estado geral, eutrófico, ativo, corado, acianótico, anictérico, afebril, ausência de hepatoesplenomegalia à propedêutica abdominal. Pele e exame de mucosas não revelaram presença de petéquias ou equimoses. A investigação clínica e laboratorial iniciais, encontramos Fe 35, IST 6% Ferritina 12, CTLF 450. Ácido fólico e vitamina B12 normais. Sorologias para hepatites virais, VDRL, HTLV e HIV não reagentes. Fator Reumatóide, FAN, Eletroforese de proteínas, C3, C4 e CH50 normais, assim como anticardiolipina (IgG e IgM), anti-beta glicoproteína 1 (IgM e IgG) e anticoagulante lúpico não reagentes. DHL 215 (VN: 120 e 246 UI/L), VHS 35 (VN: <15). TSH e t4 livres normais, TGO 18, TGP 20, Cr 0,48, Ur 30, Albumina 3,78. O esfregaço de sangue periférico confirma plaquetopenia, não demonstrando macroplaquetas ou plaquetas gigantes, assim como granulação presente. Também não foi observado células anômalas. Diante do diagnóstico de ferropenia instituído, reposição de ferro endovenoso foi iniciada. Em 7 dias, após reavaliação laboratorial, o hemograma demonstrava seguintes achados Hb 14,0 VCM 86 Rdw 14,8 Leucócitos 5200, diferencial normal, plaquetas 82000. Ainda em conformidade da propedêutica diagnóstica da ferropenia, realizou-se EDA, cujo laudo revelou achados compatíveis com Doença de Crohn em duodeno, sem indícios de doença celíaca, e a colonoscopia revelou achados de doença inflamatória em íleo, confirmados pelo exame histopatológico das biópsias obtidas. Anticorpos anti-endomísio e anti-transglutaminase foram não reagentes. **Discussão:** O caso exposto demonstra uma associação incomum, expondo a plaquetopenia como única manifestação da ferropenia em paciente com doença inflamatória intestinal, por possível componente disarbsortivo e/ou perda crônica pelo diagnóstico obtido. A maioria dos pacientes com deficiência de ferro terá contagens de plaquetas normais ou elevadas, algumas superiores a 1.000×10^9/L no momento do diagnóstico, por conseguinte, a trombocitopenia associada à deficiência de ferro é uma manifestação relativamente rara. Importante salientar e excluir possíveis diagnósticos diferenciais, como Purpura trombocitopênica imune, que depreenderia conduta diferente na condução do caso. Assim como frisar a importância de uma propedêutica laboratorial completa na presença de citopenias, especialmente referindo-se as etiologias carenciais. Paciente então fora encaminhado ao gastroenterologista a fim de continuidade da abordagem terapêutica.

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DOENÇAS DA SÉRIE VERMELHA: ANEMIAS HEMOLÍTICAS

ASSOCIATION BETWEEN HEMOGLOBIN LEVELS AND END-ORGAN DAMAGE IN SICKLE CELL DISEASE: A RETROSPECTIVE LINKED PRIMARY AND SECONDARY CARE DATABASE ANALYSIS IN ENGLAND

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Objectives: Sickle cell disease (SCD) is a chronic, multifaceted blood disorder that affects the oxygen-carrying protein hemoglobin (Hb). Along with chronic hemolysis and vaso-occlusion that often accompanies SCD, low Hb levels may contribute to downstream end-organ damage (EOD). Emerging evidence suggests an association between chronic hemolytic anemia in SCD and both short-term and long-term adverse outcomes, including EOD. Therefore, treatments that directly increase Hb may improve patients' acute symptoms while reducing the risk for long-term disease-related effects known to contribute to morbidity and mortality. This study aims to ascertain the association between Hb level variation and EOD and clinical conditions typically associated with SCD (stroke, pulmonary hypertension, chronic kidney disease [CKD], end-stage renal disease [ESRD], leg ulcers, and pneumonia) in a real-world data set. **Methods:** The Clinical Practice Research Datalink (CPRD) and the Hospital Episode Statistics (HES) databases in England were used to retrospectively identify linked Hb data among patients with SCD (1 April 2007 to 31 March 2019). Recurring results in any 90-day period were averaged. Logistic regression adjusted with demographic and clinical variables was used to determine odds ratios (ORs) of developing each EOD outcome or clinical complication. ORs, p values, 95% confidence intervals (CIs), and areas under the receiver operating curve (AUC-ROCs) and corresponding 95% CIs were reported. **Results:** Of 11,936 patients identified, 5379 (45%) had Hb results recorded in the CPRD. The logistic model for risk assessment of all outcomes studied indicated that an increase in Hb among patients with SCD was associated with a statistically significant ($p < 0.001$) decrease in adjusted ORs per 1 g/dL increase in Hb. Except for ESRD, leg ulcers, and pneumonia, the adjusted models showed statistically significant increases in AUC-ROC compared with the unadjusted models, signifying that the adjusted models were more robust and further verified a statistical OR after adjustment. Increased Hb was associated with decreased risk of respiratory-related events. Pulmonary hypertension had the strongest effect with the most robust model ($OR_{adjusted}$ of 0.66). For pneumonia, $OR_{adjusted}$ was 0.77. For renal insufficiency, ORs for developing CKD or ESRD were significantly lower than 1 ($OR_{adjusted} = 0.73$ and $OR_{adjusted} = 0.75$, respectively). After adjusting for clinical and demographic factors, the model predicted a lower risk for stroke ($OR_{adjusted} = 0.89$). The estimated AUC-ROCs suggest that the adjusted model is more robust in stroke, hypertension, and CKD. These findings did not change when testing for other covariates such as deep vein thrombosis. **Discussion:** Among patients with SCD, an increase in Hb of 1 g/dL was associated with a statistically significant reduction in risk for 6 common EOD outcomes and clinical conditions. The results were more pronounced after adjusting for demographic and clinical covariates (based on clinical opinion and literature review) and further assessed with a bivariate analysis. The results were obtained from a representative real-world evidence dataset analyzed over a 12-year period, which was sufficient to observe EOD events, and are

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.

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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.

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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)