Dapagliflozin and the Incidence of Type 2 Diabetes in Patients with Chronic Kidney Disease

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Abstract (1721 + 77 = 1798/1800 characters, not including spaces) The character count includes the abstract title, abstract body, and any images.

The DAPA-CKD trial demonstrated a significant reduction in the risk of adverse kidney and cardiovascular outcomes in participants with chronic kidney disease (CKD), with and without type 2 diabetes (T2D), treated with dapagliflozin 10 mg once daily compared to placebo (randomized 1:1). This pre-specified analysis explored the effect of dapagliflozin on incident T2D in the cohort without diabetes enrolled in DAPA-CKD. A subgroup of 1,398 participants with CKD, no prior history of diabetes, and HbA1c <6.5% at baseline were included. In this pre-specified exploratory analysis, surveillance for new-onset T2D (confirmed HbA1c ≥6.5%) was accomplished through periodic HbA1c testing (part of the study protocol) and comparison between treatment groups assessed through Cox proportional hazards model. Over a median follow-up of 2.4 years, T2D developed in 33/701 (4.7%) in the placebo group and 21/697 (3.0%) in the dapagliflozin group. This corresponded to event rates of 2.4/100-patient years and 1.5/100-patient years, respectively. Dapagliflozin led to a 38% reduction in T2D incidence (hazard ratio [95%CI] 0.62 [0.36, 1.08]). There was no heterogeneity in the effect of dapagliflozin on T2D prevention based on most key prespecified subgroups, including age, glycemic status, blood pressure, estimated glomerular filtration rate, albuminuria, race and region, but the effect was more pronounced in females (p interaction 0.03). More than 90% of the participants who developed T2D had prediabetes at baseline (HbA1c 5.7–6.4%). A meta-analysis of DAPA-CKD and DAPA-HF (dapagliflozin in heart failure with reduced ejection fraction) demonstrated that dapagliflozin reduced new-onset diabetes compared to placebo (hazard ratio 0.66 [0.51, 0.87]; p=0.003), without heterogeneity between studies

(p interaction 0.78). In this pre-specified explorative analysis of patients with CKD, treatment with dapagliflozin reduced the incidence of new T2D, an effect that was consistent across DAPA-CKD and DAPA-HF.