Title (70 characters): **AFFINITY study: 1-year results of atrasentan in IgA nephropathy (IgAN)**

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Introduction (512 characters): Endothelin A (ET_A) receptor activation is one of the drivers of kidney dysregulation in glomerular diseases. Atrasentan, a potent, selective ET_A receptor antagonist, has been shown to reduce proteinuria and may preserve kidney function in patients with IgAN and other glomerular diseases. AFFINITY is a Phase 2, open-label basket study evaluating the efficacy and safety of atrasentan in patients with glomerular disease. Here, we present the results from the IgAN cohort through 1 year (52 weeks) of treatment.

Methods (434 characters): The IgAN cohort included adults with biopsy-proven IgAN, estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73m^2, urine protein-to-creatinine ratio (UPCR) ≥0.5 g/g and <1.0 g/g (first morning void), and on maximum tolerated/stable dose of renin angiotensin system inhibitors (RASi) for ≥12 weeks. Patients took 0.75 mg oral atrasentan daily for 52 weeks. The primary endpoint was change in 24-hour UPCR from baseline to Week 12.

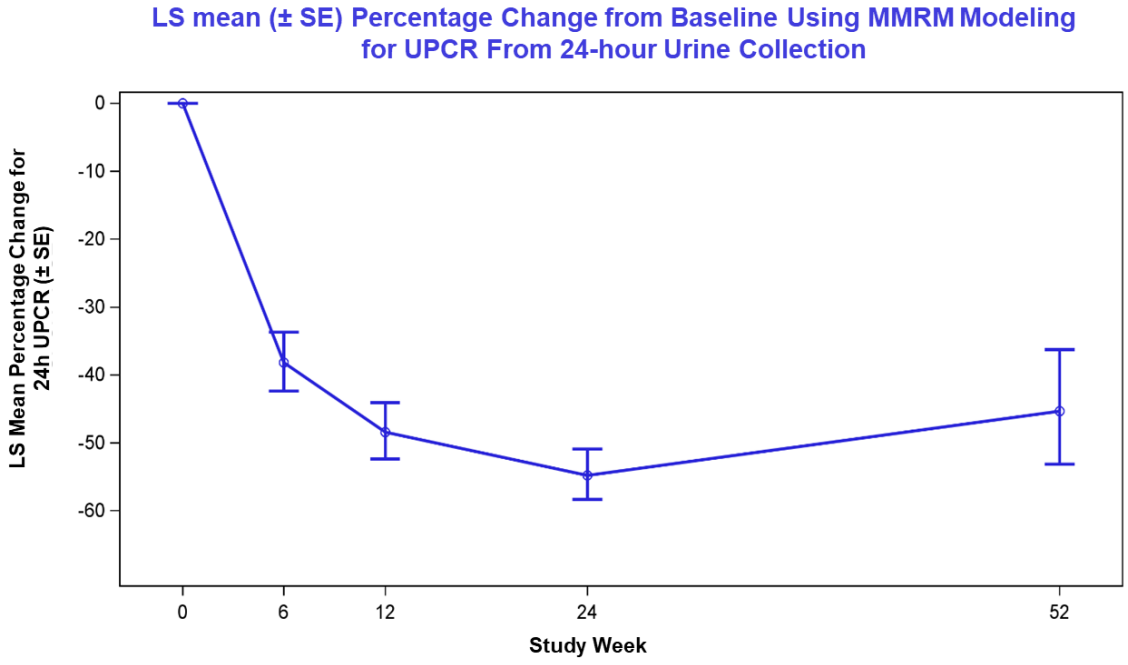
Results (996 characters): The IgAN cohort enrolled 20 patients. The median age was 44.5 years, 50% were women, 45% were White, and 45% were Asian. Overall, 19 patients completed 52 weeks of treatment. Baseline median 24-hour total urine protein was 1.2 g/d, 24-hour UPCR was 0.8 g/g, and eGFR was 46 mL/min/1.73 m^2. Systolic/diastolic blood pressure was 128/82 mmHg.

Reduction in 24-hour UPCR was evident by Week 6 (least squares mean percentage change from baseline -38.2% [95% confidence interval: -46.6, -28.5]), and sustained through Week 12 (-48.4% [-56.4, -39.0]) to Week 52 (-45.4% [-60.7, -24.0]; Figure). Atrasentan was well tolerated with no treatment-related serious adverse events (AEs) or deaths. AEs were seen in 18 (90%) patients; one patient discontinued treatment at Week 13 due to an AE of headache considered to be treatment related. There was no evidence of significant fluid retention (no clinically meaningful mean changes from baseline in body weight, brain natriuretic peptide, or blood pressure).

Conclusion (531 characters): Atrasentan, in addition to standard of care, was well tolerated and resulted in a clinically meaningful, stable reduction in proteinuria over 1 year of treatment, supporting its therapeutic potential in IgAN. The ongoing global Phase 3 ALIGN study (NCT04573478) is evaluating the effect of atrasentan on proteinuria and kidney function in patients with IgAN.

This abstract was also submitted for the ASN Kidney Week 2024: Barratt J, et al.: AFFINITY study: 1-year results of atrasentan in IgA nephropathy (IgAN) [Abstract FR-PO855].

Figure :



*n=12 patients due to a protocol amendment not requiring 24h urine collection at Week 52.
CI, confidence interval; LS, least squares; MMRM, mixed-model repeated measures; SE, standard error; UPCR, urine protein–creatinine ratio.
Efficacy analysis set (N=20). LSMean percent change and 95% CI were calculated by transforming the results on the natural log scale and used an MMRM model with unstructured variance-covariance.

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See full list here.

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