Cost-Effectiveness of Sotagliflozin for the Treatment of Recent Worsening Heart Failure with Diabetes

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Poster Code: EE429

ISPOR 2023 May 7-10 Boston, MA, USA

Introduction

The SOLOIST-WHF (Effect of Sotagliflozin on Cardiovascular Events in Patients with Type 2 Diabetes Post Worsening Heart Failure) trial illustrated that in patients with diabetes and recent worsening heart failure, sotagliflozin therapy initiated before or shortly after discharge significantly lowered a composite endpoint of cardiovascular deaths, hospitalizations, and urgent visits for heart failure. The incidence of primary events (number of events per 100 patient-years) was lower in the sotagliflozin group than in the placebo group (51.0 vs. 76.3; HR 0.67; 95% CI 0.52-0.85; P<0.001). The rate of death from cardiovascular causes was 10.6 in the sotagliflozin group and 12.5 in the placebo group (HR 0.84; 95% CI 0.58-1.22) and the rate of death from any cause was 13.5 in the sotagliflozin group and 16.3 in the placebo group (HR 0.82; 95% CI 0.59-1.14). Total events were reduced with sotagliflozin and the point estimate suggested improvement in mortality. This is a high-risk population with a high incidence of events. Thus, with 51.0 and 76.3 events per 100 patient years in the sotagliflozin and placebo groups, respectively, the number needed to treat was 4.

However, establishment of efficacy does not reflect the value of therapy. Based on the SOLOIST-WHF data, we present the results of a cost-effectiveness analysis of sotagliflozin in patients with diabetes and recent worsening heart failure.

Study Design

The SOLOIST-WHF trial was a double blind RCT in which 1222 patients meeting all eligibility criteria were randomized to sotagliflozin (200 mg, up-titrated to 400 mg as tolerated) or placebo from 2018 to 2022 at 306 sites in 32 countries. Patients were eligible if they were 18-85 years of age and had been hospitalized because of the presence of signs and symptoms of heart failure and received treatment with intravenous diuretic therapy. Patients were also required to have received a previous diagnosis of type 2 diabetes before the index admission or to have laboratory evidence to support a diagnosis of type 2 diabetes during the index admission. Exclusion criteria included end-stage heart failure or recent acute coronary syndrome, stroke, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) surgery, or an eGFR <30 ml per minute per 1.73 m2 of body surface area. Patients were followed for a median of 9 months.

Objective

In this study, we aimed to

- Perform both in-trial and lifetime health economic assessment using empirical data from the SOLOIST-WHF trial and Markov simulation model to examine the cost-effectiveness of sotagliflozin versus placebo for the primary endpoint of prevention of either death from cardiovascular causes or hospitalization for heart failure.
- Explore healthcare resource use and estimate costs.
- Calculate in-trial life-years gained and estimate quality-adjusted life-years gained.
- Conduct lifetime analysis cost-effectiveness analysis and run microsimulation model.
- Examine costs and effectiveness with different scenarios and in subgroups.
- Assess uncertainties through sensitivity analysis.

Methods

The current study was conducted in observation of the Consolidated Health Economic Evaluation Reporting Standards. Analyses were performed from a US healthcare sector perspective.

The SOLOIST-WHF dataset included patient-level baseline characteristics as well as all cardiovascular disease (CVD) and safety events recorded during the follow-up period. Patient-level events included nonfatal and fatal CVD including myocardial infarction (MI), stroke, and cardiac arrest; revascularization with PCI or CABG; hospitalization for heart failure, atrial fibrillation, ventricular tachycardia, peripheral arterial disease (PAD) requiring intervention, or unstable angina; and syncope and major bleeding. Competing risk analysis, based on the cumulative incidence function, was applied to estimate marginal probability of an event in the presence of competing events.

Patient-level acute and chronic event rates and medication use data from SOLOIST-WHF were used to inform healthcare resource use. Event costs were taken from the National Inpatient Sample. Medical care costs included pre-CVD drug costs, CVD costs (cost incurred through the first 30 days after CVD event and the rest of the first year), and chronic CVD costs (cost incurred after the first year) and were assessed using a combination of resource-based and event-based methods. Costs were inflated to 2021 US dollars (USD) using the Personal Consumption Expenditure index. In-trial and lifetime costs were estimated as the sum of background healthcare costs plus the costs of events and medications. Quality-adjusted life-years (QALYs) were calculated by multiplying the length of time in a health state by the utility score associated with that health state. As utility was not directly measured in SOLOIST-WHF, it was estimated using disability weights from the Global Burden of Disease Study. Disutility of nonfatal cardiovascular events, revascularization procedures, or stroke was estimated.

A microsimulation model based on SOLOIST-WHF was run to compare the lifetime cost-effectiveness of sotagliflozin versus placebo. Using Monte-Carlo simulation, a Markov state-transition model based on 9-month median follow-up of in-trial patient-level data was used to extrapolate costs, life expectancy, and quality-adjusted life expectancy to estimate the ICER over a lifetime horizon. The simulation was run with 3-month cycles. In each cycle, individuals could experience a fatal or nonfatal MI, stroke, angina, hospitalization or urgent visit for heart failure, or could die of other causes. The microsimulation model was run at the individual patient level.

Incremental cost-effectiveness ratios (ICERs) were calculated as the incremental costs divided by the incremental QALYs between the two treatment groups of sotagliflozin and placebo. Costs and QALYs were discounted at 3% annually. Subgroup analyses were performed including age, sex, systolic blood pressure at baseline, total cholesterol, and fasting glucose. To assess the robustness of our results, utility scores, HR, discount rate, and the cost of sotagliflozin were set to vary through possible ranges where we then performed traditional one-way sensitivity analyses. Probabilistic sensitivity analyses were performed to evaluate the impact of simultaneous changes in all the above variables.

Results

During the 9-month follow-up period, average in-trial costs were significantly higher for the sotagliflozin group ($11,565 vs $8,432; Δ $3,133; 95% UI $1,615-$4,652); this difference was driven by medication costs. During this time, patients receiving sotagliflozin gained an average of 0.80 life-years (vs. 0.77 in placebo group) and 0.51 QALYs (vs. 0.49 in placebo group; Table 1, In-Trial Analyses).

Compared with the placebo group, sotagliflozin added 0.39 QALYs (4.43 vs. 4.04 QALYs), 0.64 life-years (7.12 vs. 6.48, discounted) over the lifetime, at an incremental lifetime cost of $29,449 (95% uncertainty interval (UI) $26,610-$32,528), for an ICER of $75,510 per QALY gained (95% UI $55,640-$98,300 per QALY gained), which was lower than the threshold of $100,000 per QALY (Table 1, Lifetime Analyses). Lifetime PSA results evaluated the impact of simultaneous changes of all the variables involved in the cost and life-years gained (Table 2, Lifetime PSA).

Results from Markov simulation show that the benefit of sotagliflozin in QALY mainly come from the decrease in CVD deaths compared with the placebo group (Figure 1). Cost-effectiveness acceptability curves for sotagliflozin vs placebo are displayed in Figure 2. The cost-effectiveness acceptability curve shows more than a 95% probability that sotagliflozin was more cost-effective than placebo at the threshold of $100,000. The result of one-way sensitivity analysis is illustrated in Figure 3, where the top 10 most sensitive variables are demonstrated in the tornado diagram. The model was most sensitive to the HR of events and the monthly price of sotaglifozin, and changing the price impacts the cost-effectiveness of the treatment and affects the relationship between the status of cost-effectiveness and the willingness-to-pay thresholds (Figure 4).

Table 1. Cost-effectiveness results for sotagliflozin compared to placebo

Analysis	Mean Total Cost (2021 USD)			Mean LYs/QALYs Gained			ICER (USD/LY or USD/QALY)	SOTA Dominant	SOTA Dominated	Probability of Cost-Effectiveness		
	SOTA	Placebo	Δ (95% UI)	SOTA	Placebo	Δ (95% UI)				<$50,000	<$100,000	<$150,000
In-Trial (LYs)	11,565	8,432	3,133 (1615; 4652)	0.80	0.77	0.03 (-0.02; 0.08)	116,593	0.0%	13.8%	9.0%	43.9%	60.3%
In-Trial (QALYs)	11,565	8,432	3,133 (1615; 4652)	0.51	0.49	0.02 (-0.00; 0.06)	129,517	0.0%	7.7%	5.5%	36.0%	56.3%
Lifetime (LYs)	216,179	186,730	29,449 (26,610; 32,528)	7.12	6.48	0.64 (0.35; 0.94)	46,015	5.0%	0.5%	27.5%	85.2%	98.4%
Lifetime (QALYs)	216,179	186,730	29,449 (26,610; 32,528)	4.43	4.04	0.39 (0.31; 0.48)	75,510	2.0%	0.8%	14.3%	77.1%	93.2%
Lifetime PSA (LYs)	204,864	178,478	26,386 (22,784; 29,990)	7.14	6.55	0.59 (0.33; 0.85)	44,722	4.6%	0.2%	31.2%	88.4%	99.8%
Lifetime PSA (QALYs)	204,864	178,478	26,386 (22,784; 29,990)	4.37	4.01	0.36 (0.29; 0.44)	73,295	2.3%	0.6%	16.2%	79.5%	95.1%

National Inpatient Sample (NIS) event costs. VA Federal Supply Schedule medication costs. Sotagliflozin cost $443/30-day supply. Lifetime analysis based on microsimulation and PSA (probabilistic sensitivity analysis) utilized population means for parameters involved.
USD = US dollars; LY = life-year; QALY = quality-adjusted life-year; ICER = incremental cost-effectiveness ratio; SOTA = sotagliflozin; UI = uncertainty interval; Δ = difference between SOTA and placebo; PSA = probabilistic sensitivity analysis.

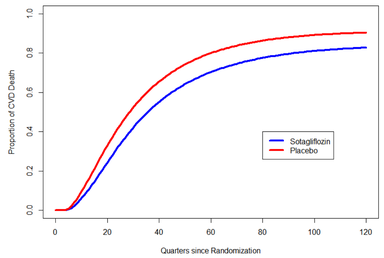

Figure 1 Mortality from Cardiovascular Causes

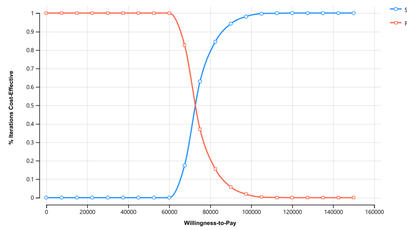

Figure 2 Cost-Effectiveness Acceptability Curve

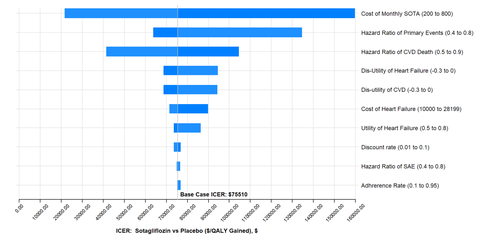

Figure 3 Sensitivity Analysis of Sotaglifozin vs Placebo

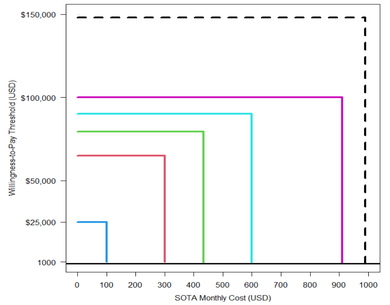

Figure 4 Sotogliflozin Monthly Cost

Conclusion

In patients with diabetes and worsening heart failure, sotagliflozin is cost-effective at commonly accepted willingness-to-pay thresholds.

Our study shows that sotagliflozin is a clinically and economically attractive medication compared with placebo.

Disclosure

Supported by an unrestricted grant from Lexicon Pharmaceuticals. The sponsor is the manufacturer of the drug. The analysis was performed entirely by the academic investigators independent of the sponsor. The original trial data from SOLOIST-WHF was provided by the sponsor to the investigators. The sponsor had no role in the design and conduct of this study; management, analysis, and interpretation of the data; or in the collection of additional supporting data for the economic analysis.