generalizable to the UK and similar populations. **Conclusions:** Our findings support the use of therapeutics that increase Hb in patients with SCD to protect against deleterious organ damage. **Disclosures:** This study and its analysis were conducted by CorEvitas LLC and sponsored by Global Blood Therapeutics.

https://doi.org/10.1016/j.htct.2022.09.018

EFFICACY AND SAFETY OF NIPOCALIMAB, AN FCRN BLOCKER, IN WARM AUTOIMMUNE HEMOLYTIC ANEMIA (WAIHA): ENERGY PHASE 2/3 STUDY DESIGN

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Objectives: Warm autoimmune hemolytic anemia (wAIHA) is characterized by the destruction of red blood cells (RBCs) by pathogenic autoantibodies which bind to RBCs and lead to their clearance in the spleen and liver. Patients with wAIHA can experience acute worsening of anemia, which can be a medical emergency, and have an increased risk of thromboembolic events and premature death. Nipocalimab is a fully human, aglycosylated, effectorless IgG1 monoclonal antibody that blocks the IgG binding site on the neonatal Fc receptor (FcRn) with high affinity. FcRn, which is expressed in endothelial cells, is responsible for recycling IgG into the circulation and for the relatively long half-life of IgG antibodies compared to other Igs. It is expected that nipocalimab, by blocking IgG binding to FcRn, will prevent IgG recycling and lower pathogenic IgG autoantibodies that cause many autoantibody diseases, including wAIHA. Nipocalimab has been studied in multiple phase 1 studies in healthy subjects and in a completed phase 2 study in subjects with Generalized Myasthenia Gravis (gMG). Treatment with nipocalimab was associated with rapid and durable total serum IgG and pathogenic IgG autoantibody reduction and meaningful clinical response. Here we share the rationale and study design for an adaptive, phase 2/3 multicenter, randomized, double-blind, placebo-controlled study in patients with wAIHA whose aim is to evaluate the efficacy, safety, tolerability, PK, and PD of nipocalimab compared with placebo (NCT04119050). **Materials and methods:** Male or female subjects ≥18 years of age who have been diagnosed with primary or secondary wAIHA and have not experienced a sufficient response or have not tolerated currently available treatments will be included in the study. Subjects with cold antibody AIHA, cold agglutinin syndrome, mixed type (i.e., warm and cold) AIHA, or paroxysmal cold hemoglobinuria will be excluded. Participants will be randomized 1:1:1 to receive nipocalimab at two different dose schedules or placebo. Following completion of 24 weeks of double-blind treatment, participants may enter an open-label extension period to receive nipocalimab. **Results:** The primary endpoint is percentage of participants achieving durable response of improvement in hemoglobin (Hgb). The main secondary endpoints are change from baseline in the total score from the FACIT-Fatigue Scale, number of participants who attain normal lactate dehydrogenase, normal haptoglobin, and normal indirect bilirubin levels at a minimum of 3 consecutive visits after baseline. **Discussion:** ENERGY is a phase 2/3 study that will evaluate the efficacy and safety of nipocalimab in wAIHA. **Conclusion:** ENERGY is currently enrolling globally. **Conflicts of interest:** IM received research support from Alexion, Annexon, Incyte, Kezar, Momenta, Rigel, and Sanofi; and served as a consultant for Apellis, Janssen, Momenta, Novartis, Rigel, and Sanofi. BF is a consultant of Alexion, Amgen, Janssen, Momenta, and Novartis. DC is an employee of Janssen Global Services, LLC, which is a wholly owned subsidiary of Johnson & Johnson, and may own stock or stock options in Johnson & Johnson; was an employee of Momenta. AMBP is an employee of Janssen Latin America, which is a wholly owned subsidiary of Johnson & Johnson, and may own stock or stock options in Johnson & Johnson. MHJ was an employee of Momenta.

https://doi.org/10.1016/j.htct.2022.09.019

LONG-TERM EFFICACY AND SAFETY OF THE ORAL PYRUVATE KINASE ACTIVATOR MITAPIVAT IN ADULTS WITH NON −TRANSFUSION-DEPENDENT ALPHA- OR BETA-THALASSEMIA

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Objectives: Thalassemic red blood cells (RBCs) have insufficient levels of adenosine triphosphate (ATP) to meet increased energy demands associated with globin chain precipitation and oxidative stress responses. Mitapivat is a first-in-class, small molecule, oral activator of pyruvate kinase (PK), a key glycolytic enzyme regulating ATP production. In a phase 2, open-label trial of mitapivat in adults with α- or β-non−transfusion-dependent (NTD) thalassemia (NCT03692052), 80% (16/20) of patients (pts) met the primary endpoint of a hemoglobin (Hb)