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Safety and Efficacy of Iptacopan in Patients with IgA Nephropathy (IgAN) with Baseline eGFR 20-<30 mL/min: Phase 3 APPLAUSE-IgAN Subcohort Results

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Introduction: Treatment of patients with advanced IgAN and estimated glomerular filtration rate (eGFR) <30 mL/min/1.73m^2 is limited to supportive care. Iptacopan specifically binds Factor B and inhibits the alternative complement pathway (AP), which is involved in IgAN pathogenesis. We present results from the APPLAUSE-IgAN subcohort with baseline eGFR 20–<30 mL/min/1.73 m².

Methods: APPLAUSE-IgAN (NCT04578834), a Phase 3, randomized, double-blind, placebo-controlled trial, enrolled adults with biopsy-confirmed IgAN with proteinuria ≥1 g/g despite stable supportive therapy. Patients were randomized 1:1 to iptacopan 200 mg or placebo twice daily for 24 months while remaining

on supportive therapy. Safety, efficacy, and pharmacokinetics (PK) of the low baseline eGFR subcohort were descriptively assessed at Month 9 at time of interim analysis (IA).

Results: The analysis included 27 patients (13 iptacopan, 14 placebo) randomized to the low eGFR cohort at time of IA. Baseline demographic and disease characteristics were similar for iptacopan vs placebo: median (IQR) 24h urine protein–creatinine ratio (UPCR) 2.1 (1.7-2.5) vs 1.8 (1.4-2.4) g/g; mean (SD) eGFR 24.7 (2.8) vs 25.8 (2.9) mL/min/1.73m^2. All patients received maximally approved/tolerated RASi doses. Serious adverse events (AEs) occurred in 2 patients in each arm and AEs leading to treatment discontinuation in 1 patient in each arm. The most frequent AE was COVID-19 (23.1% iptacopan, 35.7% placebo). Proteinuria (24h-UPCR and 24h urine albumin–creatinine ratio) decreased from baseline to Month 9 in the iptacopan arm but increased in the placebo arm (**Table**). At Month 9, the relative reduction in median 24h-UPCR was 34.5% for iptacopan vs placebo, consistent with the primary analysis. PK data will be presented.

Conclusion: In patients with baseline eGFR 20–<30 mL/min/1.73m², iptacopan was well tolerated with a favorable safety profile, and decreased proteinuria vs placebo (34.5% at Month 9). Iptacopan may therefore represent a potential treatment option for patients with low eGFR.

This abstract was also submitted for the ASN Kidney Week, 23–27 October 2024, San Diego, CA, USA.

Table. Descriptive statistics of proteinuria outcomes in the low eGFR population

Proteinuria measure	Unit	Iptacopan (n=11)*		Placebo (n=10)*	
		Baseline	Month 9	Baseline	Month 9
24h-UPCR (g/g)	Median (IQR)	2.07 (1.68, 2.54)	1.49 (1.16, 2.24)	1.78 (1.40, 2.17)	2.06 (1.39, 3.38)
	Median (IQR) % reduction	-	28 (–3, 35)	-	–10 (–56, 19)
24h-UACR (g/g)	Median (IQR)	1.66 (1.26, 2.08)	1.17 (0.90, 1.60)	1.57 (1.09, 1.80)	1.71 (1.05, 2.50)
	Median (IQR) % reduction	-	27 (–3, 45)	-	–8 (–46, 26)

*Patients with available measurements at baseline and Month 9. 24h-UACR, urine albumin–creatinine ratio from 24h collection; 24h-UPCR, urine protein–creatinine ratio from 24h collection; IQR, interquartile range.