Empagliflozin—kidney protection regardless of an initial 'eGFR dip'

June 8 2020

Empagliflozin (EMPA), a selective inhibitor of sodium/glucose cotransporter 2 (SGLT2 inhibitors, "gliflozines"), reduces CKD progression in type 2 diabetics (T2D) with cardiovascular disease, presumably by lowering intraglomerular pressure. Positive effects of the drug on the cardiovascular risk of patients have also been observed.

However, uncertainty has been generated by the initial reduction in glomerular filtration rate after introducing an SGLT2 inhibitor. The increase in tubular flow rate caused by the reduced reabsorption of glucose and sodium from the glomerular filtrate under EMPA triggers the tubuloglomerular feedback mechanism in the kidney. The increased rate of tubular filtration causes the release of vasoactive hormones at the afferent arterioles of the glomerulus and thus to constriction of the afferent arterioles, as a result of which the glomerular filtration rate (GFR) decreases. But when administration of the drug is stopped, this feedback mechanism is terminated and the GFR increases again.

A study presented at the ERA-EDTA Congress today as a "Late Breaking Clinical Trial" investigated whether this effect of the initial 'GFR dip' after EMPA initiation was influenced by baseline characteristics and/or might have an impact on the EMPA-induced risk reduction in kidney outcomes. The study analyzed data of the EMPA-REG OUTCOME trial, in which patients with T2D and established cardiovascular disease had been treated treated (1:1:1) with EMPA 10 mg, 25 mg or placebo. The new analysis presented by Bettina J. Kraus, University Hospital Würzburg, Germany, searched for patients who had

experienced an initial 'eGFR dip' of >10% from baseline at Week 4 after treatment initiation. Twenty-eight percent of participants on empagliflozin experienced an 'eGFR dip' >10%. Diuretic use and/or higher KDIGO risk category at baseline were predictive of an initial 'eGFR dip' of >10% in empagliflozin compared to placebo treatment. However, rates of kidney adverse events were consistent across subgroups based on these predictive factors. Also, an 'eGFR dip' >10% had no major impact on the risk reduction with EMPA for the composite kidney outcome.

"These data show that around one in four patients treated with EMPA experiences an initial 'eGFR dip'. This was more likely in those taking diuretics and/or in more advanced stages of chronic kidney disease, but EMPA was safe and effective even in those. For such high-risk patients, especially, any intervention is welcome that slows the progression of kidney disease and allows the need for dialysis to be postponed as long as possible", commented Professor Christoph Wanner, Würzburg, Germany, President-Elect of the ERA-EDTA.

More information: Bettina J. Kraus et al. KIDNEY IMPLICATIONS OF THE INITIAL EGFR RESPONSE TO SGLT2 INHIBITION WITH EMPAGLIFLOZIN: THE 'EGFR DIP' IN EMPA-REG OUTCOME. LBCT 4547, presented at the ERA-EDTA Congress 2020.

Provided by ERA-EDTA