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Title: AXICABTAGENE CILOLEUCEL AS SECOND-LINE THERAPY FOR LARGE B-CELL LYMPHOMA IN TRANSPLANT-INELIGIBLE PATIENTS: FINAL ANALYSIS OF ALYCANTE, A PHASE 2 LYSA STUDY

Abstract Type: Oral Presentation

Session Title: Aggressive lymphoma - CAR-T

Background:

Patients with relapsed or refractory (R/R) large B-cell lymphoma (LBCL) after first-line treatment who are unable to undergo high-dose chemotherapy (HDCT) and hematopoietic stem cell transplantation (HSCT) have poor outcomes and limited treatment options. In the ZUMA-7 study, Axicabtagene ciloleucel (axi-cel) demonstrated superior efficacy over standard of care (SOC) as second-line therapy in patients intended for transplant (Locke et al, NEJM 2022).

Aims:

The objective of the open-label, phase 2, ALYCANTE study (NCT04531046) was to evaluate the efficacy and safety of axi-cel in patients with R/R LBCL after 1 prior line of therapy not intended for HDCT/HSCT owing to age and/or comorbidities.

Methods:

Eligible patients were adults with R/R LBCL that was refractory to or had relapsed no more than 12 months after first-line chemoimmunotherapy and who were not deemed candidates for HDCT/HSCT based on physician's assessment and at least one of the following criteria: age ≥ 65 years; age ≥ 18 years and Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI) score ≥3; or age ≥ 18 years and prior ASCT (as 1st line consolidation). The primary endpoint was the complete metabolic response (CMR) at 3 months from axi-cel infusion based on investigator assessment. The protocol was amended to allow an expansion of 22 additional patients for subgroup comparisons.

Results:

At the time of data cut-off, 40 patients (out of 62 infused patients) could be analyzed for the primary endpoint. Median on-study follow-up was 10 months. Median age was 68 years (range, 49-81; 45% ≥ 70 years), 30% had HCT-CI score ≥ 3, and 52.5% were refractory to first-line treatment. Overall, 37 patients (92.5%) received bridging chemotherapy (R-GEMOX). Twenty-seven patients (67.5%) were refractory to bridging therapy. The study met its primary endpoint with a CMR at 3 months of 70% *versus* 12% expected with SOC based on historical controls (Cazelles et al, Leukemia & Lymphoma 2021). Best OR and CR rates were 92.5% and 80%, respectively. Median PFS was 11 months and median OS was not reached. CRS occurred in 90% of patients, including 10% of grade 3-4. ICANS occurred in 55% of patients, including 20% of grade 3-4. Twelve patients (30%) were admitted to ICU. Seven patients died: 2 due to lymphoma and 5 due to fatal infections. Early evaluation of response showed that 64.7% (22/34) and 44.4% (16/36) of patients had a negative PET-CT and an undetectable ctDNA at day 14 post axi-cel infusion, respectively.

Summary/Conclusion:

In the ALYCANTE study, axi-cel as second-line treatment in patients with LBCL who were not deemed candidates for HDCT/HSCT appears feasible and induces high response rates. The final analysis with 22 additional patients (N=62 vs 40 patients at current cut-off) and a longer follow-up will be presented at the meeting, including subgroup analysis.

Keywords: CAR-T, Diffuse large B cell lymphoma, Elderly