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POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Evaluating the Impact of Cryopreservation of PBMCs on CAR-T Therapy Efficacy and Safety in DLBCL Patients: An Informative Approach to Optimize Manufacturing Strategies

Teng Xu[1], *Fan Yang*[1], *Rui Liu*[1], *Zhonghua Fu*[1], *Na Li*[1], *Xiaoyan Ke*[1], *Shaomei Feng*[1], *Biping Deng*[2], *Kai Hu*[1]

[1] Department of Lymphoma and Myeloma Research Center, Beijing Gobroad Boren Hospital, Beijing, China
[2] Department of Cytology Laboratory, Beijing Gobroad Boren Hospital, Beijing, China

Background: Chimeric Antigen Receptor (CAR) T-cell therapy has emerged as a pivotal treatment modality for relapsed/refractory (R/R) B-cell malignancies. However, some patients are unable to receive CAR-T therapy due to challenges in obtaining sufficient lymphocytes through leukapheresis, often resulting from intensive prior treatments or impaired lymphocyte function after repeated tumor reductions under high tumor burden. This issue underscores the need to explore strategies such as advance collection and cryopreservation of peripheral blood mononuclear cells (PBMCs), which could provide enhanced flexibility in the pre-CAR-T treatment planning process and potentially widen the accessibility of CAR-T therapy.
Aims: This retrospective study compares the safety, efficacy, and adverse reactions of anti-CD19 CAR-T cell therapy for Diffuse Large B-Cell Lymphoma (DLBCL) patients, using cryopreserved versus freshly harvested PBMCs.
Methods: A total of 162 R/R DLBCL patients treated with an anti-CD19-CD3zeta-4-1BB CAR-T cell therapy from January 2019 to April 2023 were included in this study, excluding those who received concurrent autologous stem cell transplants. The median age was 52 (15-78) years old, and the majority (87.7%) patients had stage III-IV disease. With a median IPI score of 2 (range, 0-5), 71.0% (115/162) had extranodal lesions and 18.0% (29/162) had bulky disease > 7 cm. Among these, 136 patients received CAR-T cells derived from cryopreserved PBMCs, which were frozen with a controlled rate freezer and CryoSure-DEX40 cryoprotectant and stored in the liquid phase of liquid nitrogen. The remaining 26 patients received CAR-T cells that were directly cultured from freshly collected lymphocytes without any cryopreservation. For all patients, CAR-T cells were freshly infused post-manufacture.
The study primarily explores the attainment of CAR-T cell infusion dose (achieving $2x10^6$ cells/kg), in vivo expansion of CAR-T cells, and the persistence of CAR-T cells in the body. Secondary aims include assessing overall survival (OS), progression-free survival (PFS), 3-month complete response (CR) rate and objective response rate (ORR). The incidence of cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and levels of cytokines were also recorded. In addition, baseline characteristics of both groups were taken into analysis, including factors such as Eastern Cooperative Oncology Group (ECOG) performance status, International Prognostic Index (IPI) score, age, gender, presence of bulky disease, and extranodal lesions.
For statistical analysis, either chi-square test or Fisher's exact test was employed for categorical variables, whereas continuous variables were assessed using the rank-sum test. Survival curves between groups were compared using the log-rank test. All P-values were two-tailed.
Results: Baseline characteristics between the cryopreserved and fresh groups showed no significant differences in age, gender, IPI score≥3, ECOG score≥3, and extranodal lesions (P all > .05), while bulky disease prevalence was higher in the cryopreserved group (20.6% vs. 3.85%, P = .049).
Metrics of CAR-T cell expansion, including meeting the infusion dosage benchmark of $2x10^6$ cells/kg (46.1% vs. 44.9%, P = .90), in vivo CAR-T cell persistence (median duration: 21 days for both groups, P= .48), and the peak proportion of CART19 cells in lymphocytes (median peak: 49.6% vs. 35.2%, P = .41), revealed no significant differences between the fresh and cryopreserved groups.
Assessments of CAR-T therapy safety revealed no significant differences in the incidence of grade 3 or higher ICANS and CRS, or peak levels of cytokines including interferon gamma, IL-6, IL-10, soluble CD25, and TNFα (P all > .05) between the two groups.
Clinical efficacy measurements (3-month CR and ORR, 1-year OS and PFS) were similar between the two groups, with no statistically significant differences in CR (46.2% *vs.* 45.5%), ORR (69.2% *vs.* 61.9%), 1-year OS (75.4% *vs.* 64.1%, **Fig 1**), and 1-year PFS (52.1% *vs.* 44.5%, **Fig 2**) (P all > .05).

Conclusion: Our study affirms that cryopreservation of PBMCs has no significant influence on the safety and efficacy of anti-CD19 CAR-T therapy for patients with R/R DLBCL. These findings widen the therapeutic flexibility and accessibility of anti-CD19 CAR-T therapy for DLBCL patients.
Key words: PBMC Cryopreservation, CAR-T, DLBCL

Disclosures No relevant conflicts of interest to declare.

Figure 1, OS for cryopreserved group compared to non-cryopreserved group

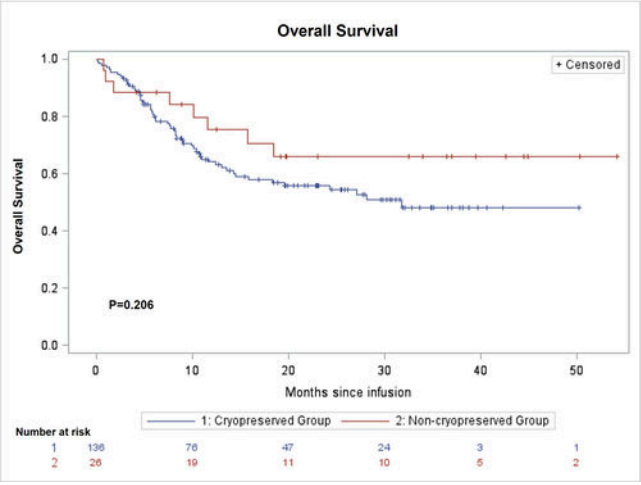

Figure 2, PFS for cryopreserved group compared to non-cryopreserved group

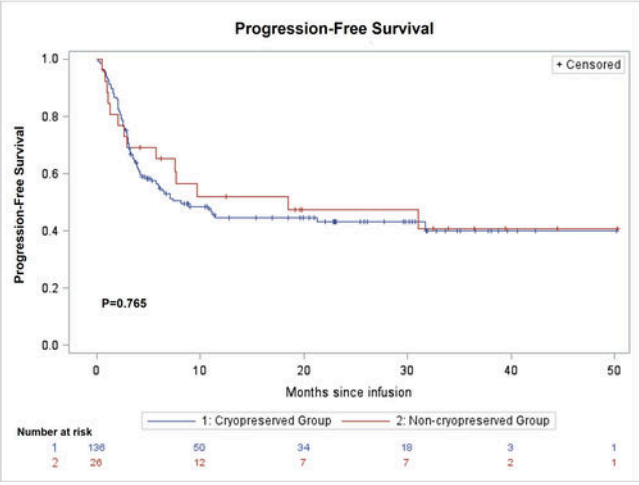

Figure 1

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