REAL-WORLD CHARACTERISTICS AND CLINICAL OUTCOMES IN RELAPSE/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA POST CAR-T FAILURE

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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].
- Progressive disease following chimeric antigen receptor T-cell (CAR-T) therapy for DLBCL is a common scenario[2]. There are limited treatment options after CAR-T failure with a poor prognosis for patients at this stage in their disease. The effectiveness of existing treatment options following CAR-T failure is still being investigated in the real-world setting.

OBJECTIVES

- To further understand the clinical outcomes of CAR-T failure in relapse/refractory (RR) DLBCL patients in the real-world setting.

METHODS

Study population

- This retrospective analysis identified adult patients diagnosed with RR-DLBCL [01/01/2014 – 12/31/2021] who received CAR-T therapy in either the investigational or real-world setting and experienced a subsequent disease progression or death. COTA's Real World Evidence (RWE) database is comprised of longitudinal, HIPAA-compliant data abstracted from electronic health records (EHR) from over 200 sites of care in US (60% academic, 40% community).

Outcome measurements

- 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).
- The first post CAR-T therapy was categorized as checkpoint inhibitor +/- other therapies (CPI), investigational therapies, tafasitamab +/- lenalidomide, polatuzumab-containing regimen (pola-containing), lenalidomide +/- anti-CD20, BTK inhibitors (BTKi), chemotherapy/chemoimmunotherapy (CT/CIT), allogenic stem-cell transplant (allo-SCT), or anti-CD20 monoclonal antibody. Overall response rate (ORR), complete response (CR), and overall survival (OS) were reported for treatment groups with at least 5 patients.

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

- Of the 110 CAR-T patients identified, 60 (55%) patients failed CAR-T therapy due to receiving subsequent line of therapy, having documented progression event, or death **(Table 1)**. Most patients who failed CAR-T received it after 2L **(Figure 1).**
- Patients who failed CAR-T were 65% males and on average 59 years old **(Table 2)**.
- Within a median follow-up of 10.9 mo, 46 (77%) of 60 patients initiated further therapy after CAR-T whereby 9 (20%) initiated investigational therapies, 9 (20%) CPI, 8 (18%) tafasitamab +/- lenalidomide, 6 (14%) pola-BR, 5 (11%) lenalidomide +/- anti-CD20, 3 (7%) CT/CIT, 2 (4%) anti-CD20 monoclonal antibody, 2 (4%) BTKi, and 2 (4%) allo-SCT as their first post CAR-T therapy **(Table 3)**. Of these patients, 46% received more than two lines of therapies after CAR-T.

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
Patients who failed CAR-T (patients with a progression, new line, or death after CAR-T)	60

Figure 1. Proportion of CAR-T lines of therapy

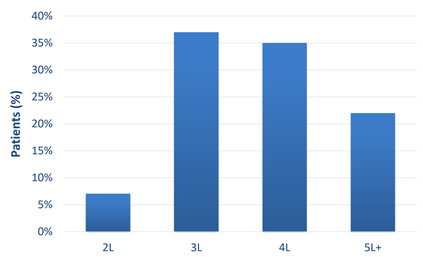

Table 2. Characteristics of Patients

Age at index (year)	
Mean (SD)	59.01 (14.88)
≥75, n (%)	8 (13.33%)
Sex, n (%)	
Male	39 (65%)
Race, n (%)	
Asian	3 (5.00%)
Black/African American	2 (3.33%)
Native Hawaiian or Other Pacific Islander	5 (8.33%)
White	47 (78.33%)
Other/Unknown	3 (5.00%)
Performance Status Results Closest to Index Date: ECOG	
0-1	40 (66.67%)
2+	15 (25.00%)
Missing	5 (8.33%)
High Grade, n (%)	
Yes	9 (15.00%)
No	51 (85.00%)
Primary Refractory, n (%)	
Yes	42 (70.00%)
No	18 (30.00%)
Ann Arbor stage, n (%)	
I-II	13 (21.67%)
III-IV	38 (63.33%)
Missing	9 (15.00%)

Table 3. Frequency of regimens 1 line after CAR-T failure

Regimen Classes, n (%)	
CPI +/- Other Therapies	9 (19.57%)
Investigational Agent	9 (19.57%)
Tafasitamab +/- Lenalidomide	8 17.39%)
Pola-BR	6 (13.04%)
Lenalidomide +/- Anti CD20	5 (10.87%)
CT/CIT	3 (6.52%)
BTKi	2 (4.35%)
AlloSCT	2 (4.35%)
Anti-CD20/CD20 monoclonal antibody	2 (4.35%)

Table 4. Overall response rate

	CPI +/- Other Therapies	Tafasitamab +/- Lenalidomide	Pola-BR	Lenalidomide +/- AntiCD20
Documented response event to post CAR-T therapy*, n (%)				
Yes	8 (89%)	7 (88%)	6 (100%)	3 (60%)
Missing	1 (11%)	1 (13%)	0 (0%)	2 (40%)
Best response rate, n (%)**				
Complete	0 (0%)	0 (0%)	0 (0%)	1 (20%)
Partial	3 (33%)	1 (13%)	2 (33%)	2 (40%)

**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.*

RESULTS CONT.

Response rates of select first therapies received after CAR-T are detailed in **Table 4**. Outside clinical trials, ORR and CRs were highest for lenalidomide +/- anti CD20 (60% & 20%), followed by CPI (33% & 0%), pola-containing (33% & 0%) and tafasitamab +/- lenalidomide (13% & 0%). OS of first post CAR-T therapy was highest for lenalidomide+/- anti CD20 (12.5 mo), then CPI (11.1 mo), pola-containing therapy (6.4 mo), and tafasitamab +/- lenalidomide (2.3 mo) **(Table 5)**.

Table 5. Overall survival

	CPI +/- Other Therapies	Tafasitamab +/- Lenalidomide	Pola-BR	Lenalidomide +/- AntiCD20
N	9	8	6	5
Death, n (%)	8 (89%)	6 (75%)	6 (100%)	2 (40%)
Median survival estimation (mo)	11.1	2.3	6.4	12.5

Note: Subsequent treatments with insufficient sample size (≤2) are not included in the presented table of results

CONCLUSIONS

- There is no existing standard of care after patients fail CAR-T therapy. Although further research is warranted in a larger sample population, poor clinical outcomes in treatment response and longevity were observed with existing treatment options. There is still a high unmet need for more effective therapies after CAR T-cell therapy has failed.

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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