



Heart Failure  
Collaboratory

Electronic & Digital Health  
Regulatory Policy & Implementation Science  
Representative Populations  
Research Networks & Societies

**Relevance of Non-Primary Endpoints in Clinical Trials**  
***Case Discussion of Heart Failure Outcomes in CVOTs in T2DM***  
**FDA Campus – March 6<sup>th</sup>, 2019**

- 8:30am – 8:40am **Welcome, Norman Stockbridge, MD, PhD and Javed Butler, MD**
- 8:40am – 8:50am **Welcome - HF Collaboratory, Mona Fiuzat, PharmD**
- 8:50am – 9:00am ***SGLT2i CVOTs and HF, Darren McGuire, MD***  
Aim:  
  1. Review briefly how and why primary endpoints were chosen for CVOTs
  2. Why HF was a secondary endpoint
  3. Changes in DECLARE
  4. Quick overview of MACE outcomes
- 9:00am – 9:10am ***HF outcomes in SGLT2i CVOTs, Marc Sabatine, MD***  
Aim:  
  1. Review HF outcomes in SGLT2i CVOTs (not RWE)
  2. Stratified by
  3. Primary prevention vs. secondary
  4. Baseline HF vs. no HF
- 9:10am – 9:25am ***HF data in CVOTs - What are the issues? Javed Butler, MD***  
Aim:  
  1. Dealing with prevention vs. treatment data in studies not designed or stratified accordingly
  2. Dealing with secondary endpoint issue, in light of
  3. Historical concern
  4. We will have HF and CKD data but will not have HF prevention in same population
  5. Are the results only positive due to undiagnosed HF in the trials?
  6. HHF as an endpoint
  7. Surrogate for new onset HF?
  8. Adjudication issues in CVOT
  9. Standalone endpoint without mortality or neutral mortality
- 9:25am – 9:40am ***Issue 1: Prevention vs. Treatment of HF, Gregg Fonarow, MD***  
Aim:  
  1. Importance of HF prevention
  2. “Phenotyping” for “HF” in prevention trial vs. treatment trial
  3. Interpretation of ‘prevention’ data from SGLT2i
  4. Interpretation of ‘treatment’ data from SGLT2i
  5. Does ‘primary’ and ‘secondary’ prevention categorization for MACE apply to HF prevention?
- 9:40am – 10:10am **Discussion, led by JoAnn Lindenfeld, MD**

<b>10:10am – 10:25am</b>	<b>BREAK</b>
10:25am – 10:40am	<p><b>Issue 2: <i>Undiagnosed Heart Failure in CVOT?</i> Milton Packer, MD</b></p> <p>Aim:</p> <ol style="list-style-type: none"> <li>1. What are the chances (clinically, statistically or otherwise) that all HF benefit is limited to ‘undiagnosed’ HF in SGLT2i CVOTs?</li> <li>2. Chances of undiagnosed vs. undocumented but known</li> <li>3. If truly undiagnosed, does it matter for prevention?</li> </ol>
10:40am – 11:10am	<b>Discussion, led by Adrian Hernandez, MD</b>
11:10am – 11:25am	<p><b>Issue 3: <i>HF hospitalization as a standalone endpoint: Pros and Con</i>, John Teerlink, MD</b></p> <p>Aim:</p> <ol style="list-style-type: none"> <li>1. Surrogate for new onset HF?</li> <li>2. Adjudication issues in CVOT</li> <li>3. Standalone endpoint without mortality or neutral mortality</li> </ol>
11:25am – 11:55pm	<b>Discussion, led by Peter Carson, MD</b>
11:55am – 12:25pm	<b>LUNCH</b>
12:25pm – 12:40pm	<p><b>Issue 4: <i>Real World Evidence (CVD REAL/EMPRISE) - Does it help?</i> Mikhail Kosiborod, MD</b></p> <p>Aim:</p> <ol style="list-style-type: none"> <li>1. Review CVD REAL, CVD REAL AP, EMPRISE etc. for HF outcomes</li> <li>2. Review data stratified by baseline HF status and by primary vs. secondary prevention status when possible</li> </ol>
12:40pm – 1:10pm	<b>Discussion, led by Mariell Jessup, MD</b>
1:10pm – 1:25pm	<p><b>Issue 5: <i>Moving forward: Secondary analyses, biobank samples, statistical analytic tools, ongoing trials?</i> James Januzzi, MD</b></p> <p>Aim:</p> <ol style="list-style-type: none"> <li>1. Will bio-banks and biomarker analysis help us?</li> <li>2. If NTproBNP is high in ‘prevention’ HF cohort – is that treatment or prevention?</li> <li>3. Will we ever have only HF prevention trials in this space</li> <li>4. Logistics</li> <li>5. Costs</li> <li>6. Stats or any other way to address HF prevention issues</li> </ol>
1:25pm – 1:55pm	<b>Discussion, led by Mona Fiazat, PharmD</b>
1:55pm – 2:10pm	<p><b>Issue 6: <i>Primary outcome vs. secondary outcome</i></b></p> <p><b><i>Statistical Perspective</i>, Sanjay Kaul (10 min)</b></p> <p><b><i>Clinical Perspective</i>, Javed Butler, MD (10 min)</b></p>
2:10pm – 2:40pm	<b>Discussion, led by Christopher O’Connor, MD and Kevin Anstrom, PhD</b>
2:40pm – 2:50pm	<b>Next steps, Javed Butler, MD</b>
2:50pm – 3:00pm	<b>Concluding Remarks - Norman Stockbridge, MD, PhD and Christopher O’Connor, MD</b>

## **Participant List**

### **Kevin Anstrom, PhD**

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