ASSIST Study Design: A Randomized, Double-blind, Placebo-controlled, Crossover Study of Atrasentan in Patients with IgA Nephropathy on SGLT2i

**Background**

Glomerular Disease and Proteinuria

- **IgA nephropathy (IgAN)** is the leading cause of primary glomerulonephritis, with approximately 30-45% of IgAN patients progressing to ESKD over a period of 20-25 years.1-4
- **Proteinuria is the strongest predictor of disease progression in IgAN.**1,5-6
- Endothelin A (ETₐ) receptor activation may contribute to mesangial cell activation, proteinuria, kidney inflammation and fibrosis in IgAN (Figure).7,8

Atrasentan* and SGLT2i

Atrasentan, a potent and selective ETₐ antagonist, has potential to reduce proteinuria and preserve kidney function in IgAN.

- Interim results of a phase 2, open-label study in patients with IgAN (AFFINITY, NCT04573920) demonstrated that atrasentan was well tolerated and resulted in clinically meaningful and sustained proteinuria reductions in patients receiving a maximally tolerated and optimized dose of a RAS inhibitor.9
- Sodium glucose cotransporter-2 inhibitors (SGLT2is) are approved for use in adults with CKD and CKD, 6-week treatment with atrasentan and SGLT2i in patients with IgAN with persistent proteinuria. Approximately 52 patients will be enrolled allowing for > 80% power to detect a ≥ 25% reduction for atrasentan relative to placebo in the primary endpoint.10
- Sodium glucose cotransporter-2 inhibitors (SGLT2is) are approved for use in adults with type 2 diabetes and CKD, 6-week treatment with atrasentan and SGLT2i in a small number of patients (n=14) further decreased albuminuria and decreased body weight, a surrogate for fluid retention, vs. atrasentan alone.11

**References**


**ASSIST Study Design**

**Study Objective:**

ASSIST™ (NCT05834738) is a randomized, double-blind, placebo-controlled, crossover study to evaluate the safety and efficacy of atrasentan vs. placebo in adults with IgAN on stable SGLT2i and RASI with persistent proteinuria. Approximately 52 patients will be enrolled allowing for > 80% power to detect a ≥ 25% reduction for atrasentan relative to placebo in the primary endpoint.

**Study Endpoints:**

- **Primary:** Change in proteinuria (UPCR from a 24-hour urine collection) from baseline to week 12
- **Key secondary:** In Treatment Period 2, the change in proteinuria (UPCR from a 24 hr urine collection) from baseline to week 24
- **Safety:** Type, incidence, severity, and relatedness of adverse events (AEs) and serious AEs
- **Exploratory:** In Treatment Period 2, change in eGFR from baseline to week 24

**Key inclusion criteria**

**All patients**

- Adults with biopsy-proven IgAN, not due to secondary causes
- Receiving max tolerated and stable RASI ≥ 12 weeks prior to screening
- eGFR ≥ 30 mL/min/1.73 m² (CKD-EPI) at screening

**SGLT2i stable**

- Receiving SGLT2i at stable dose ≥ 8 weeks prior to screening
- 24-hour total urine protein > 0.5 g/d at screening

**SGLT2i naive or non-stable**

- 24-hour total urine protein > 0.85 g/d at screening
- Complete 8-week run-in period on a stable and well tolerated dose of an SGLT2i
- After run-in:
  - 24-hour total urine protein > 0.5 g/d confirmed at end of run-in
  - eGFR of ≥ 30 mL/min/1.73 m² (CKD-EPI) at end of run-in

**Summary**

- Atrasentan, a potent and selective ETₐ antagonist, has potential to reduce proteinuria and preserve kidney function in IgAN.
- The ASSIST crossover study will evaluate the safety and efficacy of atrasentan in combination with SGLT2i in patients with IgAN with persistent proteinuria despite maximized RASI

The ASSIST study is currently enrolling For more information, scan QR or visit https://clinicaltrials.gov/ct2/show/NCT05834738

* Atrasentan is an investigational drug that has not been approved by regulatory authorities. Efficacy and safety have not been established. There is no guarantee that it will become commercially available for the use(s) under investigation.