

EFFICACY AND SAFETY OF EXPERIMENTAL CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELLS VERSUS AXICABTAGENE CILOLEUCEL (YESCARTA) FOR THE TREATMENT OF RELAPSED/REFRACTORY LARGE B-CELL LYMPHOMA: MATCHING ADJUSTED INDIRECT COMPARISONS AND SYSTEMATIC REVIEW

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Introduction: Despite the high response rates seen with Chimeric Antigen Receptor (CAR) T-cell therapy for relapsed/refractory Large B-cell lymphoma (R/R LBCL), post-therapy relapse remains a key challenge. To date, no study has evaluated the comparative efficacy and safety of experimental CAR T-cell products versus currently approved CAR T-cell therapies. **Objective:** To indirectly compare the efficacy and safety of novel, experimental CAR T-cell products against the first FDA-approved CAR T-cell construct, Axicabtagene ciloleucel (Yescarta). **Methods:** In compliance with the PRISMA guidelines, we performed a systematic review, which identified 16 independent, early-phase clinical trials consisting of 193 LBCL patients with individual patient data (IPD). We categorized eight pooled populations based on the target antigens (CD19, CD20), co-stimulatory domains (CD28, 4-1BB), and CAR T-cells administered with or without concomitant autologous stem cell transplant (ASCT). The pooled populations were categorized as follows: (1) dual targeting strategies, such as tandem CD19.CD20, n = 28; (2) co-infusion of CD19 and CD20 CARs, n = 21; (3) third-generation CARs, n = 26; (4) CD19 CARs with modified constructs for reduced toxicity, including CD19.BBz.86, n = 21; and (5) Hu19.CD828Z, n = 14; (6) CD19. 4-1BB.S manufactured in China, n = 24; (7) concomitant ASCT and CD19.CD28, n = 45; and (8) CD20 CARs with a 4-1BB co-

stimulatory domain, n = 14. A Matching Adjusted Indirect Comparison (MAIC) statistical technique was applied to account for heterogeneity in the study population across trials. Estimates for the experimental CAR T-cell trials were adjusted using patient-level data to match the ZUMA-1 (Yescarta, n = 108) study population based on mutually reported key baseline covariates, including age, disease stage, histology, refractoriness, number of prior lines of therapy, and extranodal disease. The study endpoints for this study included progression-free survival (PFS), cytokine release syndrome (CRS), and neurotoxicity (NT). **Results:** In the dual-targeting strategy, only tandem CD19.CD20.4-1BB was associated with a statistically significantly improved PFS (HR = 0.46; 95% CI, 0.23-0.92) and a safer NT profile (OR = 0.15; 95% CI, 0.03-0.76) compared to Yescarta. As for safety, significantly reduced NT (OR = 0.19; 95% CI, 0.04-0.94) was also noted with third-generation CAR T-cells. None of the other comparisons were statistically significant. Of note, no statistically significant associations regarding PFS or safety were seen with the sequential administration of ASCT followed by CAR T-cells within 4-7 days. CD19.BBz.86 and Hu19.CD828Z CAR T-cell products containing modified co-stimulatory domains aimed at reduced toxicity demonstrated no grade ≥3 CRS nor NT occurrence. Anti-CD20.4-1BB did not show a remarkable difference in terms of the selected endpoints for this study. Safety data for the co-infusion of CD19 and CD20 were not available for this trial. **Discussion and conclusion:** Our MAIC suggests a dual targeting approach using tandem CD19.CD20.4-1BB might have both superior efficacy and safety compared to Yescarta. Future studies comparing experimental CAR T-cell constructs with other CD19.4-1BB-based approved CAR T-cell products, such as Tisagenlecleucel (Kymriah) and Lisocabtagene maraleucel (Breyanzi), may further contribute to clarify these findings.

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ELABORAÇÃO DE UM LIVRO INFANTIL PARA CONVERSAR SOBRE TRANSPLANTE DE MEDULA ÓSSEA NA ANEMIA FALCIFORME

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Introdução: A Anemia Falciforme é uma doença genética pertencente ao grupo de doenças falciformes e caracteriza-se pela forma de maior gravidade clínica, sendo também a mais prevalente. O único tratamento com possibilidade curativa é o Transplante de Medula Óssea. Os autores do presente

