Efficacy and safety of finerenone in patients with chronic kidney disease and type 2 diabetes by diuretic use: A FIDELITY analysis


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Introduction: Globally, approximately 85% of patients with chronic kidney disease (CKD) suffer from hypertension; this population is at increased risk of cardiovascular (CV) disease. Thiazide and loop diuretics are commonly used to treat hypertension and heart failure, respectively, in these patients. Diuretics alter potassium levels, which are also associated with CV outcomes.

Purpose: This post hoc exploratory analysis assessed the effect of the nonsteroidal mineralocorticoid receptor antagonist finerenone on CV and safety outcomes by baseline diuretic use in the FIDELITY dataset. We assessed whether the efficacy and safety of finerenone would be consistent regardless of diuretic use status at baseline, despite the effects these medications have on potassium.

Methods: In FIDELITY, a pooled analysis of the FIDELIO-DKD and FIGARO-DKD phase III clinical trials, eligible patients with type 2 diabetes (T2D) and CKD (urine albumin-to-creatinine ratio [UACR] ≥30–<300 mg/g and estimated glomerular filtration rate [eGFR] ≥25–<90 ml/min/1.73 m², or UACR ≥300–≤5000 mg/g and eGFR ≥25 ml/min/1.73 m²) were randomized 1:1 to finerenone or placebo. Patients were up-titrated to the maximum tolerated dose of renin–angiotensin system inhibitor during the run-in phase of the studies. For this analysis, patients were categorized by baseline diuretic use (yes/no for any diuretic and diuretic type) with additional on-treatment sensitivity analyses by post-baseline diuretic status. A composite CV outcome (CV death, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for heart failure) assessed efficacy. Safety was assessed considering treatment-emergent adverse events.

Results: Of 13,026 patients, 51.5% were treated with diuretics at baseline (21.5% on loop and 24.2% on thiazide diuretics). Finerenone reduced the risk of the composite CV outcome vs. placebo and this effect was not modified by baseline diuretic use (Yes: hazard ratio [HR]: 0.86; 95% confidence interval [CI]: 0.77–0.97; No: HR: 0.86; 95% CI: 0.74–1.00; P-value for interaction = 0.95). On-treatment analysis showed concomitant diuretic use with study treatment to be mainly constant among patients during the follow-up period and sensitivity analyses revealed consistently lower incidence rates with finerenone vs. placebo on composite CV outcome across the three diuretic subgroups by corresponding on-treatment use/non-use. Hyperkalaemia rates for patients on finerenone were overall comparable by diuretic use (Yes: 13.8% vs. 5.7% for placebo; No: 14.3% vs. 8.3% for placebo). The incidence of hyperkalaemia leading to hospitalization or discontinuation of study drug for both treatment groups was low irrespective of diuretic use.

Conclusion: In this analysis, finerenone reduced the risk of CV outcomes in patients with CKD and T2D irrespective of baseline diuretic use. Overall, the incidence of hyperkalaemia leading to hospitalization was low across all subgroups of diuretic users.