Abstract: S111

Title: TREATMENT OF POST-TRANSPLANT RELAPSE IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH BCP ALL USING CD19-CAR-T: A EUROPEAN RETROSPECTIVE ANALYSIS OF REAL-WORLD DATA

Abstract Type: Oral Presentation

Session Title: Immune therapeutic treatment in ALL

Background:

Relapse after allogeneic hematopoietic stem cell transplantation (SCT) for very high-risk acute lymphoblastic leukemia (ALL) has a dismal prognosis. The potentially curative effect of a second SCT is jeopardized by a high rate of subsequent relapse or treatment related mortality. Tisagenlecleucel (Tisa-cel), a CD19-directed CAR-T cell product, has been licensed for the treatment or post-transplant relapse in patients (pts) 25 years or younger with CD19 positive ALL.

Aims:

A retrospective study aiming at assessing the outcome of patients treated with Tisa-cel for post-SCT relapse was planned. 27 centers from 7 European countries participated and reported their consecutive patients treated between September 1st, 2018 and January 1st, 2022 (Ethics Committee approval, University of Frankfurt am Main No.: 2021-376).

Methods:

145 patients (median age 9 years, range: 1-25) treated with Tisa-cel for post-SCT relapse were included in the study. Upon lymphodepleting chemotherapy (LDC), 71 patients (57%) had <5% and 53 patients (43%) >5% leukemic blasts in the bone marrow (missing data in 21 patients). Among the conditioning regimens of the original SCT, 56 (39%) consisted of TBI, 32 (23%) were treo-based, and other regimens were used in 56 (39%) patients. Post-SCT relapse had occurred within 6 months in 38 (30%) labelled as “early relapsed” and beyond 6 months in 87 (70%) “late relapsed” patients.

Results:

CRS and ICANS:

79 (63%) patients experienced cytokine release syndrome (CRS); CRS maximum grade was grade I-II in 69 (55%), grade III-IV in 8 (6%) and grade V in 2 (2%). Thirteen (11%) patients developed ICANS (grade I: n=6, grade III-IV: n=7). Data were not yet reported in 20 patients.

Response and Survival

The 2-yr EFS was 44.3% (±4.8%) and the 2-yr OS 64.0% (±4.7%). For the 135/145 patients who were in remission at d28, the 2-yr RFS was 46.1% (±5.1%), the 2-yr probability of persistent B-cell aplasia (pBCA) 46.3% (±6.7%), and the 2-yr non-relapse mortality 1.6% (±1.1%). Age, type of donor and leukemia burden at time of LDC did not influence outcome, whereas the post-SCT timing of relapse did.Only 5 patients received a furterh HSCT for consolidation while being in remission post CAR-T cell treatment.

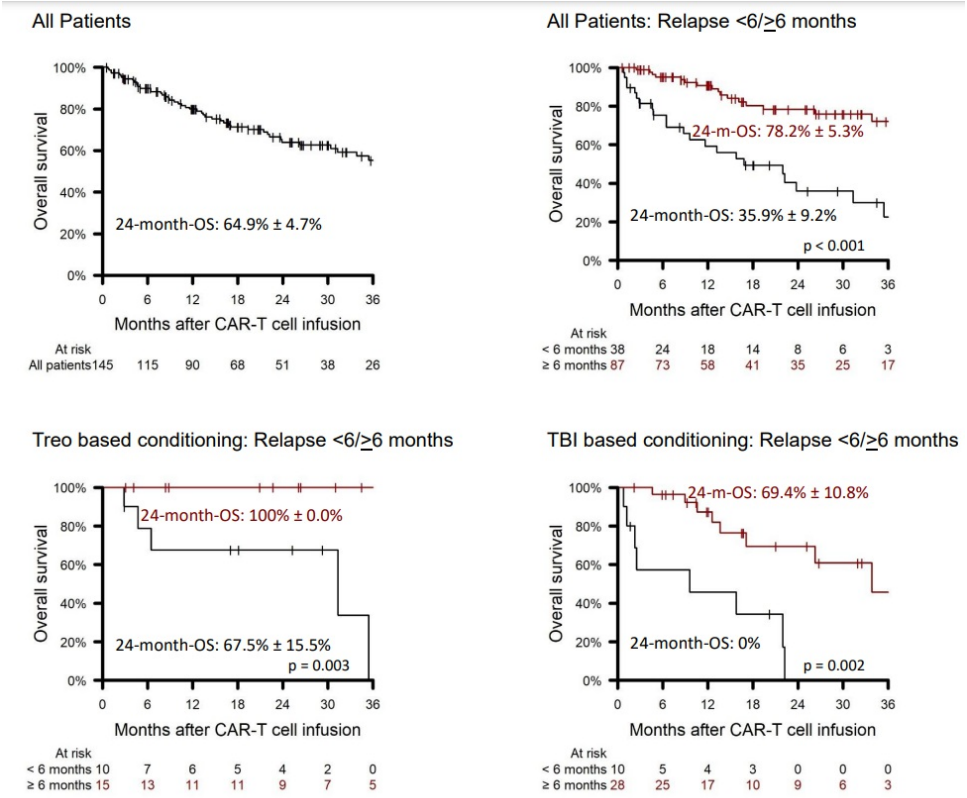
The 2-yr EFS was 19.5% (±8.3%) for early relapsed (median follow-up 29.3 months, range 1.7-41.9), and 53.0% (±6.3%) (p=0.001) for late relapsed patients (median follow-up 25.0 months, range 0.6-59.9). Similarly, the 2-yr OS was 35.9% (±9.2%) and 78.2% (±5.3%) (p<0.001) and the 2-yr RFS of 24.0% (±10.0%) and 51.9% (±6.6%) (p=0.020) for early and late relapsed patients, respectively. Such a difference was even more pronounced in patients who relapsed post SCT after conditioning with Treosulfan compared to TBI based regimen (Figure1).

The 2-yr CIR after Tisa-cel was 70.4% (±10.2%) for early relapsed, compared with 42.8% (±6.3%) for late relapsed

patients (p=0.006). Relapses tended to be CD19+ for those who early relapsed patients (CIR 43.5%±10.9%) and less frequent for late relapsed patients (CIR 24.6%±0.06%) (p=0.050). A 2-yr pBCA of 13.7% (±11.4%) was reported for early relapsed patients and of 55.8% (±7.5%) for late relapsed patients (p=0.011). This might suggest that in patients with early relapse post HSCT the generation of CAR-T cells resulted in significantly "sub-potent CAR-T cells".

Summary/Conclusion:

Patients who relapsed >6 months from HSCT have an excellent prognosis with only a single Tisa-cel infusion and no further consolidation. Early loss of CAR-T cells may be a reflection of inferior T-cell effector function, i.e. sub-potent starting material for CAR-T manufacturing, early after HSCT. These findings may become relevant for further clinical decision making.



Keywords: Immune therapy, Acute lymphoblastic leukemia, Immunotherapy