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Evaluation of iptacopan in atypical hemolytic uremic syndrome: 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 the dysregulation of the alternative complement pathway (AP). Complement inhibition via oral administration is an attractive therapeutic target in aHUS as current approved therapies require intravenous or subcutaneous administration. Furthermore, not all such intravenous therapies are available in many countries. 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. Moreover, iptacopan showed clinically meaningful results in the Phase 3 APPLY PNH study. Thus, Iptacopan 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 200 mg twice daily in adult patients with aHUS (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 is the 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 by an extension treatment period of 26 weeks of treatment with iptacopan. Upon completion, eligible patients will be offered post-trial access to iptacopan.

Results

The study is currently recruiting in 32 sites worldwide.

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Summary

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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