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

CHINOOK THERAPEUTICS

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Background/Methods

IgA Nephropathy (IgAN)

- IgAN is the leading cause of primary glomerulonephritis worldwide[1] with approximately 30-45% of IgAN patients progressing to ESKD over 20-25 years[2-5].
- Proteinuria is strongly associated with kidney disease progression in IgAN[2,6-7].

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-IgA1[8]
- In IgAN, elevated levels of APRIL are associated with increased Gd-IgA1 and proteinuria and lower eGFR[9-12].

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 m^2; Stable/optimized dose of RASi for ≥ 3 months prior to screening (or intolerant to RASi).

Cohort 1 (n=10) → 450 mg Q2W IV → 600 mg Q2W SC, up to 124 weeks[†‖] → **Ongoing**

Cohort 2 (n=30) → 600 mg Q2W de novo SC, up to 124 weeks[‖] → **Ongoing**

†Patients transitioned to SC at ≥24 weeks
‖ Optional treatment extension available to both cohorts

Demographics	Cohort 1, n=10	Cohort 2, n=30***
Age, years, *mean (min, max)*	42 (27, 59)	42 (21, 74)
Sex, male, *n (%)*	9 (90)	19 (63)
Race, White, *n (%)*	10 (100)	14 (47)
Asian, *n (%)*	0	13 (43)
Black, *n (%)*	0	1 (3)
Missing, *n (%)*	0	2 (7)
Ethnicity, Hispanic, *n (%)*	2 (20)	4 (13)
Country, US, *n (%)*	10 (100)	21 (70)
Baseline characteristics	*Median (min, max)*	*Median (min, max)*
Time from biopsy, years	2.1 (0.2, 7.7)	3.1 (0.1, 8.3)
Blood pressure (mmHg), Systolic	127 (113, 133)	126 (106, 147)
Diastolic	83 (69, 88)	82 (57, 89)
eGFR (mL/min/1.73 m^2)[§]	69 (30, 122)	64 (30, 131)
24-hour urine protein excretion (g/day)	1.2 (0.7, 6.5)	1.1 (0.3, 7.0)
24-hour UPCR (g/g)	0.6 (0.4, 4.6)	0.8 (0.2, 3.2)
Renin-angiotensin system inhibitor use (%)	100%	100%
Efficacy population (including biomarkers)	**Cohort 1, n=8****	**Cohort 2, n=27****

[§] eGFR by CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration
** Two patients withdrew from study for reasons unrelated to study drug
***Three patients discontinued for not meeting eligibility criteria #6 (biopsy-confirmed IgAN)

References

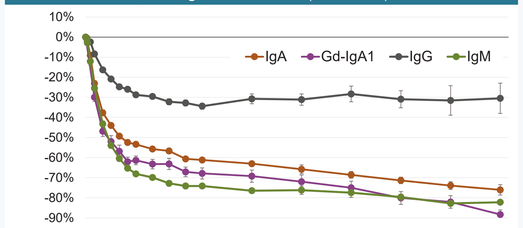
1. Mcgrogan et al, 2011, NDT; 2. Reich et al, 2007, JASN; 3. Moriyama et al, 2014, PLOS ONE; 4. Rauen et al, 2020, Kidney Int; 5. Hastings et al, 2018, Kidney Int Rep; 6. Thompson et al, 2019, CJASN; 7. Barbour et al, 2019, JAMA Int Med; 8. Suzuki et al, 2021, Sem Immunol; 9. Zhai et al, 2016, Medicine;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

Results

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

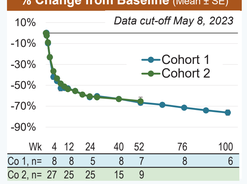
- Similar reductions in IgM were also observed; reductions in IgG were more modest.
- Data was consistent between cohorts.
- Reductions in immunoglobulins were maintained through study week 100 in cohort 1.

Immunoglobulins, Combined Cohorts
% Change from baseline (Mean ± SE)

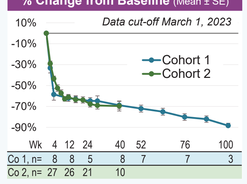


#IgA n=33 at week 12

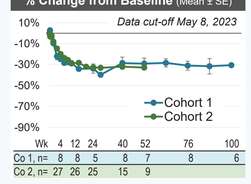
IgA
% Change from Baseline (Mean ± SE)



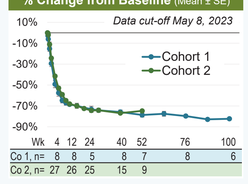
Gd-IgA1
% Change from Baseline (Mean ± SE)



IgG
% Change from Baseline (Mean ± SE)



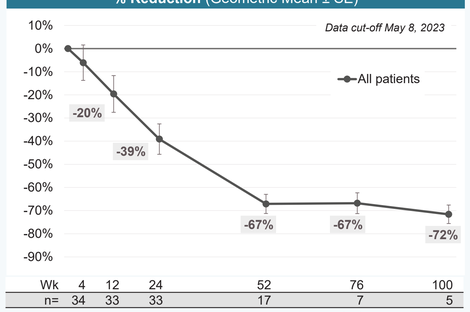
IgM
% Change from Baseline (Mean ± SE)



Zigakibart treatment results in sustained, clinically meaningful proteinuria reductions in patients with IgAN

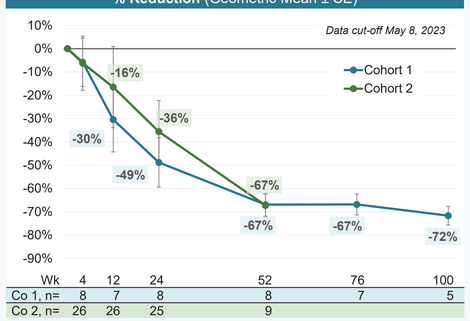
- Reductions in UPCR were seen by Week 12 in patients with IgAN across a wide range of baseline proteinuria levels.
- UPCR continued to decline through one year in both cohorts and was maintained through two years in Cohort 1, providing evidence of sustained efficacy.

UPCR, Combined Cohorts
% Reduction (Geometric Mean ± SE)



Median (range) baseline protein excretion: 1.1 (0.3, 7.0) g/day

UPCR, Cohort 1 and Cohort 2
% Reduction (Geometric Mean ± SE)



Median (range) baseline protein excretion:
Cohort 1, 1.2 (0.7, 6.5) g/day; Cohort 2, 1.1 (0.3, 7.0) g/day

Safety

Zigakibart is generally well-tolerated in patients with IgAN, with no ADAs observed and no reported deaths or AEs leading to discontinuation of study drug to date^

Safety, Cohorts 1 and 2:

- IgG < 3 g/L occurred in 2 patients; no infections were reported while IgG < 3 g/L.
- All infections have been Grade 1 or 2 in severity and only one subject had infections deemed treatment-related (Grade 1 viral upper respiratory tract infection and influenza).
- 8 subjects experienced injection site reactions. There were 16 ISRs reported from 875 SC doses (<2%). All ISRs were Grade 1 or Grade 2 in severity.
- One serious AE occurred (amnesia) that was not treatment-related and did not result in interruption of study drug.

AE Category (N=40)		n (%)
Treatment emergent AEs (TEAEs)	Subjects with any TEAE	32 (80)
	Subjects with Serious TEAE	1 (3)
	Subjects with any Infection TEAE	26 (65)
	Infection TEAE occurring in N>1 subject	
	COVID-19	10 (25)
	Upper Respiratory Tract Infection	9 (24)
	Influenza	4 (10)
	Urinary Tract Infection	3 (8)
	Asymptomatic COVID-19	2 (5)
	Bronchitis	2 (5)
	Nasopharyngitis	2 (5)
	Rhinitis	2 (5)
	Sinusitis	2 (5)
Treatment-related AEs	Subjects with any treatment-related AE	9 (23)
	Treatment-related AEs occurring in N>1 subject	
	Injection site erythema	4 (10)
	Fatigue	3 (8)

^Safety data cut-off May 8, 2023

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 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.

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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.