CARDIAC SAFETY RESEARCH CONSORTIUM

CSRC Think Tank:

NOAC Use in the Pediatric Population: Defining the Path Forward
ACC Heart House
Washington, DC

Chair for each session in red font.

7:45 – 8:00 AM
CSRC Welcome (Jonathan or Diptee)
Keynote speech, including Goals of the Think Tank: Ann Farrell, MD (FDA)

8:00 - 8:45AM Session I: Current Landscape of use of Anti-Coagulation in the Pediatric Population. Focus on Defining Unmet Medical Need

What are the current indications for which anti-coagulation is used? Treatment vs thrombo-prophylaxis? Does use differ in different age-subgroups? Where are areas of unmet medical need? What are the current industry and academic barriers for pediatric research?

- Courtney Thornburg, MD (Rady Children's Hospital, San Diego)
- Thomas Diacovo, MD (University of Pittsburgh)
- Current industry and academic barriers for pediatric research Diptee Gajjar, PharmD, PhD (Bristol-Myers Squibb)
- Patricia Massicotte, MD (University of Alberta)
- Christoph Hornik, MD (Duke)
- Shetarra Walker, MD (FDA)

Discussion: What are the major issues and needs in the development of pediatric cardiac indications for anticoagulation?

8:45 - 9:45 Session II: Introduction to Sessions III and IV: Regulatory Considerations in Using Adult Data for Pediatric Indications

- Shetarra Walker, MD (FDA)
- Mona Khurana, MD (FDA) Pediatric drug development – US Perspective
- Dirk Mentzer, MD (EMA/UK) – Pediatric drug development - European/UK Perspective
- Sudharshan Hariharan, PhD (FDA) Clinical Pharmacology Perspective on Biomarkers and Extrapolation
- Jacqueline Corrigan-Curay, JD, MD (FDA) RWE expert (panelist)

9:45am-10:00am Break

10:00 - 11:45am Session III: Thromboprophylaxis and Thrombosis treatment: need to develop NOAC for these 2 indications?

Define unmet medical need for thromboprophylaxis.
Define unmet medical need for thrombosis treatment
Define special characteristics of children for both indications
Define children age group for both indications
Are there any similarities and differences in coagulation cascade between adult and pediatric population and accordingly, the condition of thrombus development?

- Defining "unmet need" from Sponsor Perspective – Charlotte Jones-Burton, MD (Bristol-Myers Squibb)
- Sudharshan Hariharan, PhD (FDA) (panelist)
- Lori Ehrlich, MD (FDA) (panelist)

Discussion: Are currently available agents sufficient for thrombosis treatment? If not, what pediatric indication development is critical using NOACs?

11:45pm-12:15pm Lunch

12:15 - 2:00pm Session IV: Define study population and relevant endpoints for NOAC pediatric development

What are the patient characteristics (e.g., age and other demographics, underlying diagnoses and other comorbidities, more 'social' needs) that are of relevance for NOAC development for pediatric use?
What are the appropriate trial efficacy and safety endpoints? Is there a correlation between the adult and pediatric endpoint and/or biomarkers?

- Christoph Hornik, MD (Duke)
- James Revkin, MD (Pfizer)
- Mark Rothmann, PhD (FDA) Stats, panelist]
- Robert "Skip" Nelson, MD, PhD (Johnson and Johnson)
- Nicholas Richardson, MD (FDA) (panelist)

Discussion: Define pediatric population for NOAC research. Which pediatric anticoagulation outcome measures are clinically maningful for approval? Which to demonstrate long term benefit?

2:00 - 2:15 Break

CARDIAC SAFETY RESEARCH CONSORTIUM

CSRC Think Tank:

NOAC Use in the Pediatric Population: Defining the Path Forward
ACC Heart House
Washington, DC

2:15 - 3:15pm Session V: Regulatory requirements for trial design: A Practical Example

What areas of study design for pediatric studies need to be addressed in order to ensure that trials meet regulatory standards? What are the gaps in knowledge in children for these indications? What data need to be generated from pediatric clinical trials? What trials require a written request? Which meet PREA requirements? What trials require PIP? Is a trial needed to match each adult indication? How is long-term benefit demonstrated?

ROUNDTABLE DISCUSSION

- Lynne Yao, MD (FDA)
- Ann Farrell, MD (FDA)
- Lori Ehrlich, MD (FDA)
- Norman Stockbridge, MD (FDA)
- Dirk Mentzer, MD (EMA/UK)
- Diptee Gajjar PharmD, PhD (Bristol-Myers Squibb)
- Peter Aprile (Pfizer)
- Christoph Hornik, MD (Duke)
- Thomas Diacovo, MD (University of Pittsburgh)

Discussion: What type of trials are needed to address the knowledge gap? Do different pediatric age groups require different trial designs? Different indications? What are the regulatory pathways? How can populations be defined? How can we overcome trial enrollment challenges especially for young children (<6 years)?

3:15 - 3:45pm Session VI: Practical challenges for conducting pediatric clinical trial

How can a trial be designed to be successful for enrollment and getting relevant information to support regulatory approval? Role of patient network. Operational barriers? Consent issues? How to increase participation/enrollment of patients in pediatric studies, especially very young patients including neonates by overcoming the barriers. design for pediatric?

ROUNDTABLE DISCUSSION

- Daniel Keene, MD (Health Canada)
- FDA: Lynne Yao, MD, Jacqueline Corrigan-Curay, JD, MD, Donna Snyder, MD, Robert Temple, MD, Norman Stockbridge, MD, Nicholas Richardson, MD
- Dirk Mentzer, MD (EMA/UK)
- Christoph Hornik, MD (Duke)
- Janette T. Reyes, NP (University of Toronto)
- Angela Bates MD (University of Alberta)
- Sitara de Gagne, Child and Family Centered Care & Patient Advocacy.
- Liza (Miriam) Pina, MD(Johnson and Johnson)

3:45-4:15 Session VII: Summary and Next Steps

- Diptee Gajjar, PharmD, PhD (Bristol-Myers Squibb)
- Jonathan Seltzer, ACI Clinical