REAL-WORLD CHARACTERISTICS AND CLINICAL OUTCOMES IN RELAPSE/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA PATIENTS WHO RECEIVED CAR-T THERAPY

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INTRODUCTION

- Diffuse large B-cell lymphoma (DLBCL) is an aggressive B-cell malignancy and the most common form of non-Hodgkin lymphoma, accounting for approximately one-quarter of all new cases[1].
- A significant proportion of patients diagnosed with DLBCL experience refractory or relapse (RR) disease[2]. Approval of chimeric antigen receptor T-cell (CAR-T) therapies has resulted in a novel therapeutic option for eligible patients with RR-DLBCL[3]. However, progressive disease post CAR-T remains a common scenario[4] as patient identification, timing, and effectiveness of CAR-T in the real-world setting is still evolving.

OBJECTIVES

- To further understand clinical outcomes of standard of care CAR-T in RR-DLBCL in clinical practice.

METHODS

Study population

- This retrospective analysis identified adult patients diagnosed with RR-DLBCL [01/01/2014 – 12/31/2021] who received CAR-T therapy. COTA's Real World Evidence (RWE) database is comprised of longitudinal, HIPAA-compliant data abstracted from the electronic health records (EHR) of healthcare provider sites, representing diverse treatment U.S settings from over 200 sites of care; roughly 60% of patients are seen at academic sites and 40% are seen at community sites. Patients were categorized as having received CAR-T therapy in 2L, 3L, 4L, or 5L.

Outcome measurements

- Baseline characteristics were reported for CAR-T patients. Best response rate, treatment failure, and overall survival (OS) were reported by line of therapy. Disease characteristics were derived from the EHR, including the presence of high-grade lymphoma (positive rearrangement in C-MYC and BCL-2 or BCL-6 biomarkers) and primary refractory disease (2L started within 6 months not due to patient preference, drug shortage, insurance reasons, toxicity, or pandemic reasons). CAR-T treatment failure was defined as the earliest of death, initiation of subsequent line of therapy, or documented progression event after CAR-T. Follow-up was measured from CAR-T to last contact date or death.

Statistical analyses

- The analyses conducted for this study is primarily descriptive. Categorical variables are summarized using frequencies and accompanying proportions; and continuous variables characterized using descriptive statistics such as mean, median, standard deviation and interquartile range. Time to event analyses were conducted using the Kaplan-Meier method.

RESULTS

- A total of 110 CAR-T patients were identified whereby 34 received CAR-T therapy in a clinical trial setting and were excluded from this real-world evidence study **(Table 1).** Of the 76 patients that remained, 7 (9%) received CAR-T in 2L, 30 (39%) in 3L, 28 (37%) in 4L, and 11 (14%) in 5L+.
- CAR-T patients had a mean age of 60 years, most were male (54%), 17% were diagnosed with high-grade lymphoma, and 57% were primary refractory **(Table 2)**. Median time from diagnosis to initiation of CAR-T was 16.4 months.
- Overall, 35% of patients achieved a complete response with a decrease in response in later lines (2L: 100%, 3L: 63%, 4L: 36%, 5L+: 18%) **(Table 3)**.
- Within a median follow up of 12 months (2L: 11.5 mo, 3L: 16.8 mo, 4L: 9.8 mo, 5L+: 6.5 mo), treatment failure occurred in 46% of patients, with an increase in later lines (2L: 0%, 3L: 40%, 4L: 46%, 5L+: 91%) **(Table 5)**.

Table 1. Characteristics of Patient Attrition

Description	N
Patients with a DLBCL diagnosis between January 1, 2014 and December 31, 2021 in the COTA EHR database	3436
Patients with evidence of CAR-T treatment initiation during the specified study period – the treatment start date will be considered the index date	111
Patients at least 18 years or older on index date	111
Exclude patients with evidence of multiple CAR-T treatments	110
Exclude patients who received CAR-T in the investigational setting	76

Table 2. Characteristics of Patients

CAR-T type, n (%)	
Axicabtagene ciloleucel	54 (71.05%)
Tisagenlecleucel	10 (13.16%)
Lisocabtagene maraleucel	6 (7.89%)
Unknown	6 (7.89%)
Age at index (year)	
Mean (SD)	59.60 (13.02)
≥75, n (%)	7 (9.21%)
Sex, n (%)	
Male	41 (53.95%)
Race, n (%)	
Asian	5 (6.58%)
Black/African American	2 (2.63%)
White	59 (77.63%)
Other/Unknown	10 (13.16%)
Performance Status Results Closest to Index Date: ECOG	
0-1	55 (72.37%)
2+	13 (17.11%)
Missing	8 (10.53%)
High Grade, n (%)	
Yes	13 (17.11%)
No	63 (82.89%)
Primary Refractory, n (%)	
Yes	43 (56.58%)
No	33 (43.42%)
Ann Arbor stage, n (%)	
I-II	17 (22.37%)
II-IV	46 (60.53%)
Missing	13 (17.11%)

Table 3. Overall response rate

	Any line CAR-T	2L CAR-T	3L CAR-T	4L CAR-T	5L+ CAR-T
Documented response event to CAR-T therapy*, n (%)					
Yes	71 (93%)	7 (100%)	30 (100%)	24 (86%)	10 (91%)
Missing	5 (7%)	0 (0%)	0 (0%)	4 (14%)	1 (9%)
Best response rate, n (%)**					
Complete	38 (35%)	7 (100%)	19 (63%)	10 (36%)	2 (18%)
Partial	19 (17%)	0 (0%)	6 (20%)	8 (29%)	5 (45%)

*Physician noted a response to treatment. If no response was recorded, initiation of a subsequent line or death was considered no response to the treatment.
**The denominator of best response rate included patients who did not have any documented response event after CAR-T treatment.

Table 4. Overall survival

	Any line CAR-T	2L CAR-T	3L CAR-T	4L CAR-T	5L+ CAR-T
N	**76**	**7**	**30**	**28**	**11**
Death, n (%)	25 (33%)	0 (0%)	8 (27%)	7 (25%)	10 (91%)
Median survival estimation (mo)	26.5	NR	NR	28.8	8.1

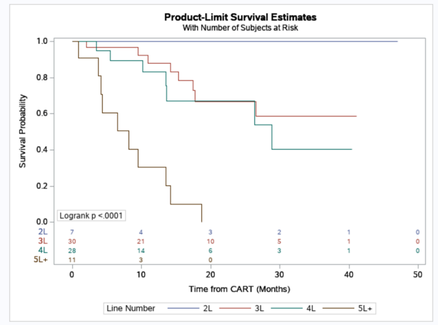
Table 5. Treatment failure rate

	Any line CAR-T	2L CAR-T	3L CAR-T	4L CAR-T	5L+ CAR-T
Follow-up (mo)					
Median (Q1, Q3)	12 (4.2, 20.3)	11.5 (4.7, 38.6)	16.8 (9.1, 26.5)	9.8 (2.5, 17.2)	6.5 (3.8, 13.5)
Initiated subsequent line, progression event, or death, n (%)					
Yes	35 (46%)	0 (0%)	12 (40%)	13 (46%)	10 (91%)
No	41 (54%)	7 (100%)	18 (60%)	15 (54%)	1 (9%)

RESULTS CONT.

- Median OS 26.5 months (Not reached (NR); 2L: NR, 3L: NR, 4L: 28.8 mo, 5L+: 8.1 mo) **(Table 4)** with unequal survival probabilities across lines of therapy (Log-rank test: p<0.001) **(Figure 1).**

Figure 1. Survival estimates



CONCLUSIONS

- CAR T-cell therapies are considered a major advance in DLBCL, yet approximately half of those patients eventually fail. Outcomes are inferior in later lines with a decrease in complete response rates, higher failure rate, and shorter survival by line of therapy, thus, highlighting the need to provide CAR T-cell therapies in earlier settings.

LIMITATIONS

- Clinical outcomes may be under reported or inaccurately documented in real-world historical EHR data.
- Subgroup analysis of outcomes according to the type of CAR-T therapy received was not performed in this study.
- The sample size of CAR T-cell treated patients was small, future analysis planned.

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