The BEYOND Trial: A Phase 3, Randomized, Double-blind, Placebo-controlled Study of Zigakibart in Adults with IgA Nephropathy

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**Background**

IgA Nephropathy (IgAN)
- IgAN is the leading cause of primary glomerulonephritis worldwide
- Approximately 30-45% of IgAN patients progress to ESKD over a period of 20-25 years
- Proteinuria is strongly associated with kidney disease progression in IgAN
- Treatments that reduce proteinuria result in improved renal outcomes in IgAN

Zigakibart* and the APRIL Pathway

Zigakibart is a novel, humanized monoclonal antibody that binds and blocks APRIL (a proliferation-inducing ligand)
- APRIL is a TNF superfamily cytokine that drives IgA class switching and survival of IgA-secreting plasma cells in IgAN, leading to elevated Gd-IgA1 and immune complex deposition in the mesangium
- Blocking APRIL with zigakibart is a potentially disease-modifying mechanism by decreasing Gd-IgA1 and preventing pathogenic immune complex formation
- Interim results from a Phase 1/2 trial of zigakibart in patients with IgAN (NCT03945318) demonstrate rapid and durable reductions in Gd-IgA1, along with sustained, clinically meaningful reductions in proteinuria and an acceptable safety profile

**References**


**Study Design**

**Study Objective:**

BEYOND™ (NCT05852938) is a Phase 3, randomized, double-blind, placebo-controlled study to evaluate the effect of zigakibart in adults with primary IgAN at risk of progressive kidney function loss. Approximately 272 patients will be enrolled across North America, South America, Europe and Asia-Pacific.

**Key Inclusion criteria:**
- Biopsy-proven IgAN within the past 10 years (not due to secondary causes)
- eGFR ≥ 30 ml/min/1.73m² (CKD-EPI)
- Total urine protein ≥ 1.0 g/day and UPCR ≥ 0.7 g/g at screening
- Receiving stable, maximally tolerated ACEi/ARB ≥ 12 weeks
- Antihypertensive agent and/or endothelin receptor antagonist ≥ 12 weeks
- eGFR < 15 mL/min/1.73m²
- 30% or 40% reduction in eGFR
- Polyuric dysfunction and proteinuria
- Tubulointerstitial injury and atrophy
- Type, incidence, severity and relatedness of adverse events (AEs) and serious AEs

**Study Endpoints**

- **Primary:** Change in proteinuria (UPCR from a 24-hour urine collection) from baseline to week 40
- **Key secondary:** Change in eGFR from baseline to week 104
- **Additional secondary:** Composite clinical outcome, including at least one of the following:
  - 30% or 40% reduction in eGFR
  - eGFR < 15 ml/min/1.73m²
  - Dialysis, kidney transplantation or all-cause mortality
  - Impact of zigakibart on disease biomarkers and health-related quality of life as well as analysis of zigakibart pharmacokinetics and immunogenicity

**Summary**

- Zigakibart provides a potentially disease-modifying approach for the treatment of IgAN that directly targets the disease pathogenesis by blocking excess production of Gd-IgA1.
- The phase 3 BEYOND registrational study will evaluate the effect 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.

For more information, scan QR or visit https://clinicaltrials.gov/ct2/show/NCT05834738

* Zigakibart (BION-1301) is an investigational drug that has not been approved by regulatory authorities. Efficacy and safety have not been established. There is no guarantee that it will become commercially available for the use(s) under investigation.

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