SGLT2 Inhibitors and Major Adverse Cardiovascular Events in Patients with Diabetes at High Risk For Atherosclerotic Cardiovascular Disease, Heart Failure or Chronic Kidney Disease: A SMART-C Collaborative Meta-Analysis

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BACKGROUND

• SGLT2i have been clearly demonstrated to reduce the risk of adverse HF and kidney outcomes.
• Treatment effects of SGLT2i on MACE have been more modest, with differences observed across trials.
• Uncertainty exists regarding the effect of SGLT2i on MACE, particularly the individual MACE components, across several important patient subgroups.

METHODS

• Collaborative meta-analysis of the SGLT2 Inhibitor Meta-Analysis Cardio-Renal Trialists Consortium (SMART-C) – includes all large, phase 3, pbo-controlled clinical outcome RCTs of SGLT2i across three primary pt populations:
  1. DM at high risk for ASCVD: EMPAREG Outcome, CANVAS, DECLARE-TIMI 58, VERTIS-CV
  2. Heart failure: DAPA-HF, EMPEROR-Reduced, EMPEROR-Preserved, DELIVER
  3. Chronic kidney disease: CREDENCE, DAPA-CKD, EMPA-KIDNEY
• Trial-level summary data, overall and by subgroup, provided by SMART-C investigators
• Outcomes of interest = MACE composite of CV death, MI and stroke, individual MACE components (inclusive of fatal & non-fatal events), death subtypes
• Trial effect estimates were meta-analyzed in each of the 3 primary pt populations using fixed and random effects
• Effect modification across subgroups was examined using RE meta-regression

RESULTS

- Overall, 80% had DM, 36% had HF, 37% had eGFR <60
- SGLT2i consistently reduce the risk of MACE across a broad range of patient populations (irrespective of ASCVD, DM, kidney function).
- Driven primarily by reduction in HF death & SCD, without clear effect on MI or stroke.
- These data may help inform the selection of SGLT2 therapies across the spectrum of cardiovascular-kidney-metabolic disease.

DISCLOSURE OF FACULTY RELATIONSHIPS: