drugs", FDA is specifically interested in soliciting feedback regarding four high-priority topics:

1. Understanding the temporal relationship between changes in blood pressure and changes in risk.
2. Interpreting results of the PRECISION study and its relevance to the pressor guidance.
3. Is there a BP increase of concern applicable across development programs or should each development program take its risk tolerance into consideration? What is the role of the patient population?
4. The necessity of using placebo groups as controls in ABPM studies.

8:30 am **Morning Refreshments**

9:00 am **Welcome and Overview**

- Mark McClellan, Duke-Margolis Center for Health Policy

9:05 am **Opening Remarks**

- Ellis Unger, U.S. Food & Drug Administration

9:15 am **FDA Perspective on the Evaluation of Blood Pressure in Drug Development**

- Norman Stockbridge, U.S. Food & Drug Administration

Part I: Issues FDA Raised in the Draft Guidance

9:30 am **Session 1A—Understanding the Temporal Relationship Between Changes in Blood Pressure and Changes in Risk**
Moderator: Mark McClellan

Objective: Discussion will consider the potential lag between changes in blood pressure and corresponding risk and whether risk is related to the integration of changes in blood pressure over time. Interventions associated with changes in blood pressure and associated with increased risk will be discussed.

Presentation:

- Michael Weber, State University of New York

Reactants and Panel Discussion:

- William Cushman, Department of Veterans Affairs
- Patrick Twomey, Genentech, Inc.
- Hector Ventura, Ochsner Health System

10:20 am **Break**

10:30 am **Session 1B—Interpreting Results of the PRECISION Study**
Moderator: Gregory Daniel, Duke-Margolis Center for Health Policy

Objective: Discussion will consider the PRECISION study and its relevance to the pressor draft guidance. Is PRECISION's nested blood pressure study an appropriate use case for the purpose of FDA guidance?

Presentation:

- Jeffrey Borer, SUNY Downstate

Reactants and Panel Discussion:

- Robert Blankfield, Case Western Reserve University
- William White, University of Connecticut

11:20 am **Session 1C—Pressor Risk & Tolerance Among Diverse Development Programs**
Moderator: Gregory Daniel

Objective: Is there a blood pressure increase of concern applicable across development programs or should each development program take its risk tolerance into consideration?

Presentation:

- George Bakris, The University of Chicago

Reactants and Panel Discussion:

- Vasilios Papademetriou, Department of Veterans Affairs
- G. Brandon Atkins, Merck Research Laboratories
- Philip Sager, Stanford University
- Mitchell Krucoff, Duke University

12:10 pm **Lunch**

1:00 pm **Session 1D—Placebo Control Groups in ABPM Studies**
Moderator: Gregory Daniel

Objective: Consider the potential need for placebo control groups in ABPM studies and how placebo groups affect study reproducibility and the interpretation of diurnal patterns of blood pressure.

Presentation:

- Tzu-Yun McDowell, U.S. Food & Drug Administration

Reactants and Panel Discussion:

- Raymond R. Townsend, University of Pennsylvania
- Milton Pressler, Pfizer Inc.
- Frank Rockhold, Duke University
- Norman Stockbridge, U.S. Food & Drug Administration

Part II: ABPM Study Design, Efficiency, and Appropriateness

1:50 pm **Session 2: Design of Efficient Ambulatory Blood Pressure Monitoring Studies**
Moderator: Mark McClellan

Objective: Discussion will consider metrics for evaluating blood pressure; pattern of missing data and its impact on study results; and influence of study size on power to exclude small increases in blood pressure.

Presentation:

- Lars Johannesen, U.S. Food & Drug Administration

Reactants and Panel Discussion:

- Charles Benson, Eli Lilly and Company
- Frank Rockhold, Duke University
- Norman Stockbridge, U.S. Food & Drug Administration

2:40 pm **Break**

2:50 pm **Session 3: Methodological Options & Outstanding Issues in Pressor Study Design for Reliable Evidence Development**
Moderator: Mark McClellan

Objective: This session will highlight high-priority methodological concerns and outstanding issues in the realm of pressor study design. Short presentations will define an outstanding issue and propose potential approaches, and the panel will then react to each presentation.

Panelists:

- Mitchell Krucoff, Duke University
- Philip Sager, Stanford University
- Michael Weber, State University of New York
- William White, University of Connecticut [Tentative]

Presentation 1: Is ABPM the Right Blood Pressure Metric for Assessing Risk

- Daichi Shimbo, Columbia University

Presentation 2: Clinical Pharmacology Considerations

- Rajnikanth Madabushi, U.S. Food & Drug Administration

Part III: Reflection & Open Audience Feedback

3:40 pm **Session 4: Open Audience Feedback**
Moderator: Mark McClellan

The audience is invited to share remarks and outstanding questions regarding the day's discussions and FDA's draft guidance "Assessment of Pressor Effects of Drugs".

4:30 pm **Closing Remarks and Adjournment**

- Douglas Throckmorton, U.S. Food & Drug Administration

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