IgA Nephropathy (IgAN) is the leading cause of primary glomerulonephritis worldwide with approximately 30-40% of IgAN patients progressing to ESKD over 20-25 years. Proteinuria is strongly associated with kidney disease progression in IgAN.

Zigakibart and the APRIL Pathway

Zigakibart is a novel, humanized monoclonal antibody that blocks APRIL (A Proliferation-inducing Ligand), a TNF superfamily cytokine that drives IgA class switching, plasma cell survival and the excess secretion of Gd-IgA.

In IgAN, elevated levels of APRIL are associated with increased Gd-IgA1 and proteinuria and lower eGFR. 1-4

Study Design and Baseline Characteristics

ADU-CL-19 (Part 3) is an ongoing phase 1/2 trial investigating zigakibart in patients with IgAN (NCT03945318).

Key objectives: Safety, tolerability, PK, immunogenicity, pharmacodynamic effects and preliminary effect on proteinuria.

Key eligibility criteria: Biopsy-proven IgAN within past 10 years; total protein excretion ≥ 0.5 g/day; OR UPCR ≥ 0.5 g/g based on 24-hour urine collection at screening; eGFR ≥ 30 mL/min per 1.73 m²; Stable/optimized dose of RASi for 3 months prior to screening (or intolerant to RASi).

Data was consistent between cohorts.

Results

Zigakibart treatment results in rapid and sustained reductions in IgA and pathogenic Gd-IgA1

• Similar reductions in IgA were also observed; reductions in IgG were more modest.

• Data was consistent between cohorts.

Repetitive reductions in immunoglobulins were maintained through study week 100 in cohort 1.

Conclusions

Interim data continues to demonstrate disease-modifying potential of zigakibart in patients with IgAN.

Zigakibart has been generally well-tolerated and directly targets IgAN pathogenesis by depleting Gd-IgA1, leading to sustained, clinically meaningful reductions in proteinuria in patients with IgAN.

The global phase 3 BEYOND registrational study (NCT05852938) will evaluate the efficacy of zigakibart vs. placebo on proteinuria, eGFR and composite clinical endpoints as well as key safety measures in adult patients with IgAN at risk of progressive kidney function loss.

Updated Interim Results of a Phase 1/2 Study of Zigakibart (BION-1301) in Patients with IgA Nephropathy

Jonathan Barratt,1 Laura Kostioga,2 Irfan Agha,2 Pablo Ruiz-Ramón1, Arvind Madan3, Hanna Thomas4, Bess Sorensen5, Jocelyn Leiske6, Zeeshan Khawaja7, Andrew King8, Charlotte Jones-Barton4

1. University of Leicester, Leicester, United Kingdom; 2. Colorado Kidney Care, Denver, United States of America; 3. Dallas Renal Group, Dallas, United States of America; 4. Florida Kidney Physicians, Tampa, United States of America; 5. Nephrology Associates of Central Florida, Orlando, United States of America; 6. Chinook Therapeutics, Seattle, United States of America

References


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