The AFFINITY Trial: An Open-label Phase 2 Study of Atrasentan in Patients with Proteinuric Glomerular Diseases

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Patients with Proteinuric Glomerular Diseases

The AFFINITY Trial: An Open-label Phase 2 Study of Atrasentan in Glomerular Disease and Proteinuria

Glomerular diseases, including IgA nephropathy (IgAN), focal segmental glomerulosclerosis (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.

Atrasentan*

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.

Atrasentan has been shown to:

- Potently and selectively block the ETA receptor.
- Reduce proteinuria and preserve kidney function in glomerular diseases.
- Potentially reduce proteinuria and inflammation in patients with glomerular disease.

The AFFINITY Study

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.

Approximately 100 patients in the United States, Australia, South Korea, Spain, Italy and United Kingdom will be enrolled.

- IgAN, DKD, Alport syndrome, and FSGS (optional dose escalation) cohort enrollments are complete.
- FSGS cohort (0.75 to 1.5 mg dose escalation) - ENROLLMENT ONGOING.

Key Eligibility Criteria:

- Proteinuria must be present in all patients
- eGFR with DKD
- Patients must be receiving maximally-tolerated SGLT2i or patients with DKD must also be on SGLT2i
- uACR > 0.5 g/g; FSGS, UPCR > 1.0 g/g; AS, UPCR > 0.5 g/g
- Proteinuria ≥ 0.5 and < 1.0 g/g

Key exploratory measures include safety, tolerability and change in eGFR from baseline to Week 52.

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.

Reference