PCN151

Impact of Adverse Events (AEs) on Healthcare Resource Utilization and Total Costs of Care (TCOC) Among Patients With Large B-Cell Lymphoma (LBCL)

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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.[1] In the United States, DLBCL has an incidence of 5.6 per 100,000 patients per year[2]
- Clinical outcomes are often poor among patients in whom first-line R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone) therapy, second-line chemotherapy, and/or stem cell transplantation have failed[3]
- In 2017, 2 chimeric antigen receptor (CAR) T cell therapies were approved for third-line use in the treatment of patients with relapsed/refractory DLBCL: tisagenlecleucel and axicabtagene ciloleucel (axi-cel)[4,5]
- Although clinical trials have demonstrated impressive outcomes among patients with DLBCL who received CAR T cell therapy, limited data on real-world outcomes exist
- Moreover, there is a growing interest in understanding the safety outcomes of CAR T cell therapies in real-world settings, given that there are specific treatment-related AEs that are common with CAR T cell therapies

Objectives

- Understand real-world demographics and characteristics of patients receiving CAR T cell therapy for DLBCL
- Describe real-world treatment patterns associated with CAR T cell infusion, including previous treatments, bridging therapy, and setting of CAR T cell administration
- Describe healthcare resource utilization associated with CAR T cell therapies, including inpatient and outpatient services and length of stay
- Describe the total costs of care (TCOC) associated with CAR T cell treatment, including inpatient, outpatient, and pharmacy costs
- Describe the incidence of select adverse events (AEs) of interest, including cytokine release syndrome (CRS) and neurological events (NEs)

Methods

- Adult patients diagnosed with DLBCL were retrospectively identified in 2 claims databases: IBM® MarketScan® Commercial & Medicare Database and Optum® Clinformatics® Data Mart. Patients who met the following criteria were included:
  - Received a CAR T cell infusion of either tisagenlecleucel or axi-cel from September 1, 2017, through June 30, 2018, in the IBM MarketScan database (index date), or through June 30, 2019, in the Optum Clinformatics Data Mart (index date)
  - Patients with ≥2 non-diagnostic medical claims for a DLBCL diagnosis (*International Classification of Diseases, Tenth Revision* [*ICD-10*] code: C83.3x) within 365 days of the index date
  - Patients were required to have continuous enrollment with medical and pharmacy benefits from ≥6 months before the CAR T cell infusion date (index date) and have ≥3 months of additional continuous enrollment after the CAR T cell infusion index date. Patients were followed from the index date until inpatient death, end of continuous enrollment, or end of the study period, whichever occurred first
  - Patients who participated in a clinical trial were excluded

Table 1. Definitions of Selected AEs

AE	Loose Requirement	Strict Requirement
CRS	**Evidence of CRS, defined as:** fever **OR** fatigue **OR** malaise **OR** headaches (must be accompanied by fever to be CRS) **OR** arthralgias **OR** tachycardia **OR** hypotension **OR** hypoxia Evidence of CRS within 14 days of CAR T cell infusion	Evidence of ≥2 CRS manifestations (listed on the left) within 14 days of CAR T cell infusion
Severe CRS	**Evidence of CRS, defined as:** fever + hypotension **OR** fever + hypoxia **OR** fever + hypotension + hypoxia Evidence of CRS + use of tocilizumab, corticosteroids, or vasopressors	Not applicable[a]
NE	**Evidence of:** encephalopathy **OR** delirium **OR** anxiety **OR** sleep disorders/insomnia **OR** dizziness **OR** tremor **OR** peripheral neuropathy **OR** seizures **OR** mutism **OR** aphasia **OR** presence of headache + MRI or CT scan within 30 days of CAR T cell infusion	Evidence of ≥2 NE manifestations (listed on the left)
Severe NE	**Evidence of:** encephalopathy + 1 additional NE manifestation (listed above) **OR** seizures	Not applicable[a]
Hematologic AE	**Evidence of hematologic AE, defined as:** neutropenia **OR** febrile neutropenia **OR** anemia **OR** thrombocytopenia Evidence of hematologic AE within 30 days of CAR T cell infusion	Not applicable[a]
Prolonged Cytopenia	Evidence of >1 hematologic AE for >28 days (at least 1 claim per week) within 90 days of CAR T cell infusion	Not applicable[a]

"Not applicable" indicates no strict definition was examined, as the loose definition was already restricted.
AE, adverse event; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; CT, computed tomography; MRI, magnetic resonance imaging; NE, neurological event.

- Newly initiated CAR T cell treatment was defined as the following: pharmacy (National Dug Code [NDC]), medical claim (Healthcare Common Procedure Coding System [HCPCS] code), or inpatient admission (*ICD-10* procedure codes) of a CAR T cell treatment from September 1, 2017, through June 30, 2018, or June 30, 2019
  - Tisagenlecleucel codes: NDC 0078-0958-19 and 0078-0846-19, and HCPCS Q2042 and Q2040
  - Axi-cel codes: NDC 71287-119-02 and HCPCS Q2041
  - *ICD-10* procedure codes: XW033C3 and XW043C3

Results

Table 2. Demographic Characteristics

	IBM MarketScan (N=19)	Optum (N=56)
Age, y		
Mean (SD)	55.3 (10)	62.5 (12.6)
Median (range)	56 (35–74)	67 (30–83)
Age category, n (%)[a]		
25–34 y	0	3 (5.4)
35–44 y	3 (15.8)	3 (5.4)
45–54 y	5 (26.3)	6 (10.7)
55–64 y	8 (42.1)	12 (21.4)
65–74 y	3 (15.8)	23 (41.1)
≥75 y	0	9 (16.1)
Sex, n (%)[a]		
Male	15 (79.0)	35 (62.5)
Female	4 (21.1)	21 (37.5)
Race,[b] n (%) [a]		
Black	—	4 (7.1)
Hispanic	—	11 (19.6)
White	—	30 (53.6)
Unknown	—	11 (19.6)
Primary payer, n (%) [a]		
Commercial	17 (89.5)	29 (51.8)
Medicare	2 (10.5)	27 (48.2)
Geographic region, n (%) [a]		
Northeast	8 (42.1)	8 (14.3)
South	4 (21.1)	24 (42.9)
West	2 (10.5)	8 (14.3)
North Central	5 (26.3)	15 (26.8)
Unknown	0	1 (1.8)

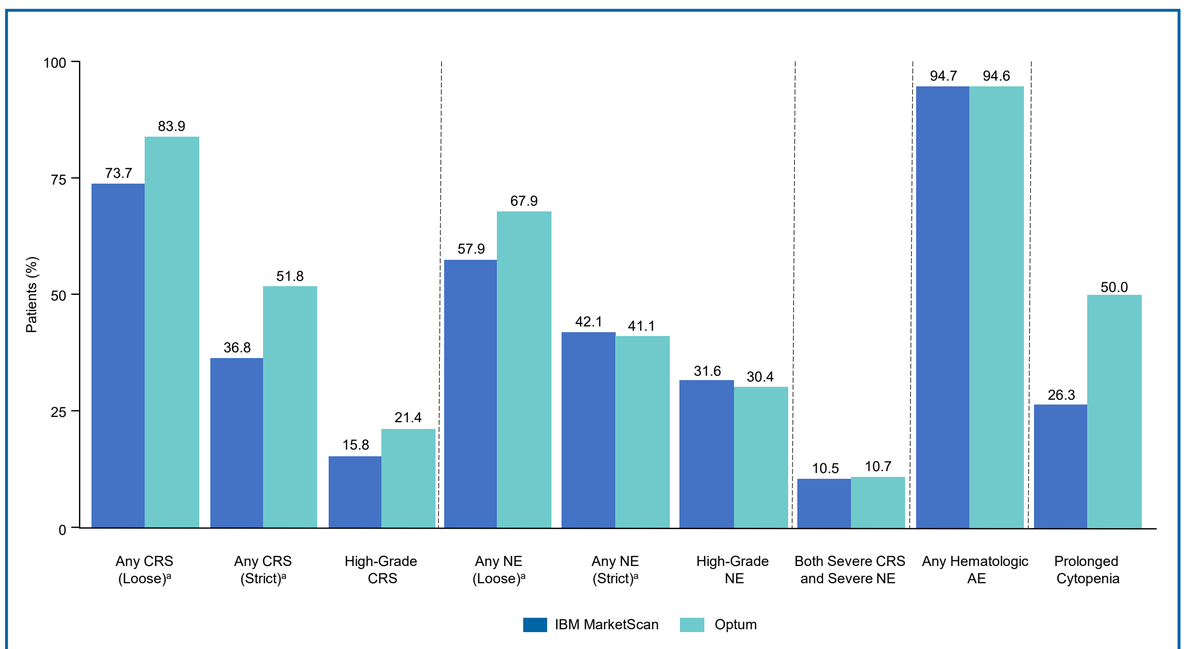
[a]Percentages may not total 100% because of rounding. [b]Race was not defined in the IBM MarketScan database.
SD, standard deviation.

Table 3. CAR T Cell Infusion Characteristics

	IBM MarketScan (N=19)	Optum (N=56)
Infusion setting, n (%)		
Inpatient	19 (100.0)	52 (92.9)
Outpatient	0	4 (7.1)
Leukapheresis		
Leukapheresis confirmed,[a] n (%)	12 (63.2)	40 (71.4)
Time from leukapheresis to CAR T cell infusion, days, median (range)	25 (14–45)	27 (14–73)
LDC		
LDC confirmed,[a] n (%)	11 (57.9)	39 (69.6)
Time from leukapheresis to LDC, days, median (range)	21 (15–28)	23 (16–69)
Time from LDC to CAR T cell infusion, days, median (range)	4 (2–5)	4 (1–6)
Duration of LDC, hours, median (range)	3 (2–3)	3 (1–3)
LDC medications, n (%)		
Cyclophosphamide + fludarabine	11 (100.0)	35 (89.7)
Bendamustine	0	3 (7.7)
Cyclophosphamide	0	1 (2.6)
Bridging therapy, n (%)		
Patients with confirmed bridging therapy	4 (21.1)	17 (30.4)

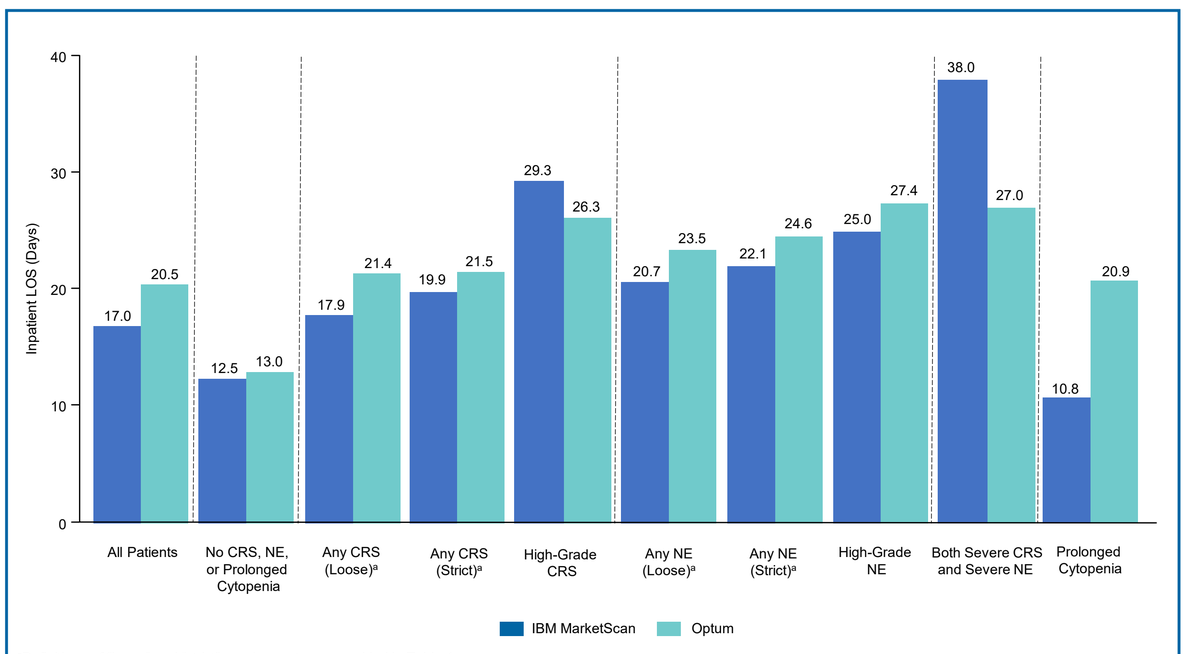
[a]Due to potential in coding errors, use of CAR T cell therapy–related services may have been missed during the time before formal procedure codes and coding guidelines were introduced.
CAR, chimeric antigen receptor; LDC, lymphodepleting chemotherapy.

Figure 1. Presence of AEs Within 14 Days of CAR T Cell Infusion



[a]Definitions of "loose" and "strict" requirements are provided in Table 1.
AE, adverse event; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; NE, neurological event.

Figure 2. Inpatient LOS 3 Months After CAR T Cell Infusion



[a]Definitions of "loose" and "strict" requirements are provided in Table 1.
CAR, chimeric antigen receptor; CRS, cytokine release syndrome; LOS, length of stay; NE, neurological event.

Table 4. Mean Total Costs After 3 Months of CAR T Cell Infusion Treatment (IBM MarketScan)

Variable	All Patients (N=19)	Any CRS[b] (n=14)	Any CRS[c] (n=7)	Severe CRS (n=3)	Any NE[b] (n=15)	Any NE[c] (n=9)	Severe NE (n=6)	Severe CRS and NE (n=2)	Prolonged Cytopenia (n=5)
Mean total cost	$428,272	$464,539	$530,974	$711,615	$434,312	$370,832	$337,490	$495,469	$565,656
Inpatient[a]	$389,265	$427,121	$483,144	$649,621	$398,667	$339,638	$308,019	$461,510	$509,959
Outpatient	$32,999	$29,863	$41,663	$59,288	$30,759	$24,944	$21,239	$30,771	$46,937
Pharmacy	$6008	$7556	$6167	$2707	$4886	$6251	$8231	$3188	$8761
Change in total cost vs all patients[d]	—	$36,267	$102,702	$283,343	$6040	($57,440)	($90,782)	$67,197	$137,384

[a]31.5% of patients were readmitted to the hospital within 3 months. Mean time to readmission was 29 days. Patients with severe CRS and NEs had the highest readmission rate (100%; n=2).
[b]Using loose requirements, as defined in Table 1. [c]Using strict requirements, as defined in Table 1. [d]Parentheses denote negative costs.
CAR, chimeric antigen receptor; CRS, cytokine release syndrome; NE, neurological event.

Table 5. Mean Total Costs After 3 Months of CAR T Cell Infusion Treatment (Optum)

Variable	All Patients (N=56)	Any CRS[b] (n=47)	Any CRS[c] (n=29)	Severe CRS (n=12)	Any NE[b] (n=50)	Any NE[c] (n=33)	Severe NE (n=19)	Severe CRS and NE (n=7)	Prolonged Cytopenia (n=28)
Mean total cost	$353,642	$375,998	$344,486	$485,110	$324,769	$344,004	$429,721	$572,131	$339,084
Inpatient[a]	$236,135	$256,355	$223,297	$313,022	$216,507	$193,424	$234,456	$258,183	$278,045
Outpatient	$112,285	$116,674	$118,753	$168,370	$101,510	$146,030	$189,976	$307,043	$55,110
Pharmacy	$5222	$2969	$2436	$3718	$6752	$4549	$5289	$6906	$5929
Change in total cost vs all patients[d]	—	$22,356	($9156)	$131,468	($28,873)	($9638)	$76,079	$218,489	($14,558)

[a]33.9% of patients were readmitted to the hospital within 3 months. Mean time to readmission was 30 days. Patients with prolonged cytopenia had the highest readmission rate (35.7%).
[b]Using loose requirements, as defined in Table 1. [c]Using strict requirements, as defined in Table 1. [d]Parentheses denote negative costs.
CAR, chimeric antigen receptor; CRS, cytokine release syndrome; NE, neurological event.

Limitations

Several limitations exist for this analysis, including:

- Use of CAR T cell therapies and related services may have been missed during the time before formal procedure codes and coding guidelines were introduced
- Due to the CAR T cell therapy coding structure, we were unable to differentiate between which of the 2 commercially available CAR T cell therapies were received
- The incidence of CRS and NEs must be interpreted with caution. Algorithms developed to identify these AEs are not validated and may overestimate or underestimate the real incidence of these AEs
- The observed number of patients treated with CAR T cell therapy is small; thus, results may be subject to variation and should be interpreted with caution

Conclusions

- Rates of AEs, particularly CRS and NEs, were high among patients treated with CAR T cell therapies
- Severe CRS was common among CAR T cell-treated patients, with 15.8%−21.4% of patients experiencing high-grade CRS. Furthermore, severe NEs were common, with 30.4%−31.6% of patients experiencing severe NEs
- Mean inpatient length of stay was longer among patients experiencing severe CRS or severe NEs compared with all patients and compared with patients without CRS, NEs, or prolonged cytopenias
- Mean total healthcare expenditures were high among CAR T cell-treated patients. Among patients experiencing severe CRS or severe NEs, mean total healthcare costs were generally higher than mean total healthcare costs for all patients
- CAR T cell therapies offer a significant advancement for the treatment of patients with relapsed/refractory DLBCL, but are associated with high costs and sometimes severe toxicities
- Bridging therapy was confirmed in 21.1%−30.4% of patients
- Outpatient use, although low, resulted in significant cost savings across the board
- There is a need for additional innovative therapies that build on CAR T cell efficacy, but offer an improved safety profile

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Disclosures

- AM is a consultant for Bristol-Myers Squibb Company; MT, MPJ, CP, SJK, and AP are employees of Bristol-Myers Squibb Company, and own Bristol-Myers Squibb Company stock
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