P1533 TRIAL IN PROGRESS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 STUDY OF THE EFFICACY AND SAFETY OF PARSACLISIB IN PATIENTS WITH PRIMARY WARM AUTOIMMUNE HEMOLYTIC ANEMIA

**Topic:** 28. Enzymopathies, membranopathies and other anemias

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**Background:** Autoimmune hemolytic anemia (AIHA) is a rare acquired disorder characterized by autoantibodies targeted against erythrocyte membrane antigens, leading to accelerated red blood cell destruction. The estimated incidence of AIHA is 1.3–2.9 per 100,000/year in North America and Western Europe, of which warm AIHA (wAIHA) accounts for 60%–70% of cases. In wAIHA, autoimmunity is typically immunoglobulin G mediated with a warm thermal reactivity range (~37°C). Approximately 50% of wAIHA cases are characterized as primary disease, in which hemolysis occurs without other coexisting disorders. There are few available treatment options for wAIHA beyond corticosteroids and rituximab. Parsaclisib is a potent inhibitor of phosphoinositide 3-kinase (PI3K)-δ that has demonstrated efficacy and safety in a phase 2 study of patients with primary AIHA.

**Aims:** To describe the study design of an ongoing double-blind, randomized, multicenter, placebo-controlled phase 3 trial evaluating the safety and efficacy of parsaclisib in patients with primary wAIHA (PATHWAY; NCT05073458).

**Methods:** Approximately 100 patients will enroll in the study and provide written informed consent before initiation of any study-related procedures. Eligible patients are ≥18 years old and must have a wAIHA diagnosis based on the presence of hemolytic anemia and serologic evidence of anti-erythrocyte antibodies; be inadequately controlled with, intolerant to, or have a contraindication to other therapies; have a hemoglobin (Hgb) level ≥7–<10 g/dL with symptoms of anemia; and have a Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) score ≤43 at screening. Exclusion criteria include other AIHA subtypes, suspected secondary AIHA, splenectomy <3 months before randomization, and prior treatment with a PI3Kδ or pan-PI3K inhibitor for any indication. Patients will be screened for up to 32 days and randomized in a 1:1 ratio to parsaclisib 2.5 mg once daily (QD) or placebo QD for 24 weeks (Figure). Concomitant treatment with low-dose corticosteroids (equivalent to ≤20 mg/d of prednisone) is permitted during the study. Patients who experience worsening wAIHA (defined as a ≥1-g/dL decrease in Hgb from prior assessment or development of new or worsening symptoms) can use rescue therapy (new or increased dose of corticosteroids, transfusions, intravenous immunoglobulin, or epoetin alfa); those who continue on rescue therapy after Week 6 will be considered nonresponders in the primary efficacy analysis. Dose reductions to 1 mg are allowed for adverse events or a rapid rise in Hgb. Patients who complete the 24-week treatment period will enter an open-label extension period and receive parsaclisib 2.5 mg QD for an additional 24 weeks; patients will be monitored for 12 weeks after the last study dose with visits every 4 weeks.

The primary endpoint is the proportion of patients attaining a durable Hgb response, defined as Hgb ≥10 g/dL with a ≥2-g/dL increase from baseline not attributed to rescue therapy at ≥3 of 4 available visits at Week 12 or later during the 24-week double-blind treatment period. The key secondary endpoint is the proportion of patients with a ≥3-point increase from baseline in FACIT-F score at Week 24. Safety will be assessed by monitoring adverse events from informed consent until ≥12 weeks after the last dose of study drug.

**Results:** The study is currently open and recruiting.

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Summary/Conclusion: This phase 3 study will provide valuable insight into the safety and efficacy of parsaclisib as a potential treatment for patients with primary wAIHA.