4503 CAR T Cell Therapy in Early Relapsed/Refractory Large B-Cell Lymphoma: Real World Analysis from the Cell Therapy Consortium

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Abstract

Introduction:

Anti-CD19 CAR T cell therapy with axicabtagene ciloleucel (axi-cel) and lisocabtagene maraleucel (liso-cel) was recently approved as second line (2L) therapy for patients (pts) with large B-cell lymphoma (LBCL) whose disease relapses within 12 months (mo) of completion of or is refractory to frontline therapy (early R/R). However, limited real-world data on CAR T outcomes for early R/R LBCL are available by line of therapy. We performed a retrospective multicenter study to evaluate the real-world outcomes of early R/R LBCL pts treated with CAR T in 2L as compared to the 3L+ setting.

Methods:

Pts aged ≥ 18 years (yrs) with early R/R LBCL who received commercial axi-cel, tisagenlecleucel (tisa-cel), or liso-cel infusion from 4/2018 – 6/2023 at 9 academic US medical centers were identified from the Cell Therapy Consortium registry. Bridging therapy (BT) initiated prior to

leukapheresis and continued until lymphodepleting chemotherapy (LDc) was not considered a separate treatment line. Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded per ASTCT consensus criteria. Tumor response was assessed per Lugano criteria.

Results:

As of 6/25/24, we identified 155 pts with early R/R disease of whom 51% had primary refractory disease. Among 53 (34%) pts receiving CAR T in 2L, 74% received axi-cel and 26% liso-cel, and among 102 (66%) pts receiving CAR T in 3L+, 48% received axi-cel, 24% tisa-cel and 28% liso-cel. Median age at leukapheresis was 63yrs (IQR: 56-70) with 26% >70yrs, 67% were male, 15% had an ECOG performance status (PS) ≥ 2, and 11% were non-Caucasian. Fludarabine/cyclophosphamide LDc was received by 76% of pts and bendamustine by 23%. Forty-seven percent of pts had elevated LDH pre-LDc, and 39% achieved an objective response to BT (complete or partial response). Baseline patient characteristics that differed between pts receiving 2L vs 3L+ CAR T were in disease status at time of referral (51% refractory in 2L vs 35% in 3L+, p<0.01), and CAR T product received (74% axi-cel in 2L vs 48% in 3L+, p<0.01).

Any grade CRS occurred in 68% of all pts (6% grade 3-4). Any grade ICANS occurred in 35% of pts (15% grade 3-4). There were no differences in rates of CRS or ICANS (no CRS/ICANS vs grade 1-2 vs 3-4) between pts receiving 2L vs 3L+ CAR T. Fifty (32%) pts died related to lymphoma. Fifteen deaths were unrelated to lymphoma with the most common causes of infection (4%), other malignancy (2%) and other causes (3%). Causes of death were similar between pts receiving 2L vs 3L+ CAR T.

Out of 137 (89%) pts evaluable at 30 days post-infusion, objective response rate (ORR) was 80% and complete response (CR) rate was 54%. Out of 122 (78%) pts evaluable at 90 days post-infusion, ORR was 70% and CR rate was 57%. There was no significant difference in either ORR or CR rate for those treated with 2L or 3L+ CAR T.

Median time of follow-up was 11.1 mo (range: 0.2-63 mo). Progression-free survival (PFS) at 9 mo was 48% (95%CI: 41-57%) for all pts. Pts treated with CAR T in 2L had a 9 mo PFS of 56% (95%CI: 44-71%) compared to 45% (95%CI: 36-56%) in 3L+ (p=0.18). Overall survival (OS) at 9 mo was 64% (95%CI: 57-72%) for all pts. Pts treated with CAR T in 2L had a 9 mo OS of 75% (95%CI: 63-88%) compared to 59% (95%CI: 50-69%) in 3L+ (p=0.11). Nine-month non-relapse mortality for all pts was 9% (95%CI: 4-13%) with no significant difference between 2L vs 3L+.

Factors included in multivariable analysis (MVA) were age at time of leukapheresis, ECOG PS, response to frontline therapy, CAR T product, elevated LDH pre-LDc, discrete number of lines of prior therapy, and response to BT. Factors associated with PFS on MVA were elevated LDH pre-LDc (HR 3.6, p<0.01) and ECOG PS (0,1,≥2) (HR 1.8, p=0.01). Factors associated with OS on MVA were elevated LDH pre-LDc (HR 2.7, p<0.01), discrete number of lines of prior therapy (HR 1.3, p<0.01), and ECOG PS (0,1, ≥2) (HR 1.9, p=0.02).

Conclusions:

In this real-world analysis of pts with early R/R LBCL after frontline therapy, outcomes of pts treated with commercial CAR T in both the 2L and 3L+ setting yield favorable response and survival outcomes. While our analysis is limited by short follow-up and limited subgroup cohort size, our data suggest similar outcomes for early R/R LBCL pts treated with CAR T in 2L

vs 3L+. Selection of more fit pts and efforts to reduce disease burden prior to infusion may improve survival outcomes for early R/R LBCL pts treated with CAR T regardless of line of therapy.

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