Efficacy and safety of dapagliflozin by glycemic status in the DAPA-CKD trial

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There is robust evidence that sodium-glucose cotransporter 2 (SGLT2) inhibitors reduce the risk of adverse cardiovascular and kidney outcomes. The DAPA-CKD trial (NCT03036150) demonstrated a significant risk reduction in participants with chronic kidney disease (CKD), with and without type 2 diabetes, treated with dapagliflozin 10 mg once daily compared with placebo, as an adjunct to standard care. In this prespecified analysis, we compared the

efficacy and safety of dapagliflozin according to baseline glycemic status. The trial included individuals with CKD with an estimated glomerular filtration rate (eGFR) of 25 to 75 mL/min/1.73 m^2 and a urinary albumin-to-creatinine ratio of 200 to 5000 mg/g. The primary outcome was a composite of sustained decline in eGFR of at least 50%, end-stage kidney disease, or death from renal or cardiovascular causes. We analyzed results by baseline glycemic status based on the American Diabetes Association criteria for HbA_{1c} level <5.7% (normoglycemia) vs. ≥5.7 to <6.5% (pre-diabetes) vs. ≥6.5% or a history of type 2 diabetes. Of the 4304 participants in the trial, 738 had normoglycemia at baseline; 660, pre-diabetes; and 2906, type 2 diabetes. The relative risk reduction for the primary composite outcome with dapagliflozin (hazard ratio [HR], 0.61; 95% CI, 0.51−0.72) was consistent in participants with normoglycemia (HR, 0.62; 95% CI, 0.39−1.01), pre-diabetes (HR, 0.37; 95% CI, 0.21−0.66) and type 2 diabetes (HR, 0.64; 95% CI, 0.52−0.79; p-interaction = 0.19). Similarly, we found no evidence of effect modification by glycemic status on secondary or exploratory outcomes. The safety profile of dapagliflozin was similar across glycemic groups, with no events of major hypoglycemia or ketoacidosis in participants with normoglycemia or pre-diabetes, and no ketoacidosis in any participant treated with dapagliflozin. In conclusion, dapagliflozin reduced the risk of kidney and cardiovascular events independent of baseline glycemic status.