with CD3ζ followed by CD19-CAR containing NKp30 as a co-stimulatory domain, aiming to enhance cytotoxic activity against malignant B cells. **Material and methods:** (i) Construction of lentiviral vectors encoding CD19-NKp30-CAR and CD3ζ, separately; (ii) production of lentiviral particles carrying CD3ζ through transfection of HEK-293T cells; (iii) transduction of NK-92 cells via spinoculation. **Results:** CD19-NKp30-CAR construct was assembled by cloning the domains followed by and ligation using Gibson assembly. The construct was validated by restriction enzyme digestion and PCR amplification of the CAR transgene. This construct will be used to transduce NK-92 cells that were previously modified with CD3ζ via lentiviral transduction. Lentiviral vectors encoding CD3ζ were produced by transfection of HEK-293T cells, associated with helper plasmids, resulting in a titer of 1.335×10^8 TU/mL. Transduction of NK-92 cells reached 17.4% of CD3ζ-positive cells detected by flow cytometry on day three post-transduction. These modified cells were enriched via cell sorting. **Discussions and conclusion:** NK-92 cells can be engineered to the stable expression of CD3ζ, enabling further modification with CD19-NKp30-CAR, thereby enhancing cytotoxic activity against B cells malignancies.

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EFFICACY AND SAFETY OF BELUMOSUDIL VERSUS BEST AVAILABLE THERAPY FOR THE TREATMENT OF CHRONIC GRAFT-VERSUS-HOST DISEASE IN THE US POPULATION

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Introduction: To date, no clinical studies have undertaken a head-to-head evaluation of the efficacy and safety of belumosudil vs best available therapy (BAT) for the treatment of relapsed/steroid-refractory chronic graft-versus-host disease (cGVHD) as lines of therapy (LOTs) 3–6. **Aim:** This non-interventional study was designed to estimate the efficacy and safety of belumosudil vs BAT in treating cGVHD patients aged ≥ 12 years who had failed 2–5 prior LOTs via emulation of a target trial. **Material and methods:** Data were collected from patient medical records across 8 sites in the United States (US) between March 1, 2015 and March 27, 2024. Adjusted comparative analysis of cGVHD treatment outcomes following belumosudil vs BAT was performed at the LOT level, with a standardized LOT algorithm applied across all sites. The primary study estimate was defined as the causal ratio of overall response rate (ORR), calculated as the ratio of average overall response (OR) for belumosudil vs BAT at LOTs 3–6 after 6 months of follow-up from the time of LOT initiation. OR was defined as complete (CR) or partial response (PR) of cGVHD based on the 2014 National Institutes of Health consensus criteria, physician-assessed CR or PR, or steroid dose taper of ≥ 50% without disease progression. Death, relapse, and initiation of a new LOT were categorized as failure to respond. The secondary study estimate was the difference in failure-free survival (FFS) between belumosudil and BAT at LOTs 3–6 after 1 year of follow-up. Targeted maximum likelihood estimation, an advanced methodology for causal inference with real-world data, was used to generate all study estimates while adjusting for biases common in non-interventional studies and accounting for correlations among multiple LOTs from the same patient. Adverse events (AEs), including those leading to hospitalization and/or death, observed in were descriptively summarized for belumosudil vs BAT LOTs 3–6 using unadjusted counts and rates per 100 LOT-years. **Results:** A total of 196 patients met all eligibility criteria. Of these, 113 were treated with belumosudil and 83 were not, resulting in 358 LOTs (113 belumosudil, 245 BAT). Baseline characteristics were generally well-balanced across belumosudil and BAT LOTs. The estimated 6-month ORR was 38.7% for belumosudil vs 26.8% for BAT. The 6-month ORR ratio between groups was 1.44 (95% confidence interval [CI]: 1.04, ∞; $p = 0.03$), corresponding to a 44% improvement with belumosudil over BAT. The estimated 1-year FFS was 61.2% for belumosudil vs 47.8% for BAT, resulting in a 1-year FFS difference of 13.5% (95% CI: 1.5%, 100.0%; $p = 0.03$). The AE rate per 100 LOT-years was 41.2% for belumosudil and 51.6% for BAT LOTs 3-6. Belumosudil LOTs had a lower AE rate per 100 LOT-years in 69% of the AE categories. **Discussion and conclusion:** This study demonstrated that belumosudil has superior efficacy compared with BAT in real-world patients with relapsed/steroid-refractory cGVHD. The safety profile of belumosudil-treated patients was consistent with its previously established clinical profile.

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EFFICACY OF CAR-T THERAPY FOR REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: A SYSTEMATIC REVIEW AND METANALYSIS

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Introduction: Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy, and although survival rates in children are high, adult B-lineage ALL (B-ALL) presents with high rates of relapse and refractoriness.[1,2] Chimeric antigen receptor (CAR)-T cell therapy, a form of personalized immunotherapy, has emerged as a revolutionary strategy for hematological cancers, showing transformative results where conventional treatments have failed.[3] This therapy involves genetically modifying a patient's T-cells to recognize and eliminate cancer cells.[3] Given its potential, this study aims to synthesize the current evidence on the efficacy and safety of CAR-T therapy in patients with relapsed or refractory (R/R) B-ALL. **Aim:** To evaluate and synthesize the results on the efficacy and safety of different CAR-T treatments in patients with refractory B-ALL through a systematic review and meta-analysis of published clinical trials. **Material and methods:** A systematic review and meta-analysis were conducted following PRISMA guidelines. A search of PubMed, SciELO, BVS, Cochrane Library, and Web of Science databases was performed for clinical trials published between 2014 and 2025 that evaluated CAR-T therapy for R/R B-ALL. A total of 27 single-arm, non-randomized clinical trials were included. Data on measurable residual disease negativity, cytokine-release syndrome and neurotoxicity were extracted. A meta-analysis of proportions was performed using a random-effects model to calculate pooled estimates and 95% confidence intervals. **Discussion and conclusion:** The pooled analysis showed an overall MRD-negativity rate of 78.89% (95% CI: 73.17%–84.16%). Subgroup analysis showed rates of 79.70% for anti-CD19 constructs, 83.17% for dual anti-CD19/CD22, and 56.45% for anti-CD22 alone. The incidence of CRS of any grade was 80.91% (95% CI: 74.38%–86.79%), while severe CRS (Grade ≥ 3) occurred in 14.62% (95% CI: 9.35%–20.66%) of patients. Neurotoxicity of any grade was observed in 22.66% (95% CI: 14.17%–32.27%) of patients. Heterogeneity was observed across the analyses (I^2 from 66%–87%). CAR-T cell therapy induces high rates of complete remission and MRD negativity in adult patients with R/R B-ALL, representing a major advance for this historically poor-prognosis population. However, adverse events such as CRS and neurotoxicity are frequent. The significant heterogeneity among studies highlights the influence of factors like patient characteristics, CAR-T construct, and treatment protocols on outcomes. Future research should focus on optimizing CAR-T cell persistence, overcoming resistance, and refining patient selection to maximize the curative potential of this therapy.

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ERROS INATOS DA IMUNIDADE E TCTH: URGÊNCIA, BARREIRAS E OPORTUNIDADES

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Introdução: Os erros inatos da imunidade (EII) constituem um grupo heterogêneo de doenças genéticas caracterizadas por disfunções no sistema imunológico. Em determinadas formas, especialmente nas imunodeficiências combinadas graves, o transplante de células-tronco hematopoéticas (TCTH) é a única intervenção potencialmente curativa, decisiva para a sobrevida e a qualidade de vida. **Objetivos:** Este estudo teve como objetivo descrever o perfil epidemiológico de pacientes com EII e indicação de TCTH acompanhados em um centro de referência. **Material e métodos:** Estudo retrospectivo, observacional, baseado em registros eletrônicos hospitalares e no banco nacional de receptores de medula óssea (REREME), envolvendo pacientes acompanhados entre 2011 e 2025 (14 anos) com indicação formal de TCTH. **Resultados:** Foram incluídos 42 pacientes, 76% do sexo masculino, mediana de idade de 1 ano (0–16). Desses, 57% (24) realizaram TCTH, sendo 71% (17) meninos, com mediana de idade ao procedimento de 0,7 anos (0–11) e tempo mediano de espera de 135 dias (22–1.571). As principais indicações foram SCID (17) — mutações ADA, JAK3, NOD2, ILR7 —, Síndrome de Wiskott-Aldrich (3), doença granulomatosa crônica (1), deficiência de receptor de IL-10 (1), deficiência de NFKB (1) e outras imunodeficiências combinadas (1). A mortalidade foi de 26% (6), principalmente por VOD e infecção por CMV. Entre os 43% (18) não transplantados, 5 perderam seguimento e 5 evoluíram a óbito antes da realização. Oito permaneciam em busca de doador compatível ou fora da faixa etária, com mediana de espera de 1.769 dias (67–1.862), período anterior à ampla adoção dos transplantes haploidênticos (2018) e à implantação da triagem neonatal (2021) no país. **Discussão e conclusão:** O TCTH é pilar terapêutico nos EII graves. O atraso diagnóstico e a escassez de doadores compatíveis comprometem a sobrevida. Medidas para detecção precoce e ampliação do acesso a centros especializados são cruciais para melhores desfechos.

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ESTADO NUTRICIONAL DE CRIANÇAS SUBMETIDAS A TRANSPLANTE DE CÉLULAS-TRONCO HEMATOPOIÉTICAS (TCTH)

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