Empagliflozin Maintains Cardiorenal Benefit After Treatment

Empagliflozin reduces progression of chronic kidney disease (CKD) and cardiovascular death, with benefits persisting for up to 12 months after drug discontinuation in a post-trial follow-up.

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28 September 2025 — In an extended follow-up of the EMPA-KIDNEY trial, patients originally randomized to empagliflozin experienced lower rates of the composite outcome of kidney disease progression or cardiovascular death than those randomized to placebo.

Dr William G. Herrington, with the University of Oxford, United Kingdom, and the EMPA-KIDNEY Collaborative Group reported their findings in the October 25, 2024, online issue of the *New England Journal of Medicine.*

Importantly, "In a broad range of patients with chronic kidney disease at risk for progression, empagliflozin continued to have additional cardiorenal benefits for up to 12 months after it was discontinued," Dr Herrington and colleagues noted.

Empagliflozin is a sodium–glucose cotransporter-2 (SGLT2) inhibitor that reduces proximal tubular glucose reabsorption and produces natriuresis and hemodynamic changes that reduce intraglomerular pressure. Empagliflozin has also been associated with slower loss of estimated glomerular filtration rate (eGFR*)* in multiple trials.

Because the active EMPA-KIDNEY trial was stopped early for efficacy after a median of approximately 2 years, investigators implemented a prespecified 2-year post-trial observational follow-up to determine whether benefits persisted after discontinuation and to accrue additional hard end points such as end-stage kidney disease.

Among the 6609 patients randomized in the active trial, 4891 (74%) entered the post-trial period. During the post-trial period, local clinicians could prescribe open-label SGLT2 inhibitors, and their use was similar between groups (43% in the empagliflozin arm and 40% in the placebo arm).

To evaluate clinical efficacy, the prespecified primary outcome was a composite of progression of kidney disease (sustained greater than 40% eGFR decline, sustained eGFR of less than 10 mL/min/1.73 m^2) or having died of kidney or cardiovascular causes, assessed across the active and post-trial periods.

During the combined follow-up, the primary outcome occurred in 865 of 3304 (26.2%) patients assigned to empagliflozin versus 1001 of 3305 (30.3%) assigned to placebo— hazard ratio (HR) 0.79 (95% CI, 0.72–0.87). In the post-trial period alone, the HR was 0.87 (95% CI, 0.76–0.99), with most of the carryover concentrated in the first 6 months (HR for 0-month to 6-month post-trial, 0.60; 95% CI, 0.38–0.93).

Benefits were also observed in key secondary outcomes. Kidney failure occurred in 9.0% versus 11.3% (HR 0.74), and cardiovascular death in 3.8% versus 4.9% (HR 0.75) for empagliflozin versus placebo over combined follow-up. There was no observed effect on death of non-cardiovascular causes (5.3% in both groups).

Safety during post-trial follow-up showed no new serious adverse event signals attributed to trial empagliflozin. Investigators note, however, that because local clinicians could start open-label SGLT2 inhibitors, post-trial medication use and differences in who initiated open-label therapy complicate causal interpretation of longer-term effects.

According to the researchers, "the carry-over effect on the primary outcome was less than the effect of taking empagliflozin during the active trial period and appeared to last for up to 12 months, with most additional benefit exerted in the first 6 months after the active trial ended." They added that although "not demonstrated directly, this suggests that to maximize the cardiorenal clinical benefits of SGLT2 inhibitors in CKD requires long-term treatment."

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Reference

EMPA-KIDNEY Collaborative Group, Herrington WG, Staplin N, et al. Long-Term Effects of Empagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med*. 2025;392(8):777-787. doi:10.1056/NEJMoa2409183