Chimeric Antigen Receptor T-Cell Therapy Utilization Patterns for Relapsed/Refractory Diffuse Large B-Cell Lymphoma Among United States Community Hematologists/Oncologists

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Objectives

- Patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) initially treated by community hematologists or oncologists (cH/Os) and referred for chimeric antigen receptor T-cell (CAR-T) therapy have a complex journey.
- This study assessed that journey from the cH/O perspective.

Methods

- Retrospective, observational, multicenter chart review of R/R DLBCL patients receiving CAR-T therapy in 2019.
- Charts were abstracted by treating cH/Os capturing patient characteristics, treatment patterns, and outcomes.
- Data were:
  - **Compared by months from initial diagnosis to CAR-T therapy (<18 [n=29] or >18 [n=36]) using <18-month surrogate end point for poor prognosis (e.g., refractory disease, rapid progression).**
  - Compared by patient United States (US) region of residence (Northeast [NE], Midwest [MW], South [S], West [W]).
  - Measured using chi-square, t-, or Wilcoxon tests.

Results

Cohort Treatment Characteristics

- 65 patients were identified by 11 cH/Os:
  - Most (92%) received first-line (1L) R+CHOP, 79% had 2 pre-CAR-T infusion therapeutic lines, and 32% had prior autologous stem cell transplantation (ASCT).
  - Patients with >18 months between initial diagnosis and CAR-T therapy:
    - Were more likely to receive ASCT (53% vs 7%, *P=0.0056*) (**Figure 1**).
    - Had longer median time from 1L initiation to CAR-T therapy (26.1 vs 11.1 months, *P<0.0001*) (**Table 1**).
    - Had longer median overall survival (OS) post-CAR-T therapy (64.8 vs 40.3 months, *P=0.0488*) (**Table 1**).
    - Were significantly less likely to have disease progression by 12 months after CAR-T therapy (69% vs 56% without disease progression, *P=0.0395*).
  - Median times to other key events for overall sample (**Table 1**):
    - Referral to leukapheresis (LP), 4.6 weeks.
    - LP to CAR-T therapy, 3.6 weeks.

Cohort Region of Residence

- 65 patients were identified by 11 cH/Os:
  - Distributions within each US region (NE, MW, S, W):
    - Time to CAR-T therapy <18 months: 74%, 33%, 42%, 14% (*P=0.0056*) (**Figure 4A**).
    - ASCT received pre-CAR-T therapy (n=21): 11%, 83%, 71%, 15% (*P<0.0001*).
    - Axicabtagene ciloleucel CAR-T therapy received (n=39): 48%, 17%, 100%, 58% (*P=0.0006*) (**Figure 4B**).
    - <12 months of post-CAR-T therapy progression-free survival (PFS) (n=23): 11%, 33%, 43%, 50% (*P=0.0332*) (**Figure 4C**).

ASCT and Lines of Therapy

Figure 1. ASCT Prior to CAR-T Therapy

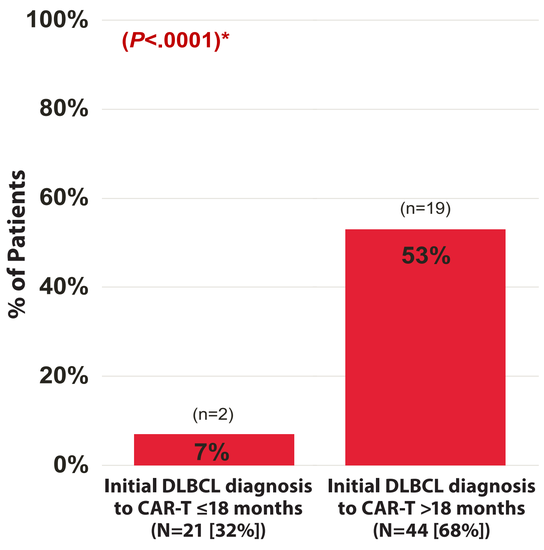
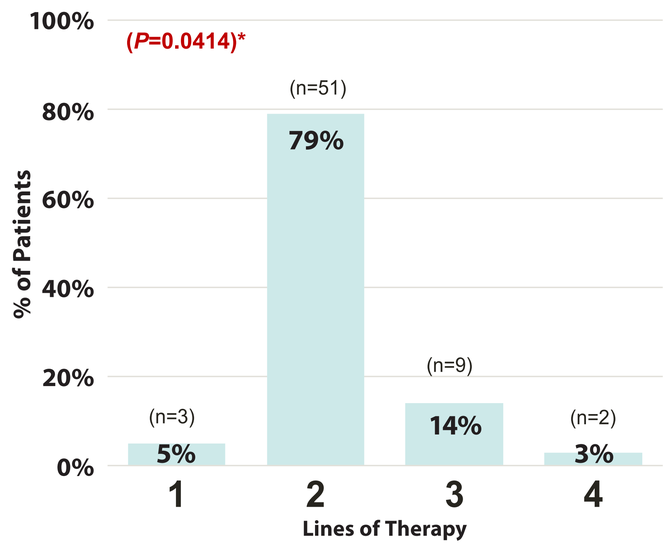


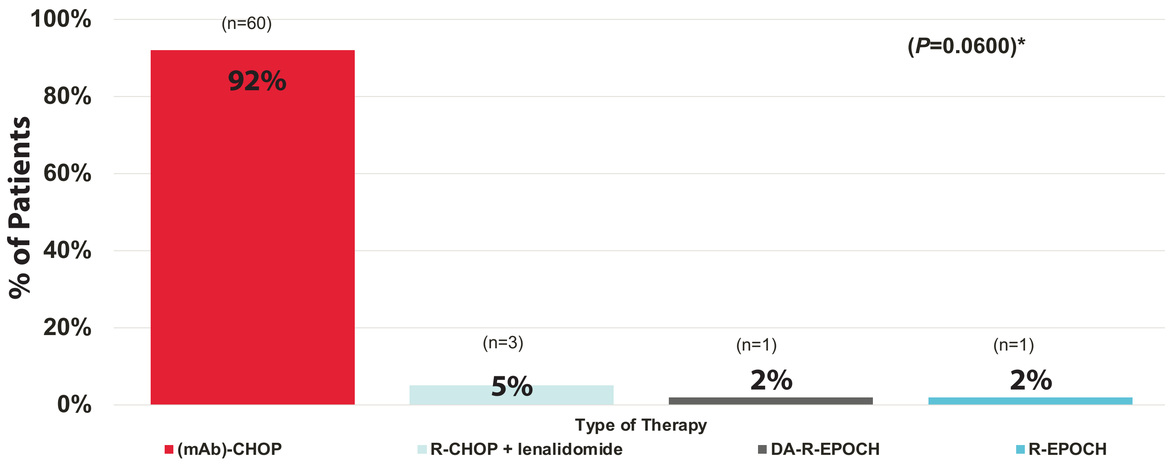
Figure 2. Lines of Therapy Prior to CAR-T



***Bolded red font indicates statistical significance (*P≤0.05*).** P-values compared across the two subgroups using t-tests and Wilcoxon tests.

1L Regimens Prior to CAR-T Therapy

Figure 3. 1L Regimens Prior to CAR-T Therapy Among All Patients (N=65)



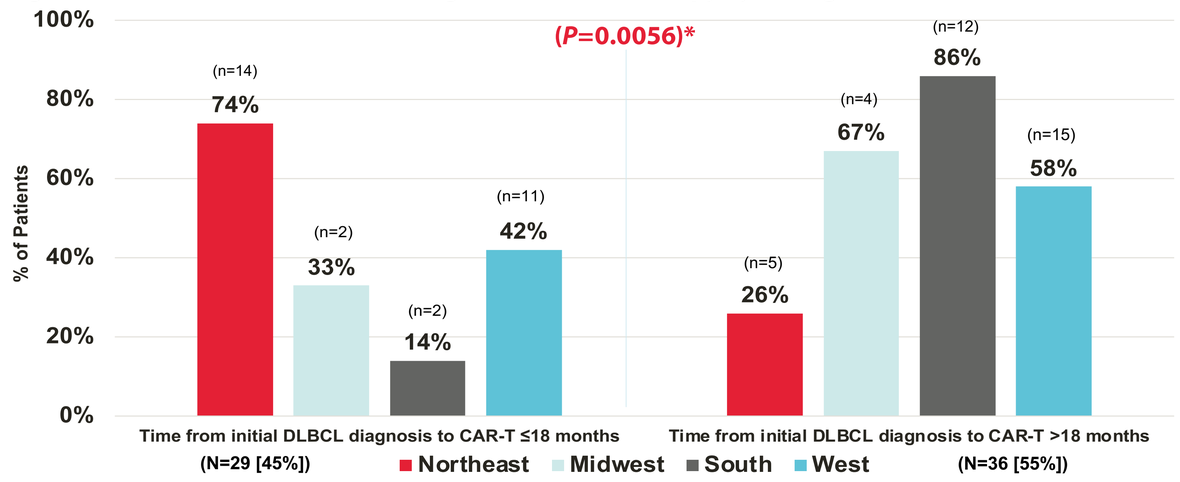
*P-values obtained using t-tests and Wilcoxon tests.

Table 1. Events Around CAR-T Therapy Among All Patients

	All treated patients (N=65)		Patients with time from initial DLBCL diagnosis to CAR-T ≤18 months (n=29)		Patients with time from initial DLBCL diagnosis to CAR-T >18 months (n=36)		*P*-value[1]
Median (IQR) time from initial DLBCL diagnosis to CAR-T infusion, months	20.3	12.3-33.1	11.4	9.0-13.7	30.6	22.2-40.3	<0.0001
Median (IQR) time from 1L initiation to CAR-T infusion, months	18.8	11.8-30.1	11.1	8.8-13.1	26.1	21.6-37.7	<0.0001
Median OS from CAR-T infusion, months (95% CI)	53.7	(40.4, 65.4)	40.3	(22.4, 57.7)	64.8	(45.8, 78.6)	0.0488
Time from CAR-T therapy referral to LP (among patients for whom LP date was reported), weeks (n, %)[2]	28	43.1	15	51.7	13	36.1	0.1879
Median (IQR)	4.6	1.9-9.4	5.9	3.0-9.6	2.0	1.6-4.9	
Time from LP (among patients for whom the date was reported) to CAR-T infusion, weeks (n, %)	28	43.1	15	51.7	13	36.1	0.1056
Median (IQR)	3.6	3.1-4.1	3.1	2.1-3.6	4.0	3.7-4.6	

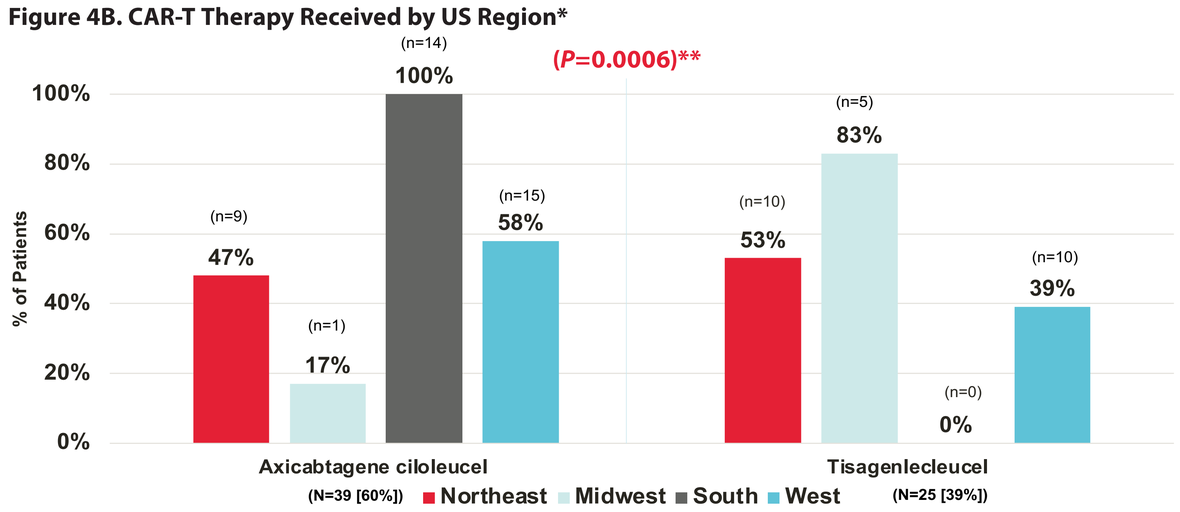
Bolded red font indicates statistical significance (*P≤0.05*).
[1]P-values compared across the two subgroups using t-tests and Wilcoxon tests. [2]All 65 patients who had CAR-T infusion had the preceding leukapheresis; however, dates of leukapheresis were entered for 28/65 patients (43%), likely due to an option of "Unknown" having been available to the physicians for this question.

Figure 4A. Time From Initial DLBCL Diagnosis to CAR-T Therapy by US Region, Months



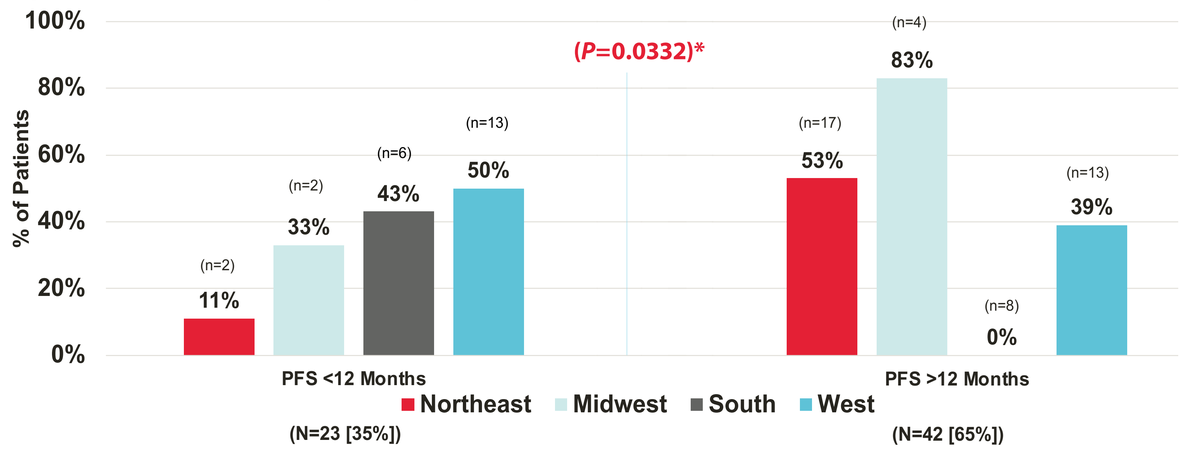
***Bolded red font indicates statistical significance (*P≤0.05*).** P-values compared across the two subgroups using t-tests and Wilcoxon tests.

Figure 4B. CAR-T Therapy Received by US Region*



*1 patient (2%) received lisocabtagene maraleucel. **Bolded red font indicates statistical significance (*P≤0.05*). P-values compared across the two subgroups using t-tests and Wilcoxon tests.

Figure 4C. PFS After CAR-T by US Region



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Conclusions

- Regional differences in patterns of community care existed for important CAR-T therapeutic patterns and outcomes among DLBCL patients.
  - These included CAR-T treatment received and timing.
  - Future studies should focus on differences in geographic access and practice patterns.
- Median time from referral to LP of 4.6 weeks among overall sample could impact availability and outcomes of CAR-T therapy.
  - Future studies should investigate how to shorten the time from referral to LP.
- Shorter real-world OS for patients with time from diagnosis to CAR-T treatment <18 months is consistent with recent trials.
  - The surrogate end point chosen of < and > 18 months from diagnosis to CAR-T therapy may have predictive value for poor outcomes following CAR-T therapy.
- These data were collected prior to FDA approval of CAR-T for 2L treatment of DLBCL in April 2022, following reports from the ZUMA-7 trial of improved event-free survival relative to standard treatment.

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Abbreviations: 1L, first-line; 2L, second-line; CAR-T, chimeric antigen receptor T-cell; cH/O, community hematologist/oncologist; DLBCL, diffuse large B-cell lymphoma; R/R, relapsed/refractory; MW, Midwest; NE, Northeast; S, South; US, United States; W, West; ASCT, autologous stem cell transplantation; CAR-T, chimeric antigen receptor T-cell; cH/O, community hematologist/oncologist; LP, leukapheresis; OS, overall survival; R+CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), vincristine sulfate (Oncovin), and prednisone; PFS, progression-free survival; CHOP, cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), vincristine sulfate (Oncovin), and prednisone; DA-R-EPOCH, dose-adjusted rituximab, etoposide phosphate, prednisone, vincristine sulfate (Oncovin), cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin); R-EPOCH, rituximab, etoposide phosphate, prednisone, vincristine sulfate (Oncovin), cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin); CI, confidence interval; IQR, interquartile range; Midwest (IA, IL, IN, KS, MI, MN, MO, ND, NE, OH, SD, WI); Northeast (CT, DE, MA, ME, MD, NH, NJ, NY, PA, RI, VT); South (AL, AR, DC, FL, GA, KY, LA, MS, NC, OK, SC, TN, TX, VA, WV); West (AK, AZ, CA, CO, HI, ID, MT, NM, NV, OR, UT, WA, WY); FDA, U.S. Food and Drug Administration.

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