The World Congress of Nephrology (WCN) 2024
Buenos Aires, Argentina, April 13 – 16, 2024

Abstract submission deadline: October 31, 2023

Late-breaking abstract deadline: January 11, 2024 – a placeholder abstract must be submitted by the regular abstract deadline

[Notification of acceptance: December 14, 2023]

Character count: [Title: 156 + abstract: 3243] **3399/3400** characters [including spaces, excluding tables and graphs if inserted as an image, author names and affiliations, and keywords]

Tables and figures: Images must be in JPEG or PNG format (uploaded images cannot exceed 640w x 480h pixels and 1.5 Megabytes)

Standard of English: US

Encores: It is permissible to present encore abstracts if both the first and subsequent conferences allow this. However, abstract authors must declare this at the end of the abstract in the following way: This abstract was also submitted for the (insert meeting title) congress. By submitting the abstract to WCN'24, abstract authors declare that re-submitting the abstract is permitted by the organizers of the previous meeting

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Abstract title (156 characters)

SAFETY AND EFFICACY OF IPTACOPAN IN ADOLESCENT PATIENTS WITH IDIOPATHIC (PRIMARY) IMMUNE-COMPLEX-MEDIATED MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (IC-MPGN)

Abstract text (3243 characters)

Introduction: IC-MPGN is an ultra-rare, fast-progressing complement-mediated kidney disease characterized by immunoglobulin deposits in the kidneys, which may be idiopathic (primary) or secondary to chronic infections, autoimmune disorders, or monoclonal gammopathies. The clinical presentation and disease course are comparable to complement 3 glomerulopathy, also characterized by membranoproliferative histology. Dysregulation of the alternative pathway (AP) is strongly implicated in the pathogenesis of both glomerulonephritis entities including children and adults.

Primary IC-MPGN is frequently diagnosed by adolescence with no approved treatments that target the underlying complement-mediated pathophysiology. Given the fast-progressing nature of the disease, there is a high unmet need for treatment in patients with IC-MPGN. Iptacopan (LNP023) is an oral, highly potent proximal complement inhibitor that specifically binds to factor B and inhibits the AP.

Methods: This randomized, double-blind, placebo-controlled, pivotal Phase 3 study is the first to evaluate the efficacy and safety of iptacopan in patients with idiopathic IC-MPGN (see Figure). Approximately 68 patients will be randomized to a 1:1 ratio (iptacopan:placebo), including at least 10 adolescents aged 12–17 years, (recruited in cohorts of 5). All patients will have biopsy-confirmed idiopathic (primary) IC-MPGN (within 12 months [adults] and 3 years [adolescents]) prior to enrollment, proteinuria ≥1 g/g, and eGFR ≥30 mL/min/1.73 m^2 and will receive maximally tolerated renin-angiotensin inhibitors (e.g., ACEi/ARBs) and vaccination against encapsulated bacteria. Patients with an organ transplant, secondary IC-MPGN, kidney biopsy with >50% interstitial fibrosis/tubular atrophy, as well as those receiving systemic prednisone >7.5 mg/day or other immunosuppressants (except mycophenolic acids), within 90 days of iptacopan administration will be excluded.

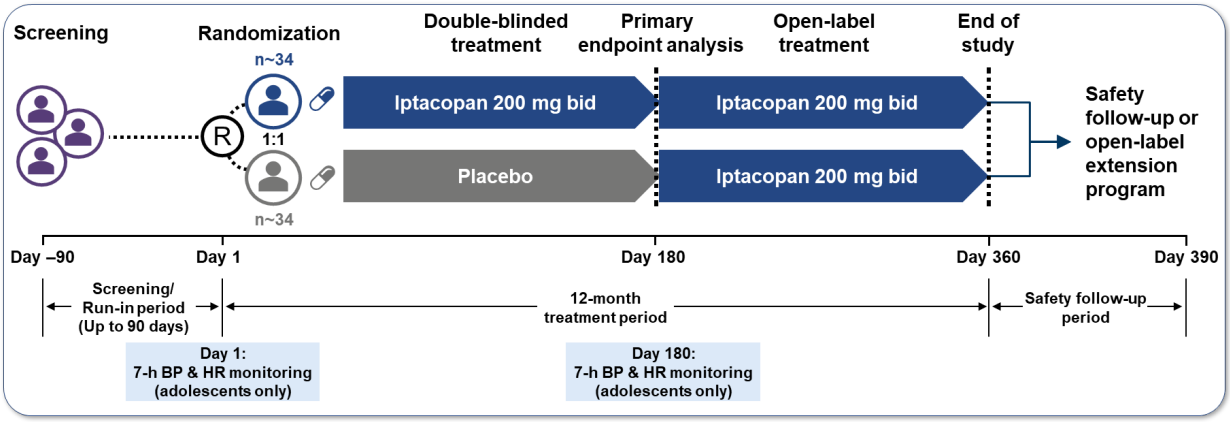
Study treatment phase comprises a 6-month double-blind period (either iptacopan 200 mg [2 x 100 mg capsules for adolescents] twice daily [bid] or placebo) followed by a 6-month open-label period (iptacopan 200 mg bid) for all study participants.

The primary objective is to demonstrate the superiority of iptacopan versus placebo on proteinuria reduction as measured by UPCR (24h urine collection) at 6 months. Key secondary endpoints will assess improvement in eGFR, proportion of patients who achieve a proteinuria–eGFR composite endpoint, and improvement in patient-reported fatigue. The safety objectives will evaluate the safety and tolerability of iptacopan in all patients. Adolescents will be evaluated for blood pressure and heart rate effects at the first open-label dosing. Supplementary cardiovascular safety surveillance will be carried out in these patients to assess the potential effect of iptacopan on blood pressure, heart rate, cardiac function and biomarkers of cardiac injury at study visits.

Results: The study has already started (NCT05755386) and is expected to start recruiting adolescent patients in 2024.

Conclusion: This study will provide evidence towards the efficacy and safety of iptacopan in adult as well as adolescent patients with idiopathic (primary) forms of IC-MPGN.

Figure: Study design and endpoints



Participants	Adults and adolescents aged 12–60 years with biopsy-confirmed native kidney IC-MPGN, UPCR ≥1 g/g, and eGFR ≥30 mL/min/1.73 m^2
Primary objective	To demonstrate the superiority of iptacopan vs. placebo in reducing proteinuria at 6 months
Secondary objectives	• To demonstrate the superiority of iptacopan vs. placebo in improving – eGFR – the proportion of participants achieving a composite renal endpoint (a stable or improved eGFR [≤15% reduction in eGFR] and a ≥50% reduction in UPCR compared with the baseline visit) – patient-reported fatigue • To perform cardiovascular surveillance (adolescents only) • To evaluate safety and tolerability

bid, twice daily; BP, blood pressure; eGFR, estimated glomerular filtration rate; HR, heart rate; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; UPCR, urine protein-to-creatinine ratio

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Key words (up to 5): iptacopan, immune complex-mediated membranoproliferative glomerulonephritis, IC-MPGN, clinical trial, Phase 3

Abstract Category:

- The Kidney Losing Function: Dialysis, CKD-MBD, anemia and interventional nephrology

Abstract topics:

- Chronic kidney disease complications
- Chronic kidney disease, experimental models, biomarkers, precision medicine
- Other CKD

See complete list of topics here

Transparency declaration and ethics statement:

This study was conducted according to International Council for Harmonization E6 Guidelines for Good Clinical Practice that have their origin in the Declaration of Helsinki.

Declaration of funding and interests:

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Nicholas Webb, UdayKiran Veldandi, Yaqin Wang, and Matthias Meier are employees and stockholders of Novartis.

David Kavanagh: scientific founder of and hold stocks in Gyroscope Therapeutics. He has received consultancy income from Gyroscope Therapeutics, Alexion Pharmaceuticals, Novartis, Apellis and Sarepta. His spouse works for GSK.

Andrew S Bomback: consulting honoraria from Achillion, Alexion, Chemocentryx, Novartis, Silence, Catalyst, and Principio.

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Marina Vivarelli: honoraria for advisory boards and consulting fees, participation in clinical studies sponsored by the following pharmaceutical companies: Achillion, Alexion, Apellis, Bayer, Catalyst, Novartis, Roche, Retrophin/Travere, GSK, BioCryst Pharmaceuticals, Chinook Therapeutics.