Better Oral Health May Reduce Mortality Risk For Patients with End Stage Renal Disease

A novel compound in development, emapticap pegol (emapticap; NOX-E36, Noxxon Pharma), a drug with anti-inflammatory properties, may be the first disease-modifying drug for the nephropathy in type 2 diabetes mellitus (T2DM). In a presentation at the European Renal Association—European Dialysis and Transplant Association Congress in Amsterdam in June, researchers presented evidence that emapticap had positive effects on the kidney that persisted for several weeks after the drug was stopped.

Emapticap specifically binds and inhibits the pro-inflammatory chemokine CCL2 (also called monocyte chemotactic protein 1, MCP-1). Phase 1 studies showed it to be safe and well tolerated, and there were hints of renoprotective effects. These signals have now been followed up in a study involving 75 T2DM patients with albuminuria.

In the trial, the drug was on stable anti-diabetic therapy and on drugs to block the renin-angiotensin system (e.g., ACE inhibitors or angiotensin receptor blockers). They had an albumin-to-creatinine ratio (ACR) >100 mg/g, an estimated glomerular filtration rate (eGFR) >25 mL/min/1.73 m², and a glycated hemoglobin (HbA1c) between 6.0 percent and 10.5 percent, Patients received emapticap or placebo subcutaneously twice a week for 12 weeks and were followed for an additional 12 weeks without drug or placebo.

Haller reported that the drug reduced pharmacologically active levels at the dose given and had the expected effect of reducing the number of monocytes bearing receptors for CCL2. Preclinical work had shown that this effect prevented the migration of inflammatory cells into the kidney, thereby preserving its structure and function, according to a news release from the company developing the drug.

Compared to placebo, emapticap reduced the mean ACR by 32 percent (p = 0.014) in the group of 49 patients deemed to be most relevant for future studies for this indication (i.e., censoring patients with kidney disease not from diabetes). Thirty-one percent of patients receiving the active drug had a 50 percent or greater reduction in ACR, compared to only 6 percent of patients receiving placebo. No differences were seen in blood pressure or eGFR between the emapticap and placebo groups, so the effect on ACR occurred independently of changes in blood pressure or eGFR and was thus presumably working through a different mechanism.

The patients on emapticap continued to receive benefit even after the drug was stopped and throughout the second 12-week (off-drug) period. The maximum decrease in ACR was seen 8 weeks after the last dose and was a mean 39 percent lower than for the placebo group (p = 0.011). At the end of the initial 12-week period, HbA1c trended downward with emapticap compared to placebo (an absolute change from baseline of −0.52 percent vs. +0.06 percent, respectively; p = 0.096). This difference became statistically significant 4 weeks after the last dose (p = 0.036).

The researchers concluded that the drug is safe, well tolerated, and effective in reducing ACR and HbA1c, with prolonged administration in patients with T2DM and albuminuria. They noted that the renoprotective effect independent of blood pressure reduction distinguishes this compound from other drugs and is a novel approach.

Haller noted that the residual beneficial effect after the drug is stopped may indicate that emapticap ameliorates the underlying pathophysiology of the disease and "may hence be the first disease-modifying drug for this indication." The research group suggests further clinical studies to assess the potential of the drug to stop end stage renal disease and cardiovascular events.

Aside from the renal effects, the reduction in HbA1c suggests that emapticap also can benefit glycemic control.

In light of positive early results but then failure of some drugs in larger trials, confirmation of these phase 2 results is clearly warranted. Bardoxolone, a compound that reduced inflammation and oxidative stress, looked good in increasing eGFR among T2DM patients in phase 2b but failed in phase 3 because of higher cardiovascular mortality in the group receiving the drug.