Title (57 characters): **A Phase 1/2 Trial of Zigakibart in IgA Nephropathy (IgAN)**

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Introduction (478 characters): IgAN is the leading cause of primary glomerulonephritis with limited treatment options. Zigakibart is a novel investigational, humanized monoclonal antibody that blocks A PRoliferation-Inducing Ligand (APRIL), a cytokine elevated in patients with IgAN, which promotes pathogenic galactose-deficient IgA1 production, leading to inflammation and kidney injury. Here, we present the 76-week results from Part 3 of ADU-CL-19, an ongoing Phase 1/2 trial (NCT03945318) of zigakibart.

Methods (691 characters): ADU-CL-19 Part 3 enrolled patients ≥18 years with biopsy-proven IgAN, total urine protein ≥0.5 g/24h or urine protein-to-creatinine ratio (UPCR) ≥0.5 g/g, estimated glomerular filtration rate (eGFR) ≥30 mL/min per 1.73 m^2, and on stable/optimized dose of renin-angiotensin system inhibitors (RASi) for ≥3 months prior to screening (or RASi intolerant). Patients received zigakibart 450 mg once every 2 weeks (Q2W) intravenously, transitioning to 600 mg Q2W subcutaneously at ≥24 weeks (Cohort 1) or 600 mg Q2W subcutaneously (Cohort 2) for up to 124 weeks. Key objectives include safety, tolerability, immunogenicity, pharmacodynamic effects, and preliminary effects on proteinuria and eGFR.

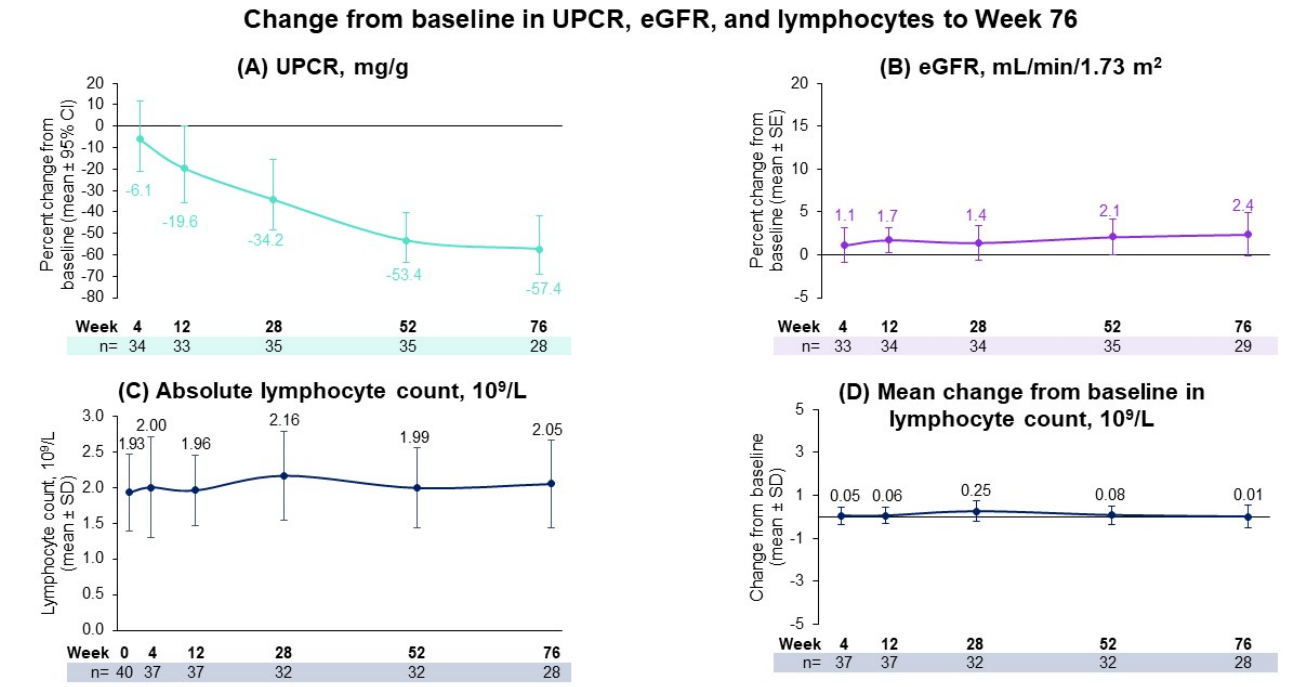
Results (805 characters): Overall, 40 patients were enrolled (n=10 [Cohort 1], n=30 [Cohort 2]); median age 38.5 years; 70% male; 60% White and 33% Asian. Zigakibart was well-tolerated with no adverse events (AEs) leading to study drug discontinuation or deaths. AEs were observed in 34 (85%) patients, most commonly infections (78%) of Grade 1 or 2 in severity; one patient experienced Grade 3 infections. One patient experienced infections deemed treatment related. IgA and IgM levels were reduced by 71% and 79% from baseline, respectively, through Week 76, while reduction in IgG was mild to modest (35%). At Week 76, proteinuria, measured as UPCR from a 24-hour collection, was reduced by 57% from baseline, and eGFR remained stable (Fig. 1A, 1B). Circulating lymphocyte counts remained stable through the study (Fig. 1C, 1D).

Conclusion (419 characters): Zigakibart was well tolerated and led to sustained, clinically meaningful reductions in proteinuria and eGFR stabilization in patients. The global Phase 3 BEYOND study (NCT05852938) is also evaluating the efficacy and safety of zigakibart in adults with IgAN.

Zigakibart WCN 2025 encore abstract

This abstract was also submitted for the ASN Kidney Week 2024: Barratt J, et al.: A Phase 1/2 Trial of Zigakibart in IgA Nephropathy (IgAN) [Abstract FR-PO856].

Figure:



Data cut-off: March 20, 2024. Data presented are mean percent change from baseline in natural log-transformed UPCR ± 95% CI for UPCR and mean percent change from baseline ± SE for eGFR. Biomarker analysis set used for UPCR and eGFR (N=35). Safety analysis set used for lymphocyte analyses (N=40). Baseline is defined as the last non-missing value collected prior to receiving first dose of study drug. All post-baseline assessments were considered, scheduled and unscheduled.

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See full list here.

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