Sibeprenlimab in patients with IgA nephropathy: a Phase 2 trial

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1 Background

Up to 85% of individuals with IgA nephropathy (IgAN) progress to kidney failure within 50 years of kidney biopsy diagnosis.1 Multiple lines of evidence support a key role for APRIL in the pathogenesis of IgAN.2-3 Sibeprenlimab is a recombinant IgG, monoclonal antibody that binds to and inhibits APRIL.

The first-in-human Phase 1 trial of sibeprenlimab concluded that sibeprenlimab was well tolerated, and generally suppressed APRIL, and some surrogate markers of IgAN activity.4

2 Methods

• A Phase 2, 2-center, randomized, double-blind placebo-controlled, multiple-dose, parallel-group study (NCT02570378) was conducted in adults with active IgAN, proteinuria, despite background treatment.

• Eligible patients were aged ≥18 years, with proteinuria ≥2.0 g/g at screening or >2.0 g/g at baseline.

• The primary endpoint was change from baseline in geometric mean uPCR (g/g) at 12 months (Figure 1; Table 2) with a non-inferiority margin of −20%.

• Patients were stratified by region (Japan, rest-of-world), and baseline uPCR ≥2.0 g/g or >2.0 g/g at screening.

• Sibeprenlimab was administered as a 2 mg/kg or 4 mg/kg or 8 mg/kg intravenous infusion monthly for 12 months as an add-on to standard-of-care treatment. Randomization was stratified by region and baseline uPCR ≥2.0 g/g or >2.0 g/g at screening.

• The primary endpoint was change from baseline in geometric mean uPCR (g/g) at 12 months. Secondary endpoints included change in 24-hour proteinuria and 24-hour albuminuria, and safety monitoring, at 12 months and 24 months.

• Renal safety measures included change in estimated glomerular filtration rate (eGFR) and proteinuria, stabilization of estimated glomerular filtration rate (eGFR), and robust suppression of serum APRIL.4

3 Results

• Patient characteristics. Baseline characteristics were generally similar between treatment groups (Table 1). The profile of patients in this study was consistent with other Phase 2 trials of sibeprenlimab in IgAN.2-3

• Median duration of follow-up was 16 months.

4 Discussion

• In patients with IgAN, 12 months of sibeprenlimab treatment demonstrated significant reduction in proteinuria, stabilization of eGFR decline, and robust suppression of serum APRIL, compared to placebo.

• Of the available therapies for IgAN, none have demonstrated a sustained impact on proteinuria stabilization and/or suppression of the magnitude observed in the present study.

• Robust suppression of serum APRIL was also observed.

Sibeprenlimab was generally safe and well tolerated, without evidence of unacceptable toxicity.

• A Phase 3 trial is underway to investigate the efficacy and safety of sibeprenlimab in a larger population of patients with IgAN (NCT03246074), the Valeriana study – please scan the QR code for more information.

References