Experimental drug lowers serum phosphate in phase 3 trial of hemodialysis patients

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An investigational drug that blocks intestinal phosphate absorption may help reduce the dangerously high blood levels of phosphate commonly seen in patients with kidney failure. The findings appear in an upcoming issue of the *Journal of the American Society of Nephrology* (*JASN*).

Patients with kidney failure who are receiving dialysis often have elevated levels of phosphate in their blood, which can contribute to cardiovascular and bone disease. Strategies used to reduce serum phosphate are currently limited to taking phosphate binder medications and reducing dietary phosphate intake.

An investigational drug called tenapanor reduces intestinal phosphate absorption by inhibiting a transporter protein called the sodium/hydrogen exchanger 3. To test the drug's potential for lowing serum phosphate in patients receiving maintenance hemodialysis, Glenn M. Chertow, MD, MPH (Stanford University School of Medicine) and his colleagues conducted a phase 3 randomized, double-blind trial.

The investigators randomly assigned patients with high serum phosphate who were receiving maintenance hemodialysis to receive twice-daily oral tenapanor (3 mg, 10 mg, or 30 mg [the latter down-titrated, if needed]) for 8 weeks. Patients were then re-randomized 1:1 to receive either their previously assigned dose or placebo for a 4-week "withdrawal" period. The researchers assessed the average change in serum phosphate over the 4-week withdrawal period for the tenapanor group versus the placebo group.

Of 219 patients randomized, 152 completed both study phases. During the initial 8- week treatment period, all 3 treatment groups experienced significant decreases in average serum phosphate (reductions of 1.00 mg/dL, 1.02 mg/DL, and 1.19 mg/dL, corresponding to the 3 mg, 10 mg, or 30 mg dose groups, respectively). Tenapanor also showed a significant benefit over placebo during the withdrawal period, with an average increase of 0.85 mg/dL in patients taking placebo versus an average increase of 0.02 mg/dL in patients taking tenapanor. Side events associated with tenapanor were largely limited to softened stool and a modest increase in bowel movement frequency, resulting from increased stool sodium and water content.

"I am extremely excited about the therapeutic potential of tenapanor in patients with advanced chronic kidney disease. Tenapanor is not a phosphate binder, but rather, a novel agent that inhibits the intestinal absorption of phosphorus," said Dr. Chertow. "I am eagerly looking forward to results of the second, ongoing phase 3 ("PHREEDOM") trial in patients receiving hemodialysis with hyperphosphatemia and additional studies using tenapanor in conjunction with phosphate binders."

More information: "Efficacy and Safety of Tenapanor in Patients Receiving Maintenance Hemodialysis with Hyperphosphatemia: A Randomized Phase 3 Trial," *Journal of the American Society of Nephrology* (2019). DOI: 10.1681/ASN.2018080832

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