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

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Background

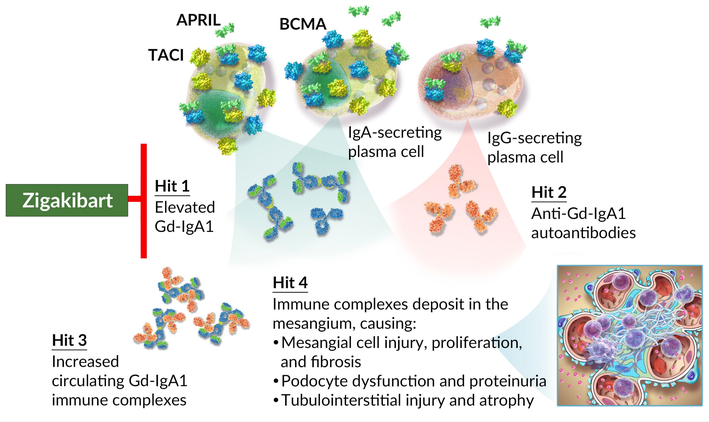
IgA Nephropathy (IgAN)

- IgAN is the leading cause of primary glomerulonephritis worldwide[1]
- Approximately 30-45% of IgAN patients progress to ESKD over a period of 20-25 years[2-5]
- Proteinuria is strongly associated with kidney disease progression in IgAN[2,6-7]; treatments that reduce proteinuria result in improved renal outcomes in IgAN[8-9]

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 (Figure)[10-12]
- 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[13]



References

1. Mcgrogan et al, 2011, NDT; 2. Reich et al, 2007, JASN; 3. Moriyama et al, 2014, PLOS ONE; 4. Rauen et al, 2020, Kidney Int; 5. Hastings et al, 2018, Kidney Int Rep; 6. Thompson et al, 2019, CJASN; 7. Barbour et al, 2019, JAMA Int Med; 8. Inker et al 2016 AJKD; 9. Inker et al, 2019, CJASN; 10. Suzuki et al, 2021, Sem Immunol; 11. Zhai et al, 2016, Medicine; 12. McCarthy et al, 2011, J Clin Invest; 13. J Barratt, et al. ASN Kidney Week 2022; FR-PO659

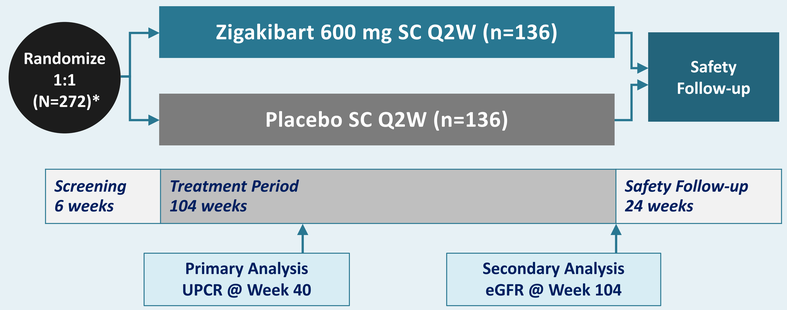
BEYOND Study Design

BEYOND™

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.



** Up to 20 additional patients with eGFR 20 to <30 mL/min/1.72m² will be enrolled in an exploratory cohort for a total n=292. SC, subcutaneous.*

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 prior to screening or intolerant
- May be on a stable dose of SGLT2i, mineralocorticoid receptor antagonist, and/or endothelin receptor antagonist ≥ 12 weeks prior to screening

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
Safety	➢ Type, incidence, severity and relatedness of adverse events (AEs) and serious AEs
Exploratory	➢ 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

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* 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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