



## The 65th ASH Annual Meeting Abstracts

## ORAL ABSTRACTS

## 705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALY AVAILABLE THERAPIES

**Multicenter, Real-World Study in Patients with R/R Large B-Cell Lymphoma (LBCL) Who Received Lisocabtagene Maraleucel (liso-cel) in the United States (US)**

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**Background:** Liso-cel is an autologous, CD19-directed, 4-1BB CAR T cell product administered at equal target doses of CD8<sup>+</sup> and CD4<sup>+</sup> CAR<sup>+</sup> T cells that has demonstrated efficacy and favorable safety based on clinical studies. Liso-cel is approved in the US for the treatment of adults with R/R LBCL after 1 or more lines of systemic therapy, but data describing outcomes in patients treated with liso-cel in the real-world setting are limited. We report real-world clinical effectiveness and safety of commercial liso-cel in patients with R/R LBCL based on a postmarketing study using data collected at the Center for International Blood and Marrow Transplant Research (CIBMTR).

**Methods:** This is a noninterventional, observational, multicenter study of US patients who were followed in the CIBMTR Cellular Therapy Registry between February 2021 and November 2022 after infusion with commercial liso-cel (conforming product only) for the treatment of R/R LBCL. Patients who received nonconforming product are being followed in a separate postmarketing study. The primary objective was to evaluate the real-world clinical effectiveness and safety outcomes of patients with R/R LBCL receiving liso-cel, including ORR, CR, duration of response (DOR), progression-free survival (PFS), overall survival (OS), and risk of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Results were analyzed and reported descriptively.

**Results:** At data cutoff (May 4, 2023), 323 patients who received commercial liso-cel across > 50 treatment sites were included in the analysis. The median vein-to-vein time (from leukapheresis to liso-cel infusion) was 36 days (IQR, 34–42), which is consistent with clinical studies of liso-cel. The median age was 70 years (range, 24–91). Patients included those with high-risk disease (Table). Most patients had DLBCL not otherwise specified (NOS; 81%), 27% had disease transformed from indolent lymphoma, 12% had high-grade B-cell lymphoma (HGBCL), 37% had International Prognostic Index (IPI)  $\geq$  3, 6% had active CNS involvement, and 15% had prior transplant. The median number of prior lines of systemic therapy was 3 (range, 0–11), with 25% of patients having received  $\geq$  4 lines. The median time from diagnosis to liso-cel infusion was 1.4 years (range, 0.2–29.7). At a median follow-up of 7.4 months, ORR was 79%, with a 65% CR rate. Median time to response was 1.2 months

(IQR, 1.0–3.1). The median DOR has not been reached; DOR rate at 6 months was 73% (95% CI, 66%–79%). The median PFS and median OS had not been reached at the time of data cutoff. Estimated 6-month PFS and OS rates were 64% and 82%, respectively. Most events of CRS and ICANS were of low grade, with no CRS and ICANS reported in 48% and 70% of patients, respectively. Overall, 52% of patients had CRS and 3% had grade  $\geq 3$  events. There was a high concordance on CRS grading per Lee 2014 and American Society for Transplantation and Cellular Therapy criteria. The most common treatments for CRS were tocilizumab (20%) and corticosteroids/tocilizumab (12%). ICANS was seen in 30% of patients, with grade  $\geq 3$  events in 11%. ICANS was mostly treated with corticosteroids (12%) and corticosteroids/antiepileptics (5%). Based on the attributed cause of death, grade 5 CRS or ICANS were observed in 3 and 3 patients, respectively, and all but 2 patients had concomitant causes of death, including disease progression ( $n = 3$ ) and hemophagocytic lymphohistiocytosis ( $n = 2$ ). Prolonged cytopenia (grade 4 thrombocytopenia and/or neutropenia persistent at 30 days postinfusion) occurred in 10% of patients.

Conclusions: This is the first large, multicenter, real-world study of patients with R/R LBCL who received commercial liso-cel in the US. Baseline characteristics of patients treated in the real-world setting were consistent with or worse than the liso-cel registrational study experience, including the percentage of patients who had received  $\geq 4$  lines of prior systemic therapy (25% vs 26% in TRANSCEND). One-time infusion of liso-cel demonstrated deep and durable responses in patients with R/R LBCL across a broad age range, including those with high-risk features characteristic of poor prognosis. The incidence of severe (grade  $\geq 3$ ) CRS and ICANS was low. These results further support liso-cel as a therapeutic option with a favorable benefit/risk profile for a broad, real-world population of patients with R/R LBCL.

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**Table. Baseline demographics and disease characteristics**

Characteristic	All patients (N = 323)
Male, n (%)	204 (63)
Age, median (range), years	70 (24–91)
< 65, n (%)	107 (33)
≥ 65, n (%)	216 (67)
≥ 75, n (%)	89 (28)
Histology, n (%)	
DLBCL	270 (84)
DLBCL NOS	263 (81)
Transformed from CLL (Richter's)	22 (7)
Transformed from other lymphoma histology	66 (20)
PMBCL	2 (1)
FL3B	4 (1)
HGBCL	38 (12)
HGBCL with <i>c-MYC</i> and either <i>BCL2</i> and/or <i>BCL6</i> translocation at infusion	32 (10)
Other	9 (3)
ECOG PS, n (%)	
0–1 / ≥ 2	274 (85) / 18 (6)
Comorbidities, n (%)	
Pulmonary (moderate/severe)	82 (25)
Cardiac	80 (25)
Obesity	30 (9)
Renal (moderate/severe)	8 (2)
Hepatic (moderate/severe)	6 (2)
Other	32 (10)
Active CNS involvement, n (%)	18 (6)
IPI score, n (%)	
0–1 / 2	84 (26) / 121 (37.5)
3 / 4–5	92 (28.5) / 26 (8)
Number of prior lines of systemic therapy, median (range)	3 (0–11)
Received standard LDC (FLU/CY), n (%)	294 (91)

CY, cyclophosphamide; FL3B, follicular lymphoma grade 3B; FLU, fludarabine; LDC, lymphodepleting chemotherapy; PMBCL, primary mediastinal B-cell lymphoma.

**Figure 1**

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