CHINOOK THERAPEUTICS

A Phase 3, Randomized, Double-Blind, Placebo-Controlled

Study of Atrasentan in Patients with IgA Nephropathy (The ALIGN Study)

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Study Background – Atrasentan

- Atrasentan is a potent endothelin A (ET_A) receptor antagonist (Ki = 0.034 nM) with >1,800 fold selectivity over ET_B (Ki = 63.3 nM).[1]
- Blocking ET_A leads to rapid and sustained reductions in proteinuria and has direct anti-inflammatory and anti-fibrotic effects.[2]
- Atrasentan has been studied extensively in more than 5,300 patients with type 2 diabetes and kidney disease (DKD), demonstrating clinically significant and sustained reductions in proteinuria when administered on top of a maximum tolerated dose of a RAS inhibitor (RASi).[3, 4]
- In a Phase 2 study in DKD (RADAR), atrasentan reduced urine albumin-creatinine ratios by an average of 35% (95% confidence interval [CI]: 24, 45; P = 0.001).[3]
- In a global Phase 3 outcome study in DKD (SONAR), the atrasentan treatment group demonstrated a 35% reduced risk of the primary composite outcome of doubling serum creatinine or end stage kidney disease (95% CI: 0.49, 0.88; P = 0.005).[4]

Figure 1.
UACR change in the percent geometric mean from baseline to recovery in RADAR

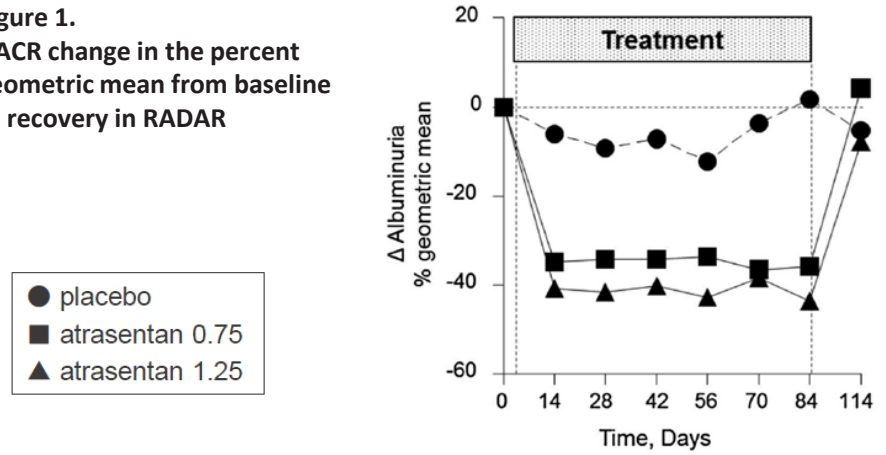
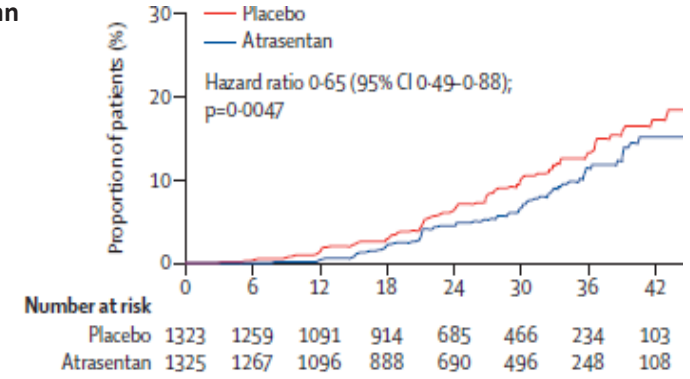
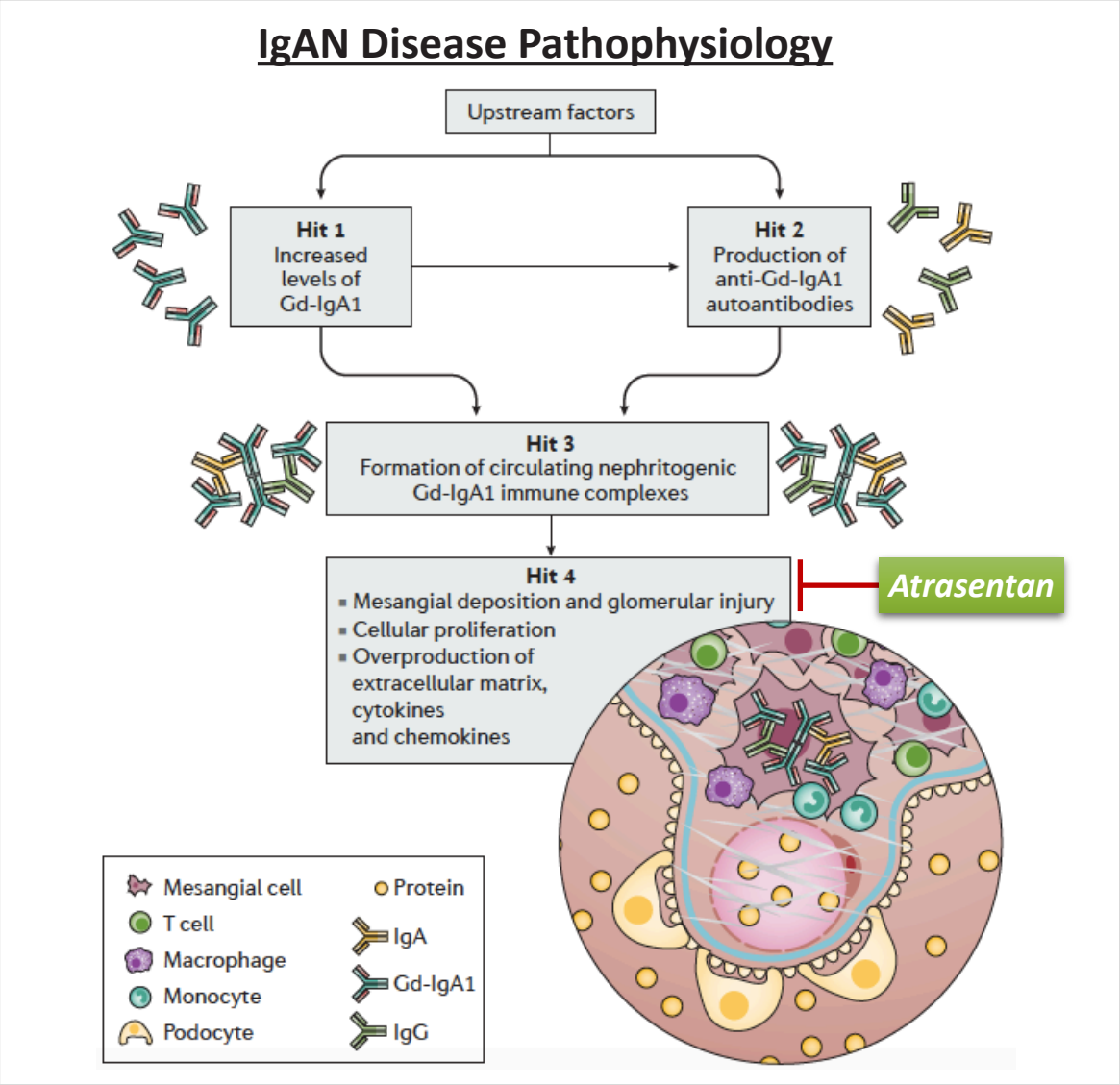


Figure 2.
Effects of atrasentan on the primary composite renal outcome in SONAR



Rationale for Atrasentan Use in IgA Nephropathy

- ET_A activation results in mesangial cell collagen and cytokine production[5], podocyte injury[6], proteinuria[4] and tubulointerstitial inflammation and fibrosis[7], all hallmark characteristics of progressive IgAN.
- The use of selective ET_A blockade in IgAN has been clinically validated in an exploratory trial of sitaxsentan demonstrating significant reduction in proteinuria and intraglomerular pressure in CKD patients on standard of care therapy[8]



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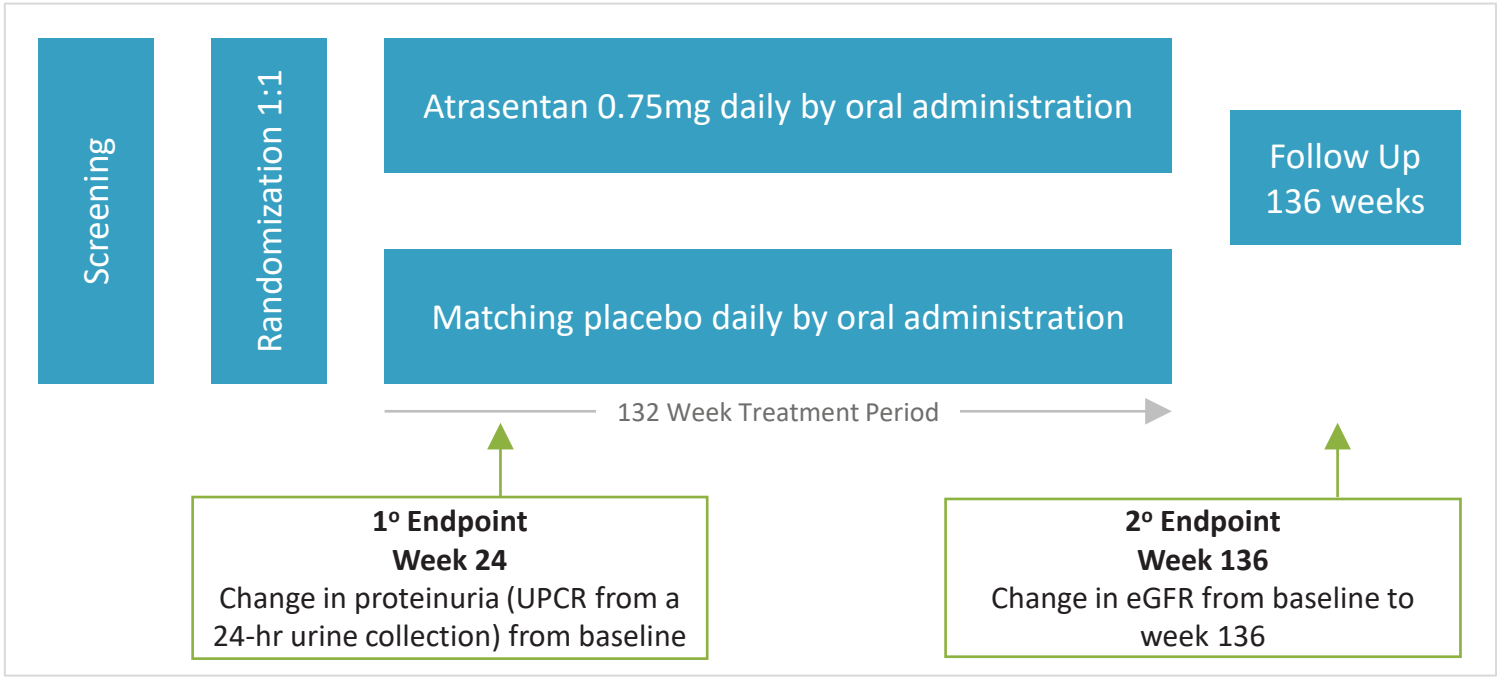
ALIGN Study Methods

The Phase 3 ALIGN trial will assess the efficacy, safety and tolerability of atrasentan in IgAN patients at risk of progressive kidney function loss, despite optimized RAS blockade

Key Eligibility Criteria (~320 patients)

- Age 18 and older
- Biopsy proven IgAN - no time limit on biopsy
- Stable, optimized dose of ACE inhibitor or ARB for ≥ 12 weeks or unable to tolerate RASi
- UPCR ≥1 g/g based on first morning void
- eGFR of at least 30 mL/min/1.73m^2
- No use of systemic immunosuppressants, such as steroids, for more than 2w in the past 3m
- No current diagnosis with another chronic kidney disease, including DKD
- No history of kidney or other transplantation
- No history of heart failure



- Virtual trial options may include telemedicine and home health nurse visits
- Provides a flexible solution for patients and clinicians in the era of COVID-19 and reduces the burden to patients for trial participation
- Open label extension study available to participants completing the study
- Currently selecting trial sites in North America, South America, Europe, and Asia-Pacific. Enrollment started in March 221

ClinicalTrials.gov Identifier: NCT04573478

References

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