Cost-effectiveness of sodium-glucose cotransporter-2 inhibitor empagliflozin in patients with chronic heart failure irrespective of left-ventricle ejection fraction in the Netherlands

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Objectives

Sodium-glucose cotransporter-2 inhibitors (SGLT2i) have been recently found to be an effective treatment option for patients with type-2 diabetes, in reducing cardiovascular and renal outcomes.[1]

SGLT2i reduce the renal glucose absorption in the kidneys and thus lead to an increase in the secretion of glucose through the urine. This helps in managing a major risk factor for diabetic, cardiovascular (CV) and renal disease, but also and chronic heart failure.[2]

In the particular case of chronic heart failure, the level of left-ventricle ejection fraction (LVEF), being either reduced at LVEF of <40% (HFrEF), medium reduced at ≥40-49% (HFmrEF), or preserved at ≥50% (HFpEF), is used by physicians to classify and segment the condition and adapt treatment strategy accordingly for their patients.

Subsequently, for chronic heart failure patients with HFrEF and HFmrEF/HFpEF the clinical efficacy of the treatment option of the SGLT2i empagliflozin was assessed separately in two clinical trials, irrespective of T2DM status. These trials have subsequently shown the efficacy of the SGLT2i empagliflozin in preventing hospitalisation for heart failure (hHF) or CV mortality in with HFrEF[3] and HFmrEF/HFpEF patients.[4]

The aim of this research is to estimate the cost-effectiveness of empagliflozin added to standard-of-care (SoC) compared to SoC in adult patients suffering from chronic heart failure irrespective of LVEF.

Methods

Two identically structured, monthly cycle, Markov-models were build using the New-York Heart Association (NYHA) classification of states I, II and III/IV, paired with states for hospitalisation due to heart failure (hHF), mortality due to heart failure or other causes, as depicted in Figure 1.

The models further allowed for patients in the treatment group to discontinue SGLT2i-treatment based on a risk function and both treatment arms included the occurrence of adverse events.

Transition probabilities were calculated based on time-dependent probability matrices from the EMPEROR-Reduced[3] and –Preserved[4] clinical trials for respectively the HFrEF and HFmrEF/HFpEF model.

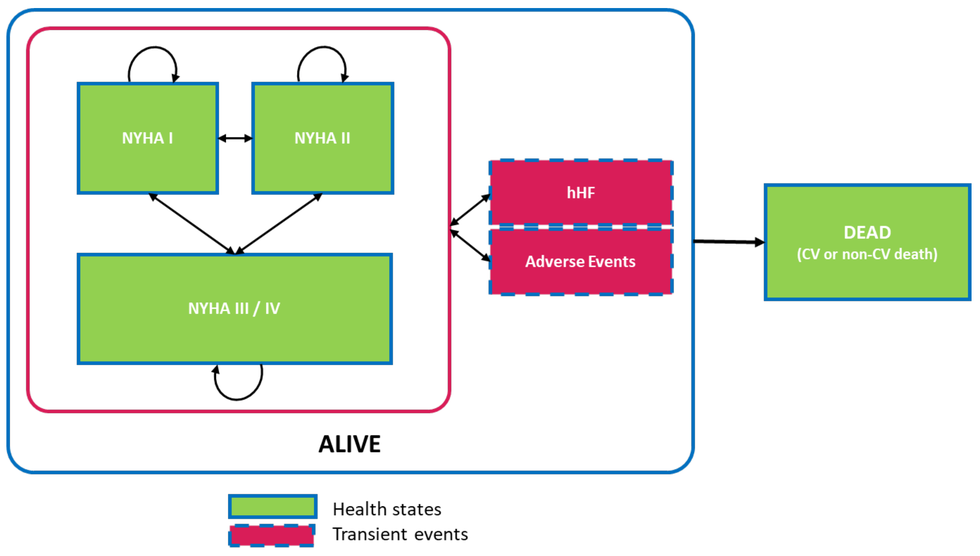
Published trial data was used to determine stage-specific event rate functions of hHF, as well as CV and all-cause mortality in both models. A repeated-measures Poisson generalised estimating equation model was used for the estimation of hHF over time. For both types of mortality estimates, survival curves were fitted following the NICE DSU guidelines.[5]

The costs included in the model were those of medication, clinical events, disease monitoring and adverse events management costs in euros at 2022 price level. Dutch drug acquisition costs were obtained from the GIP database, as well as the G-standard of the Z-index. Other costs were quantified using the Dutch guidelines for conducting economic analyses.[6] Costs were included to represent the Dutch setting from a societal perspective with an applicable willingness-to-pay threshold (WTP) of €50,000 per quality adjusted life-years (QALYs).

Data on quality of life was derived from trial data based on using the standardised EQ-5D-5L scale measured throughout both trials. The final utilities were estimated using a linear mixed-effects regression model including variables for study population characteristics, NYHA health states and clinical events.

Disutility's for hHF and adverse events were separately sourced from the EMPEROR-Reduced and -Preserved trials.3,4 The robustness of the deterministic results of the two models were each tested performing a deterministic sensitivity analysis (DSA) as well as a probabilistic sensitivity analysis (PSA) with 1,000 replications.

Figure 1. Model structure



The model structure was identical for both models.

Results

In the HFrEF model, patients treated with empagliflozin + SoC reported 4.25 QALYs compared to 4.13 with SoC, resulting in an incremental discounted QALY gain of 0.12. For HFmrEF/HFpEF patients, treatment with empagliflozin + SoC compared to SoC results in 5.60 versus 5.49 discounted QALYs per patient, respectively. This corresponds with an incremental QALY gain of 0.11.

Empagliflozin in the treatment of patients with HFrEf resulted in a dominant incremental cost-effectiveness ratio (ICER), whereas the ICER for the HFmrEF/HFpEF setting was determined to be €5,606. The management costs, productivity losses and informal care prevented through less hospitalisations resulted to be the main drivers for both ICERs.

Probabilistically confirmed robustness of the results, with the likelihood of empagliflozin to be cost-effective by applying a WTP threshold of €50,000 per QALY was estimated at 97% and 99% for HFrEF and HFmrEF/HFpEF, respectively.

"Empagliflozin is highly cost-effective by reducing mortality and resource utilization in the 2nd treatment line, irrespective of LVEF classification used in treatment guidelines."

Figure 3. Cost-effectiveness plane

Conclusion

Empagliflozin is a highly cost-effective intervention, preventing hospitalisations due to heart-failure or CV mortality in patients with chronic heart-failure. Notably, these favourable cost-effectiveness outcomes resulted to be irrespective of the level of LVEF.

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