studies, and informing public health and precision medicine policies.

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IMUNOTERAPIA COM USO DE CÉLULAS CART-T EM PACIENTES DIAGNOSTICADOS COM LEUCEMIA LINFOBLÁSTICA AGUDA PEDIÁTRICA

RH Ramos, GB Miranda, DFA Lopes, NKU Nogueira, NC Trovo

Universidade Nove de Julho, São Paulo, SP, Brasil

Introdução: A leucemia linfoblástica aguda de células B (LLA-B) é a neoplasia hematológica mais comum na infância. Apesar dos avanços terapêuticos, casos recidivantes/refratários ainda representam desafio clínico significativo, com prognóstico reservado e poucas opções terapêuticas. Nos últimos anos, a imunoterapia com células T geneticamente modificadas para expressar receptores quiméricos de antígeno (CAR-T cells), especialmente direcionadas contra o antígeno CD19, tem emergido como alternativa promissora. Essa tecnologia vem demonstrando resultados encorajadores quanto às taxas de remissão, sobrevida e controle da doença residual sobretudo em faixas etárias mais vulneráveis. **Objetivos:** Este trabalho objetiva revisar e sintetizar as evidências científicas disponíveis sobre a eficácia clínica da terapia com células CAR-T em pacientes pediátricos com LLA-B, com foco na população prevalente e nos principais fatores prognósticos associados aos desfechos terapêuticos. **Material e métodos:** Foi realizada uma revisão integrativa da literatura acerca da eficácia da terapia com células CAR-T em pacientes pediátricos com LLA-B. A estratégia de busca foi conduzida na base de dados PubMed utilizando os descritores em inglês "immunotherapy", "CAR-T cell" e "pediatric leukemia". Aplicaram-se filtros para apenas artigos disponíveis na íntegra, publicados entre 2017 e 2025, redigidos em inglês. Como critérios de inclusão, adotou-se a necessidade dos estudos abordarem eficácia clínica e as taxas de remissão da doença em pacientes pediátricos com idade entre 2 e 5 anos, faixa etária de maior prevalência da LLA-B. **Discussão e conclusão:** A análise de estudos clínicos sobre pacientes pediátricos com LLA-B recidivante/refratária demonstrou alta eficácia da terapia CAR-T anti-CD19. As taxas de remissão completa variaram entre 83% e 100% (KATO et al., 2025; WANG et al., 2024; MYERS et al., 2025; NCT 03827343), com negativação de doença residual mínima (MRD) em até 96,5% dos casos (WANG et al., 2024). A sobrevida global (OS) em 1 ano foi de até 82% (KATO et al., 2025), e a sobrevida livre de eventos (EFS) variou conforme a carga tumoral — 80% para pacientes com < 5% de blastos e 24% nos com doença avançada (KATO et al., 2025). A toxicidade mais comum foi a síndrome de liberação de citocinas (SRC) presente em até 77% dos pacientes (ELIANA STUDY, 2017), seguida de neurotoxicidade (ICANS), controlada com medidas como dexametasona intratecal precoce (JI et al., 2024). A terapia mostrou-se viável em crianças menores de 3 anos (com peso < 10 kg) com sucesso na produção e infusão do produto em 94% dos casos (ESTUDO MULTINACIONAL, 2023). Fatores como carga tumoral elevada, mutação TP53 e ausência de transplante alogênico pós-CAR-T foram associados a pior prognóstico (ZHANG et al., 2021). Isoformas alternativas de CD19 já presentes no diagnóstico foram identificadas como possíveis mecanismos de resistência, reforçando a necessidade de terapias combinadas ou multialvo (FISCHER et al., 2017; MYERS et al., 2025).

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INFLUENCE OF CONDITIONING, DONOR AGE, AND TRANSPLANT PERIOD ON ALLOGENEIC TRANSPLANT OUTCOMES IN ACUTE LYMPHOBLASTIC LEUKEMIA: A LATIN AMERICAN COHORT OF 748 PATIENTS

WF Silva [a], A Gómez de León [b], ME Zelada [c], MN Kerbauy [d], ME Mas [e], DN Cysne [a], I Colturato [f], AC Cordeiro [g], LLA Luna [h], AA WU [a], VRCV Sampaio [a], GG Salas [b], AEG Lozano [b], I Domínguez [i], J Rojas [j], JEC Pedraza [b], N Quinteros [k], VIU Ceniceros [l], E Zapata [m], J Schmidt-Filho [g], L Tucunduva [n], G Navarro [o], VA Colturato [f], N Hamerschlak [d], AL Basquiera [e], V Rocha [a]

[a] *Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HCFMUSP), São Paulo, SP, Brazil*
[b] *Universidad Autónoma de Nuevo León, Mexico*
[c] *Clínica Dávila, Chile*
[d] *Hospital Israelita Albert Einstein, São Paulo, SP, Brazil*
[e] *Hospital Privado Universitario de Cordoba, Argentina*
[f] *Hospital Amaral Carvalho, Jaú, SP, Brazil*
[g] *A.C. Camargo Cancer Center, São Paulo, SP, Brazil*
[h] *Centro Medico Nacional 20 de Noviembre, Mexico*
[i] *Hospital Sótero del Río, Chile*
[j] *Hospital Regional de Talca, Chile*
[k] *Hospital San Borja de Arriarán, Chile*
[l] *Instituto Nacional de Cancerología, Mexico*
[m] *Fundación Arturo López Pérez, Chile*
[n] *Hospital Sírio-Libanês, São Paulo, SP, Brazil*
[o] *Hospital de Amor, Barretos, SP, Brazil*

Introduction: Allogeneic hematopoietic stem-cell transplantation (HCT) remains a key component of consolidation

therapy for many adults with acute lymphoblastic leukemia (ALL). The role of HCT is especially critical in settings where pediatric-inspired protocols may be excessively toxic or difficult to implement, and novel agents for B-cell ALL are not readily available. In recent years, the use of haploidentical donors and reduced-intensity conditioning (RIC) regimens expanded treatment options for selected patients. However, there are currently no comprehensive data describing HCT outcomes for ALL in Latin America (LA). **Aim:** In this study, we aimed to assess survival and response outcomes in a large, multicenter cohort, with an additional focus on less-studied subgroups of the disease. **Material e methods:** This is a retrospective registry-based study that included HCT data from 18 centers in LA. We included patients aged ≥ 15 years with ALL or ambiguous lineage leukemia who underwent a first HCT between January 2007 and December 2024. Primary endpoints were overall survival (OS), disease-free survival (DFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM). Multivariate Cox regression analyses (MVA) were performed. Country was incorporated as a frailty term in the models. **Results:** A total of 748 patients were included (median age 29; 84% B-cell ALL). Transplants occurred in Brazil (49.9%), Mexico (22.7%), Argentina (15.4%), and Chile (12%). Ph+ ALL was present in 28.5%, CNS disease in 16.9%. HCT was performed in CR1 (57.2%), CR2+ (37.4%), or refractory disease (5.4%); pre-HCT MRD was positive in 22.8%. Donors were haploidentical (40.6%), MSD (39.3%), MUD (11.6%), MMUD (5.5%), or cord blood (2.7%); 78.1% used peripheral blood. Myeloablative conditioning (MAC) was predominant (84.3%), with TBI in 69.6%. At 47.7 months' median follow-up, 4-year OS and DFS were 46.8% and 42.5% (45.4% excluding refractory). CIR and NRM were 29.9% and 28.5%. Donor type did not affect OS, but MUD lowered relapse risk (HR 0.551, $p = 0.027$). OS predictors included age (HR 1.014, $p = 0.005$), CR2+ (HR 1.398, $p = 0.01$), TBI (HR 0.749, $p = 0.02$), donor age (HR 1.01, $p = 0.035$), and HCT from 2019 (HR 0.759, $p = 0.038$). TBI improved DFS ($p = 0.0003$) and reduced relapse ($p = 0.003$) without raising NRM, persisting in MAC ($p = 0.044$) but not RIC ($p = 0.25$). Donor age predicted DFS ($p = 0.036$) and NRM ($p = 0.03$). HCT from 2019 protected against relapse (HR 0.546, $p = 0.0005$). MRD positivity worsened all outcomes ($p < 0.05$). In Ph+ ALL ($n = 196$), donor age impacted OS (HR 1.02, $p = 0.004$) via higher NRM; TBI and age were not significant. In patients ≥ 50 ($n = 116$), RIC reduced NRM (HR 0.49, $p = 0.032$) without affecting relapse; TBI lowered relapse (HR 0.413, $p = 0.046$) without increasing NRM. Country of transplant was not significant in any model. **Discussion and conclusion:** These findings demonstrate that allogeneic HCT for ALL in LA yields survival outcomes comparable to international benchmarks despite marked heterogeneity in practice. TBI-based conditioning and more recent transplant periods were associated with improved disease control without increasing NRM, while donor age remains an important predictor of adverse outcomes. RIC regimens reduced toxicity in older patients without apparently compromising relapse risk. These results highlight the importance of optimizing conditioning strategies, careful donor selection, and regional collaboration to improve HCT outcomes in LA.

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INITIAL EXPERIENCE WITH ANTI-CD19 CAR-T CELL THERAPY IN PATIENTS WITH RELAPSED/ REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: A SERIES OF CASES IN A BRAZILIAN CANCER CENTER

NM Santana, ML Garcia, JA Balthazar, GA Peruzini, LM Brandão, BA de Souza, JF Campos, JC Amarante, AGO Braga, AC Cordeiro, VA Bovolenta, MM Nascimento, JS Filho

AC Camargo Cancer Center, São Paulo, SP, Brazil

Introduction: B-cell Acute Lymphoblastic Leukemia (B-ALL) has a 90% overall survival (OS) rate in children and young adults. However, in the relapsed/refractory (R/R) setting, 5-year OS drops to 50% after the first relapse, falling to 20–30% in R/R B-ALL post-allogeneic hematopoietic stem cell transplantation (allo-HSCT). Given this scenario, the ELIANA trial evaluated the CD19-targeting CAR T-cell therapy Tisagenlecleucel (Tisa-Cel) in R/R B-ALL, reporting complete response (CR) rates of 81%. A 3-year follow-up showed event-free survival and OS rates of 44% and 63%, respectively. Among grade 3 or 4 adverse events, Cytokine Release Syndrome (CRS) occurred in 48% of cases and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) in 13%, though real-world studies report lower rates of 16% for CRS and 9% for ICANS. Another less frequent, but more serious, adverse event is Macrophage Activation Syndrome (MAS). Tisa-Cel was approved in Brazil in 2022 for R/R B-ALL patients up to 25 years of age, including post-allo-HSCT. Therefore, this study aims to retrospectively report the cases of patients with R/R B-ALL treated with Tisa-Cel at our institution between 2022 and 2024, based on the analysis of medical records. **Case report:** We report a series of three R/R B-ALL cases, aged 15 to 24, all heavily pre-treated with a median of 3 therapy lines; two had relapsed post-allo-HSCT. Following leukapheresis, all patients received Fludarabine and Cyclophosphamide lymphodepletion and a Tisa-Cel infusion. With a median follow-up of 10 months (10-13), two of the three patients remain alive and in CR without cytopenias. Patient 1: A 15-year-old male with Philadelphia (Ph)-like B-ALL, refractory to two lines (including use of Blinatumomab), and relapse in central nervous system post-allo-HSCT, received CAR-T therapy while in CR. He had no CRS or ICANS and remains with no evidence of disease. Patient 2: A 23-year-old male with lymphoblastic lymphoma Ph negative localized in the tibia (no medullary involvement), refractory to two lines and not yet submitted to allo-HSCT, received CAR-T in a partial response (PR). He developed grade 1 CRS without ICANS and achieved PR at D30, and CR at D60. Patient 3: A 24-year-old female with Ph positive B-ALL, refractory after more than 3 lines of therapy lines and relapsed post-allo-HSCT, received CAR-T with active disease (7.6% blasts in bone marrow). She developed grade 3 CRS and grade 1 ICANS, managed with IL-1 and IL-6 inhibitors, intensive care and dexamethasone. She achieved CR at D+30 but died at D+55 from complications, including severe fungal infection, occlusive-venous-disease and MAS. **Conclusion:** Despite the