The Dual SGLT1 and SGLT2 Inhibitor, Sotagliflozin, Significantly Reduces Hospitalization for Heart Failure, Urgent Heart Failure Visit, and CV Mortality in Patients with Type 2 Diabetes, Chronic Kidney Disease, and a History of Heart Failure Regardless of Left Ventricular Ejection Fraction: Subgroup Analysis from the SCORED Trial

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INTRODUCTION

- Patients with type 2 diabetes (T2DM) and chronic kidney disease (CKD) have a high risk for heart failure (HF), ischemic events, and hospitalization.
- Patients with a history of HF have an increased risk of hospitalization and mortality, highlighting an unmet need that improves clinical outcomes and reduces the economic burden of hospitalization for heart failure (HHF).
- The dual SGLT1 and SGLT2 Inhibitor, sotagliflozin, significantly reduced the risk of cardiovascular (CV) death, HHF, and urgent visit for heart failure (UVHF) in patients hospitalized with worsening HF (SOLOIST-WHF) and in patients with T2DM, CKD, and CV risk factors (SCORED).[1,2]
- The present post hoc analysis of the SCORED trial was undertaken to evaluate the effects of sotagliflozin on the primary endpoint (composite of CV death, HHF, and UVHF) and its individual components in a subgroup of patients with a reported history of HF. Secondly, this analysis will examine the outcomes in this subgroup of patients across a range of ejection fraction.

METHODS

- SCORED (Effect of Sotagliflozin on Cardiovascular and Renal Events in Patients with Type 2 Diabetes and Moderate Renal Impairment Who Are at Cardiovascular Risk) was a randomized, double-blind study in 10,584 patients with T2D (HbA1c ≥7%), CKD (eGFR 25-60 mL/min/1.73 m^2 regardless of UACR), and increased CV risk[1]
- Eligible patients were randomized to sotagliflozin (200 mg/d up-titrated to 400 mg/d at the discretion of the investigator) vs. placebo (1:1) and followed for a median of 16 months
- Primary endpoint was total occurrences of CV death and worsening HF (HHF and UVHF)

Present Analysis:

- Identify patients with a reported history of HF collected in Medical History at baseline (N = 3281)
- Determine event rates for the primary endpoint in patients with HF with LVEF < 50% and LVEF ≥ 50%

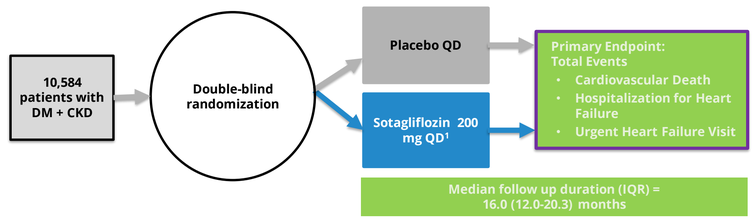
PATIENT DEMOGRAPHICS

Table 1. SCORED Baseline Characteristics in Patients with a Reported History of HF by LVEF

Baseline Characteristics in Patients with Heart Failure	Sotagliflozin N = 795 LVEF < 50%	Placebo N = 819 LVEF < 50%	Sotagliflozin N = 843 LVEF ≥ 50%	Placebo N = 824 LVEF ≥ 50%
Age, years; mean (SD)	69.0 (8.3)	68.1 (8.4)	69.4 (8.3)	69.6 (8.4)
Female sex; N (%)	252 (31.7)	253 (30.9)	458 (54.3)	451 (54.7)
HbA1c, %; mean (SD)	8.7 (1.5)	8.7 (1.4)	8.7 (1.4)	8.8 (1.4)
BMI, kg/m^2; mean (SD)	31.4 (5.9)	31.7 (6.3)	34.2 (6.5)	34.3 (6.4)
UACR, mg/g categories; N (%)				
< 30 (normal)	279 (35.1)	280 (34.2)	307 (36.5)	320 (38.8)
≥ 30 to 300 (microalbuminuria)	315 (39.6)	304 (37.1)	305 (36.2)	291 (35.3)
≥ 300 (macroalbuminuria)	201 (25.3)	235 (28.7)	230 (27.3)	213 (25.8)
eGFR, ml/min/1.37m^2; mean (SD)	43.3 (9.5)	43.3 (9.4)	43.4 (9.2)	44.0 (9.6)
LVEF; mean (SD)	36.6 (7.3)	36.3 (7.9)	59.6 (6.4)	59.7 (6.7)
NT-proBNP, pg/mL; mean (SD)	2007.9 (2925.9)	2063.9 (3162.1)	789.3 (1457.0)	824.8 (1574.7)
SBP, mmHg; mean (SD)	130.9 (16.1)	130.9 (17.2)	138.2 (15.7)	137.9 (15.7)
DBP, mmHg; mean (SD)	75.7 (10.7)	75.3 (10.7)	77.1 (10.9)	76.8 (11.0)
History of CVD; N (%)				
Myocardial infarction	337 (42.4)	353 (43.1)	199 (23.6)	167 (20.3)
Stroke	91 (11.4)	83 (10.1)	96 (11.4)	93 (11.3)
Coronary revascularization	333 (41.9)	317 (38.7)	218 (25.9)	207 (25.1)
Peripheral vascular disease	189 (23.8)	201 (24.5)	228 (27.0)	232 (28.2)
Major CV risk factors				
Hospitalization for HF during last 2 yrs	281 (35.3)	280 (34.2)	241 (28.6)	234 (28.4)
Left ventricular hypertrophy	418 (52.6)	408 (49.8)	542 (64.3)	536 (65.0)
Coronary artery calcium score ≥ 300	3 (0.4)	7 (0.9)	4 (0.5)	6 (0.7)
NT-proBNP ≥ 400 pg/mL	577 (72.6)	629 (76.8)	381 (45.2)	378 (45.9)
High-sensitivity troponin	686 (86.3)	713 (87.1)	686 (81.4)	676 (82.0)
High-sensitivity C-reactive protein > 3 mg/L	396 (49.8)	395 (48.2)	488 (57.9)	456 (55.3)
UACR ≥ 300 mg/g	201 (25.3)	235 (28.7)	230 (27.3)	213 (25.8)

TRIAL DESIGN

Figure 1: SCORED Trial Design



[1]Up titrated to 400mg at the discretion of the investigator.

Key inclusion criteria:
- Type 2 diabetes with HbA1c≥7%
- eGFR 25-60 mL/min/1.73m^2 - with no requirement for macro- or microalbuminuria
- CV risk factors

Key exclusion criteria:
- Planned start of SGLT2 inhibitor

Results

Table 2: Efficacy of Sotagliflozin on CV Death, HHF, and UVHF in Subgroup of Patients with Reported History of Heart Failure

	Sotagliflozin Events per 100 p-y [events/patients]	Placebo Events per 100 p-y [events/patients]	HR (95% CI); P-value
Total Occurrences of HHF, UVHF, & CV Death			
HF subgroup (N = 3281)	1,638 (12.61)	1,643 (16.83)	0.750 (0.615-0.915); 0.004
Baseline LVEF < 50% (n = 1614)	176 (16.89)	230 (21.81)	0.777 (0.606-0.997); 0.048
Baseline LVEF ≥ 50% (n = 1667)	98 (8.69)	134 (12.09)	0.727 (0.530-0.997); 0.048
Total Occurrences of HHF			
Baseline LVEF < 50%	95 (9.12)	136 (12.90)	0.721 (0.526-0.989); 0.042
Baseline LVEF ≥ 50%	54 (4.79)	83 (7.49)	0.647 (0.429-0.975); 0.038
Total Occurrences of UVHF			
Baseline LVEF < 50%	23 (2.21)	25 (2.37)	0.933 (0.494-1.762); 0.831
Baseline LVEF ≥ 50%	13 (1.15)	18 (1.62)	0.722 (0.342-1.523); 0.392
Total Occurrences of CV Death			
Baseline LVEF < 50%	58 (5.57)	69 (6.54)	0.838 (0.592-1.186); 0.319
Baseline LVEF ≥ 50%	31 (2.75)	33 (2.98)	0.921 (0.567-1.498); 0.741

SUMMARY

- In patients with T2DM and CKD, SOTA significantly reduced the composite of total CV deaths, HHF, and UVHF by 25%.
- In a subgroup population of patients with a history of HF enrolled in SCORED, SOTA significantly reduced the composite of total CV deaths, HHF, and UVHF by 25%.
- In patients with a history of HF and an LVEF < 50%, SOTA significantly reduced the composite of total CV deaths, HHF, and UVHF by 22%.
- In patients with a history of HF and an LVEF ≥ 50%, SOTA significantly reduced the composite of total CV.

CONCLUSIONS

- **The SCORED trial enrolled a large population of patients with a history of HF. In this subgroup including those with LVEF < 50% and ≥ 50%, sotagliflozin significantly reduced the primary endpoint of CV death and HF-related events.**
- **All endpoints of the composite positively contributed to the findings; however, HHF was the predominant influencing factor.**

REFERENCES

References

1. *Bhatt DL et al. N Engl J Med. 2021;384(2):117-128.*
2. *Bhatt DL et al. N Engl J Med. 2021;384(2):129-139.*

DISCLOSURE INFORMATION

This analysis was supported by Lexicon Pharmaceuticals, Inc.

Dr. Deepak Bhatt received research funding from Sanofi and Lexicon for his role as Chair of SCORED.

Dr. Bertram Pitt discloses the following relationships – consulting fees from Lexicon, Bayer, Astra Zeneca, Boehringer Ingelheim, Merck, and Phasebio and consulting fees and/or stock options from Viror, KBP Biosciences, Cereno scientific, Tricida, SC Pharmaceuticals, SQ Innovations, G-3 Pharmaceuticals, Protonintel, and Brainstorm medical and holds US Patent 9931412 on site specific delivery of eplerenone to the myocardium and US Patent pending 63/045,783 on histone-modulating agents for the protection and treatment of organ damage.

Drs. Hardin, Carroll, and Davies are Lexicon employees.

Presented at the 2023 WCIRDC, Universal City, CA, December 7-9, 2023