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POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Second-Line Chimeric Antigen Receptor T Cell Therapy (CAR-T) As Standard of Care for Relapsed-Refractory Large B-Cell Lymphoma (LBCL)

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Introduction:
The randomized registrational ZUMA-7 (Locke, NEJM 2022) and TRANSFORM (Kamdar, Lancet 2022) trials in second line (2L) LBCL showed superiority of CAR T when compared to standard of care (SOC) chemotherapy-based regimens with a goal of consolidative autologous stem cell transplant. These results led to the FDA approval of axicabtagene ciloleucel (axi-cel) and lisocabtagene maraleucel (liso-cel) in 2L for LBCL with refractory disease or relapse within 1 year of completing induction chemotherapy. Significant differences exist between the registrational trial patient population and the real-world commercial CAR-T recipients in 3L+ setting (Nastoupil, JCO 2020, Jacobson, JCO 2020). Herein, we describe the outcomes of patients with LBCL treated with 2L commercial CAR T therapy.

Methods:
Five US academic institutions contributed data to this retrospective study. CAR T associated toxicities were graded by ASTCT consensus grading criteria (Lee, TCT 2019) and investigator assessed responses were reported per Lugano 2014 criteria. Patients who received CAR T therapy in 2L after the histologic diagnosis of LBCL were included, with leukapheresis between SOC approval on 4/1/2022, and 4/25/23. Patients were included if they received intermediary therapies before CAR T-cell infusion. These intermediary therapies included disease-holding therapy, defined as therapy given between relapse and the time of leukapheresis, given with the intent to "hold" patients' disease under control until CAR T-cell therapy was arranged (Bucklein, Hemasphere 2023). Patients who received therapy after relapse with the intent of restaging to decide on subsequent CAR T-cell therapy were excluded. Patients who received bridging therapy, defined as therapy given between leukapheresis and the start of lymphodepleting (LD) chemotherapy were also included. Kaplan-Meier analysis was used to calculate median progression-free survival (PFS) and overall-survival (OS).

Results:
112 patients were leukapheresed with intention to receive commercial CAR T as 2L (103 axi-cel, 9 liso-cel). All but two patients received CAR T infusion (one manufacturing failure and one delayed due to infection). The median follow-up of the cohort was 6.2 months (95%CI 4.32 - 7.61). Median age of the cohort was 66.5 yrs (range 23-83) with male predominance (66%). The

median international prognostic index (IPI) score was 3 (range 0-5) and 72% of the patients had stage III/IV disease. Fifty-nine percent of the patients had primary refractory disease.
The median time between documentation of progression after 1L therapy and patient evaluation for 2L CAR T was 22 days (IQR 15-32). The median time from patient evaluation to CAR T infusion was 47.5 days (IQR 36.25 - 67). Forty-two patients (37.5%) received disease-holding therapy and 77 (69%) received bridging therapy. Twenty-nine patients (26%), received both disease-holding therapy and bridging therapy. Receipt of these therapies was associated with longer CAR T evaluation-to-infusion times, with a median time of 61 days for patients who received both disease-holding therapy and bridging therapy, as opposed to 38 days for patients who didn't receive either therapy. This is presumably related to washout requirements and the time needed to allow for count recovery prior to either leukapheresis or LD therapy.
Among 110 CAR T infused patients, cytokine release syndrome(CRS) occurred in 88% (n=97) of the patients with grade 3 or 4 in 6.3% (n=7). Immune effector cell associated neurologic syndrome (ICANS) occurred in 59% (n= 65) with grade 3 or 4 in 30% (n= 33). No deaths from CRS or ICANS were observed.
Overall response rate (ORR) was 82.7% and complete remission rate was 61.8%. Median PFS and OS were not reached. Point estimates of PFS and OS at six months were 64.1% (95% CI: 52.8 - 73.4), and 84.4% (95% CI: 73.8 - 90.9), respectively (**Figure 1)**.

Conclusions:
This multicenter retrospective study provides insights into practice and outcomes of SOC CAR T therapy for 2L relapsed-refractory LBCL. In clinical practice, patients commonly receive "disease-holding therapy" to control disease while organizing CAR T-cell consultation and leukapheresis. Despite the relatively short follow-up duration, the best response and toxicity profiles were comparable to those observed in the pivotal clinical trials. Updated follow-up and subgroup analysis will be presented at the meeting.
SD and JYS contributed equally.

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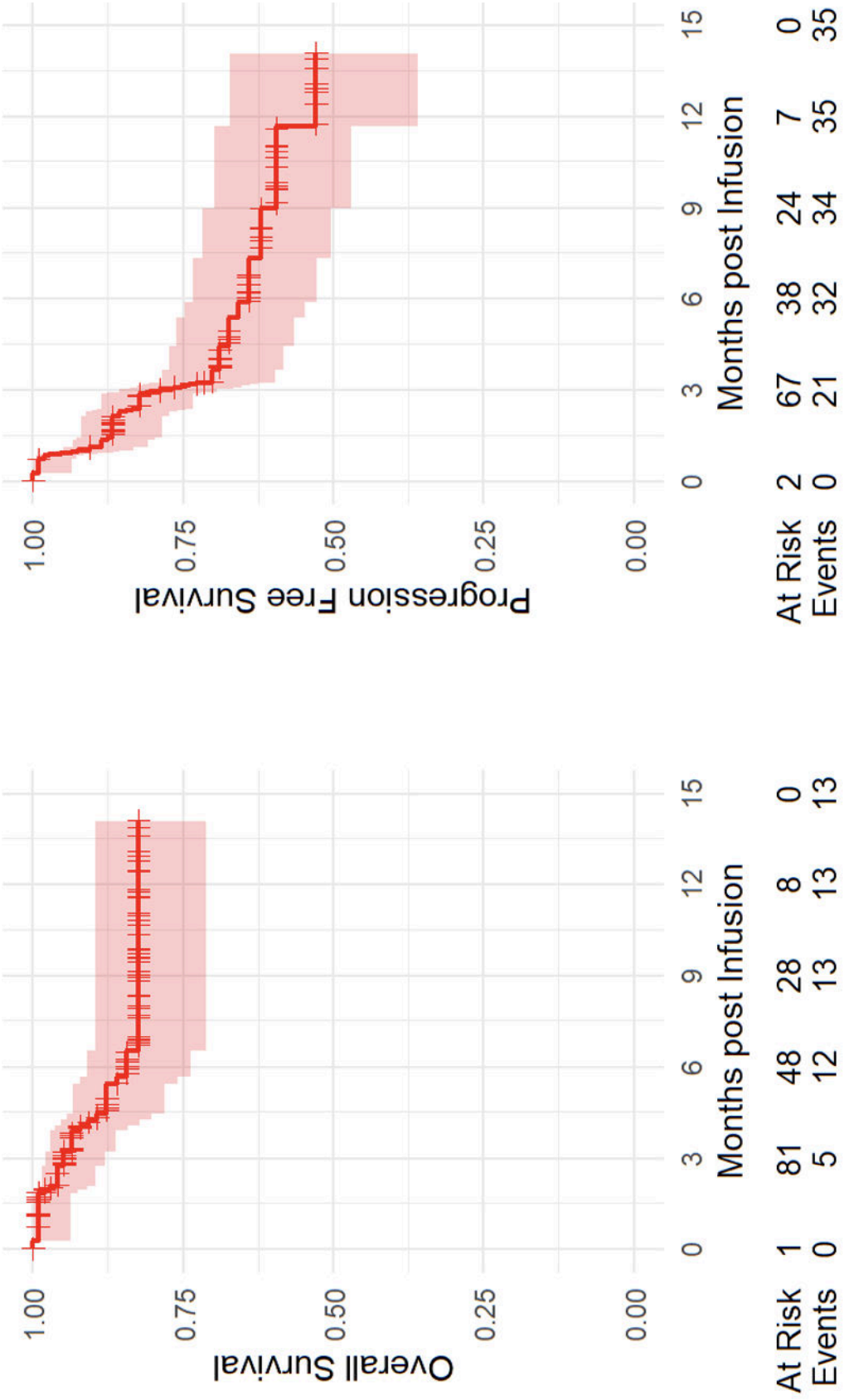

Figure 1: OS and PFS for the 110 patients who received 2nd line standard of care CAR T therapy.

Figure 1