A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Atrasentan in Patients with IgA Nephropathy - The ALIGN Study

**IgA and the Endothelin Pathway**

- IgA nephropathy (IgAN) is the leading cause of primary glomerulonephritis, with a global incidence of 2.5 per 100,000 individuals per year\(^1\).
- Approximately 30-45\% of IgAN patients progress to end-stage kidney disease (ESKD) over a period of 20-25 years\(^2,4\).
- Proteinuria is strongly associated with kidney disease progression in IgAN\(^2,7\) and treatments that reduce proteinuria result in improved clinical outcomes in IgAN\(^8-9\).

**Atrasentan**

Blockade of the ET\(_A\) receptor with atrasentan, a potent and selective ET\(_A\) antagonist, represents a potential approach to reduce proteinuria and preserve kidney function in IgAN\(^15\).

In preclinical studies, atrasentan attenuates mesangial cell activation, glomerular and tubulointerstitial injury, and reduces proteinuria associated with IgAN\(^16-18\).

**The ALIGN Study**

- **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 m\(^2\)
    - 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

- **The primary endpoint** is change in proteinuria from baseline at Week 24.
- **Key Secondary endpoint** is change in eGFR from baseline at week 136

**References**


**Modified from Liu et al, 2016, Nat Rev Dis Primers**

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