SGLT-1/SGLT-2 Inhibitor Shows Promise in Patients with T2DM, Renal Impairment

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The investigational LX4211 may one day fill a need for these patients who are unable to eliminate a lot of glucose in urine and who respond poorly to selective SGLT2 inhibitors.

The dual sodium glucose cotransporter (SGLT) 1 and 2 inhibitor LX4211 reduces systolic blood pressure and improves glycemic control in patients with type 2 diabetes and moderate to severe renal impairment, according to results of a study presented at the American Heart Association Scientific Sessions 2014.

Unlike the SGLT2-only inhibitors, LX4211 (sotagliflozin) inhibits both SGLT2 in the kidney and SGLT1 in the gastrointestinal tract.

“The difference may be relevant in the setting of renal impairment because patients with moderate to severe renal impairment cannot eliminate a lot of glucose in their urine,” study author Pablo Lapuerta, MD, Lexicon Pharmaceuticals, Inc. told Endocrinology Network. “That is why selective SGLT2 inhibitors have shown limited efficacy at controlling glucose for these patients.”

Lapuerta and colleagues1 hypothesized that LX4211 would reduce post-prandial glucose in the setting of moderate to severe renal impairment because of its action on SGLT1 in the gastrointestinal tract. They randomly assigned 31 patients to treatment with 400-mg LX4211 (n=16) or placebo (n=15) for 7 days. Patients had a mean age of 64.4 years and at baseline, mean estimated glomerular filtration rate (eGFR) of 43.4 mL/min/1.72 m² and a mean systolic blood pressure of 130.9 mm Hg.

Results showed that postprandial glucose area under the curve decreased by 169.3 mg per hour/dL in patients assigned LX4211 compared with placebo (P=.003). Patients assigned the study drug also had a mean reduction of 11.4 mm Hg in systolic blood pressure compared with no reduction in patients assigned placebo (P=.045).

Among patients with an eGFR of less than 45 mL/min/1.72 m² treated with LX4211 there was a mean 10.5 mm Hg reduction in systolic blood pressure compared with a 0.3 mm Hg reduction in patients assigned placebo.

“Sotagliflozin reduced post-prandial glucose significantly in the setting of moderate to severe renal impairment. This occurred despite relatively low urinary glucose excretion,” Lapuerta said. The researchers reported that there were no serious adverse events and no patients discontinued treatment in response to an adverse event.

“Renal impairment is common in the setting of diabetes, and we need better ways of achieving glucose control in this population,” Lapuerta said. “Additionally, hypertension in the setting of renal impairment is very common and difficult to treat. The encouraging results from this trial on glucose and blood pressure support the conduct of longer-term studies with sotagliflozin.”

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