CAR T Cell Therapy Referral Patterns and Characteristics of Patients with Relapsed or Refractory Large B-Cell Lymphoma in the United States

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Introduction

- CAR T cell therapies are a pivotal advancement in the treatment of R/R large B-cell lymphoma (LBCL) that offer the potential for long-lasting deep remissions[1–10]
- Real-world access to CAR T cell therapy remains limited to specialized academic centers, with systemic and logistical barriers limiting equitable access for eligible patients[11]
- Patients outside of CAR T sites must be referred to receive treatment
- Here, we report results of a retrospective cohort study using Unites States (US)-based real-world claims data to assess CAR T cell therapy referral patterns and characteristics of patients with R/R LBCL in the US

Methods

Study design

- Data from the Komodo Health® claims database from October 2016 to May 2025 were used to identify patients in the US with ≥ 2 diagnoses of LBCL recorded ≥ 30 days apart
- Eligible patients had continuous claims enrollment, initiated ≥ 2 lines of LBCL therapy after initial diagnosis, and had no evidence of prior LBCL-approved treatment before first recorded diagnosis
- Patients receiving ≥ 1 line of therapy (LOT) between January 2021 and May 2025 were included
- Referral rates were evaluated among patients who received treatment at non-CAR T sites (ie, centers that do not administer any approved CAR T cell therapy for LBCL) at any point during their treatment journey, and rates were assessed in aggregate and stratified by individual LOT from second (2L) to fifth line (5L) depending on data availability
- CAR T cell therapy treatment rates were analyzed for all referred patients, both overall and by LOT, and for patients who continually received care at CAR T sites across LOTs
- Baseline patient characteristics were evaluated for eligible patients and compared between referred versus nonreferred and CAR T cell therapy—treated versus non-CAR T cell therapy—treated patients
- Time to next treatment (TTNT) was tracked from the date of therapy to end of enrollment or death or end of study period (whichever came first)
- Health care resource utilization (HCRU) estimates for each population were calculated as an aggregate of inpatient, outpatient, and emergency department visit rates, as well as total medical and pharmacy costs
- Statistical significance of differences was assessed by Pearson's chi-square test, with a significance threshold of $P < 0.05$

Results

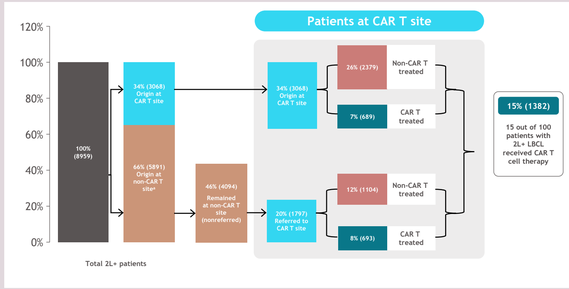
Table 1. Baseline characteristics of patients who began care at non-CAR T sites in the study period

	Nonreferred (N = 4094)	Referred (N = 1797)	*P* value[a]
Mean age, (SD), y	67.3 (15.4)	61.5 (13.8)	
Age group, n (%)			
18–34	158 (3.9)	89 (5.0)	< 0.001
35–59	902 (22.1)	661 (36.8)	
60–75	1565 (38.3)	773 (43.0)	
76+	1459 (35.7)	274 (15.2)	
Missing	10	0	
Gender, n (%)			
Male	2364 (59.0)	1113 (62.9)	0.005
Female	1645 (41.0)	656 (37.1)	
Missing	85	28	
Race/ethnicity, n (%)			
White	2500 (70.6)	976 (66.4)	0.012
Black or African American	300 (8.5)	122 (8.3)	
Hispanic or Latino	449 (12.7)	225 (15.3)	
Asian or Pacific Islander	171 (4.8)	94 (6.4)	
Other	122 (3.4)	53 (3.6)	
Missing	552	327	
US census region, n (%)			
North Central	875 (21.6)	405 (22.7)	0.002
Northeast	676 (16.7)	337 (18.9)	
South	1590 (39.3)	611 (34.2)	
West	902 (22.3)	434 (24.3)	
Missing	51	10	
Insurance type, n (%)			
Commercial	994 (26.7)	688 (44)	< 0.001
Medicare	2337 (62.7)	683 (44)	
Medicaid	376 (10.1)	186 (12)	
Veterans Affairs	18 (0.5)	1 (0.1)	
Missing	369	239	
Mean (SD) CCI	6.2 (3.82)	6.28 (3.92)	
CCI group, n (%)			
0	38 (0.9)	22 (1.2)	0.455
1–4	1788 (43.7)	804 (44.7)	
5–7	616 (15.0)	249 (13.9)	
8+	1652 (40.4)	722 (40.2)	

[a]$P < 0.05$ is considered significant.
CCI, Charlson Comorbidity Index; SD, standard deviation.

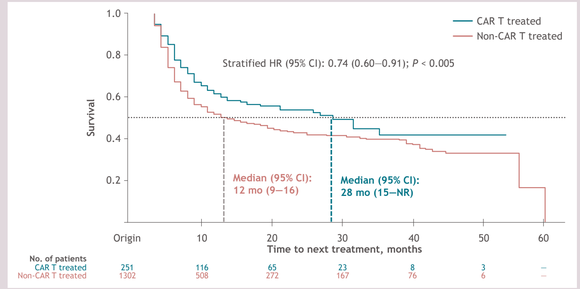
Overall, only 15% of patients with second-line or later (2L+) LBCL received CAR T cell therapy, including 7% of patients who began treatment at a CAR T site and 8% of patients who began treatment at a non-CAR T site. Among 2L patients who received CAR T cell therapy, median TTNT was 28 months, significantly longer than the 12 months in those who received therapies other than CAR T cell therapy

Figure 1. Treatment journey for patients with 2L+ LBCL



[a]Of 5891 patients identified, 21 began treatment at a CAR T site and later received treatment at a non-CAR T site, making them eligible for referral back to a CAR T site.

Figure 2. TTNT for patients with a closed claim[a] who received 2L CAR T cell therapy versus non-CAR T cell therapy



[a]Closed claim patients included those who initiated treatment at CAR T cell therapy sites and those who were referred to a CAR T cell therapy site. NR, not reached.

- Of 8959 patients with 2L+ LBCL, 34% began and remained at a CAR T site throughout their treatment journey and 66% began care at a non-CAR T site for ≥ 1 LOT (**Figure 1**)
  - Of those who began care at a non-CAR T site, 31% (1797/5891) were referred to CAR T sites during the study period, of which 39% (693/1797) received CAR T cell therapy
  - Of those who began at a CAR T site, 22% (689/3068) received CAR T cell therapy
  - Overall, 1382 (15%) patients received CAR T cell therapy (only 15 of 100 patients with 2L+ LBCL), including 689 (7%) who originated from CAR T sites and 693 (8%) referred to CAR T sites during the treatment journey
- In the overall closed-claims 2L cohort, patients treated with CAR T cell therapy had a significantly longer median TTNT than those receiving non-CAR T cell therapies (28 vs 12 months, respectively; $P < 0.005$; **Figure 2**)

- Among the 5891 patients who received ≥ 1 treatment at a non-CAR T site, significant differences in referral patterns were observed based on demographics (age, sex, race/ethnicity, geographic region, and insurance type), while comorbidity burden (CCI) had less impact (**Table 1**)
  - A higher proportion of patients who were younger, male, Hispanic or Asian, or had commercial insurance were referred to CAR T sites
  - Compared to other regions, fewer patients from the South were referred to CAR T sites
- When assessed by LOT, referral rates increased from 19% at 2L to 25% at third line (3L) and declined to 23% at fourth line (4L) and 13% at 5L
  - CAR T cell therapy treatment rates followed a similar pattern (2L: 6%, 3L: 12%, 4L: 11%, and 5L: 4%)

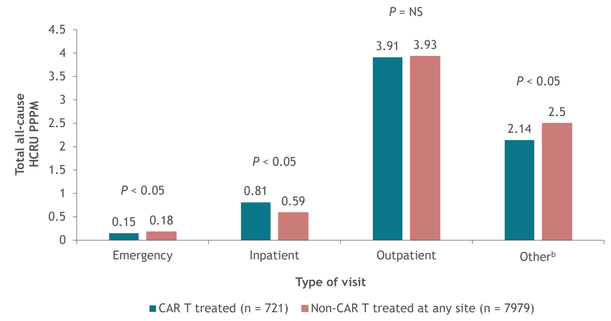
Table 2. Distance to nearest CAR T sites

	Nonreferred (N = 4094)[a]	Referred (N = 1797)	*P* value[b]
Median (range) distance to nearest CAR T site, miles	24 (0–1430)	17 (0–1514)	
Patients by distance to CAR T site, n (%)			
0 miles[c]	315 (7.9)	167 (9.3)	< 0.001
1–25 miles	1696 (42.6)	864 (48.1)	
26–50 miles	652 (16.4)	281 (15.6)	
51–80 miles	510 (12.8)	160 (8.9)	
81+ miles	805 (20.2)	325 (18.1)	

[a]116 nonreferred patients had missing data for distance. Percentage calculations are out of 3978 patients. [b]Comparing distance to nearest CAR T site between nonreferred and referred patients. $P < 0.05$ is considered significant; [c]Zero miles indicates that the patient had a CAR T site located in the same zip code as the non-CAR T site where they were receiving treatment.

- Median distance to the nearest CAR T site was greater for nonreferred versus referred patients (24 vs 17 miles; **Table 2**)
- More than half (57.4%) of referred patients lived within 25 miles of a CAR T site, compared with only 50.6% of nonreferred patients
  - Greater distances may be a barrier: Nonreferred patients were more likely to live farther away (≥ 81 miles: 20.2% vs 18.1%)

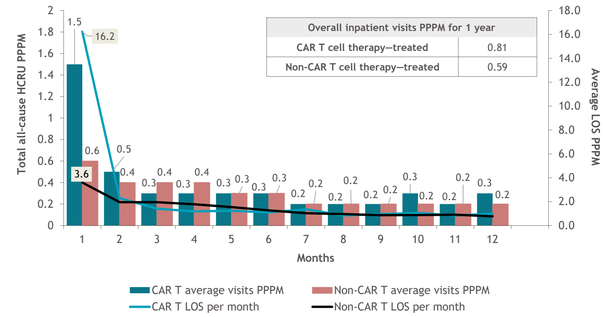
Figure 3. Mean total all-cause HCRU PPPM within 1 year of treatment initiation for patients with 2L LBCL[a]



[a]Patients were observed for a follow-up window of 1 year, where all treatment activity, including treatments after line progression were considered; [b]Includes ambulatory, urgent care, ambulatory surgery center, and home.
NS, not significant; PPPM, per patient per month.

- Patients who received CAR T cell therapy incurred higher inpatient visit rates than those who received non-CAR T cell therapy (**Figure 3**)
- For inpatient stays, the mean (SD) total length of stay (LOS) during Year 1 was 24.4 days (27.3) for CAR T cell therapy—treated patients and 12.4 days (21.0) for non-CAR T cell therapy—treated patients ($P < 0.05$)

Figure 4. Temporal view for inpatient visits within 1 year of treatment initiation



- The increase in inpatient visits with CAR T cell therapy was mainly due to utilization concentrated in the first month after infusion (**Figure 4**). Beyond the first month, HCRU was comparable between both CAR T treated and non-CAR T-treated groups

Limitations

- As the timeframe for collection of these data occurred before the Food and Drug Administration label update, which reduced requirements for patient monitoring after CAR T cell therapy, future HCRU for these patients may change

Conclusions

- This analysis of comprehensive claims data shows that, although CAR T cell therapy offers curative potential as a new standard of care for 2L+ LBCL, approximately 85% of patients do not receive CAR T cell therapy due to significant barriers, particularly limited referral
- Differences in referral patterns appeared to be linked to patient demographics, with comorbidity having less impact
- Geographic proximity likely plays an important role in access to CAR T cell therapy, as findings suggest distance longer than 25 miles may present a barrier to be referred to a CAR T site
- CAR T cell therapy—treated patients had higher inpatient visit rates and LOS within the first month of treatment initiation, likely owing to required post-infusion monitoring. Their inpatient stays were comparable to non-CAR T cell therapy—treated patients after the first month following infusion. HCRU was comparable between both CAR T cell therapy—treated and non-CAR T cell therapy—treated groups beyond the first month of treatment initiation
- When focusing on overall closed-claims patients treated in 2L, CAR T cell therapy—treated patients demonstrated significantly longer TTNT than non-CAR T cell therapy—treated patients
- These findings underscore the need to improve equitable access by expanding CAR T site availability and strengthening referral pathways from non-CAR T sites to ensure broader reach of innovative treatments across LBCL patient populations

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