Abstract: P1468

Title: COMPARABLE OUTCOMES OF CD19-TARGETING CAR-T THERAPY IN TRANSFORMED FOLLICULAR LYMPHOMA AND DE NOVO DIFFUSE LARGE B-CELL LYMPHOMA

Abstract Type: Poster Presentation

Topic: Gene therapy, cellular immunotherapy and vaccination - Clinical

Background:

CD19 CAR-T cell therapy has changed the treatment landscape of refractory/relapsed large B cell lymphoma, including transformed from follicular lymphoma (tFL). Axicabtagene ciloleucel (axi-cel), lisocabtagene maraleucel (liso-cel), and tisagenlecleucel (tisa-cel) are now FDA-approved for the treatment of tFL, but limited data are available on their clinical activity in patients (pts) with tFL, although 3 pivotal studies suggested that outcomes in those pts were better than those with de novo diffuse large B-cell lymphoma (dDLBCL).

Aims:

Here, we report a real-world outcome of pts with tFL treated with CD19 CAR-T cell therapy and compared to dDLBCL.

Methods:

We performed a multicenter retrospective analysis of pts with tFL and dDLBCL treated with commercial CD19 CAR-T products from April 2016 to August 2023. The main clinical-biological characteristics of the pts were extracted from the electronic medical records. Cytokine release syndrome (CRS) and neurotoxicity were graded according to ASTCT guidelines. Progression-free (PFS) and overall survival (OS) were measured from the time of CAR-T cell infusion; PFS events were death, relapse, and disease progression.

Results:

A total of 399 pts were included (291 dDLBCL and 108 tFL). Within both cohorts of pts, the median age was 65 years. There were no statistically significant differences on sex, performance status, pre-apheresis levels of LDH or presence of bulky disease. Pts with tFL had more advanced stage disease at time of CAR-T apheresis (82% vs 68%, $p<0.008$). As expected, tFL was enriched in a germinal center B-cell origin (GCB) subtype by Hans' algorithm (84 vs 55%, $p<0.001$).

Pts with tFL received a median of 3 prior lines of therapy (range 1-13), including those specific for FL, vs, 2 lines (range 1-10) in pts with dDLBCL ($p<0.001$). Among tFL pts, 61 (63%) were refractory to the last therapy, with 41 (38%) exhibiting primary refractory disease, compared to 172 (63%) in the dDLBCL cohort, with 133 (46%) having primary refractory disease (p-values of 0.33 and 0.15 respectively). Moreover, a higher proportion of pts in the tFL cohort received axi-cel therapy (67% vs. 49%), whereas in the dDLBCL cohort, the percentage treated with tisa-cel was higher (31% vs. 19%) ($p< 0.009$). A comparable proportion of pts received bridging therapy (35% in tFL vs. 32% in dDLBCL).

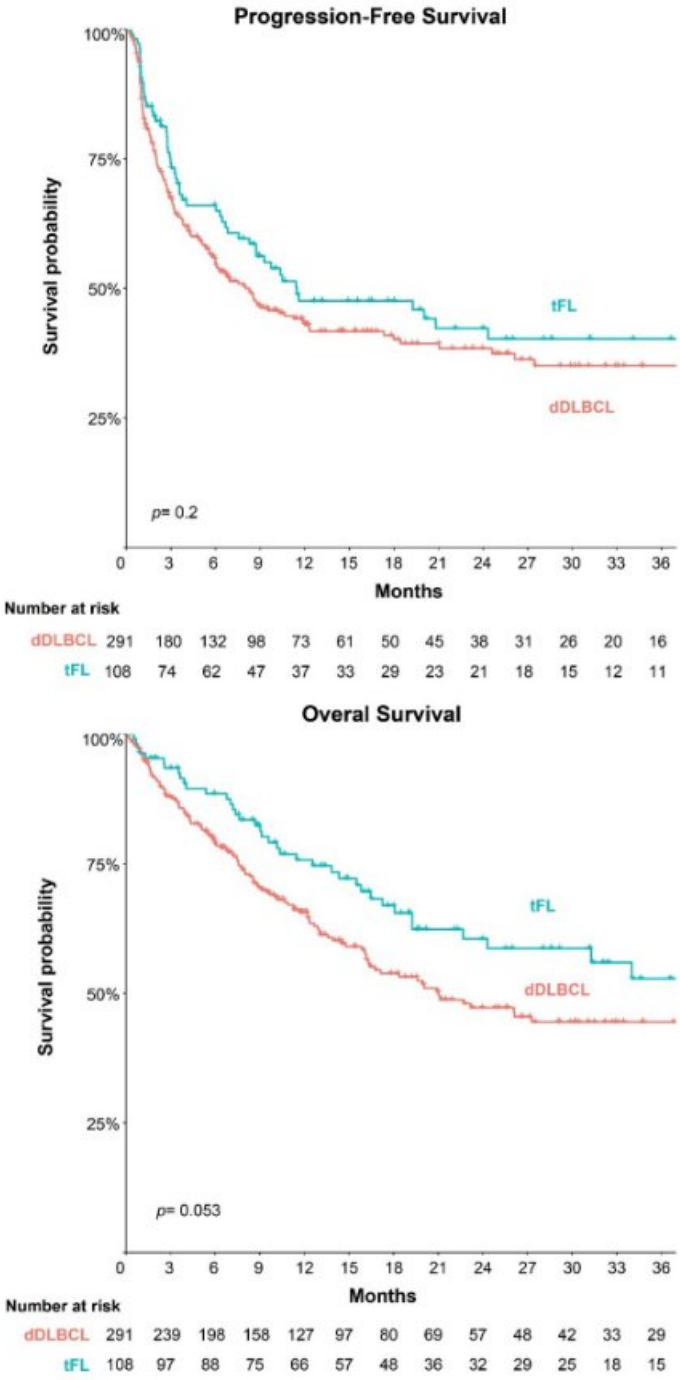
CRS of any grade was observed in 86 (80%) pts with tFL and 212 (80%) with dDLBCL, with grades ≥3 seen in 7(6%) and 28 (10%) pts, respectively. Neurologic toxicity of any grade was more prevalent in pts with tFL, occurring in 39 (36%) individuals, compared to 71 (24%) pts with dDLBCL ($p=0.02$). However, no significant differences were observed in the frequency of grade ≥3 events, with 16 (14.8%) and 30 (10%) pts in the tFL and dDLBCL cohorts, respectively ($p=0.2$). The overall response rate (ORR) and complete response (CR) rate was 79%/64% in tFL and 70%/56% in dDLBCL. With a median duration of follow-up of 19.76 months (10.62-34.65) the median PFS in the tFL cohort was 11 months and 8 months in the dDLBCL. The estimated 2-year PFS in the tFL was 42% (95% CI: 33-54%) and 38% (95% CI: 32-46%) in the dDLBCL. The median OS was 44 months in the tFL and 31 months in the dDLBCL, with an estimated 2-year OS rate of 61% (95% CI: 51–72%) in the tFL

and 47% (95% CI: 41-55%) in the dDLBCL group (Figure). High LDH serum levels were associated with a significantly lower PFS and OS in the tFL group in the univariate analysis.

Summary/Conclusion:

This study represents one of the largest analyses to date, demonstrating that CD19 CAR-T cell therapy in pts with relapsed/refractory tFL exhibits efficacy and toxicity profiles similar to those observed in pts with dDLBCL. These findings offer valuable insights into the therapeutic impact and safety profile of CD19 CAR-T cell therapy in this historically challenging patient population.

Figure. PFS and OS in the tFL and dDLBCL Cohorts



Keywords: Diffuse large B cell lymphoma, Follicular lymphoma, Transformation, CAR-T