Real-World Evaluation of Health Care Resource Utilization, Clinical Effectiveness, and Safety of Lisocabtagene Maraleucel and Axicabtagene Ciloleucel Administered in the Outpatient Setting for Relapsed or Refractory Large B-Cell Lymphoma

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Sagar S. Patel, MD,[1] Elise A. Chong, MD,[2] Farah Toron, MSc,[3] Fei Fei Liu, GDCE, MBA,[4] Fangyi Gu, ScD,[4] John H. Baird, MD,[5] Sameh Gaballa, MD[6]

[1]University of Utah, Huntsman Cancer Institute, Salt Lake City, UT, USA; [2]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [3]Bristol Myers Squibb, Uxbridge, UK; [4]Bristol Myers Squibb, Princeton, NJ, USA; [5]City of Hope National Medical Center, Duarte, CA, USA; [6]Moffitt Cancer Center, Department of Malignant Hematology, Tampa, FL, USA

Introduction

- Use of CD19-directed CAR T cell therapies has transformed treatment of patients with large B-cell lymphoma (LBCL)[1,2]
- Outpatient (OP) administration has the potential to improve access, reduce health care resource utilization (HCRU), and lower costs; however, direct real-world data on safety, HCRU, and effectiveness of liso-cel and axi-cel remain limited[3,4]

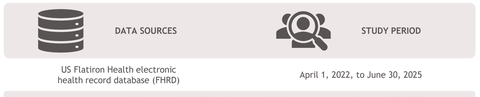
Objectives

- Report results of a retrospective study evaluating real-world HCRU, clinical outcomes, and safety of lisocabtagene maraleucel (liso-cel), an autologous, CD19-directed, 4-1BB CAR T cell product, and axicabtagene ciloleucel (axi-cel) in the OP setting for R/R LBCL

Methods

Study design

Figure 1. Data sources and inclusion/exclusion criteria



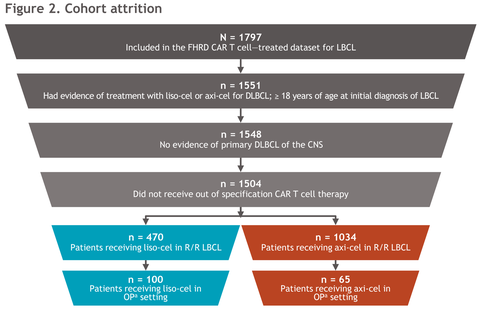
[a]Patients dropped from the cohort between the earlier data cutoff (October 31, 2024) and the current data cutoff (June 30, 2025), which includes longer follow-up time. Patients dropped from the cohort either due to changes in the Flatiron network (when sites are dropped from the Flatiron network, patients from those sites are no longer eligible for inclusion) or updated documentation leading to patients no longer qualifying based on the inclusion/exclusion criteria; [b]For the HCRU analysis, only patients with ≥ 3 months of electronic health record activity after index date were included.
ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision.

- This was a retrospective observational study using the Flatiron Health oncology-specific electronic health record database that included patients diagnosed with R/R LBCL (**Figure 1**)
- Primary objectives were to describe CAR T cell therapy–related AEs (cytokine release syndrome [CRS], cytopenia, infections, and immune effector cell–associated neurotoxicity syndrome [ICANS]), AE management, and HCRU among patients with R/R LBCL treated with liso-cel or axi-cel in an OP setting
- Secondary objectives were to describe OS and PFS
- Descriptive statistics were used to analyze AEs and HCRU
- KM landmark survival analysis was used to estimate OS and PFS

Results

Patients

Figure 2. Cohort attrition



[a]OP designation was based on how CAR T cell therapy infusion was coded.

- A total of 1504 patients with R/R LBCL were identified; 470 received liso-cel and 1034 received axi-cel (**Figure 2**)
- The analysis included 165 patients treated in the OP setting, of whom, 100 of 470 (21.3%) received liso-cel and 65 of 1034 (6.3%) received axi-cel

Table 1. Patient characteristics

Characteristic	Liso-cel (n = 100)	Axi-cel (n = 65)
Median (range) age, y	67 (23–84)	63 (28–80)
Male, n (%)	51 (51.0)	35 (53.8)
Practice type[a] at infusion, n (%)		
Community	26 (26.0)	13 (20.0)
Academic	72 (72.0)	48 (73.8)
Missing	2 (2.0)	4 (6.2)
Median (range) length of follow-up, months	7.8 (0.03–45.4)	11.0 (0.1–81.2)
Disease subtype, n (%)		
DLBCL, not otherwise specified (NOS)	89 (89.0)	51 (78.5)
HGBCL with double-/triple-hit	4 (4.0)	9 (13.8)
Primary mediastinal B-cell lymphoma	2 (2.0)	2 (3.1)
Other	5 (5.0)	3 (4.6)
Cell of origin,[b] n (%)		
Germinal center B cell	41 (41.0)	30 (46.2)
Nongerminal center B cell/activated B cell	35 (35.0)	18 (27.7)
Missing	24 (24.0)	17 (26.2)
ECOG PS at CAR T cell therapy infusion, n (%)		
0–1	72 (72.0)	41 (63.1)
2 / 3–4	6 (6.0) / 0	10 (15.4) / 0
Missing	22 (22.0)	14 (21.5)
Received transplant before CAR T cell therapy infusion, n (%)		
Allogeneic	1 (1.0)	0
Autologous	8 (8.0)	6 (9.2)
No evidence of transplant	91 (91.0)	58 (89.2)
Elevated LDH at CAR T cell therapy infusion, n (%)		
Yes	24 (24.0)	11 (16.9)
No	47 (47.0)	19 (29.2)
Missing	29 (29.0)	35 (53.8)
Presence of bulky disease[c] at CAR T cell therapy infusion, n (%)		
Yes	68 (68.0)	43 (66.2)
No/Unknown	32 (32.0)	22 (33.8)

[a]Academic cancer centers currently are NCI-designated cancer centers and are part of larger, multispecialty academic medical centers, which include both IP and OP facilities affiliated with a medical school and teaching hospital(s). Non-NCI–designated cancer centers are considered a community practice; [b]Cell of origin designation determined per the Hans algorithm[5]; [c]Presence of bulky disease determined per Lugano criteria.[6]
EBV+, Epstein Barr virus positive; IP, inpatient.

- Baseline and disease characteristics between patients treated with liso-cel and axi-cel were broadly similar (**Table 1**)
- Median (range) age was 67 years (23–84) and 63 years (28–80), and the proportion with ECOG PS ≤ 2 was 78.0% and 78.5%, respectively
- The proportion of patients with elevated LDH and DLBCL NOS was greater for liso-cel versus axi-cel (LDH: 24.0% vs 16.9%; DLBCL NOS: 89.0% vs 78.5%)
- A greater proportion of patients treated with liso-cel versus axi-cel received treatment in non-NCI–designated community centers (26.0% vs 20.0%)

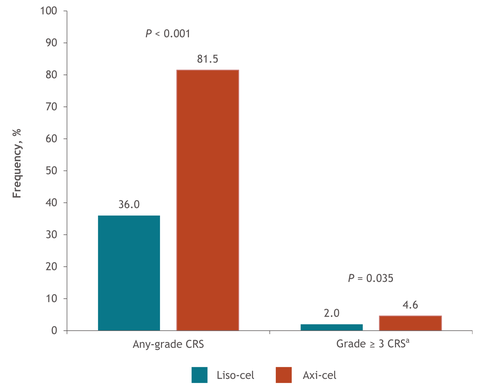
Table 2. Bridging therapy

	Liso-cel (n = 100)	Axi-cel (n = 65)
Immunotherapy, n (%)		
Polatuzumab + BR, single-agent polatuzumab, bispecific antibodies, or other (eg, brentuximab vedotin, rituximab)	34 (34.0)	15 (23.1)
Chemotherapy based, n (%)		
CHOP ± rituximab, EPOCH ± rituximab, GemOx ± rituximab, ICE ± rituximab	18 (18.0)	12 (20.0)
Targeted small molecules, n (%)		
Ibrutinib, lenalidomide ± rituximab, venetoclax	6 (6.0)	0
Steroid, n (%)	0	4 (6.2)
Radiation therapy, n (%)	19 (19.0)	7 (10.8)
Other, n (%)	8 (8.0)	5 (7.7)
No evidence of bridging therapy, n (%)	26 (26.0)	27 (41.5)

BR, bendamustine rituximab; EPOCH, etoposide, prednisone, vincristine, cyclophosphamide, and hydroxydaunorubicin; GemOx, gemcitabine and oxaliplatin.

- Use of bridging therapy was more common in patients receiving liso-cel than those receiving axi-cel (74.0% vs 58.5%)
- Immunotherapy was the most commonly used bridging therapy overall, while radiation therapy was more common with liso-cel and chemotherapy was more common with axi-cel (**Table 2**)

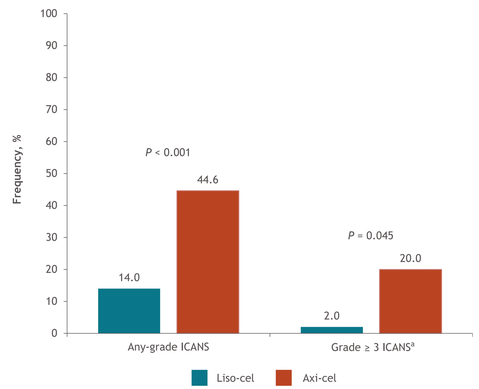
Figure 3. CRS with liso-cel and axi-cel



[a]No grade 4 events of CRS were observed in patients treated with liso-cel or axi-cel.

- A significantly lower proportion of liso-cel versus axi-cel recipients had any-grade CRS ($P < 0.001$)

Figure 4. ICANS with liso-cel and axi-cel



[a]No grade 5 events of ICANS were observed in patients treated with liso-cel.

- A significantly lower proportion of liso-cel versus axi-cel recipients had any-grade ICANS ($P < 0.001$)

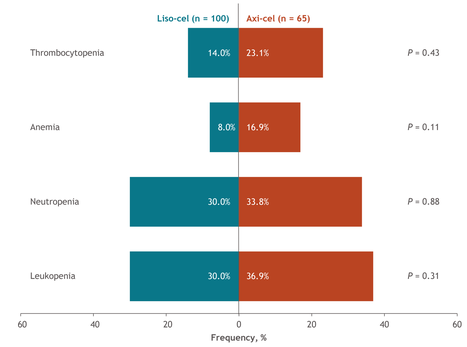
Table 3. Immune-related AE treatment management[a]

	Liso-cel (n = 100)	Axi-cel (n = 65)
Tocilizumab only, n (%)	11 (11.0)	11 (16.9)
Tocilizumab + steroid, n (%)	12 (12.0)	21 (32.3)
Steroid only (dexamethasone or other), n (%)	3 (3.0)	9 (13.8)
Anakinra/Siltuximab + steroid, n (%)	0	1 (1.5)
Tocilizumab + anakinra/siltuximab + steroid, n (%)	2 (2.0)	5 (7.7)

[a]Treatment for ICANS or CRS (use records with admin date or start date from CAR T cell therapy infusion until start date of the next line of therapy or date of end of follow-up).

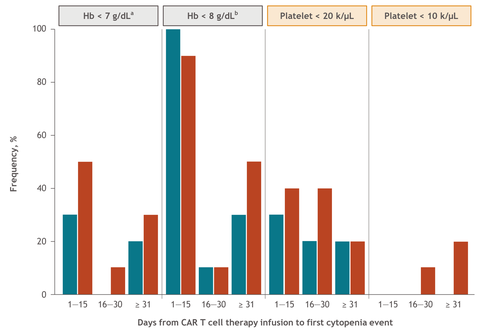
- Overall, significantly fewer liso-cel versus axi-cel recipients required any pharmacologic AE management ($P < 0.001$)

Figure 5. Grade ≥ 3 cytopenias with liso-cel and axi-cel from 30 days after infusion until next LOT or end of follow-up[a]



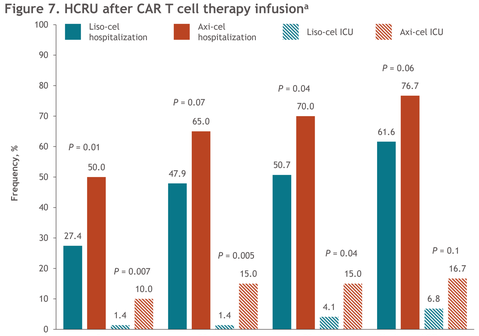
[a]*P* values are by grade.
LOT, line of therapy.

Figure 6. Frequency of hemoglobin and platelet events by time since CAR T cell therapy infusion



[a]At least 1 Hb lab result after CAR T cell therapy infusion < 7 g/dL from CAR T cell therapy infusion until next line or end of follow-up; [b]At least 1 Hb lab result after CAR T cell therapy infusion < 8 g/dL from CAR T cell therapy infusion until next line or end of follow-up.
Hb, hemoglobin.

Figure 7. HCRU after CAR T cell therapy infusion[a]



[a]For the HCRU analysis, only patients with a follow-up of ≥ 90 days were included (liso-cel [n = 73], axi-cel [n = 60]). Patients who died within 90 days were also included.

- From 30 days after CAR T cell therapy infusion until start of next LOT, numerically lower rates of grade ≥ 3 anemia and thrombocytopenia were reported for liso-cel versus axi-cel recipients, whereas rates of neutropenia and leukopenia were similar (**Figure 5**)
- The proportions of patients with infections were also similar for liso-cel versus axi-cel (19.0% vs 23.1%)
- A lower proportion of patients receiving liso-cel versus axi-cel had ≥ 1 Hb level, < 7 g/dL (n = 5; 5.3% vs n = 9; 14.8%), and < 8 g/dL (n = 14; 14.7% vs n = 15; 24.6%) after CAR T cell therapy infusion (**Figure 6**)
- Similarly, fewer patients in the liso-cel group had ≥ 1 platelet count of < 20,000/μL after CAR T cell therapy infusion than the axi-cel group (n = 7 [7.4%] vs n = 10 [16.7%])
- For patients who were hospitalized within all 3 time points (3, 30, and 90 days after infusion), the median length of stay for liso-cel and axi-cel was 8.0 and 12.0 days, respectively (**Figure 7**)
- Overall, liso-cel recipients experienced a significantly ($P < 0.05$) lower proportion of hospitalizations, shorter stays, and lower proportion of ICU admissions

Table 4. OS in patients treated with liso-cel or axi-cel

OS estimates	Liso-cel (n = 100)	Axi-cel (n = 65)
Survival probabilities at time point, % (SE)		
6 months	90.4 (3.5)	86.1 (4.6)
9 months	86.7 (4.2)	72.2 (6.2)

- Early results show that OS at 9 months was 86.7% for liso-cel and 72.2% for axi-cel (**Table 4**)

Table 5. PFS in patients treated with liso-cel or axi-cel

PFS estimates	Liso-cel (n = 100)	Axi-cel (n = 65)
Survival probabilities at time point, % (SE)		
6 months	72.0 (5.4)	61.9 (6.4)
9 months	66.1 (6.0)	57.9 (6.6)

- Early results show that PFS at 9 months was 66.1% for liso-cel and 57.9% for axi-cel (**Table 5**)

Conclusions

- Patients treated with liso-cel demonstrated more favorable HCRU outcomes compared with those treated with axi-cel, including fewer hospitalizations and shorter inpatient stays after infusion
- Liso-cel was associated with a lower incidence of all-grade CRS and ICANS compared with axi-cel, suggesting a more manageable safety profile
- Treatment with liso-cel required significantly fewer interventions for immune-related AEs (eg, tocilizumab, corticosteroids) than axi-cel, indicating reduced treatment burden
- Early results suggest that PFS at 9 months was comparable between liso-cel and axi-cel, indicating similar efficacy in disease control
- The data collectively indicate that liso-cel offers a more favorable safety and resource utilization profile without compromising efficacy compared with axi-cel
- These findings support the feasibility of OP administration of CAR T cell therapy as a treatment option for the management of R/R LBCL, alleviating the hospital-based burden of patients who receive CAR T cell therapy

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