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Abstract specifications for WCN 2025

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Abstract topic: Clinical Glomerulonephritis

Character count: 1708/3400 characters [including spaces, excluding tables and graphs if inserted as an image, author names and affiliations, and keywords]

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Standard of English: US or UK (Current: US)

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Efficacy and safety of iptacopan in patients with IgA nephropathy (IgAN): Interim analysis (IA) of the Phase 3 APPLAUSE-IgAN study

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Introduction: There is growing evidence for involvement of the alternative complement pathway in IgAN pathogenesis. No currently approved therapies specifically target this pathway.

Methods: APPLAUSE-IgAN (NCT04578834) is a Phase 3, randomized, double-blind, placebo-controlled study of iptacopan on top of optimized supportive care in patients with biopsy-confirmed IgAN and proteinuria ≥1 g/g by UPCR from 24h urine collection (UPCR-24h) despite maximally tolerated RAS inhibition for ≥3 months. Patients were randomized 1:1 to iptacopan 200 mg or placebo twice daily.

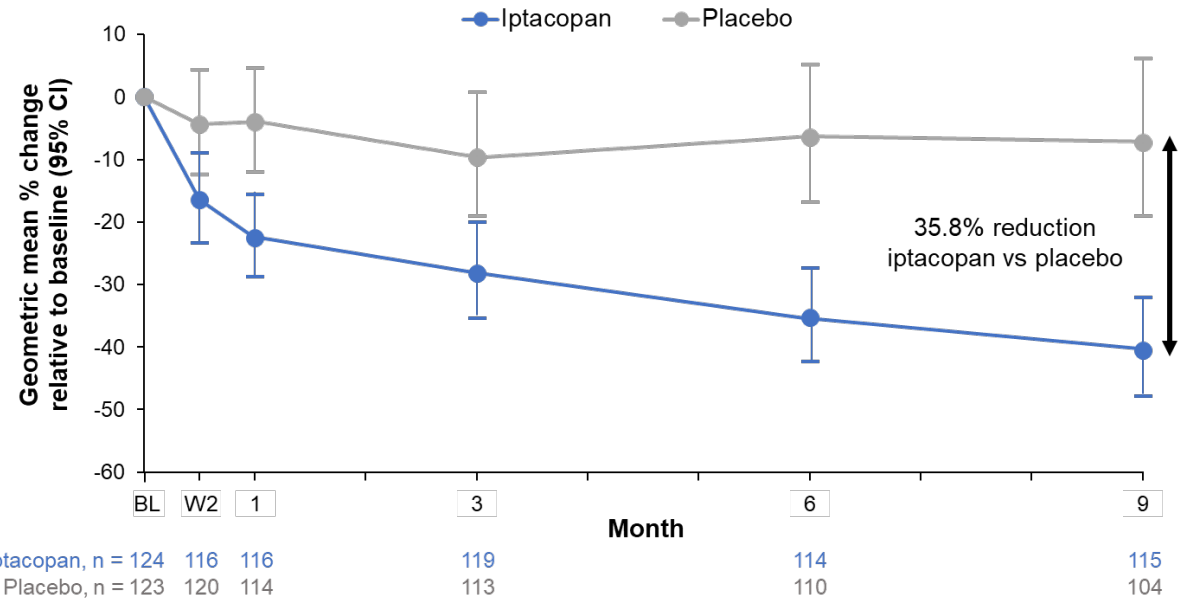
Results: Efficacy analyses at the pre-specified IA included 125 patients each for iptacopan and placebo; safety analyses included 222 and 221 patients, respectively. Baseline characteristics were balanced across treatment arms. Iptacopan was superior to placebo in reducing UPCR-24h from baseline at Month 9: 38.3% (95% CI 26.0%–48.6%; 1-sided $p<0.0001$) reduction relative to placebo. UPCR from first morning void decreased as early as Week 2 and continued to decrease to Month 9: 35.8% (95% CI 22.6%–46.7%) reduction relative to placebo at Month 9 (**Figure**). Approximately twice as many patients on iptacopan reached UPCR-24h <1 g/g at Month 9 vs placebo (marginal proportion 42.5% [95% CI 34.5%–50.5%] vs 21.9% [95% CI 14.8%–29.0%], respectively). Iptacopan was well tolerated (treatment

was discontinued due to AEs in 2.7% patients in each arm) and the infection rate in the iptacopan arm did not exceed that of placebo.

Conclusion: APPLAUSE-IgAN demonstrated superiority of iptacopan vs placebo in proteinuria reduction at Month 9, with early onset and consistency of effect. Iptacopan was well tolerated with a favorable safety profile.

This abstract was also submitted for the National Kidney Foundation Spring Clinical Meetings, 14–18 May 2024, Long Beach, CA, USA.

Figure: Geometric mean % change relative to baseline in UPCR FMV by treatment arm and timepoint



n = number of patients with values non-missing and not imputed as per the intercurrent event handling strategy.
Log transformed ratio to baseline was analyzed using MMRM including treatment, timepoint (as categorical variable), randomization strata as fixed effects, treatment*timepoint and timepoint*log(baseline UPCR FMV) as interaction terms and baseline log(UPCR FMV) as a fixed covariate. Results were back-transformed to geometric means and are presented on the percentage scale.
BL, baseline; CI, confidence interval; FMV, first morning void; MMRM, mixed model for repeated measures; UPCR, urine protein–creatinine ratio; W2, Week 2.