Among the total patients, 46% were diabetic.

Empagliflozin treatment was associated with an acute dip in eGFR (2.12 mL/min/1.73 m²) for a relative reduction of 6%. After 2 months, the chronic slope was reduced by about half (from -2.75 to -1.37 mL/min/1.73 m² per year).

Effects on the chronic slope varied according to diabetes status as well as baseline eGFR and UACR. Patients with lower initial UACR had a lower absolute difference in chronic slope. However, because this group had a slower rate of CKD progression, they had a larger relative difference in chronic slope: 86% among patients with a baseline UACR less than 30 mg/g compared with 29% among those with an initial UACR of 2000 mg/g or greater.

The findings suggest substantial slowing of long-term progression of CKD with empagliflozin treatment.

“If widely implemented, use of SGLT2 inhibitors could have a substantial effect on the public health impacts of chronic kidney disease,” the investigators conclude. They cite a companion paper (see reference 12 in the article) reporting broadly similar effects of empagliflozin in patients with different types of primary kidney diseases (EMPA-KIDNEY Collaborative Group. Effects of empagliflozin on progression of chronic kidney disease: A prespecified secondary analysis from the EMPA-KIDNEY trial. Lancet Diabetes Endocrinol 2024; 12:39–50. doi: 10.1016/S2213-8587(2300321-2).)

JYNARQUE® (tolvaptan) has been proven effective in the 2 largest clinical trials of over 2800 patients with ADPKD across CKD stages 1–4.3

TEMPO 3:4 Trial—A 36-month trial in patients with CKD Stages 1, 2, and 3.4

The difference in TKV between treatment groups was most prominent within the first year, at the earliest assessment; the difference was minimal in years 2 and 3. JYNARQUE had little effect on kidney size beyond what accrued during the first year of treatment.4

Study design: TEMPO 3:4 was a double-blind, placebo-controlled randomized trial of 1445 patients with ADPKD. The inclusion criteria were 18 to 50 years of age, early, rapidly progressing ADPKD (meeting modified Ravine criteria): TKV >750 mL; creatinine clearance ≥60 mL/min. Patients were treated for up to 3 years. The primary endpoint was annual rate of change in the total kidney volume.4

REPRISE Trial—A 12-month trial of patients with CKD late Stage 2 to early Stage 4.

Study design: REPRISE was a double-blind, placebo-controlled randomized withdrawal trial of 1370 patients with ADPKD. The inclusion criteria were: CKD with an eGFR between 25 and 65 mL/min/1.73 m² if younger than age 56, or eGFR between 25 and 44 mL/min/1.73 m², plus eGFR decline ≥2.0 mL/min/1.73 m²/year if between ages 56-65. Subjects were to be treated for 12 months; after completion of treatment, patients entered a 3-week follow-up period to assess renal function. The primary endpoint was the treatment difference in the change of eGFR from pre-treatment baseline to post-treatment follow-up, evaluated by each subject’s treatment duration.4

Most common observed adverse reactions with JYNARQUE (incidence >10% and at least twice that for placebo) were thirst, polyuria, nocturia, poliuriopia and poliuriopia.

Data only included those patients who remained in the study for 3 years; effect in those who discontinued is unknown.5

In years 4 and 5 during the TEMPO 3:4 extension trial, both groups received JYNARQUE and the difference between the groups in TKV was not maintained.

Ravine criteria defined as at least 2 unilateral or bilateral kidney cysts in at-risk individuals between 15 and 30 years of age; 2 cysts in each kidney in individuals between 30 and 50 years of age, and at least 4 cysts in each kidney in individuals older than 60 years of age.6

(e.g., ketoconazole, itraconazole, Iopiniavir/ritonavir, indinavir/ritonavir, ritonavir, and conivaptan) increases tolvaptan exposure. Use with strong CYP3A inhibitors is contraindicated; dose reduction of JYNARQUE is recommended for patients taking moderate CYP3A inhibitors. Patients should avoid grapefruit juice beverages while taking JYNARQUE.

Adverse Reactions: Most common observed adverse reactions with JYNARQUE (incidence ≥10% and at least twice that for placebo) were thirst, polyuria, nocturia, poliuriopia and poliuriopia.

Other Drug Interactions:
- Strong CYP3A Inducers: Co-administration with strong CYP3A inducers reduces exposure to JYNARQUE. Avoid concomitant use of JYNARQUE with strong CYP3A inducers.
- V₁ₐ- Receptor Agonist: Tolvaptan interferes with the V₁ₐ agonist activity of desmopressin (DDAVP). Avoid concomitant use of JYNARQUE with a V₁ₐ agonist.

Pregnancy and Lactation: Based on animal data, JYNARQUE may cause fetal harm. In general, JYNARQUE should be discontinued during pregnancy. Advise women not to breastfeed during treatment with JYNARQUE.

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka America Pharmaceutical, Inc. at 1-800-438-9927 or FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).

Please see Brief Summary of FULL PRESCRIBING INFORMATION, including BOXED WARNING, on the following page.

References:
Findings

Reduced Kidney Mass
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The study provides new evidence regarding the association of tubulointerstitial disease with maternal-fetal outcomes. ["Even a small reduction in functional kidney mass, such as a pyelonephritic scar, is associated with a shorter duration of pregnancy and an increased risk of preterm delivery," the researchers write. They add that their findings “highlight” the importance of being particularly attentive to all patients with even early CKD in pregnancy.”] [Piccoli GB, et al. Any reduction in maternal kidney mass makes a difference during pregnancy in gestational and fetal outcomes. Kidney Int, published online January 29, 2024. doi: 10.1016/j.kint.2023.12.018.]

Since 1990s, Slower Declines in GFR with Standard Care for CKD

Outcomes data on standard-of-care (SOC) control groups from chronic kidney disease (CKD) treatment trials over the past 3 decades suggest slower declines in kidney function, reports a systematic review in the American Journal of Kidney Disease.

The researchers analyzed “secular trends” in glomerular filtration rates (GFRs) among patients with nonrandomized CKD randomized to SOC treatment in clinical trials published from 1990 to 2025. A meta-analysis included data on 32,202 patients assigned to SOC groups in 92 trials.

The analysis suggested dramatic improvement in the rate of GFR decline among patients assigned to SOC. Annual decline in GFR was 5.44 mL/min/1.73 m² for studies published from 1991 to 2000 versus 3.20 mL/min/1.73 m² from 2011 to 2025, a reduction of approximately 41%. This was despite a similar age range (from 51 to 58 years, respectively) and comorbidity in the study cohorts.

Slowing of estimated GFR (eGFR) decline was associated with rising use of renin-angiotensin-aldosterone system inhibitors: 16% from 1990 to 2000 versus 85% from 2011 to 2025. Other significant factors included improved blood pressure control and decreased proteinuria. In a multivariable meta-regression model, age and baseline proteinuria level were the only factors independently associated with eGFR decline.

The researchers note some key limitations of their observational study, including variation in methods of assessing GFR.

Recent studies have provided evidence that “multifaceted nephropathy care” can substantially slow the rate of progression of CKD—representing a major paradigm shift in treatment. “Nevertheless,” the researchers write, “solid evidence demonstrating that CKD management has improved over the years is still lacking.”

The meta-analysis shows substantial improvement in rates of GFR decline among patients assigned to SOC for nonrandomized CKD from the 1990s to the current decade. The authors discuss relevant changes in patient characteristics and evidence-based treatment for CKD, along with implications for future randomized clinical trials (Garnelo C, et al. Secular trend in GFR decline in non-dialysis CKD based on observational data from standard of care of arms trials. Am J Kidney Dis, published online November 11, 2023. doi: 10.1053/j.ajkd.2023.09.014).