Bardoxolone Boosted eGFR in Kidney Disease

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A 24-week course of bardoxolone methyl, an experimental antioxidant inflammation modulator, improved glomerular filtration rates in chronic kidney disease patients with type 2 diabetes, according to a randomized phase IIb study funded by the drug's sponsor, Reata Pharmaceuticals Inc.

A phase III study slated to start next year will test whether the mean improvement of 10.1 mL/minute per 1.73 m^2 leads to better patient outcomes, according to nephrologist Dr. Pablo Pergola of the University of Texas Health Science Center, San Antonio, who presented the findings.

"You want to make sure this drug will be associated with a clinical outcome," said Dr. Pergola, the lead investigator of the phase IIb study.

Patients in the randomized, double-blind, placebo-controlled trial were assigned to 25-mg, 75-mg, or 150-mg daily doses of bardoxolone or to placebo.

A phase III study slated to start next year will test whether the mean improvement in estimated glomerular filtration rate of 10.1 mL/minute per 1.73 m^2 leads to better outcomes.

Each group had 57 subjects, except the 150-mg group, which had 56.

In addition to type 2 diabetes, subjects had stage 3b or 4 chronic kidney disease (CKD), with an estimated glomerular filtration rate (eGFR) of 20-45 mL/minute per 1.73m^2. The median age of the patients was 67 years, and all were on standard-of-care therapy – 98% of patients took ACE inhibitors or angiotensin-receptor blockers.

At the end of 24 weeks, bardoxolone patients had a mean eGFR gain of 10.1 mL/minute per 1.73 m^2, with gains noted in each group ranging from 8.3 to 11.5 mL/minute per 1.73 m^2. There was a 0.1-mL/minute per 1.73 m^2 eGFR gain in the placebo group. The treatment effect of bardoxolone relative to placebo was significant.

About 73% (124) of patients in each bardoxolone group had at least a 10% eGFR increase; approximately 25% (43) had more than a 50% increase.

Increased eGFRs also correlated with decreased blood-urea-nitrogen levels, decreased serum phosphorus and uric acid levels, and improved CKD stage.

"The maximal effect seems to be at 75 mg," Dr. Pergola said, with smaller eGFR gains at 25 mg and no greater gains at 150 mg.

Adverse events were more common in the bardoxolone groups; 49% of bardoxolone patients reported muscle spasms, compared with 12% in the placebo group.

The spasms were thought to be treatment related, as were nausea, hypomagnesemia, and diminished appetite.

The muscle cramps led to slightly higher discontinuation rates in bardoxolone subjects, Dr. Pergola said. But "the [spasms] seem to be transient and, importantly, there is no increase in biochemical markers of muscle damage."

Reata plans to release 52-week outcomes early next year.

Dr. Pergola said he has no disclosures. ■

VITALS

Major Finding: Bardoxolone methyl, an experimental antioxidant inflammation modulator, improved estimated glomerular filtration rates in diabetic CKD patients by a mean of 10.1 mL/minute per 1.73 m^2, and reduced blood urea nitrogen, serum phosphorus, and uric acid levels.

Data Source: Phase IIb randomized, double-blind, placebo-controlled trial enrolling 227 patients.

Disclosures: The study was funded by the drug's sponsor, Reata Pharmaceuticals. The lead investigator said he had no conflicts of interest.