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

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Abstract

Introduction:
IgA nephropathy (IgAN) is the most common primary glomerulonephritis. Up to 40% of patients with IgAN are at risk of progressing to end-stage kidney disease (ESKD). Proteinuria is the strongest predictor of progression. Endothelin A (ETA) receptor activation promotes proteinuria, along with kidney inflammation and fibrosis. Atrasentan, a potent and selective ETA antagonist, has been studied in >5,000 patients in a global phase 3 outcome clinical trial in patients with diabetic kidney disease who were on a maximum tolerated dose of RAS inhibitor (RASi). Results showed a 35% reduced risk of the primary composite outcome of doubling of serum creatinine or ESKD (95% CI: 0.49, 0.88; P = 0.005). The most common adverse event was fluid retention. Selective ETA blockade represents a promising approach to reduce proteinuria and preserve kidney function in patients with IgAN at high risk of progression.

Objective:
A global, phase 3, double-blind, placebo-controlled study is in progress to determine the effect of atrasentan on reduction of proteinuria and slowing down kidney disease progression in patients with IgAN at high risk of kidney disease progression.

Methods:
Approximately 320 patients across North America, South America, Europe, and Asia-Pacific with biopsy-proven IgAN will be randomized to receive 0.75 mg atrasentan or placebo daily for 12 weeks. Patients will continue receiving a maximally tolerated and stable dose of a RASi as a standard of care. The study will also include a final renal secondary outcome measure including:
- Rate of change in eGFR during 2 years on treatment at Week 12 through to Week 120
- Percent of patients achieving proteinuria <1 g/day at Week 24 and 40% reduction in proteinuria with from baseline at Week 130
- Percent of patients experiencing at least a 30% reduction in eGFR or reach ESKD during the study
- Percent of patients experiencing at least a 40% reduction in eGFR or reach ESKD during the study

Study Design
- Approximately 320 patients across North America, South America, Europe, and Asia-Pacific
- Atrasentan 0.75 mg daily by oral administration for 132 weeks following discontinuation of treatment.

Study Eligibility & Schema
- 18 years old and older
- Biopsy proven IgAN-no time limit on biopsy
- Age 18 and older
- No history of heart failure or a previous hospital admission for fluid overload
- No history of heart failure or a previous hospital admission for fluid overload
- No history of chronic kidney disease or a previous hospital admission for fluid overload

References