EVALUATION OF IPTACOPAN IN ATYPICAL HEMOLYTIC UREMIC SYNDROME (aHUS): DESIGN AND RATIONALE OF THE PHASE 3 OPEN-LABEL MULTICENTER APPELHUS STUDY

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Introduction

Atypical hemolytic uremic syndrome (aHUS) is a rare, progressive, and life-threatening form of thrombotic microangiopathy (TMA) caused by dysregulation of the alternative complement pathway (AP). Complement inhibition is an attractive therapeutic target in aHUS although current approved therapies require intravenous administration and increase the risk of infection by encapsulated organisms. Iptacopan (LNP023) is an oral, first-in-class, highly potent, selective inhibitor of factor B, a key regulator of the AP. In Phase 2 studies in IgA nephropathy, paroxysmal nocturnal hemoglobinuria and C3 glomerulopathy, iptacopan inhibited the AP, showed clinically relevant benefits, and was well tolerated. Iptacopan thus has the potential to become an effective and safe treatment for aHUS, with the convenience of oral administration.

Methods

APPELHUS (NCT04889430) is a multicenter, single-arm, open-label, Phase 3 study evaluating the efficacy and safety of iptacopan 200mg twice daily in adult aHUS patients (N=50) naïve to complement inhibitor therapy. Eligible patients must have evidence of TMA (platelet count $<150\times10^9$/L, LDH ≥1.5×ULN, hemoglobin ≤LLN, serum creatinine ≥ULN). Primary endpoint: proportion of patients achieving complete TMA response without the use of plasma exchange/plasma infusion or anti-C5 antibody during 26 weeks of treatment. This treatment period is followed trial extension of 26 weeks of iptacopan treatment. Upon completion of this, eligible patients may be offered post-trial access to iptacopan.

Results

The study is currently recruiting in India and 13 other countries worldwide.

Conclusion

APPELHUS will determine if iptacopan is safe and efficacious in patients with aHUS.

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Keywords

LNP023, iptacopan, aHUS, alternative pathway, APPELHUS.

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