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ORAL ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Lisocabtagene Maraleucel in Relapsed/Refractory Large B-Cell Lymphoma: Real World Analysis from the Cell Therapy Consortium

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Introduction

Lisocabtagene maraleucel (liso-cel) is an autologous CD19-directed CAR T cell therapy approved for the treatment of relapsed/refractory (R/R) large B-cell lymphoma (LBCL) based on the TRANSCEND (Abramson et al, *Lancet* 2020), TRANSFORM (Kamdar et al, *Lancet* 2022), and PILOT studies (Sehgal et al, *Lancet Oncol* 2022). Extending clinical trial results for liso-cel to the real-world setting, we performed a multicenter retrospective study to evaluate the safety and efficacy of liso-cel in standard of care practice.

Methods

Patients (pts) aged ≥18 years with LBCL who received commercial liso-cel infusion between February 2021 (time of FDA approval) and June 2023 at 7 academic US medical centers were identified from the Cell Therapy Consortium registry. Pt and treatment characteristics were summarized descriptively, and the Kaplan Meier method was used for survival outcomes. 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 locally by the treating clinician.

Results

As of 6/10/2023, 101 pts underwent liso-cel infusion. Detailed baseline pt characteristics are shown in **Table 1**. Median age at apheresis was 71 years (range: 30-85) with 35% of pts ≥75 years, 60% were male, 16% had an ECOG PS of ≥2 at apheresis, and 11% had active secondary CNS involvement. By histology, 86% of pts had DLBCL, 7% HGBL, 5% TFL, and 2% PMBCL. Baseline comorbidities included diabetes (18%), stage IV chronic kidney disease (5%), cerebrovascular disease (5%), impaired cardiac ejection fraction (2%), pulmonary dysfunction (2%), impaired hepatic function (2%), and active infection (3%), with 68% having a Charlson Comorbidity Index score of ≥3. Due to comorbidities, 30% of pts would have been ineligible for the TRANSCEND

clinical trial. The median number of prior therapies was 3 (range: 1-8) and 16% of pts underwent prior autologous stem cell transplant. Bridging therapy was used in 62% of pts including 41% receiving polatuzumab-based treatment, 24% chemoimmunotherapy, and 21% radiation therapy. Seven (7%) pts received liso-cel on an expanded access trial (NCT04400591) due to a non-conforming product. Median time from apheresis to CAR T-cell infusion was 39 days (IQR: 34-43) and 85% of CAR T-cell infusions occurred inpatient.

Any Grade CRS occurred in 49% (3% were Grade ≥3) and any Grade ICANS occurred in 26% (10% were Grade ≥3). Median onset of CRS and ICANS was 4 and 6 days following liso-cel infusion, respectively. Tocilizumab was administered in 31% and 31% of pts received steroids for toxicity management. Nine deaths (9%) unrelated to lymphoma progression occurred at a median of 1.2 months (range: 0.3-4.3) with 2 due to infectious complications, 2 due to other malignancy, 1 due to grade 5 neurologic toxicity, 1 due to concurrent grade 5 neurologic toxicity and grade 5 CRS, 1 due to accidental death, and 2 due to unknown causes. The 6-month incidence of non-relapse mortality was 8% (95% CI, 3.4% - 15%).

The overall response rate (ORR) to bridging therapy, as assessed prior to lymphodepletion, was 45% with 17% achieving a complete response (CR). Following liso-cel infusion, response assessment was performed at day 30 and/or day 90 according to treating center practice, or in those determined to have clinical progression. Of the 89 pts evaluable at day 30, the ORR was 81% with 63% achieving a CR. Among 76 pts evaluable at day 90, the ORR was 63% with 58% achieving a CR. With a median follow-up of 10.3 months (range 0.3-22.8), month 6 outcomes were 62.7% (95% CI, 52.8% - 74.3%) for progression-free survival, 71.6% (95% CI, 60.9% - 84.1%) for duration of response, and 77.1% (95% CI, 68.4% - 86.9%) for overall survival (**Figure 1**).

Conclusions

These analyses confirm that efficacy and safety are similar or superior to those of patients enrolled in liso-cel prospective clinical trials for R/R LBCL. Notably, these outcomes were achieved in pts predominately of advanced age and with a significant comorbid burden, recognizing that one-third would have been ineligible for TRANSCEND. These results also likely reflect advancements in patient selection and toxicity management including the real world utilization of novel bridging therapy to temporize and debulk disease. Follow-up is ongoing and updated data will be presented at the meeting.

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Table 1: Characteristics of Patients Receiving Liso-cel

Characteristic	N = 101
Age at apheresis	
Median, years (range)	71 (30-85)
<65, n (%)	28 (28%)
65-74, n (%)	38 (38%)
≥75, n (%)	35 (35%)
Male, n (%)	61 (60%)
ECOG, n (%)	
0	19 (22%)
1	53 (62%)
≥2	14 (16%)
Missing	15
Charlson Comorbidity Index, n (%)	
0-1	7 (7%)
2	25 (25%)
≥3	69 (68%)
Ineligible for TRANSCEND due to comorbidities, n (%)	30 (30%)
Diagnosis, n (%)	
DLBCL	87 (86%)
HGBL	7 (7%)
TFL	5 (5%)
PMBCL	2 (2%)
Disease stage III/IV, n (%)	69 (80%)
Missing	15
Bulky disease (≥10cm), n (%)	18 (18%)
Missing	1
Active secondary CNS lymphoma, n (%)	11 (11%)
Pre-lymphodepletion LDH > institutional ULN, n (%)	41 (44%)
Missing	8
Number of prior therapies	
Median, n (range)	3 (1-8)
1, n (%)	16 (16%)
2, n (%)	31 (31%)
3, n (%)	26 (26%)
4+, n (%)	28 (28%)
Prior autologous SCT, n (%)	16 (16%)
Bridging therapy, n (%)	63 (62%)
Bridging therapy regimen, n (%)	
Polatuzumab-based	26 (41%)
Chemotherapy	15 (24%)
Radiation therapy	13 (21%)
Targeted therapy	8 (13%)
Steroids	1 (1%)
Days from leukapheresis to infusion, median (IQR)	39 (34-43)
Disease status at time of lymphodepletion, n (%)	
Active disease	74 (82%)
Complete response	16 (18%)
Missing	11
Lymphodepleting chemotherapy, n (%)	
Fludarabine and cyclophosphamide	75 (74%)
Bendamustine	26 (26%)

Abbreviations: ECOG = Eastern Cooperative Oncology Group; DLBCL = diffuse large B-cell lymphoma; HGBL = high-grade B-cell lymphoma; TFL = transformed follicular lymphoma; PMBCL = primary mediastinal B-cell lymphoma; CNS = central nervous system; LDH = lactate dehydrogenase; ULN = upper limit of normal; SCT = stem cell transplant; IQR = interquartile range

Figure 1: Progression-free Survival

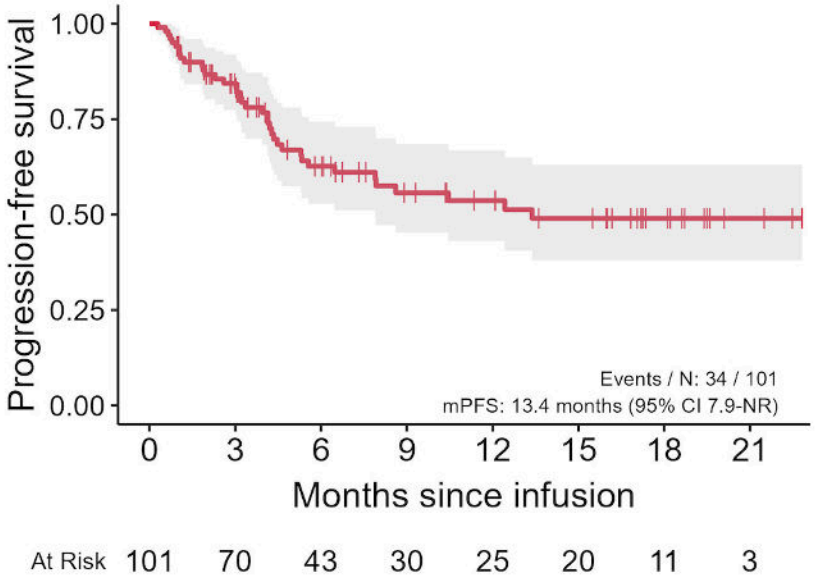

Figure 1