Atrasentan in Patients with Proteinuric Glomerular Diseases – The AFFINITY Study

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Globular Disease and Proteinuria

Atrasentan*

Glomerular diseases, including IgA nephropathy (IgAN), focal segmental glomerular sclerosis (FSGS), diabetic kidney disease (DKD) and Alport syndrome together are a leading cause of ESKD worldwide.

• Proteinuria is a predictor of disease progression and ESKD in glomerular disease.
• Endothelin 1 (ET-1) expression is elevated in patients with glomerular disease.
• Endothelin A (ETA) receptor activation drives proteinuria, inflammation, and fibrosis.

Blockade of the ETA receptor with atrasentan, a potent and selective ETA antagonist, represents a potential approach to reduce proteinuria and preserve kidney function in glomerular diseases.

• In preclinical studies, atrasentan attenuates mesangial cell activation, glomerular and tubulointerstitial injury, and reduces proteinuria associated with IgAN.
• Atrasentan has demonstrated clinically significant and sustained proteinuria reduction with an acceptable safety profile in over 5,100 patients with DKD.

The AFFINITY study (NCT04573920) is an ongoing global phase 2 open-label basket study of safety and efficacy of atrasentan in IgAN, FSGS, Alport syndrome and DKD patients at risk of progressive loss of kidney function.

Interim results from the IgAN cohort of the ongoing AFFINITY study demonstrate atrasentan is generally well-tolerated and results in a mean 54.7% reduction in proteinuria at Week 24 (N=19; ASN 2022, TH-PO497)

• Proteinuria in patients with proteinuric glomerular diseases and DKD.
• Proteinuria is a predictor of disease progression and ESKD in glomerular disease.
• Endothelin 1 (ET-1) expression is elevated in patients with glomerular disease.
• Endothelin A (ETA) receptor activation drives proteinuria, inflammation, and fibrosis.

The primary endpoint is change in proteinuria (IgAN, FSGS, AS) or albuminuria (DKD) from baseline at Week 12 for IgAN, AS and DKD, and at Week 24 post dose escalation for FSGS. Key exploratory measures include safety, tolerability and change in eGFR from baseline to Week 52.

Key Eligibility Criteria:
- Proteinuria must be present in all patients - IgAN, urine protein creatinine ratio (UPCR) ≥ 0.5 and < 1.0 g/g; FSGS, UPCR > 1.0 g/g; AS, UPCR > 0.5 g/g; DKD, urine albumin creatinine ratio (UACR) ≥ 0.5 g/g.
- eGFR ≥ 30 mL/min/1.73 m² in patients with IgAN, AS, or FSGS; eGFR ≥ 45 mL/min/1.73 m² in patients with DKD.
- Patients must be receiving maximally-tolerated RASi and patients with DKD must also be on SGLT2i.

% Reduction in UPCR

% Change from baseline (Geometric mean ± SEM)

Wk 0 6 12 24
N 19 20 20 19

Medians (range) baseline protein excretion: 1.2 (0.9, 1.5) g/day

The AFFINITY Study

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Approximately 100 patients in the United States, Australia, South Korea, Spain, Italy and United Kingdom will be enrolled.
- IgAN cohort enrollment complete
- DKD, Alport syndrome, and FSGS cohorts - ENROLLMENT ONGOING

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