Empagliflozin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus at High Cardiovascular Risk

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Patients with type 2 diabetes mellitus (T2DM) and established cardiovascular (CV) complications are at particularly high risk of further CV events, including hospitalization for heart failure (HF) and premature death. However, the long-term benefit of glucose-lowering therapies on CV outcomes has been highly controversial. We recently reported the initial results of EMPA-REG OUTCOME™ (NCT01131676.) In this trial, a total of 7028 patients with overt CV disease from 42 countries and 590 sites were randomized between September 2010 and April 2013 to one of two doses of the SGLT2 inhibitor empagliflozin (empa; 10 or 25 mg) or placebo. 7020 patients were treated and included in the primary analysis. At baseline, the mean HbA1c was 8.1%, BMI 30.6 kg/m2, and 71.5% were males. Virtually all (99.2%) patients had a prior history of CVD: MI 46.6%, CABG 24.8%, stroke 23.3%, and peripheral arterial disease 20.8%. There was high usage of evidence-based CV therapies, such as statins, renin-angiotensin system (RAS) blockers, and aspirin. All CV events were adjudicated by an independent, blinded expert committee. Nearly 97% of the original cohort completed the study, and vital status was known in >99%. Empa (pooled doses) demonstrated superiority to placebo for the primary outcome, 3-point MACE, composed of time to first event of the composite of non-fatal MI, non-fatal stroke or CV death (HR 0.86 [95% CI, 0.74, 0.99; p=0.0382.]) This was driven primarily by a 38% relative risk reduction (RRR) in CV death (p<0.0001.) Empa also reduced the secondary endpoints of HF hospitalization (HFH) (RRR 35%, p=0.0017) and all-cause death (RRR 32%, p<0.0001). The presentation will include the additional outcomes of HF mortality, HFH or CV death, and recurrent HFH in the entire cohort. In addition we will describe the baseline characteristics and subsequent outcomes in patients with versus without a history of HF prior to trial enrollment. These expanded results from the first-in-class, large CV outcome trial involving an SGLT2 inhibitor will further inform clinicians of empagliflozin’s CV effectiveness, including mortality reduction, in high-risk patients with T2DM.

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