THE KOREAN SOCIETY OF NEPHROLOGY
APCN & KSN 2024
June 13(Thu) - 16(Sun), 2024 Coex, Seoul, Korea
Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

Abstract Submission No.: A-0699

Hematuria Resolution with the APRIL-Blocking Monoclonal Antibody, Sibeprenlimab, in Patients with IgA Nephropathy in a Phase 2 Randomized Controlled Trial

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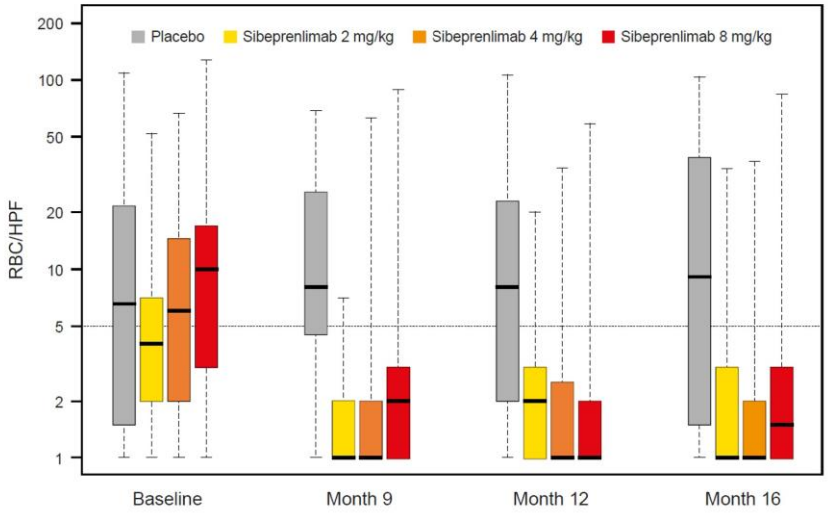
Objectives : Sibeprenlimab, a humanized IgG_2 monoclonal antibody that blocks A PRoliferation-Inducing Ligand (APRIL), demonstrated acceptable safety with uPCR reduction and eGFR stability at 12 months in a Phase 2 study in IgAN patients. Defined IgAN clinical remission criteria include reduction of proteinuria below certain thresholds and remission in hematuria (reduction in red blood cell [RBC] count to <5 RBC/HPF-high power fields). We report the effects of sibeprenlimab on these parameters.
Methods : ENVISION (NCT04287985) is a multi-center randomized (1:1:1:1) study evaluating monthly intravenous (IV) sibeprenlimab (2, 4, or 8 mg/kg) vs placebo over 12 months (with 4 months follow-up) in adults with IgAN on supportive treatment, eGFR ≥30 mL/min/1.73m^2, and proteinuria ≥1.0 g/d or urine protein creatinine ratio (uPCR) ≥0.75 g/g. Efficacy endpoints include change from baseline in 24-hour uPCR at Months 9 & 12, change in eGFR at Months 12 and 16, monthly change in spot-urine proteinuria and change in microscopic hematuria (RBC/HPF). Hematuria was assessed using central-laboratory automated urine microscopy.
Results : 155 patients were randomized (sibeprenlimab 2 mg/kg n=38; 4 mg/kg n=41; 8 mg/kg n=38; placebo n=38); 146/155 (94.2%) received all treatment doses. Baseline characteristics were balanced between groups. Median follow-up was 16.0 months. Sibeprenlimab recipients showed reduction in microscopic hematuria at Months 9, 12 and 16 vs placebo (Figure 1). At month 12, 21 patients had proteinuria ≤300 mg/day, and 10 (47.6%) of these patients had ≤5 RBC/HPF. Hematuria response corresponded to proteinuria response
Conclusions : A majority of patients receiving sibeprenlimab experienced hematuria resolution from Months 9-16, while hematuria persisted in placebo recipients. Observed improvements in proteinuria and hematuria, coupled with eGFR stability over the period of observation suggest that APRIL inhibition with sibeprenlimab may be a promising therapeutic strategy. These data support further evaluation of sibeprenlimab as a disease-modifying agent for IgAN.

Hematuria Figure.jpg

Figure 1: *Change from Baseline in Hematuria (RBC/HPF) Over Time.*



Box plots show median, 25%–75%, and minimum and maximum values. RBC/HPF, red blood cells per high power field