The World Congress of Nephrology (WCN) 2023
Bangkok, Thailand, March 30 – April 2, 2023

Abstract title:

An open-label, non-randomized extension study to evaluate the long-term efficacy, safety and tolerability of LNP023 in subjects with C3 glomerulopathy: Interim analysis of a Phase 2 study

Abstract text:

Introduction:

Iptacopan (LNP023) is an oral, first-in-class, selective inhibitor of factor B, a key component of the alternative complement pathway (AP). We have previously reported data from a Phase 2 study in native and recurrent Complement 3 glomerulopathy (C3G) showing that 12 weeks iptacopan treatment results in a 45% reduction in proteinuria in native C3G (NCT03832114). Here we present the effects of 12 months iptacopan treatment.

Methods:

Adults with native (Cohort A) or recurrent C3G post kidney transplant (Cohort B) received iptacopan for at least 12 weeks before entering this Phase 2 extension trial (NCT03955445). The primary efficacy objective was to assess the effect of iptacopan on a composite endpoint of 1) stable/improved (≤10% reduction from baseline) estimated glomerular filtration rate (eGFR), 2) ≥50% reduction from baseline in urine protein:creatinine ratio (UPCR), and 3) ≥50% increase from baseline in serum C3 after 12 months treatment.

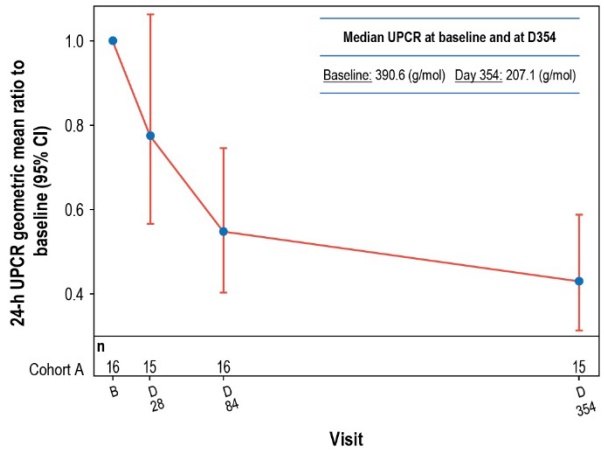
Results:

Of 27 patients completing the 12 week Phase 2 study, 26 (16 Cohort A, 10 Cohort B) entered the extension for treatment with iptacopan 200 mg b.i.d. 53% of Cohort A patients met the composite renal endpoint criteria at 12 months; proteinuria was reduced by 57% ($p<0.0001$; Fig 1), eGFR increased by 6.83 mL/min/1.73 m^2 ($p=0.0174$; Fig 2) and C3 increased by 253% ($p<0.0001$). eGFR was stable and C3 levels increased by 96% in Cohort B. Proteinuria reduction was not assessed in Cohort B, as median baseline proteinuria was normal (18.4 g/moL). Iptacopan was generally well-tolerated and most adverse events were of mild severity in both cohorts. Biomarkers demonstrated substantial AP inhibition.

Conclusion:

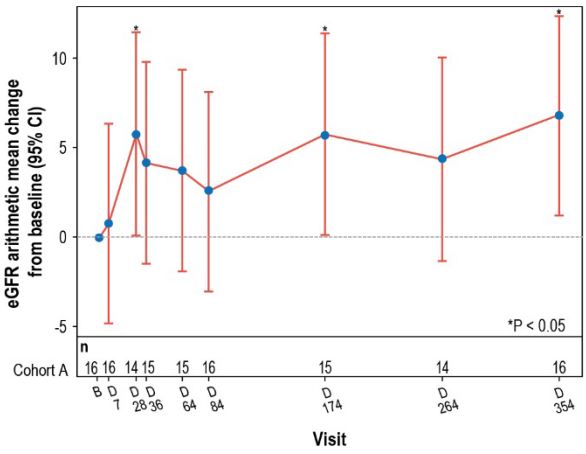
Long-term treatment with iptacopan results in further proteinuria reduction and eGFR improvement beyond that previously reported following 12 weeks treatment in native C3G. Stable eGFR was seen in recurrent C3G, with stable increases in serum C3 levels found in both cohorts. The ongoing Phase 3 APPEAR-C3G (NCT04817618) study is evaluating the efficacy of iptacopan in native C3G patients.

Figure 1: Primary endpoint Cohort A – UPCR



57% reduction in UPCR **(p<0.0001)**

Figure 2: Primary endpoint Cohort A – eGFR



+6.83 mL/min/1.73 m^2 **(p=0.0174)** increase in eGFR

Key words: C3G, glomerular diseases, clinical trials, alternative complement pathway

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Abstract Category:

Option 1) Kidney Failure (Former ESKD), incl. Dialysis, Transplantation, Conservative Care

Option 2) Chronic Kidney Disease, Hypertension, Diabetes and CVD

Abstract topic: 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:

This analysis was funded by Novartis Pharma AG.

Professional medical writing assistance was provided by Nupur Chaubey at Novartis [Healthcare Pvt. Ltd., Hyderabad, India], funded by Novartis Pharma AG.

[**Author disclosures** to be added]