**Heart Failure Association Update on Sodium glucose co-transporter-2 inhibitors in heart failure**

**(Update on: Sodium–glucose co-transporter 2 inhibitors in heart failure: beyond glycaemic control. The position paper of the Heart Failure Association of the European Society of Cardiology)**

The Heart Failure Association (HFA) of the European Society of Cardiology (ESC) has recently issued a position paper on the role of sodium-glucose co‐transporter 2 (SGLT2) inhibitors in heart failure (HF) [1].  This document was published awaiting the results of ongoing clinical trials that have since become available. Hence, the present document provides an update on the role of STGL2 inhibitors in the prevention and treatment of HF in light of new evidence from clinical trials.

Recently, the VERTIS-CV trial demonstrated that ertugliflozin reduces the risk for total and recurrent HF hospitalisations in patients with type 2 diabetes mellitus (T2DM) at high cardiovascular (CV) risk, with a hazard ratio (HR) of 0.70 (95% confidence interval (CI), 0.54-0.90, with a nominal p value = 0.006) (Presented by Professor Cosentino at the ESC Congress, August 31st, 2020). The benefit was similar in patients with and without a history of HF, and with left ventricular ejection fraction (LVEF) ≤45% or >45%. These findings are consistent with those of empagliflozin, canagliflozin and dapagliflozin, and solidify the evidence that SGLT2 inhibitors have a beneficial effect in reducing the risk of hospitalisations for HF in patients with T2DM and CV risk factors or established CV disease.

Furthermore, in 3730 patients with symptomatic HF and reduced ejection fraction (HFrEF), with or without T2DM, the EMPEROR-Reduced trial demonstrated a significant risk reduction in the primary combined endpoint of CV death or hospitalisation for HF (HR 0.75; 95% CI, 0.65 to 0.86, p<0.001) [2]. The benefit was observed regardless of the presence of T2DM, or the use of medications for HF treatment, including sacubitril/valsartan (~20% of the trial patients). Risk reduction was primarily driven by a substantial decrease in HF hospitalisations (HR 0.69; 95% CI, 0.59 to 0.81, p<0.001). The trial has also shown a significant reduction in the two prespecified secondary outcomes, namely, the total number of HF hospitalisations (first and repeated; HR 0.70; 95% 0.58 to 0.85, p<0.001) and a decline in renal function (eGFR slope).

A meta-analysis which used study-level data from DAPA-HF and patient level data from EMPEROR-Reduced further explored the effect of SGLT2 inhibition with dapagliflozin or empagliflozin in a broader spectrum of HF patients from both trials [3]. The meta-analysis demonstrated a reduction in both CV (HR, 0.86: 95% CI, 0.76–0.98, p=0.027) and all-cause mortality (HR, 0.87, 95% CI, 0.77–0.98, p=0.018) with SGLT2 inhibition, without any evidence of a statistical heterogeneity between dapagliflozin and empagliflozin. Similarly, SGLT2 inhibition reduced the risk of the combined endpoint of HF hospitalisation or CV death (HR, 0.74; 95% CI, 0.68–0.82), as well as the first HF hospitalisation (HR, 0·69; 95% CI, 0.62–0.78) and worsening renal function (HR, 0.62; 95% CI, 0.43–0.90). The results were consistent in patients with or without T2DM. Data on the safety profile of both agents were reassuring given that no excess risk in adverse events was noted compared with placebo, including the risk of severe hypoglycaemia.

In addition, a secondary analysis of DAPA-CKD trial in patients with chronic kidney disease with or without T2DM, revealed a significant risk reduction in hospitalisations for HF or CV death (HR, 0.71; 95% CI 0.55 to 0.92; p=0.0089) with dapagliflozin vs. placebo (Presented by Professor Heerspink at the ESC Congress, August 30th, 2020).

Assessing the landscape for the use of SGLT2 inhibitors in the prevention and treatment of HF, it can be concluded:

* Canagliflozin, Dapagliflozin Empagliflozin, or Ertugliflozin are all effective for the prevention of HF hospitalisation in patients with T2DM and established CV disease or at high CV risk, and this is consistent with a class effect of SGLT2 inhibitors. The specifically listed agents are recommended.
* Dapagliflozin or empagliflozin are recommended to reduce the combined risk of heart failure hospitalisation and CV death in patients with heart failure and reduced ejection fraction, with or without T2DM, and as yet there is insufficient evidence to claim any class effect.

**REFERENCES**

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