CARDIAC SAFETY RESEARCH CONSORTIUM

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

American College of Cardiology
Heart House
2400 N Street, NW
Washington, DC

April 5th, 2019

8:00am – 8:15am Introduction and Purpose of Think Tank
TBD

- Introduction to CSRC
- Anatomy of a Think Tank

8:15am – 9:45am Session I: Advantage and Disadvantages in the use of serum biomarkers during clinical development
Moderator: TBD

- 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** ( )(10 min)
- When surrogates fail **Jim Januzzi, MD** (Duke)(10 min)
- Cardiac Safety Biomarkers in Early Drug Discovery: Hope or Hype **Gary Gintant, PhD** (Abbvie)(10 min)
- Variability in circulating cardiac biomarkers levels by sex and ethnicity - to factor or not to factor? (10 min)

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: TBD

- **Serum Biomarkers of cardiomyocyte toxicity/ischemia**
  - Preclinical/In Vitro/Translational considerations **John Canty, MD** (University at Buffalo) (10 min)
  - Use in efficacy and safety studies **Marvin Konstam, MD** (Tufts) (10 min)
  - Use as a peri-procedural marker for PCI studies **Donald Cutlip, MD** (Harvard)(10 min)
- **Serum Biomarkers of myocardial dysfunction**
  - Preclinical/Translational considerations **Christopher deFilippi, MD** (INOVA) (10 min)
  - Use in efficacy studies and safety studies **Curtis Rambaran, MD** and **Maribel Salas, MD, PhD, MS** (Daiichi Sankyo)(10 min)
  - Use in post-market patient monitoring **Marty Lefkowitz, MD** (Novartis) (10 min)

Discussion: When can we use (or not) these biomarkers as validated endpoints, inclusion/exclusion criteria, stopping rules? When do we need (or not) to have these as fully validated?

11:50am – 12:30 LUNCH BREAK

12:30pm – 2:00pm Session III: Novel biomarkers in development
Moderator: TBD

- Pre-clinical Development issues **Tanja Zabka, DVM** (Roche)(10 min)
- Use of serum biomarkers in other therapeutic areas (10 min)

- **Overview of new markers—are they needed, how can they be used, pitfalls**
  - Metabolomic BM development **Mark Benson, MD, PhD** (Harvard) (10 min)
  - Multimarker panels/proteomics **Rhonda Rhyne, MBA** (Prevencio)(10 min)
  - Epigenetic markers **Saumya Das, MD, PhD** (Massachusetts General)(10 min)

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: TBD

- Biomarker Qualification Program (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 (10 min)
- Safety and Efficacy demonstrated through BM—Review Issues **Norman Stockbridge, MD, PhD** (US FDA)(10 min)

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