Empagliflozin and Cardiovascular Outcomes in Patients With Chronic Kidney Disease: The EMPA-KIDNEY Trial

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Background: More evidence is needed on the effects of sodium-glucose co-transporter (SGLT)-2 inhibition on cardiovascular and renal outcomes in patients with chronic kidney disease (CKD), in particular those without diabetes mellitus (DM) and low estimated glomerular filtration rate (eGFR).

Methods: Between May 2019 and April 2021, 6609 participants were randomly allocated empagliflozin 10mg once daily or matching placebo in the EMPA-KIDNEY trial. Eligible patients had an eGFR of 20 to <45 ml/min/1.73m^2; or 45 to <90 ml/min/1.73m^2 with a urinary albumin-to-creatinine ratio of ≥200 mg/g and were receiving standard of care (including a renin angiotensin system inhibitor, where indicated and tolerated). The primary outcome is a composite of kidney disease progression or cardiovascular death. Key secondary outcomes are the composite of hospitalization for heart failure (HHF) or cardiovascular death; all-cause hospitalizations; and all-cause death. Subgroup analyses for the composite outcome of HHF or cardiovascular death were pre-specified.

Results: Mean eGFR at baseline was 37.5 mL/min/1.73m^2 (SD 14.8), including 78% of participants with an eGFR <45 mL/min/1.73m^2. 54% of participants had no history of DM and 27% had a history of cardiovascular disease. Based on a planned interim analysis, the Independent Data Monitoring Committee recommended that the trial be stopped early for benefit on the primary outcome. Final follow-up visits are complete and data are undergoing analysis, but the Steering Committee remains blind to the results. Over 900 participants have had a primary outcome and about 280 participants have experienced HHF or cardiovascular death, there have been ~3500 hospitalizations, and ~310 participants have died.

Conclusion: EMPA-KIDNEY is the largest trial to assess SGLT-2 inhibition in patients with CKD. Detailed results for the primary outcome will be presented at the American Society of Nephrology Meeting ‘22 (02-05 November 2022), along with a summary of key secondary outcomes. More detailed unblinded results of the major cardiovascular and renal outcomes in pre-specified subgroups with cardiovascular relevance, such as by history of cardiovascular disease, will be presented at American Heart Association ‘22, with results placed in the context of the other large SGLT-2 inhibitor trials (in a collaborative meta-analysis).

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