ISN **World Congress of Nephrology (WCN '25)**
February 6–9, 2025 | New Delhi, India

Abstract cover sheet	
Abstract short title	C3G Phase 2 ROE 33-month data (*encore of ERA 2024 abstract*)
Lead / presenting author	Carla M. Nester
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Submission deadline	September 4, 2024
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Proposed category and topic	Accepted abstracts will be presented as posters or e-posters at WCN'25 **Category:** • The Kidney Losing Function **Topic:** • (11) Other CKD
Keywords:	• C3 glomerulopathy • Phase 2 study • Glomerular diseases • Alternative complement pathway • Clinical trials
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ABSTRACT: 3,290/3,400 characters including spaces.

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UPDATE TO THE LONG-TERM SAFETY AND EFFICACY OF IPTACOPAN IN C3G: 33-MONTH EXTENSION STUDY DATA FROM PATIENTS ENROLLED IN A PHASE 2 STUDY

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Introduction: Complement 3 glomerulopathy (C3G), due to overactivation of the alternative complement pathway (AP), is an ultra-rare primary glomerulonephritis. Iptacopan (LNP023) is an oral, proximal complement inhibitor that specifically targets factor B and inhibits the AP. We previously reported the primary endpoint data from the Phase (Ph) 2 extension study (NCT03955445), showing proteinuria reduction (57% [p<0.0001]) and estimated glomerular filtration rate (eGFR) improvement (by +6.83 mL/min/1.73 m^2 [p=0.0174]) from baseline, following 12 months (M) of treatment with iptacopan in patients with C3G. Here we present further long-term efficacy and safety data from patients with native C3G and recurrent C3G (post-kidney transplantation), who completed 33M of treatment with iptacopan (NCT03955445).

Methods: Adults with native C3G disease (Cohort A) or C3G recurrence post-transplantation (Cohort B) received iptacopan 200 mg twice-daily (bid) for at least 12 weeks in the Ph2 study (NCT03832114) before entering the open label extension study (NCT03955445). Long-term efficacy was assessed by a number of renal endpoints, including a 2-component composite renal endpoint (eGFR stability [≤10% reduction] and ≥50% proteinuria reduction). Long-term safety and tolerability of iptacopan was continually monitored.

Results: Of 27 patients completing the Ph2 study (NCT03832114), 26 (16 Cohort A, 10 Cohort B) entered the extension study treatment with iptacopan 200 mg bid; 22 patients (14 Cohort A, 8 Cohort B) completed the 33M visit (i.e., 3M in the Ph2 study and 30M in the extension study). In Cohort A, 42.9% of

patients met the 2-component composite renal endpoint criteria at 33M. Proteinuria (first morning void [FMV] urine protein–creatinine ratio [UPCR]) was reduced by 41% (p=0.0097) compared to baseline. eGFR stabilized or improved in most patients (10/14) over time and change from baseline at the 33M time-point was -3.18 mL/min/1.73 m^2 (p=0.3512). C3 levels increased by 275% (p<0.0001) from baseline. In Cohort B, eGFR change from baseline at the 33M time-point was -6.34 mL/min/1.73 m^2 (p=0.0571), and C3 levels increased by 102%. Baseline proteinuria values (FMV UPCR) were within the normal range for most participants in Cohort B and remained so during iptacopan treatment. Iptacopan was generally well-tolerated, and most adverse events were of mild severity in both cohorts. Biomarkers demonstrated substantial AP inhibition.

Conclusion: Long-term treatment with iptacopan was associated with sustained reduction in proteinuria in patients with native C3G (Cohort A), and stabilization of eGFR. These improvements in kidney function were associated with substantial inhibition of the AP leading to normalization of serum C3. Iptacopan a favorable safety and tolerability profile in the long term, in patients with C3G, including those with recurrence post-transplantation on top of broad triple immunosuppression. The ongoing Ph3 APPEAR-C3G study (NCT04817618) is evaluating the efficacy and safety of iptacopan in patients with C3G.

This abstract was also submitted to the ERA Congress in 2024. Nephrology Dialysis Transplantation, Volume 39, Issue Supplement_1, May 2024, gfae069-0140-277. Encore submission of this abstract to WCN 2025 is permitted by the organizers of the original meeting (ERA 2024).