**Sotagliflozin, a dual SGLT1 and SGLT2 inhibitor, reduces the risk of cardiovascular and renal disease as assessed by Steno Risk Engines in adults with type 1 diabetes**

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**Background and aims:** Sotagliflozin (SOTA) as an adjunct to insulin therapy improves glycemic control, without an increased risk of hypoglycaemia, reduces body weight and blood pressure (BP), and increases time in range in adults with type 1 diabetes (T1D). Treatment with SOTA is associated with an increased risk of diabetic ketoacidosis (DKA). SOTA demonstrated CV and renal benefits in high-risk adults with type 2 diabetes. The cardiorenal benefits along with the cardiometabolic effects may collectively outweigh the risk of DKA when evaluating SOTA for adults with T1D. The present analysis estimated the risk of CVD and end-stage kidney disease (ESKD) in adults with T1D treated with SOTA.
**Materials and methods:** Patient-level data were used from the three Phase 3 inTandem trials evaluating 2977 adults with T1D randomized to once-daily placebo, SOTA 200 mg, or SOTA 400 mg for 24 weeks. Analyses focused on 3 cohorts (1. SOTA 200 mg; 2. SOTA 400 mg; 3. SOTA pooled). A subgroup analysis was performed in patients with a BMI ≥27 kg/m$^2$. For each patient, the cumulative risks of developing CVD and ESKD were estimated using the Steno T1 Risk Engines, which are validated prediction models for predicting 5- and 10-year risk of CVD and 5-year risk of ESKD. For CVD risk estimation, only patients without previous CVD (98% of overall cohort) at baseline were included. Baseline values for age and duration of diabetes were used in the model at Week 24. Missing albuminuria values were set to normal. Smoking and exercise history were not collected, and these variables were set to No. The estimated risk was calculated at baseline and Week 24 in both treatment groups. If a participant did not have a Week 24 assessment, a baseline observation carried forward approach was used. The difference in least-square mean percent change in estimated risk from baseline (95% CI and p-value) was compared between groups using a mixed model with percent change from baseline as dependent and including the treatment group as fixed effect, and the baseline value as covariate.
**Results:** SOTA significantly reduced 5- and 10-year CVD risk scores by approximately 4 to 7% compared to placebo at 24 weeks (Table). ESKD risk score was numerically reduced with SOTA 200 mg and significantly reduced with SOTA 400 mg relative to placebo. Similar results were observed with SOTA pooled and in patients with baseline BMI ≥27 kg/m$^2$.
**Conclusion:** Using the Steno T1 Risk Engines, the estimated risk of CVD and ESKD was significantly reduced with SOTA compared to placebo in adults with T1D. This analysis provides additional clinical results that may positively enhance the benefit/risk assessment of SOTA use in T1D.

Table. Effect of sotagliflozin on CVD and ESKD Risk Score using Steno T1 Risk Engines

| | Sotagliflozin 200 mg N = 524 | | Placebo N = 526 | | Difference in LSM % change (95% CI) |
|---|---|---|---|---|---|
| | BL mean (SD) | Mean % change from baseline (SD) | BL mean (SD) | Mean % change from baseline (SD) | |
| 5-yr CVD risk | 7.5% (6.6) | -3.5 (18.5) | 6.8% (6.4) | 1.5 (17.3) | -4.6 (-6.8, -2.5)* |
| 10-yr CVD risk | 14.0% (11.4) | -3.4 (17.7) | 12.7% (11.0) | 1.4 (16.6) | -4.4 (-6.5, -2.4)* |
| 5-yr ESKD risk | 0.9% (0.9) | 6.2 (44.5) | 0.9% (0.9) | 11.4 (66.7) | -5.2 (-12.1, 1.7) |
| | Sotagliflozin 400 mg N = 1225 | | Placebo N = 1231 | | |
| 5-yr CVD risk | 7.6% (7.2) | -6.3 (18.0) | 7.0% (6.7) | 1.0 (20.2) | -7.1 (-8.6, -5.5)* |
| 10-yr CVD risk | 14.1% (12.0) | -6.0 (17.3) | 13.1% (11.5) | 0.9 (19.4) | -6.8 (-8.2, -5.3)* |
| 5-yr ESKD risk | 0.9% (0.9) | 5.0 (42.7) | 1.0% (1.2) | 12.8 (62.8) | -7.8 (-12.1, -3.6)* |

*P ≤ 0.003; BL = baseline; SD = standard deviation; LSM = least square means

*Disclosure:* **E.B. Stougaard:** None.