IgAN and the Endothelin Pathway

Atrasentan®

Blockade of the ET₄ receptor with atrasentan, a potent and selective ET₄ antagonist, represents a potential approach to reduce proteinuria and preserve kidney function in IgAN¹⁵

In preclinical studies, atrasentan attenuates mesangial cell activation, glomerular and tubulointerstitial injury, and reduces proteinuria associated with IgAN¹⁶-¹⁸

Atrasentan has demonstrated clinically significant and sustained proteinuria reduction with an acceptable safety profile in over 5,100 patients with DKD¹⁹-²⁰

Interim results from the IgAN cohort of the ongoing AFFINITY study (NCT04573920) demonstrate that atrasentan is generally well-tolerated and results in a mean 54.7% reduction in proteinuria at Week 24 (N=19; ASN 2022, TH-PO497)

The ongoing ALIGN study (NCT04573478) is a global phase 3, randomized, double-blind, placebo-controlled study of atrasentan in patients with IgAN who are at high risk of kidney function loss

The primary endpoint is change in proteinuria from baseline at Week 24. Additional endpoints include safety and tolerability, and quality of life.

Key Secondary endpoint is change in eGFR from baseline at week 136.

Approximately 320 patients will be enrolled across North America, South America, Europe, and Asia-Pacific

Major inclusion criteria:
- Biopsy-proven IgAN with total protein excretion ≥1 g per 24 hrs and eGFR ≥30 mL/min/1.73 m²
- Receiving max-tolerated and optimized dose of RASI for ≥12 weeks prior to screening; a limited number of patients (up to 5%) that are unable to tolerate RASI therapy may be enrolled
- An additional stratum of up to 64 patients receiving a stable dose of SGLT2i for at least 12 weeks will be enrolled

Reference

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