

ID – 2665

**SÍNDROME RESPIRATÓRIA AGUDA GRAVE DEVIDO A METAPNEUMOVÍRUS HUMANO EM PACIENTE COM LINFOMA LINFoblástico DURANTE A TERAPIA DE INDUÇÃO**

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**Introdução:** O quadro respiratório agudo em pacientes durante o tratamento de leucemia tem sido fonte de grande preocupação entre médicos hematologistas. Diversas causas etiológicas já foram descritas, sendo que infecções virais podem causar grave repercussão clínica, inclusive levando ao óbito. Casos de infecção por Metapneumovírus humano (hMPV) têm sido relatados em pacientes submetidos a transplante de medula óssea ou em indução quimioterápica intensiva, com desfechos clínicos variados. O hMPV é um vírus respiratório da família Paramyxoviridae, identificado pela primeira vez em 2001, responsável por infecções do trato respiratório superior e inferior em crianças, adultos e imunocomprometidos. Em pacientes com câncer hematológico e transplantados, a infecção pode evoluir de forma fulminante, com taxas de mortalidade que variam de 10% a 40%. **Objetivos:** Relatar um caso de síndrome respiratória aguda após recuperação medular em paciente recebendo quimioterapia intensa. **Resultados:** Paciente masculino, 36 anos, com diagnóstico prévio de artrite idiopática juvenil, cursando com deformidades articulares. Foi internado no serviço de hematologia devido à presença de massa mediastinal, perda ponderal e dispneia. Realizou biópsia da massa, cujo histopatológico evidenciou positividade nas células de interesse para CD3, CD7, TdT e C-Kit, com negatividade para CD1a, CD10 e CD34, além de Ki-67 >90%, compatível com linfoma/leucemia linfoblástica T. Ao diagnóstico, não havia invasão medular e a doença apenas supradiaphragmática. Iniciou tratamento quimioterápico com o protocolo HyperCVAD, com boa resposta clínica após o bloco IA e desaparecimento da massa mediastinal. Foi reinternado para o bloco IB do mesmo protocolo. Evoluiu com neutropenia febril no D11 do ciclo, com documentação microbiológica de *Moraxella* sp., mantendo estabilidade clínica após terapia antimicrobiana adequada. No entanto, três dias após, desenvolveu quadro respiratório com dor torácica, crepitações pulmonares e tosse. PCR qualitativo em swab nasal identificou infecção por hMPV. A evolução foi rapidamente desfavorável, com hipoxemia grave, choque hemodinâmico e taquidispneia. O paciente foi encaminhado à UTI, necessitando intubação orotraqueal e uso de drogas vasoativas, sem resposta às medidas adotadas, evoluindo a óbito oito dias após o início do quadro clínico. **Conclusão:** A infecção por hMPV constitui uma etiologia relevante de insuficiência respiratória aguda em pacientes imunocomprometidos, particularmente durante ou após quimioterapia intensa. Dada a ausência de terapias antivirais específicas e a limitação de estratégias profiláticas eficazes, o

diagnóstico precoce por PCR e o monitoramento rigoroso de sintomas respiratórios são essenciais. O presente relato reforça a importância da inclusão sistemática de vírus respiratórios, incluindo hMPV, no diagnóstico diferencial de síndrome respiratória aguda em hematologia, sobretudo em períodos de sazonalidade aumentada e em pacientes em tratamento mielossupressor.

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<https://doi.org/10.1016/j.htct.2025.104056>

ID - 2667

**SUCCESSFUL PREGNANCY IN A WOMAN WITH BETA-THALASSEMIA MAJOR: A CASE REPORT**

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**Introduction:** Beta-thalassemia major is a transfusion-dependent hemoglobinopathy associated with chronic anemia, transfusion-related complications, and iron overload. Pregnancy in these patients is rare and requires multidisciplinary planning due to increased transfusion demands and temporary interruption of chelation therapy. Case description: A 29-year-old white female was diagnosed with beta-thalassemia major at 8 days of life and has since received regular red blood cell (RBC) transfusions. She underwent cholecystectomy in 2009 and splenectomy in 2015. In 2020, transfusion reactions required the use of washed RBCs. Iron overload was managed with different chelation regimens. In 2022, while on deferoxamine, her serum ferritin was 403ng/mL, and liver T2\* MRI showed no hepatic involvement. Chelation was discontinued in December 2022 for conception planning. Pregnancy was confirmed in April 2023, approximately 90 days later. Prenatal care was conducted at focusing on maintaining hemoglobin >10 g/dL, with transfusions every 15 days. At 6 weeks, she presented mild vaginal bleeding, successfully treated with progesterone. No chelation was performed during pregnancy. Delivery occurred at 38 weeks via elective cesarean section. Moderate intraoperative vaginal bleeding was controlled without transfusion. The newborn weighed 3,170 g, with Apgar scores of 9 and 9 at one and five minutes, respectively. She exclusively breastfed for 6 months. Four months postpartum, serum ferritin had increased to 4,463ng/mL. In September 2024, liver MRI demonstrated a hepatic iron concentration of 17.5 mg/g dry weight, confirming significant iron overload. Chelation therapy with deferoxamine was resumed in June 2024. The patient remains on regular transfusions with stable

hemoglobin levels and no major maternal or infant complications reported. Conclusion: This case highlights that a well-controlled iron burden before conception, strict hemoglobin maintenance during pregnancy, and multidisciplinary follow-up can result in a successful pregnancy and delivery in beta-thalassemia major. It also emphasizes the need for early postpartum reassessment of iron status and timely resumption of chelation therapy to prevent iron-related organ damage.

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<https://doi.org/10.1016/j.htct.2025.104057>

ID – 16

#### SYSTEMATIC REVIEW AND META-ANALYSIS OF CROVALIMAB (C5 INHIBITOR) IN THE TREATMENT OF PAROXYSMAL NOCTURNAL HEMOGLOBINURIA: EFFICACY AND SAFETY

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**Introduction:** Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired disease of hematopoietic stem cells, characterized by hemolytic anemia caused by the susceptibility of blood cells to complement-mediated lysis. C5 inhibitors work by blocking the C5 protein, preventing complement activation and red blood cell destruction. This study systematically reviews and analyzes the impact of adding C5 inhibitors to standard treatment in patients with PNH. **Objectives:** To evaluate the safety and efficacy of the C5-inhibitor Crovalimab in patients with Paroxysmal Nocturnal Hemoglobinuria (PNH). **Material and methods:** PubMed, Scopus, Web of Science, and Cochrane Library were searched for studies on the use of C5-inhibitor crovalimab in patients with PNH (CRD420251026255). Outcomes included hemolysis control (HC) (defined as centrally assessed LDH  $\leq 1.5 \times$  ULN), Stabilized Hemoglobin (SH), proportion of patients with Transfusion Avoidance (TA), and safety outcomes, including: Patients with > 1 adverse event (AE) - of any- cause, Serious-Adverse-Events (SAE), or treatment-related AEs; AE leading-to-dose-modification of the study treatment; AE leading-to-treatment- discontinuation; grade 3–5 AEs; and infections. All safety events were evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0 (CTCAE v5.0). A comparative analysis between Crovalimab and Eculizumab was also performed regarding efficacy outcomes. Pooled relative risk (RR) and

hazard ratios (HR) with 95% confidence intervals were calculated using a random-effects model, with heterogeneity evaluated via the  $I^2$  statistic. **Results:** Four studies involving 275 patients were included in this study. The pooled prevalence of patients with HC (defined as centrally assessed LDH  $\leq 1.5 \times$  ULN) was 83% (95% CI: 0.75–0.91;  $I^2 = 60\%$ ). SH was observed in 61% of patients (95% CI: 0.48–0.75;  $I^2 = 76\%$ ), and TA was achieved in 65% (95% CI: 0.56–0.74;  $I^2 = 55\%$ ). Regarding safety outcomes, the pooled prevalence of patients experiencing  $\geq 1$  any-grade adverse event (AE) of any cause was 90% (95% CI: 0.78–0.99;  $I^2 = 82\%$ ), and serious adverse events (SAEs) occurred in 14% (95% CI: 0.05–0.23;  $I^2 = 68\%$ ). Treatment-related AEs were observed in 47% of patients (95% CI: 0.18–0.75;  $I^2 = 95\%$ ). AEs leading-to-dose-modification of the study treatment occurred in 2% (95% CI: 0.05–3.75;  $I^2 = 0\%$ ), while treatment-discontinuation due to AEs occurred in only 0.4% (95% CI: 0.01–1.51;  $I^2 = 0\%$ ). Grade 3–5 AEs were reported in 19% of patients (95% CI: 0.14–0.22;  $I^2 = 0\%$ ), and infections were observed in 50% of cases (95% CI: 0.23–0.77;  $I^2 = 96\%$ ). A comparison between Crovalimab and Eculizumab for TA (RR = 0.93; 95% CI: 0.79–1.09;  $I^2 = 0.0\%$ ) and SH (RR = 0.89; 95% CI: 0.63–1.25;  $I^2 = 62.6\%$ ) showed no significant differences between groups. The analysis of HC (RR = 1.01; 95% CI: 0.92–1.12;  $I^2 = 0.0\%$ ) indicated therapeutic equivalence between the drugs. **Discussion and conclusion:** Crovalimab demonstrated promising efficacy in HC, SH levels, and reducing transfusion needs in patients with PNH. Despite a high rate of overall AEs, treatment-related and severe events were relatively infrequent, supporting a favorable safety profile. These findings reinforce its potential as a viable therapeutic option.

<https://doi.org/10.1016/j.htct.2025.104058>

ID - 83

#### USO DO ÍNDICE DE MENTZER NO AUXÍLIO DO DIAGNÓSTICO DE TALASSEMIA BETA MENOR

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**Introdução:** As anemias microcíticas e hipocrômicas representam uma parte importante dos achados hematológicos na rotina laboratorial. As principais causas desse tipo de anemia são carência ou deficiência de ferro e as talassemias (1). O diagnóstico diferencial das talassemias se dá pela eletroforese de hemoglobina, em que o nível de Hemoglobina A2 (HbA2) é maior que 3.5% (2). A Talassemia é um tipo de anemia hereditária causada por um desequilíbrio na síntese das cadeias de globinas resultando em uma eritropoiese ineficaz e é considerada a desordem genética mais comum no mundo. Dentre os índices que são usados para auxiliar o diagnóstico, destaca-se o índice de Mentzer que é calculado pela razão entre o volume corpuscular médio e a contagem de hemácias (VCM/RBC). Pacientes que apresentam razão < 13 são sugestivos do diagnóstico de talassemia beta menor enquanto pacientes com razão > 13 são prováveis deficientes de ferro. A