# A cost-effectiveness analysis of dapagliflozin in heart failure with preserved or mildly reduced ejection fraction in Portugal

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## Background and Objective

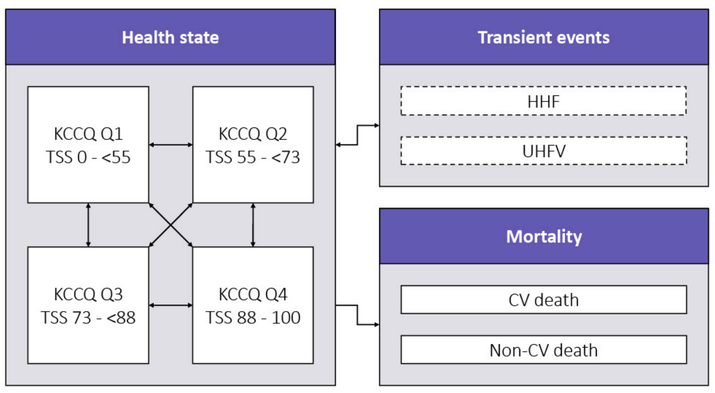
- Heart failure (HF) is a leading cause of hospitalization and mortality worldwide, affecting 1% to 3% of the general adult population. [1] HF is associated with reduced quality of life, high morbidity, mortality, and significant excess financial expenditure.
- Dapagliflozin is a sodium-glucose co-transporter-2 (SGLT2) inhibitor, which was originally developed as a glucose-lowering agent for the treatment of type 2 diabetes mellitus, that reduces the risk of death and other adverse outcomes among patients with chronic heart failure and a reduced ejection fraction (i.e., a left ventricular ejection fraction of ≤ 40%) and in those with chronic kidney disease, regardless of the presence or absence of type 2 diabetes mellitus. [2]
- The DELIVER clinical trial is an international, multicentre, double-blind, randomized placebo-controlled Phase III trial aimed to evaluate the effect of dapagliflozin versus placebo in reducing the composite of cardiovascular (CV) death or HF events [Hospitalization for HF (HHF) or Urgent HF visit (UHFV)] in patients with chronic HF and an ejection fraction >40%. The study concluded that dapagliflozin is associated with statistically significant reductions in the primary composite of CV death and HF events (HR: 0.82; 95% CI: 0.73-0.92; p<0.001) and for HHF individually (HR: 0.79; 95% CI: 0.69-0.91). [2]
- The aim of this analysis was to assess the cost-effectiveness of dapagliflozin added to standard-of-care therapy (SOC), versus SOC only, in patients with heart failure with preserved (>50%) or mildly reduced (40% - 50%) ejection fraction (HFpEF/HFmrEF), in the Portuguese setting.

## Methods

### Effectiveness model

- A lifetime Markov state-transition model was developed by HEOR Ltd., to quantify the long-term health economic impact of dapagliflozin plus SOC versus SOC in the treatment of patients with HF. **(Figure 1)**

**Figure 1. Model Structure**




- Disease progression is captured through transitions between discrete health states characterized by the quartiles of the total symptom score (TSS) of the Kansas City Cardiomyopathy Questionnaire (KCCQ) calculated across all patients at baseline, independent of treatment arm. The KCCQ-TSS quantifies patients' symptom frequency and severity.
- In addition to the health states, the model captures the incidence of HHF and UHFV (transient events), where patients incur in additional event-specific cost and utility decrement only in the cycle of incidence.
- Patient mortality is captured through the application of parametric survival equations describing CV death and non-CV death, calculated as the difference between all-cause death and CV death.
- The baseline patient characteristics are derived from the DELIVER clinical trial and used to determine the cohort's initial health state distribution across KCCQ-TSS quartiles, as well as inform the adjusted risk equations and survival equations.
- The analysis was conducted from the Portuguese National Health Service perspective assuming a 4% discount rate for costs and consequences and a lifetime time horizon.

### Adverse Events (AEs)

- The serious adverse events with a frequency > 1% of the trial population (acute kidney injury, fracture, urinary tract infection, and volume depletion) or of special clinical interest (amputation) were included in the model.

### Utilities

- Modelled utility values were derived from the analysis of individual patient data from the DELIVER clinical trial assigned to KCCQ-TSS quartile health state, mapped using the Portuguese value sets [3] and used in the model.

### Costs

- The model included costs associated with health state resources use, transient events, treatment, and adverse events, which were obtained from Portuguese databases and literature.

## Results

### Basecase scenario

- The modelled time in each health state by treatment arm are presented in **Figure 2**, and cost-effectiveness results for the base-case scenario are presented in **Table 1**.

**Figure 2. Modelled time in each health state by treatment arm**

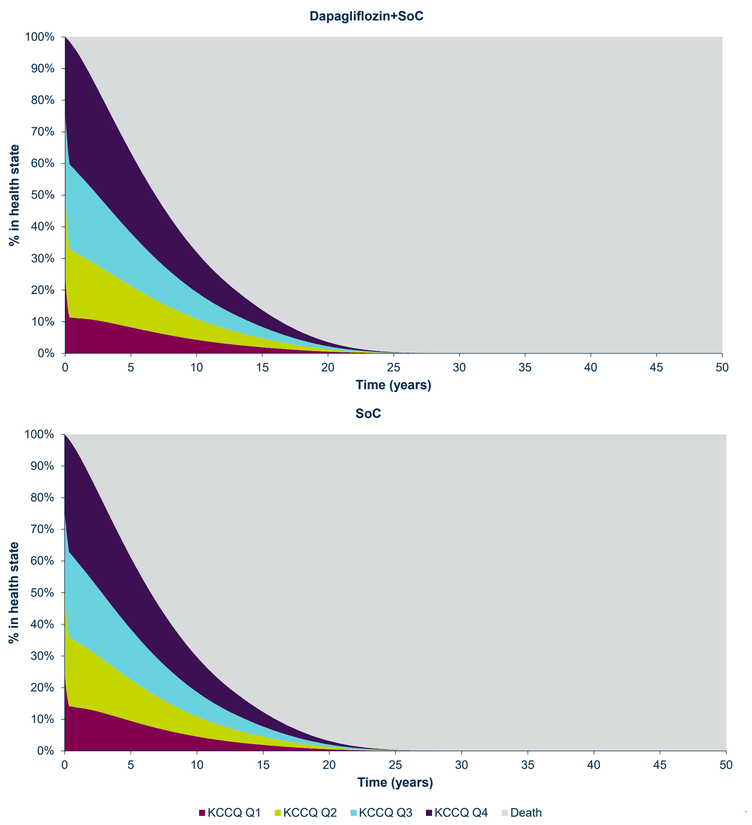



**Table 1. Cost-effectiveness results for the base-case scenario.**
LY, QALY and Costs break down by category

| | Dapagliflozin | SOC | Incremental |
|---|---|---|---|
| **Health outcomes - life years (LY)** | | | |
| KCCQ Q1 | 0.830 | 0.949 | -0.119 |
| KCCQ Q2 | 1.350 | 1.336 | 0.014 |
| KCCQ Q3 | 1.702 | 1.629 | 0.073 |
| KCCQ Q4 | 2.549 | 2.282 | 0.267 |
| **Total** | **6.431** | **6.197** | **0.234** |
| **Health outcomes - quality-adjusted life years (QALY)** | | | |
| KCCQ Q1 | 0.564 | 0.645 | -0.081 |
| KCCQ Q2 | 1.064 | 1.053 | 0.011 |
| KCCQ Q3 | 1.345 | 1.287 | 0.057 |
| KCCQ Q4 | 2.014 | 1.803 | 0.211 |
| Transient events | 0.009 | 0.011 | -0.002 |
| Adverse events | -0.022 | -0.026 | 0.003 |
| **Total** | **4.973** | **4.774** | **0.200** |
| **Cost outcomes (€)** | | | |
| Health states | 2,719.30 € | 2,620.25 € | 99.05 € |
| Transient events | 1,162.48 € | 1,447.08 € | -284.60 € |
| Death | 1,026.66 € | 1,105.46 € | -78.80 € |
| Treatment | 3,814.51 € | 1,733.16 € | 2,081.35 € |
| Adverse events | 531.74 € | 644.93 € | -113.19 € |
| **Total** | **€9,255** | **€7,551** | **€1,704** |

- Dapagliflozin plus SOC was more effective than SOC alone, leading to a mean 0.234 additional LYs (6.431 versus 6.197) and a mean 0.200 additional QALY (4.973 versus 4.774), per patient.
- Dapagliflozin plus SOC versus SOC alone was associated with incremental cost-effectiveness ratios (ICER) of 7,273.39€/LY and 8,539.98€/QALY (**Figure 3**).

### Sensitivity analysis

- Model robustness was demonstrated through scenario analyses.
- The probabilistic sensitivity analysis (PSA) also showed robust results with probabilistic ICERs of 7,220.18 €/LY and 8,495.03 €/QALY (**Figure 3**).
- The cost-effectiveness acceptability curve shows that, at a willingness-to-pay threshold of 20,000€/QALY, dapagliflozin has a probability of cost-effectiveness of approximately 87% (**Figure 4**).

**Figure 3. Cost-effectiveness plan**

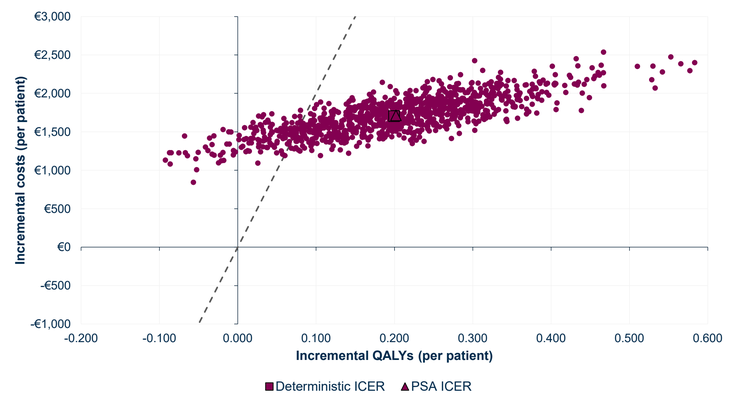
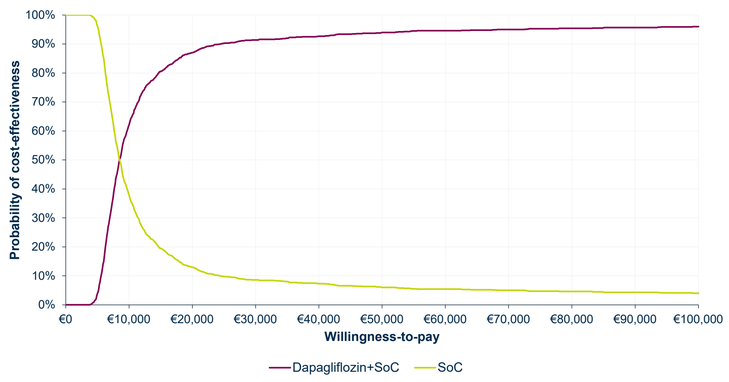



**Figure 4. Cost-effectiveness acceptability curve**




## Conclusions

- Dapagliflozin, added to SOC, was considered cost-effective compared with SOC alone in patients with HFpEF/HFmrEF.
- This cost-effectiveness analysis was considered valid and supported the reimbursement decision in Portugal.

### Disclosures

All authors disclose employment by AstraZeneca.

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### References

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