Abstract Type : Oral
Abstract Submission No. : 1391

ATRASENTAN FOR THE TREATMENT OF IGA NEPHROPATHY: INTERIM RESULTS OF THE AFFINITY STUDY

Seung Hyeok Han[1], Lesley A. Inker[2], David K. Packham[3], Dwarakanathan Ranganathan[4], Anjay Rastogi[5], Michelle N. Rheault[6], Mark Vishnepolsky[7], Andrew J. King[8], Charlotte Jones-Burton[9], Sung Gyun Kim[10]
[1]Department of Internal Medicine, College of Medicine, Institute of Kidney Disease Research, Yonsei University, Seoul, Korea, Republic of
[2]Department of Division of Nephrology, Tufts Medical Center, United States
[3]Department of Nephrology, Melbourne Renal Research Group, Australia
[4]Department of Nephrology, Royal Brisbane and Women's Hospital, Australia
[5]Department of Nephrology, University of California Los Angeles, United States
[6]Department of Pediatric Nephrology, University of Minnesota, United States
[7]Department of Nephrology, Kidney Specialists of Southern Nevada, United States
[8]Department of Research and Development, Chinook Therapeutics, United States
[9]Department of Clinical Development, Chinook Therapeutics, United States
[10]Department of Internal Medicine-Nephrology, Hallym University Sacred Heart Hospital, Korea, Republic of

Objectives: Endothelin A (ET_A) receptor activation drives proteinuria, inflammation, and fibrosis in patients with glomerular diseases. Atrasentan, a potent and selective ET_A receptor antagonist, represents a potential therapy to reduce proteinuria and preserve kidney function in patients with IgA nephropathy (IgAN) and other glomerular diseases. AFFINITY is a phase 2, open-label study evaluating efficacy and safety of atrasentan in adult patients with proteinuric glomerular diseases.

Methods: Eligibility criteria for the IgAN cohort include adults with biopsy-proven IgAN; eGFR ≥30 mL/min/1.73m^2, UPCR ≥0.5 to <1.0 g/g (first morning void) and on maximally-tolerated/stable RASi. Patients are treated orally with 0.75 mg atrasentan daily for 52 weeks. The primary endpoint is change in 24-hour UPCR from baseline to Week 12.

Results: Twenty patients have enrolled in the IgAN cohort. Median age was 45 years, with 50% women, 45% White and 45% Asian. Median baseline 24-hour total urine protein was 1.2 g/day (geometric mean; GM), 70% of patients had total urine protein of >1 g/day, and median eGFR was 46 mL/min/1.73m^2.

Mean (range) treatment duration was 45 (13-53) weeks as of data cut-off (19 October 2022). Atrasentan was generally well-tolerated with no serious and no treatment-related severe adverse events (AEs). Treatment-emergent AEs observed in 16 patients were mild or moderate; most have resolved. One patient discontinued due to a related AE of headache. No significant fluid retention was observed. GM reduction from baseline in 24-hour UPCR was 48.3% at week 12 (95% CI 38.9,56.3; n=20) and 54.7% at week 24 (95% CI 46.1,61.9; n=19**; Figure**).

Conclusions: Treatment with atrasentan in addition to standard of care was generally well-tolerated and resulted in durable and clinically meaningful reduction in proteinuria at weeks 12 and 24, strongly supporting the therapeutic potential of ET_A receptor blockade with atrasentan in patients with IgAN.

Figure. Percent reduction in UPCR with atrasentan in patients with IgAN