CARDIAC SAFETY RESEARCH CONSORTIUM

CSRC Think Tank: Driving Efficiencies in Clinical Trials through the use of Cardiac Biomarkers

FDA White Oak Campus
10903 New Hampshire Avenue
Silver Spring, MD

January 22, 2020

8:00am – 8:15am Introduction and Purpose of Think Tank
Jonathan Seltzer, MD FACC (WCG-ACI Clinical, CSRC Executive Director)
Introduction to CSRC

- Anatomy of a Think Tank

8:15am – 9:45am Session I: Advantages and disadvantages in the use of serum biomarkers during clinical development
Moderator: Jonathan Seltzer, MD FACC (WCG-ACI Clinical, CSRC Executive Director)

- Biomarkers used to alter clinical development in AF and CTEP inhibition **Thomas Povsic, MD, PhD** (Duke)(10 min)
- Biomarkers used for evaluation of CHF patients **Ileana Pina, MD** (FDA)(10 min)
- When surrogates fail intermediate vs. surrogate endpoints **Ellis Unger, MD** (FDA)(10 min)
- Cardiac safety biomarkers in early drug discovery: bridging nonclinical and clinical studies **Gary Gintant, PhD** (Abbvie)(10 min)
- Variability in circulating cardiac biomarkers levels by sex and ethnicity - to factor or not to factor? **Allan Jaffe, MD** (Mayo Clinic)(10 min)

Lead Discussant: James Januzzi, MD (Massachusetts General Hospital)
Discussion: What are the major issues in use of serum biomarkers for clinical trials? When should they be encouraged? When discouraged?

9:45am – 10:00am BREAK

10:00am – 11:50am Session II: Current use of serum biomarkers in clinical trials
Moderator: James Januzzi, MD *(Massachusetts General Hospital)*

- **Serum biomarkers of cardiomyocyte toxicity/ischemia**
  - Preclinical/In Vitro/Translational considerations **John Canty, MD** (University at Buffalo)(10 min)
  - Use as a peri-procedural marker for PCI studies **Thomas Povsic, MD, PhD** (Duke)(10 min)
- **Serum biomarkers of myocardial dysfunction**
  - Preclinical/Translational considerations **Christopher deFilippi, MD** (INOVA)(10 min)
  - Use in efficacy studies and safety studies **Maribel Salas, MD, PhD, MS** (Daiichi Sankyo)(10 min)
  - Use in post-market patient monitoring **Victor Shi, MD** (Novartis)(10 min)

Lead Discussant: Jacob Udell, MD (Women's College Hospital)
Discussion: When can we use (or not use) these biomarkers as validated endpoints, inclusion/exclusion criteria, stopping rules? When do we need (or not need) to have these as fully validated?

11:50am – 12:30pm LUNCH BREAK

12:30pm – 2:00pm Session III: Novel biomarkers in development
Moderator: Leslie Lipka, MD, PhD *(Merck)*

- Pre-clinical development issues **Tanja Zabka, DVM** (Roche)(10 min)
- Use of preclinical biomarkers in noncardiac drug development **Emily Kaushik, PhD** (Takeda)(10 min)

Overview of new markers—are they needed, how can they be used, pitfalls?

- Multimarker panels/proteomics **Rhonda Rhyne, PhD** (Prevencio)(10 min)
- Epigenetic markers **Saumya Das, MD, PhD** (Massachusetts General)(10 min)

Lead Discussant: Allan Jaffe, MD (Mayo Clinic)
Discussion: What will be the impact of these tools on clinical trials? What criteria should be used to demonstrate a need for new biomarkers? How can clinical utility be evaluated?

2:00pm – 2:15pm BREAK

2:15pm – 3:45pm Session IV: Regulatory considerations for the use of serum biomarkers in clinical development
Moderator: James Januzzi, MD *(Massachusetts General Hospital)*

- Biomarker Qualification Program **Christopher Leptak, MD, PhD** (FDA)(10 min)
  - Dose selections, targets, patient selection, toxicity, clinical trial design, endpoint establishment
- Characteristics of studies that should collect biomarkers **David Gutstein, MD** (Janssen)(10 min)
- Adaptive study designs based on response across baseline CV biomarkers **Cyrus Mehta, PhD** (Cytel Statistical Software) (10 min)
- Safety and efficacy demonstrated through biomarkers—Review Issues **Norman Stockbridge, MD, PhD** (FDA)(10 min)

Lead Discussant: James Januzzi, MD (Massachusetts General Hospital)
Discussion: What are the realistic options to use biomarkers to improve clinical development? Short term? Long term? How is clinical benefit demonstrated to the regulatory agencies? What specific proposals can we make to encourage proper BM use and development?

Closing Remarks