unadjusted analyses, platelet engraftment occurred later in HIV-positive participants. Multivariable analysis confirmed HIV-positive status as an independent predictor of delayed platelet engraftment ($\beta = 1.85$ days; 95% CI: 0.63–3.07; p = 0.003) and leukocyte engraftment ($\beta = 1.002$ days; 95% CI: 0.13–1.87; p = 0.025). Neutrophil engraftment was not significantly associated with HIV status (p = 0.075). Higher infused $CD34^+$ doses were consistently associated with faster recovery across all cell lineages, whereas the use of 10% DMSO as the cryopreservation solution was associated with longer engraftment times. **Discussion and conclusion:** In conclusion, this study provides novel evidence that HIV infection independently delays platelet and leukocyte engraftment after ASCT, even when controlling for cell dose and other key transplant variables. The magnitude of the effect on platelet recovery is clinically meaningful, with potential to increase bleeding risk, prolong transfusion dependence, and delay full hematologic recovery. These findings underscore the need for tailored supportive care, optimized $CD34^+$ collection, and proactive post-transplant monitoring in PLHIV. By addressing modifiable factors and integrating HIV-specific considerations into transplant planning, clinicians may mitigate the adverse impact of HIV on hematopoietic recovery. Future multicenter prospective studies with comprehensive immunologic profiling are warranted to elucidate underlying mechanisms and inform evidence-based guidelines. Overall, HIV infection should be recognized as an independent predictor of delayed engraftment after ASCT, reinforcing the importance of individualized transplant strategies for this population.

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IMMUNE EFFECTOR CELL-ASSOCIATED HLH IN HIGH TUMOR BURDEN PATIENTS TREATED WITH CAR-T: LESSONS FROM BRAZILIAN CASES

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Introduction: CAR-T cell therapy is based on the modification of T lymphocytes to express chimeric receptors. Although effective in the treatment of B-cell malignancies, these therapies are associated with inflammatory toxicities such as Cytokine Release Syndrome (CRS), Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), and, more rarely, Immune Effector Cell-Associated Hemophagocytic Lymphohistiocytosis (IEC-HLH). We report two cases of IEC-HLH in patients who received anti-CD19 CAR-T infusion as part of a Brazilian academic study. **Case report:** Case 1: Male, 70 years old, with refractory CLL (TP53 mutated, 11 prior lines, including allo-HSCT). Pre-CAR-T bone marrow showed 83% clonal lymphocytes. Developed grade I CRS on D+1, treated with tocilizumab 8 mg/kg. On D+15, presented with fever, cytopenias, hyperferritinemia (7,417 ng/mL), hypofibrinogenemia, hypertriglyceridemia, elevated transaminases and LDH, with an H-Score of 200. Treated with a cumulative dose of 329 mg dexamethasone and anakinra (10–5 mg/kg/day) for 7 days, achieving complete resolution. Case 2: Male, 9 years old, with ALL and bone marrow showing 95% blasts, received prophylactic tocilizumab. Developed grade III CRS (D+1) and grade IV ICANS (D+5), both treated with immunosuppressants. On D+6, presented with findings suggestive of IEC-HLH: ferritin 43,044 ng/mL, cytopenias, hypofibrinogenemia, elevated transaminases, and triglycerides, with an H-Score of 184. Received anakinra (10–7 mg/kg/day for 7 days) with complete clinical and laboratory response. On D+30 bone marrow reassessment, he achieved MRD-negative complete remission, maintained to date (D+367). **Conclusions:** Both patients had high tumor burden and developed IEC-HLH later than CRS onset. The CLL patient showed late CAR-T cell expansion (0.45% to 38.1% between D+14 and D+21) coinciding with a decline in CD19+ cells (82.2% to 1.2%), suggesting a correlation between cell expansion and IEC-HLH. Both cases were treated with anakinra, in line with prior experience in secondary HLH. Therapeutic response was satisfactory. Both patients remain in complete remission (>1 year post-infusion). These cases highlight the importance of recognizing IEC-HLH in patients with high tumor burden. The favorable outcomes with anakinra suggest its potential as a standardized therapeutic strategy. Specific protocols are essential for the diagnosis and management of this rare but potentially severe complication.

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IMPACT OF SHORT-TERM TRANSFER FROM NITROGEN TO -80°C FREEZER ON THE VIABILITY OF CRYOPRESERVED CELLULAR THERAPY PRODUCTS: AN IN VITRO STUDY

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Introduction: Liquid or vapor nitrogen is considered the gold standard for the storage of cellular therapy products, ensuring long-term viability and stability. However, contingency planning remains a challenge, as each cryopreserved unit requires an available slot in another tank for redundancy in case of failure. Additionally, most transplant centers in Brazil lack liquid nitrogen storage tanks, and cryopreserved cellular products should be delivered before conditioning begins. **Aim:** This study aimed to evaluate the impact of short-term

transfer of cryopreserved cell therapy units from nitrogen storage to a -80°C freezer, using in vitro assays. **Material and methods:** This experimental study included cellular therapy units from individuals referred for autologous stem cell transplantation. Cryopreservation was performed at a single processing facility between 2014 and 2024. Cryopreserved units authorized for discard and aliquoted into at least two bags were included. One bag was thawed immediately after removal from the vapor nitrogen tank, while the paired bag was stored at -80°C for three months before being thawed. The -80°C freezer was continuously monitored, with brief door openings, but temperatures never exceeded -76°C. Thawing was performed using a 37°C water-bath. A resuspension solution (3% human albumin, 2% hydroxyethyl starch 130/0.4, and 2.5% ACD) was added at double the final concentration in a 1:1 volume ratio. Samples were collected for total nucleated cell count, CD34+ immunophenotyping, and colony-forming assays. Data were described using medians with interquartile ranges or percentages, and continuous variables were compared using the non-parametric Wilcoxon paired test. **Results:** To date, seven paired bags have been analyzed. The median total nucleated cell count was 292.9 (272.4) $\times 10^8$ in the liquid nitrogen group and 270.4 (255.9) $\times 10^8$ in the -80°C group ($p = 0.109$). Viable CD34+ cell counts were comparable between groups, with medians of 50.4 (102.5) $\times 10^6$ and 62.5 (50.5) $\times 10^6$, respectively ($p = 0.469$). The number of GM colonies did not differ significantly, with 11 (31.5) colonies per 400 CD34+ cells/mL in the nitrogen group and 8 (39.5) colonies per 400 CD34+ cells/mL in the -80°C group ($p = 0.313$). **Discussion and conclusion:** The study suggests that -80°C freezers can be a viable short-term storage solution for cryopreserved cellular therapy products, offering a feasible contingency option. This method could significantly reduce costs by lowering operational expenses and infrastructure needs. Furthermore, it could improve access to cellular therapies, especially in under-resourced settings and transplant centers lacking nitrogen storage. This would facilitate the decentralization and broader distribution of transplants across the country, enhancing the availability and delivery of life-saving treatments and contributing to more sustainable healthcare practices. These preliminary results indicate that -80°C freezers may serve as a short-term contingency storage strategy for cell therapy products, provided they are maintained under strict conditions to prevent transient warming events. However, the limited number of thawed units and lack of in vivo validation highlight the need for further research before clinical guidelines can be established.

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IMPACTO CLÍNICO DA TERAPIA COM CÉLULAS CAR T ANTI-CD19 EM NEOPLASIAS DE CÉLULAS B: UMA REVISÃO SISTEMÁTICA E METANÁLISE

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Introdução: As células T com receptores de antígeno quimérico (CAR) direcionados ao CD19 representam uma das terapias celulares mais notáveis para o manejo de neoplasias de células B. No entanto, a sobrevida livre de doença a longo prazo ainda é um desafio a ser superado. **Objetivos:** Avaliar a influência de diferentes domínios hinge, transmembrana (TM) e coestimulatórios do CAR, bem como das condições de produção, tipo de produto celular, doses, idade dos pacientes e tipos tumorais, nos desfechos clínicos de pacientes com cânceres de células B tratados com células CAR T anti-CD19. **Material e métodos:** Foi realizada uma revisão sistemática e metanálise de acordo com as diretrizes PRISMA, registrada no PROSPERO (CRD42022360268). Foram incluídos 56 estudos (3.493 pacientes) na revisão sistemática e 46 estudos (3.421 pacientes) na meta-análise. As covariáveis analisadas incluíram: tipo de domínio hinge, TM e coestimulatórios no CAR; condições de produção das células CAR T; população celular transduzida com o CAR; número de infusões; dose de células CAR T injetadas/kg; tipo de CAR T anti-CD19 (nome); tipo tumoral e idade. **Discussão e conclusão:** A taxa global de resposta completa (BCR) foi de 56%, com sobrevida global (OS) de 60% e taxa de melhor resposta objetiva (BOR) de 75%. Pacientes mais jovens apresentaram prevalência significativamente maior de BCR, sem diferenças na OS. A presença de CD28 nos domínios hinge, TM e coestimulatórios do CAR melhorou todos os desfechos avaliados. Doses entre 1 e 4,9 milhões de células/kg resultaram em melhores resultados clínicos. Os dados também sugerem que, independentemente de apresentarem altas respostas objetivas, os pacientes podem obter benefícios de sobrevida com a terapia CAR T anti-CD19. Esta meta-análise constitui um instrumento crítico para geração de hipóteses, captando efeitos presentes na literatura sobre CAR T anti-CD19, especialmente diante da escassez de ensaios clínicos randomizados e grandes estudos observacionais.

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