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

Abstract cover sheet	
Abstract short title	APPEAR-C3G: 12 months results (*encore of ASN 2024 abstract*)
Lead / presenting author	Carla M Nester
Target congress	ISN World Congress of Nephrology (WCN'25) February 6–9 2025 | New Delhi, India
Submission deadline	September 4, 2024
URL to instructions for authors	https://www.theisn.org/wcn/abstracts/#abstract-submission-instructions
Proposed category and topic	Accepted abstracts will be presented as posters or e-posters at WCN'25 **Category:** • The Kidney Losing Function **Topic:** • (5) Chronic Kidney Disease Diagnosis, Classification and Progression • (6) Chronic Kidney Disease Complications • (8) Chronic Kidney Disease, Experimental Models, Biomarkers, Precision Medicine
Character count limit	**Limit:** 3,400 characters including spaces. • Tables and graphs do not count as characters if inserted as an image. Abstract authors/co-authors' names, affiliations, and keywords do not count towards the 3,400-character allowance.
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ABSTRACT: 2,886/3,400 characters including spaces.

Title: (120 characters including spaces)

EFFICACY AND SAFETY OF IPTACOPAN IN PATIENTS WITH C3 GLOMERULOPATHY: 12-MONTH RESULTS FROM THE PHASE 3 APPEAR-C3G STUDY

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Introduction: Complement 3 glomerulopathy (C3G), is an ultra-rare primary glomerulonephritis caused by the overactivation of the alternative complement pathway (AP). Iptacopan (LNP023) is an oral, proximal complement inhibitor that specifically targets factor B and inhibits the AP. Here we present the 12-month data from the pivotal APPEAR-C3G Phase 3 study, conducted to evaluate the efficacy, safety, and tolerability of iptacopan compared to placebo on top of supportive care in patients with native C3G.

Methods: APPEAR-C3G (NCT04817618) was a multicenter, randomized, double-blind, placebo-controlled, pivotal Phase 3 study that included adult patients with biopsy confirmed C3G. The study comprised 3 periods with a screening period (≤90 days), followed by randomized double-blinded treatment with iptacopan 200 mg b.i.d. vs. placebo (6 months) and open-label iptacopan treatment (6 months), as previously described.[1]

Results: 74 patients were randomized 1:1 to either iptacopan (n=38) or placebo (n=36). Baseline pt demographics were generally balanced; the iptacopan arm exhibited a more severe disease phenotype. 43 (58.1%) patients in the iptacopan (n=22) and placebo (n=21) arms completed 12 months treatment at data cut-off (when all patients completed 6 months of treatment). The study met its primary endpoint, demonstrating a statistically significant reduction in 24h UPCR with iptacopan treatment at 6 months (35.1%, 1-sided p=0.0014, 95% CI:13.8%, 51.1%) vs. placebo, sustained up to 12 months (**Figure**).

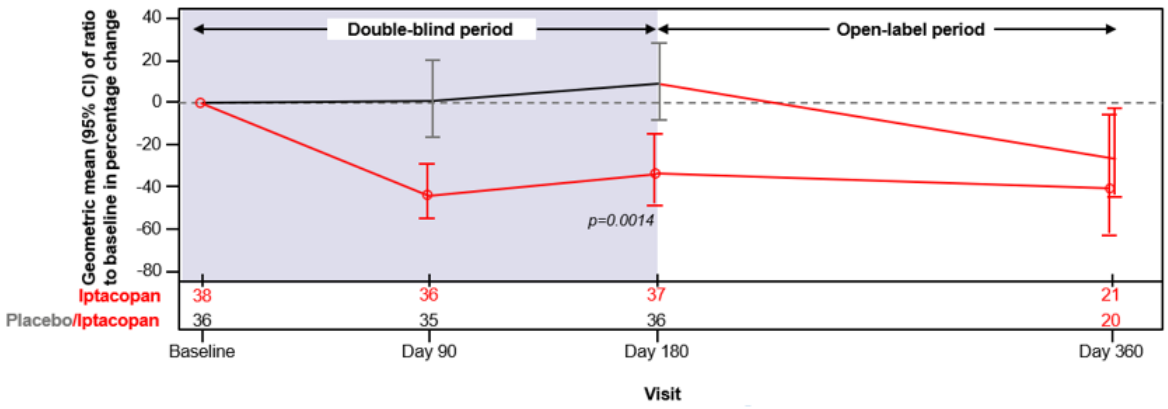
Iptacopan showed a sustained improvement in patients meeting the composite renal endpoint (≥50% reduction UPCR + ≤15% reduction in eGFR at 12m), 43.5% (iptacopan vs. placebo) and 25.0% (switched to iptacopan). Iptacopan led to improvements in the trajectory of eGFR compared to patients historical eGFR decline. Iptacopan demonstrated a favorable safety profile with no new safety signals identified. Other 12-month primary and key secondary endpoints will be presented.

Conclusion: Iptacopan demonstrated a significant and clinically meaningful proteinuria reduction on top of supportive care at 6 months in the APPEAR-C3G study; sustained up to 12 months. Iptacopan was well tolerated with a favorable safety profile in C3G patients.

This abstract was also submitted for the ASN Congress in 2024.

Reference: 1. Bomback AS, et al. *Kidney Int Rep*. 2022;7:2150–9

Figure. Proteinuria reduction (UPCR 24h) sustained to 12m



Full analysis set. Note that there was one intercurrent event of increasing corticosteroid dose on Day 106 in the iptacopan group
Robustness of primary endpoint results demonstrated by consistency of results across sensitivity analyses.

Author disclosures

Carla M Nester: clinical trial research support from Biocryst, Achillion, Novartis, Apellis, consulting fee from Silence Therapeutics; and participated on data safety monitoring board of Kira

Richard J H Smith: research funding from NIH, consultant for 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.

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Matthias Meier, Yaqin Wang, Nicholas J.A. Webb, Angelo J. Trapani, Induja Krishnan: employees and stockholders of Novartis

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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