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DIABETES

Further insights into SGLT2 inhibitors

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Sodium/glucose cotransporter 2 (SGLT2) inhibitors were developed to be used in patients with type 2 diabetes mellitus to reduce hyperglycaemia. Surprisingly, cardiovascular clinical trials, such as the CANVAS trial on canagliflozin and the EMPA-REG OUTCOME trial on empagliflozin, demonstrated not only cardiovascular safety of this drug class, but also cardiovascular benefit. Two new studies presented at the 2017 AHA Scientific Sessions in Anaheim, California, USA, provide further insight into the potential benefits of SGLT2 inhibitors.

Mahaffey and colleagues report the results of a prespecified analysis of the CANVAS trial to compare the use of canagliflozin for primary prevention versus secondary prevention. In the overall cohort of patients with type 2 diabetes and high cardiovascular risk, the rate of the primary end point of major adverse cardiovascular events (MACE; cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke) was lower in the group receiving canagliflozin than in the placebo group (HR 0.86, 95% CI 0.75–0.97, $P < 0.001$ for noninferiority, $P = 0.02$ for superiority). No evidence of heterogeneity was observed for the effect of canagliflozin between patients without a history of cardiovascular disease (primary prevention group; $n = 3,486$) and patients with previous cardiovascular events (secondary prevention group; $n = 6,656$): canagliflozin induced similar reductions in both cohorts in the rates of MACE and of secondary outcomes (hospitalization for heart failure and a composite of renal outcomes).

A new analysis of the EMPA-REG OUTCOME trial reports the effects of empagliflozin in the group of patients with peripheral artery disease (PAD), one of the most common complications in patients with type 2 diabetes. Findings in patients with PAD at baseline ($n = 1,461$) were consistent with findings in the overall cohort ($n = 7,020$), showing that use of empagliflozin in addition to standard care reduced the rates of cardiovascular death by 43%, all-cause death by 38%, MACE by 16%, hospitalization for heart failure by 44%, and progression of renal disease by 46% compared with placebo, with no increase in the risk of lower limb amputation.

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ORIGINAL ARTICLES Mahaffey, K. W. *et al.* Canagliflozin for primary and secondary prevention of cardiovascular events: results from the CANVAS program (Canagliflozin Cardiovascular Assessment Study). *Circulation* http://dx.doi.org/10.1161/CIRCULATIONAHA.117.032038 (2017) | Verma, S. *et al.* Cardiovascular outcomes and safety of empagliflozin in patients with type 2 diabetes mellitus and peripheral artery disease: a subanalysis of EMPA-REG OUTCOME. *Circulation* http://dx.doi.org/10.1161/CIRCULATIONAHA.117.032031 (2017)