admissions. Pts who complete the double-blind period will be eligible to receive mitapivat in the open-label extension period in each ph. **Results:** Pending. **Discussion:** N/A. **Conclusion:** This ph 2/3 study will investigate the efficacy and safety of mitapivat in pts with SCD. Enrollment is currently ongoing.

https://doi.org/10.1016/j.htct.2022.09.021

SELECTIVE TARGETING OF FCRN AND IGG CLEARANCE BY NIPOCALIMAB PRESERVES KEY IMMUNE FUNCTIONS

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Objectives: Autoantibody disorders are caused by immune-system-produced antibodies that can damage the body's tissues or organs. In the case of warm autoimmune hemolytic anemia (wAIHA), pathogenic autoantibodies lead to the destruction of red blood cells. There is an unmet need for innovative targeted therapies that address the underlying pathogenesis of wAIHA in a safe and efficacious way. Nipocalimab is a fully human, aglycosylated, effectorless IgG1 monoclonal antibody that blocks the IgG binding site on the neonatal Fc receptor (FcRn) which prevents IgG recycling, leading to reduced serum levels of total IgGs, including pathogenic IgG autoantibodies. Nipocalimab is in clinical development for the treatment of multiple IgG-mediated autoantibody diseases, including wAIHA (NCT04119050). Rapid, sustained lowering of IgG was observed in the phase 2 VIVACITY study in generalized myasthenia gravis (gMG) and in phase 1 healthy volunteers. In gMG patients, nipocalimab induced rapid and sustained lowering of anti-AChR autoantibodies and MG-ADL scores, but no serious adverse events including clinically significant infections. Here, we characterize the effect of nipocalimab on immune function. **Materials and methods:** Nipocalimab was evaluated extensively *in vitro* and in nonhuman primate-based chronic toxicology studies to evaluate selectivity, tolerability, safety and immunopharmacology. Safety, tolerability and immune-focused assessments in clinical phase 1 and Phase 2 MG studies were also completed (NCT02828046, NCT03772587). **Results:** Nipocalimab binds specifically *in vitro* to FcRn without activation of effector function or inhibition of antigen presentation. In nonhuman primates administered up to 300 mg/kg nipocalimab QW for up to 6 months, sustained lowering of IgG was observed without adverse effects. Immunotoxicology identified no effect on immune cell phenotypes; CD8 T cell, NK or innate cell functions; T-dependent neoantigen IgM responses. Neoantigen IgG production was observed, but with lowered peak IgG titers consistent with the anticipated increase in IgG clearance with nipocalimab. In clinical studies, nipocalimab demonstrated a reproducible selective decrease in total serum IgG, including all subclasses of IgG, with no effect on IgM, IgA, IgE, CH50, C3, C4, inflammatory cytokines or acute phase proteins including, C-reactive protein (CRP). **Discussion:** These data suggest that nipocalimab can selectively lower IgG and IgG autoantibodies while preserving cellular immunity, complete IgM response and IgG production after neoantigen challenge. **Conclusions:** Overall, nipocalimab's selective effect on IgG recycling provides a mechanistic rationale for potentially decreased infection risk despite substantial IgG lowering. **Conflicts of interest:** LEL *, FY *, CJB *, JB *, RX *, AMBP are employed by the Janssen Pharmaceutical Companies of Johnson & Johnson and may hold stock or stock options in Johnson & Johnson; ST * is an employee of Orna Therapeutics; SK * is an employee of Checkmate Pharmaceuticals; JD * is an employee of Faze Medicines; WA * is an employee of Kisbee Therapeutics. *Former employees of Momenta Pharmaceuticals which was acquired by Janssen Pharmaceutical Companies of Johnson & Johnson.

https://doi.org/10.1016/j.htct.2022.09.022

A PHASE 1 PLACEBO-CONTROLLED SINGLE-DOSE STUDY OF NIPOCALIMAB ADMINISTERED AT DIFFERENT RATES OF INTRAVENOUS INFUSION IN HEALTHY ADULTS

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Objectives: Warm autoimmune hemolytic anemia (wAIHA) is a rare, life-threatening disorder characterized by the destruction of red blood cells by pathogenic IgG autoantibodies. There is currently no approved treatment for wAIHA. 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, which is in clinical development for the treatment of wAIHA. In a prior phase 1 study in healthy adults receiving single and multiple ascending doses infused intravenously (IV) over 2 hours, nipocalimab was well-tolerated with an adverse event profile comparable to placebo. However, shorter durations of nipocalimab infusion may be more convenient for patients. Here we assess the safety and tolerability of single doses of nipocalimab administered at different IV infusion rates in healthy adults to support the potential use of shortened infusions in future studies. **Materials and methods:** The trial was a single dose, sequential, randomized, double-blind, placebo-controlled, escalating dose and infusion rate study. Eligible

participants were males or females aged 18-55 years with no clinically significant medical or physical conditions. Participants were randomized to 1 of 5 cohorts (n = 8 per cohort [6 nipocalimab, 2 placebo]) to receive nipocalimab 30 mg/kg IV infused over 60, 30, 15 or 7.5 min (0.5, 1, 2, or 4 mg/kg/min), nipocalimab 60 mg/kg IV infused over 15 min (4 mg/kg/min) or matching placebo. Escalation to the next dose level was permitted following review by a safety monitoring committee. Safety was assessed by the frequency and nature of treatment-emergent adverse events (TEAEs). **Results:** A total of 40 participants (70% female, 93% white) received study drug and were included in the safety analysis; 39 completed the study. A total of 12 participants (40%) experienced TEAEs across all nipocalimab dosing cohorts and 1 (10%) participant experienced TEAEs following administration of placebo. The most frequently reported TEAE was headache, reported by 6 participants with nipocalimab and 1 participant with placebo. Nausea was reported by 3 participants receiving nipocalimab. Grade 2 injection site reactions were reported by 2 participants but were considered unrelated to the investigational agent. None of the TEAEs were severe, and no participants discontinued treatment due to TEAEs; there were no serious adverse events or deaths. Only 4 participants experienced AEs that occurred within 24 hours after the infusion that were considered related to the study drug. Lower rates of nipocalimab infusion were associated with fewer TEAEs, while participants receiving 4 mg/kg/min (as either 30 mg/kg infused over 7.5 min or 60 mg/kg infused over 15 min) reported more TEAEs. **Discussion:** Single doses of nipocalimab, when administered at doses up to 60 mg/kg and infusion rates up to 4 mg/kg/min were safe and well-tolerated in healthy adults. **Conclusion:** The frequency of reported TEAEs was lower in participants receiving IV nipocalimab at rates of 1 or 2 mg/kg/min, providing a target infusion rate for current and future studies. **Conflicts of interest:** JHL, AV, LEL are employees of Janssen Research & Development, LLC, and AMBP is an employee of Janssen Latin America, which are a wholly owned subsidiaries of Johnson & Johnson, and may own stock or stock options in Johnson & Johnson.

https://doi.org/10.1016/j.htct.2022.09.023

ANEMIA HEMOLÍTICA AUTOIMUNE PRECEDENDO ENDOCARDITE POR STREPTOCOCCUS GALLOLYTICUS ASSOCIADA À PROVÁVEL NEOPLASIA COLORRETAL

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Objetivos: Apresentar caso clínico de paciente com anemia hemolítica autoimune (AHAI) precedendo endocardite por *Streptococcus gallolyticus* (antigo *Streptococcus bovis*), em provável associação à neoplasia colorretal. Trata-se de condição incomum, raramente relatada em literatura médica, destacando-se assim sua relevância científica. **Material e métodos:** Trabalho descritivo retrospectivo de caso clínico realizado através da coleta de dados registrados em sistema operacional do IAMSPE e revisão de literatura. **Resultados:** Paciente do sexo feminino, 80 anos, com diagnóstico de AHAI por anticorpos quentes, tratada a princípio com prednisona 1 mg/kg/dia que apresentou recaída após redução da dose. Recebeu após 4 meses do diagnostico Rituximabe 375 mg/m^2 por 4 semanas, não obtendo resposta adequada. Atendida no Pronto Socorro do HSPE, com piora de queixas constitucionais e visto em exames anemia macrocítica, com hemoglobina (Hb) de 5,2 g/dL, provas de hemólise positivas, pesquisa de anticorpos extraíveis do núcleo negativa, cinética do ferro, vitamina B12 e ácido fólico normais, sorologias para HBV, HCV, HIV e sífilis negativas e estudo medular sem alterações relevantes. Realizado corticoterapia e Azatioprina por 5 semanas, sem melhora nos níveis de Hb. Durante internação paciente apresentou febre, com identificação de *S. Gallolyticus* em hemoculturas e vista insuficiência valvar mitral em ecocardiograma transtorácico que não existia em exame prévio. Foi instituído tratamento com antibioticoterapia para endocardite, sem melhora hematimétrica. Feito imunoglobulina humana, 40 mg/kg/dia por 5 dias, no entanto sem sucesso. Devido às condições clínicas da paciente não foi possível prosseguir investigação com colonoscopia em busca de neoplasia colorretal e a paciente evoluiu a óbito. **Discussão:** A AHAI é definida como o aumento da destruição das células vermelhas por mecanismos autoimunes, usualmente mediada por autoanticorpos contra antígenos de superfície dos eritrócitos. É relativamente rara e pode ser primária/idiopática ou secundária à infecções, doenças autoimunes, malignidades, principalmente desordens linfoproliferativas, e drogas. Há associação da AHAI com infecções virais, bacterianas e parasitárias, como HCV, HIV, CMV, pneumococo e leishmaniose. Não há, entretanto, em literatura casos descritos de associação entre infecção pelo *S. gallolyticus* e AHAI. A relação entre sua infecção e o câncer colorretal já é bem estabelecida. A presença de endocardite por *S. gallolyticus* incrementa a possibilidade de carcinoma colorretal. No presente caso a paciente apresentava AHAI, infecção pelo *S. gallolyticus* e endocardite. Analisando a refratariedade do caso ao tratamento instituído e sabendo da alta incidência de neoplasia colorretal em associação com endocardite e infecção pelo *S. gallolyticus* é possível que o caso descrito se tratasse de AHAI secundária à neoplasia colorretal e endocardite por *S. gallolyticus*. **Conclusão:** O presente relato de caso reitera a vasta apresentação clínica com diferentes causas de AHAI e a necessidade de se entender a fisiopatologia e os mecanismos envolvidos em cada apresentação, bem como sua associação com quadros infecciosos e neoplásicos. O conhecimento dos mecanismos mediadores dessas condições pode determinar tratamento e abordagens específicas com melhores respostas clínicas.

https://doi.org/10.1016/j.htct.2022.09.024

DOENÇA POR CRIOAGLUTININAS COM RESPOSTA INICIAL A CORTICOTERAPIA E IMUNOGLOBULINA: RELATO DE CASO

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