SGLT2 inhibitors can slow progression of chronic kidney disease

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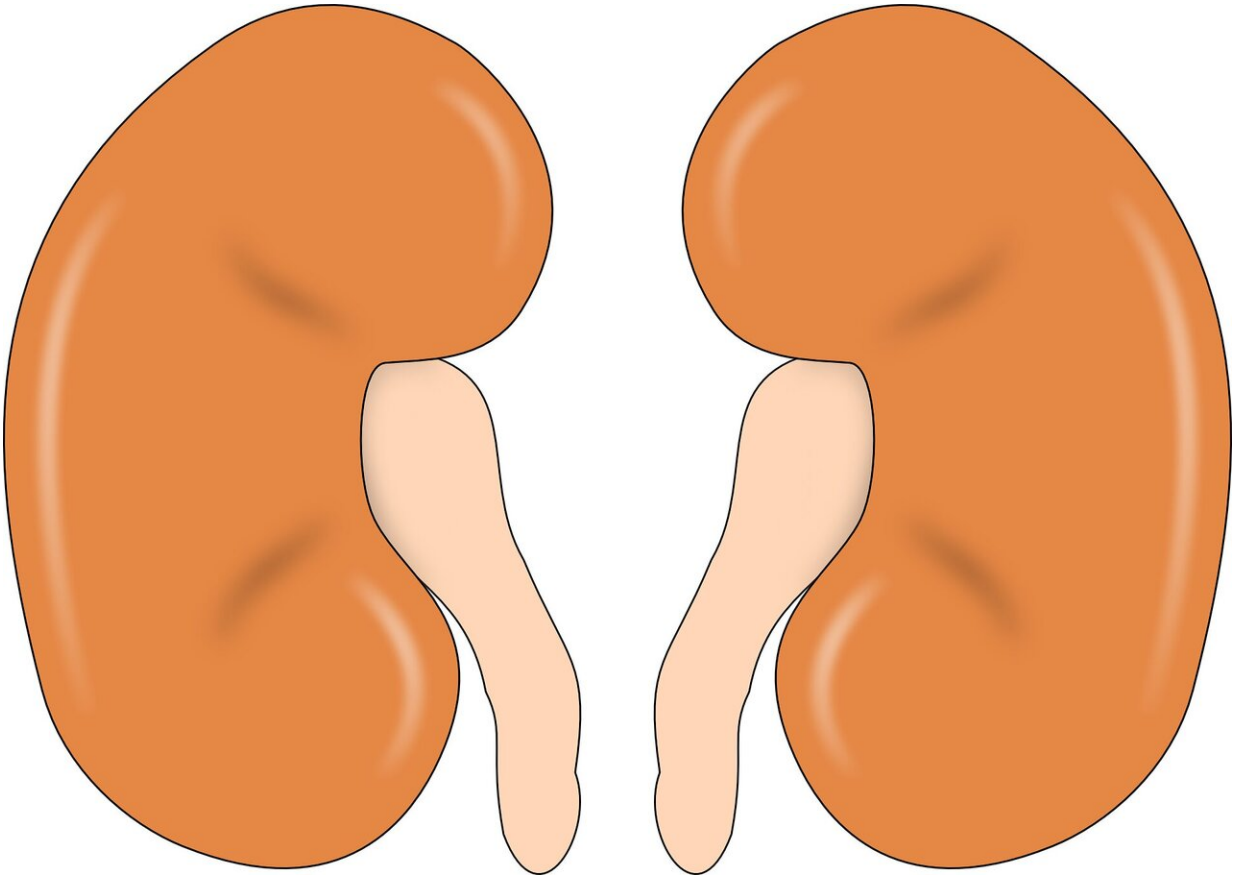

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Worldwide, 850 million people are affected by chronic kidney disease (CKD)—a worrying figure, and one that continues to rise. Treatment

options for patients with CKD are multiple and often determined by the etiology of CKD. So far, RAAS blockade (ACE inhibitors or angiotensin receptor blockers) was one of the most effective therapeutic intervention which has been shown to affect CKD disease progression. Now, SGLT2 inhibitors add significantly to the armentarium and have provided another breakthrough in the management of CKD.

The first to realize this potential of SGLT2 inhibitors was Professor Christoph Wanner, co-author of the EMPA-REG OUTCOME trial and President of the ERA-EDTA. Wanner and his colleagues conducted the EMPA-REG OUTCOME trial, the aim of which was to investigate whether the SGLT2 inhibitor Empagliflozin could lower the rate of cardiovascular events in patients with T2D.

"It could, but the much more exciting result for me as a nephrologist was an incidental finding of the study, which we analyzed and published in a second paper. It seemed that the medication could also slow progression of CKD. At that moment the effect was 'too good to be true,'" Wanner remembers. But this effect was confirmed in subsequent cardiovascular outcome trials (CVOTs) with other SGLT2 inhibitors. However, the proportion of patients with CKD in these CVOTs, which were conducted among patients with T2D, was relatively low.

At that point, the kidney study program with Canagliflozin was already underway. It was not until 2019 that the CREDENCE trial provided evidence that the SGLT2 inhibitor Canagliflozin could slow CKD progression in patients with T2D and CKD with albuminuria who were already on standard RAAS blockade and baseline glucose lowering therapy.

An important link was still missing, however. In about one third of all CKD patients, diabetes is the cause of kidney failure, but what about the other two thirds? Can SGLT2 inhibitors really help these patients, too,

and prevent them from reaching end stage kidney disease in need of regular dialysis treatments or renal transplantation?

A new study (DAPA-CKD) was initiated to answer these questions and the results were presented at the virtual ESC Congress. Cardiologists welcomed the prominent treatment originating its effects in the kidney and extending to the heart. The rationale and protocol of the study had been published in *Nephrology Dialysis Transplantation*, the premier kidney journal in Europe, earlier this year. The results were groundbreaking: 4304 patients (67.5% had diabetes) were randomized 1:1 to dapagliflozin or placebo. The primary outcome of worsening of kidney function was a composite of sustained -50% eGFR decline, occurrence of end stage kidney disease, or renal or CV death. There were 197 events in the dapagliflozin group and 312 in the placebo group; the HR for the primary endpoint was 0.61 (95% CI, 0.51-0.72; P=0.000000028) resulting in a number needed to treat of 19. The benefit of dapagliflozin on the primary endpoint was consistent in patients with and without T2D. No concerning safety signals were observed.

A study on the SGLT2 inhibitor Empagliflozin in 3730 heart failure patients (EMPEROR-Reduced) with and without T2D was already published the day before, saturday morning 8:30 am Eastern US-Time in The *New England Journal of Medicine*. Although kidney parameters were analyzed as secondary endpoints, the results point in the same direction: The annual rate of decline in the estimated glomerular filtration rate was significantly slower in the empagliflozin group than in the placebo group (-0.55 vs. -2.28 ml/min/1.73 m^2 per year, P