ORIGINAL ARTICLE

Economic Burden of Neurologic Toxicities Associated with Treatment of Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma in the United States

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BACKGROUND: Chimeric antigen receptor (CAR) T-cell therapy, which is approved for the treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL), can be associated with potentially severe and costly neurologic adverse events (AEs).

OBJECTIVES: To develop an evidence-based list of treatment-related neurologic AEs in patients with relapsed or refractory DLBCL, including AEs related to CAR T-cell therapies, and to estimate the healthcare costs associated with these neurologic AEs in a real-world setting.

METHODS: We identified grade ≥3 neurologic AEs that occurred in ≥2% of patients by reviewing drug prescribing information and published clinical trials with therapies used for relapsed or refractory DLBCL. Data from 3 nationally representative claims databases were used to identify adults with relapsed or refractory DLBCL, who were eligible for the study if they received 1 of 4 types of therapy, including CAR T-cell therapy, high-intensity cytotoxic therapy, low-intensity cytotoxic therapy, or targeted therapies. The rates of neurologic AEs and total healthcare costs were calculated for patients with and without neurologic AEs within 30 days of treatment. The costs were inflated to 2019 first-quarter US dollars.

RESULTS: A total of 16 types of neurologic AEs were identified, including 13 events related to CAR T-cell therapy and 5 related to conventional immunochemotherapy regimens, with 2 overlapping event types. Of these AEs, 11 were included in the claims analysis, based on available diagnosis codes. Of the 11,098 adults with relapsed or refractory DLBCL in the study, 118 patients received CAR T-cell therapy, 9483 received a high-intensity cytotoxic therapy, 1259 received a low-intensity cytotoxic therapy, and 238 received a targeted therapy. A total of 299 (2.7%) patients had ≥1 neurologic AEs during the 30-day postindex period. Of these patients, 43 received CAR T-cell therapy (36.4% of the 118 CAR T-cell therapy users). The mean total healthcare cost was $71,982 higher for patients with neurologic AEs than for patients without neurologic AEs. The trend of higher costs in patients with neurologic AEs was consistent across the treatment groups and was most pronounced in CAR T-cell therapy users ($143,309; 95% confidence interval, $5838-$280,779).

CONCLUSION: Patients with relapsed or refractory DLBCL who had severe or life-threatening neurologic AEs incur substantially higher costs than their counterparts who do not have neurologic AEs, with the largest cost difference in patients who receive CAR T-cell therapy.

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KEY WORDS: CAR T-cell therapy, cytotoxic therapy, healthcare costs, neurologic adverse events, relapsed or refractory diffuse large B-cell lymphoma, targeted therapy

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KEY POINTS

- CAR T-cell therapy has been linked to costly neurologic AEs in patients with relapsed or refractory DLBCL.
- This study analyzed retrospective cohort data to estimate the healthcare costs associated with treatment-related neurologic AEs in this patient population.
- All patients received 1 of 4 types of therapies, including CAR T-cell therapy, high-intensity cytotoxic, low-intensity cytotoxic, or targeted therapies.
- Of 11,098 patients with relapsed or refractory DLBCL, 299 (2.7%) had ≥1 neurologic AEs within 30 days of therapy, including 43 patients who received CAR T-cell therapy.
- Patients with neurologic AEs had $71,982 higher mean total healthcare costs than patients without neurologic AEs.
- Patients receiving CAR T-cell therapy had the greatest difference in mean total healthcare costs between those with or without neurologic AEs.
- In patients with neurologic AEs, 70% of the healthcare costs were for inpatient medical services versus 78% for outpatient services in those without neurologic AEs.
- Patients with neurologic AEs incur higher healthcare costs than patients without neurologic AEs, regardless of the treatment type.

Non-Hodgkin lymphoma (NHL) is the seventh most frequently diagnosed cancer in the United States, and is expected to account for 4.23% of all new cancer cases in 2020.[1] Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of NHL, with more than 18,000 new cases diagnosed annually.[2] The prevalence of DLBCL is projected to increase by nearly 20% in the next 15 years.[3]

Approximately 66% of patients with DLBCL respond to standard therapy with rituximab and an anthracycline-containing regimen, such as R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).[4-6] However, between 20% and 50% of patients have disease that is refractory to initial therapy or that relapses after standard therapy, and the response rate to conventional salvage immunotherapies decreases with each additional line of therapy.[4,7-10]

High-dose chemotherapy followed by autologous stem-cell transplantation (ASCT) is the standard treatment for relapsed or refractory DLBCL.[4] However, 40% to 50% of patients with relapsed or refractory DLBCL are ineligible for ASCT, primarily because of chemorefractory disease or the failure to collect stem cells.[11-13]

Second-line regimens that are recommended for the treatment of patients with relapsed or refractory DLBCL have varying overall response rates, complete response rates, overall survival, and progression-free survival (PFS).[14] For example, lenalidomide monotherapy has been shown to induce an overall response rate of 27.5%, a median overall survival of 31 weeks, and a median PFS of 13.6 weeks[15]; however, treatment with gemcitabine plus oxaliplatin or with the combination of gemcitabine, oxaliplatin, and rituximab resulted in complete response rates of 30% and 50%, respectively, and at 42 months, in overall survival rates of 7% and 37%, respectively.[16]

A regimen of bendamustine plus rituximab was associated with a complete response rate of 37.3% and a median PFS of 6.7 months.[17] In a recent retrospective meta-analysis of 636 patients with relapsed or refractory DLBCL, the rate of objective response to the next line of therapy was 26%, with a complete response rate of 7% and a median overall survival of 6.3 months.[10] These poor outcomes reinforce the unmet need for new therapeutic options for patients with relapsed or refractory DLBCL.[4]

Chimeric antigen receptor (CAR) T-cell therapies that target CD19 antigens can yield durable remissions based on clinical trials and real-world evidence.[14,18-20] The treatment options for relapsed or refractory DLBCL expanded with the approvals of the 2 CAR T-cell therapies axicabtagene ciloleucel and tisagenlecleucel. Currently, these 2 drugs are recommended by the National Comprehensive Cancer Network (NCCN) for the treatment of patients who have had a partial response to second-line therapy (regardless of transplant eligibility) and patients whose disease relapsed after a complete response to second-line therapy or those who have progressive disease.[14]

A real-world, retrospective study demonstrated that the majority (82%) of patients with relapsed or refractory DLBCL are eligible for CAR T-cell therapy based on clinical trial criteria.[21] However, CAR T-cell therapy has been associated with the unique acute toxicities of cytokine release syndrome and neurologic adverse events (AEs) known as immune effector cell-associated neurotoxicity syndrome (ICANS) that are not often seen with traditional anticancer therapies.[18,19,22,23] ICANS typically presents as encephalopathy, aphasia, and confusion, but can progress in more severe cases to depressed levels of consciousness, coma, seizures, motor weakness, and cerebral edema.[23]

The economic burden of managing neurologic AEs is not well-known. We found no studies reporting healthcare costs associated with treatment-related neurologic

AEs in patients with relapsed or refractory DLBCL. The objectives of this study were to develop an evidence-based list of relapsed or refractory DLBCL treatment-related neurologic AEs, including those with the 2 CAR T-cell therapies approved for this indication (axicabtagene ciloleucel and tisagenlecleucel), and to estimate the healthcare costs associated with these neurologic AEs using real-world data.

Methods

Grade ≥3 neurologic AEs that occurred in ≥2% of patients included in this study were first identified by reviewing US drug prescribing information, European Medicines Agency summaries of drug characteristics, and published phase 2 and phase 3 clinical trials for the treatment of relapsed or refractory DLBCL (see **Appendix Table 1**, available at **www.AHDBonline.com**). Neurologic AEs were graded using the National Cancer Institute's Common Terminology Criteria for Adverse Events (version 4.03).[18,19] Neurologic AEs that were consistent with ICANS and their corresponding *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) or *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) diagnosis codes were then identified based on inputs from clinical experts.

A retrospective cohort data analysis was then performed using the deidentified Optum Clinformatics Data Mart database, IQVIA PharMetrics Plus, and IBM MarketScan Commercial and Medicare Supplemental (MarketScan is a trademark of IBM Corporation) databases. The Optum data cover more than 10 years of patient experience and contain deidentified claims and clinical data from multiple health plans and healthcare providers for more than 150 million people. The database includes plan enrollment information, medical and pharmacy claims, and laboratory results from multiple payers.

PharMetrics Plus includes fully adjudicated pharmacy, hospital, and medical claims at the anonymized patient level, which are sourced from commercial payers covering more than 150 million enrollees from 2007 to the present. The MarketScan Commercial and Medicare Supplemental databases represent the health services of more than 43.6 million employees, dependents, and retirees in the United States with primary or Medicare supplemental coverage through privately insured fee-for-service, point-of-service, or capitated health plans. The databases include enrollment information and claims with healthcare utilization information (eg, inpatient and outpatient services, and prescription drug claims).

All data were deidentified and were compliant with the Health Insurance Portability and Accountability Act of 1996, exempting this study from Institutional Review Board approval. In addition, only claims with complete medical, pharmacy, and enrollment information were used in the current analysis. Data with incomplete information were excluded from the study.

Adults (aged ≥18 years) were included in the analysis if they received second-line or later therapy during the identification periods of January 1, 2007, to December 31, 2018, for Optum; January 1, 2007, to January 15, 2019, for PharMetrics Plus; or January 1, 2007, to March 31, 2019, for MarketScan. The patients also had to have at least 1 inpatient or at least 2 outpatient claims for DLBCL (*ICD-9-CM* code 200.7X; *ICD-10-CM* code C83.3X) during the identification periods, with at least 1 claim having occurred before or on the date of the second-line or later therapy. The second-line or later therapies were selected based on NCCN Clinical Practice Guidelines in Oncology and input by clinical experts.

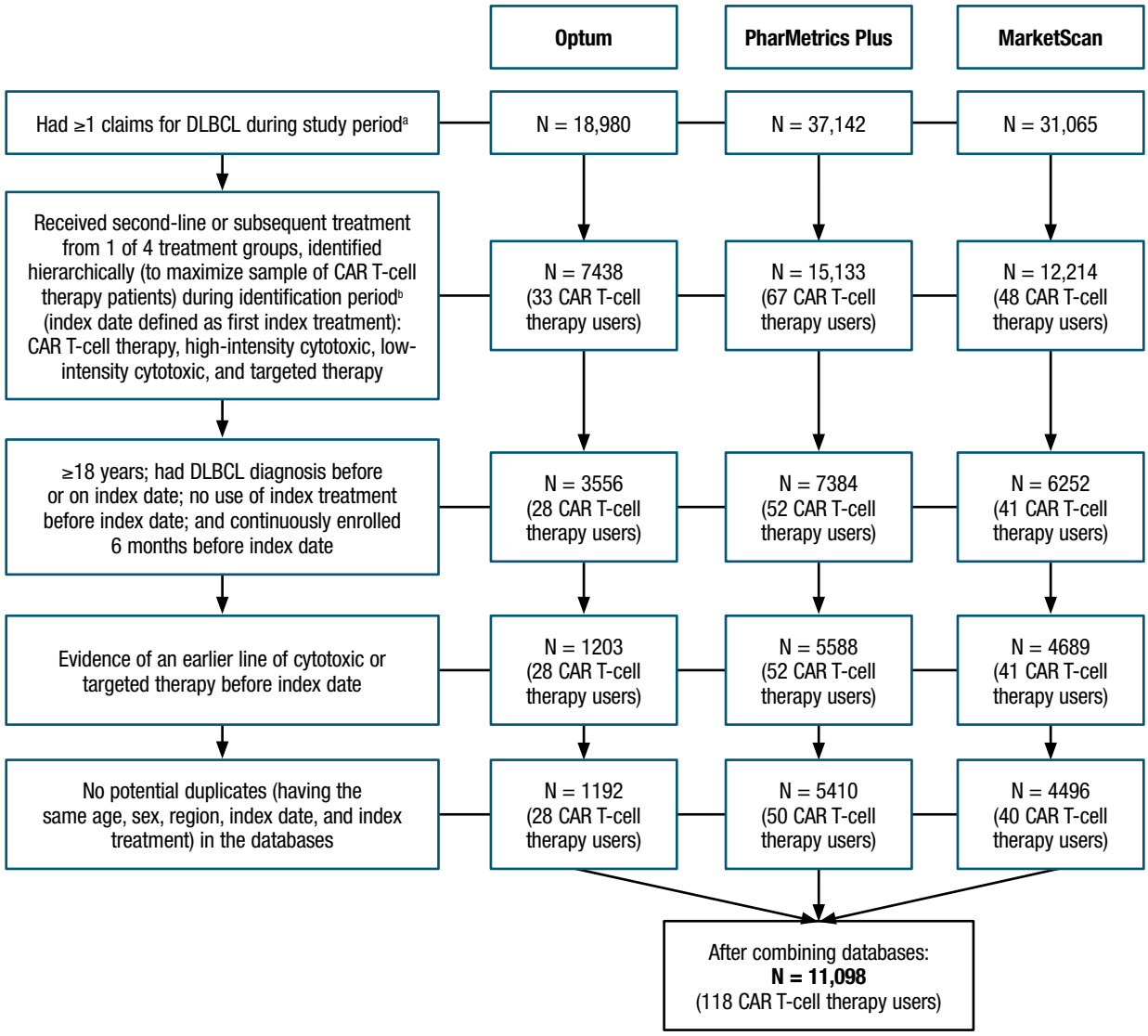
To ensure an adequate CAR T-cell therapy sample size, the therapies were categorized hierarchically into 4 groups, including CAR T-cell therapy, high-intensity cytotoxic therapy (defined as treatment regimens containing ≥1 of the following agents: carboplatin, cisplatin, cyclophosphamide, or ifosfamide), low-intensity cytotoxic therapy (defined as treatment regimens containing ≥1 of the following agents: bendamustine, lenalidomide, or gemcitabine), and targeted therapy (including rituximab alone, ibrutinib alone, or brentuximab vedotin); see **Appendix Table 2** (available at **www.AHDBonline.com**), for detailed treatment regimens based on the agent. The treatment initiated on the index date was considered to be the index treatment. The patients were further required to have at least 6 months of continuous enrollment with medical and pharmacy benefits before the index date.

To prevent the inclusion of potential duplicate records, for patients with the same age, sex, region, index date, and index treatment in the multiple databases, patients from one of the databases were randomly selected to be included in the analysis. Patients were followed until the first evidence of inpatient death in the claims data, the end of health plan enrollment, the end of the study period, or 30 days after the index date, whichever occurred first. Based on clinical trials, neurologic AEs are most likely to occur early after treatment, with a median time to onset of 6 days (range, 1-17 days) with tisagenlecleucel, and 5 days (range, 1-17 days) with axicabtagene ciloleucel; a median duration of 14 days with tisagenlecleucel; and a median resolution on day 17 after infusion with axicabtagene ciloleucel.[18-20] Therefore, a 30-day postindex time period was used for the cost analysis.

Study Measures

The baseline variables, including patient demograph-

Figure 1 Patient Attrition



[a]From January 1, 2007, to December 31, 2018, January 15, 2019, and March 31, 2019, for Optum, PharMetrics Plus, and MarketScan, respectively.
[b]From July 1, 2007, to December 31, 2018, January 15, 2019, and March 31, 2019, for Optum, PharMetrics Plus, and MarketScan, respectively.
CAR indicates chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma.

ics (age, sex, region) and Charlson Comorbidity Index (CCI) score, were measured during the 6-month preindex period.[24,25] The primary outcomes of interest, which were measured during the 30-day postindex period, included the rates of neurologic AEs and the differences in total healthcare costs between patients with and without neurologic AEs.

The inpatient service costs were calculated as the sum of the inpatient claims (room and board, inpatient pharmacy, and hospitalization services included); the outpatient service costs as the sum of the outpatient claims (office visit, emergency department visits, and outpatient hospitalization); and the outpatient pharmacy costs as the sum of the outpatient pharmacy claims. All of these primary outcomes of interest were reported for the total population and by treatment groups.

Statistical Analysis

Descriptive, unadjusted analyses were performed to assess the differences among the treatment groups at baseline. The total healthcare costs related to neurologic AEs were reported in full descriptive analysis, including

Table Patient Demographics and Charlson Comorbidity Index Score

Patient demographics	CAR T-cell therapy cohort (N = 118; 1.1%)	High-intensity therapy cohort (N = 9483; 85.4%)	Low-intensity therapy cohort (N = 1259; 11.3%)	Targeted therapy cohort (N = 238; 2.1%)	All patients (N = 11,098; 100%)
Age, yrs, mean (SD)	58.5 (10.5)	61.2 (13.7)	66.0 (13.3)	60.2 (14.2)	61.7 (13.7)
18-34, N (%)	6 (5.1)	433 (4.6)	21 (1.7)	14 (5.9)	474 (4.3)
35-44, N (%)	5 (4.2)	623 (6.6)	45 (3.6)	11 (4.6)	684 (6.2)
45-54, N (%)	23 (19.5)	1479 (15.6)	158 (12.5)	43 (18.1)	1703 (15.3)
55-64, N (%)	52 (44.1)	3318 (35.0)	378 (30.0)	91 (38.2)	3839 (34.6)
≥65, N (%)	32 (27.1)	3630 (38.3)	657 (52.2)	79 (33.2)	4398 (39.6)
Female, N (%)	35 (29.7)	4207 (44.4)	570 (45.3)	111 (46.6)	4923 (44.4)
Region					
Midwest, N (%)	26 (22.0)	2743 (28.9)	364 (28.9)	62 (26.1)	3195 (28.8)
Northeast, N (%)	32 (27.1)	1797 (18.9)	234 (18.6)	62 (26.1)	2125 (19.1)
South, N (%)	52 (44.1)	3805 (40.1)	480 (38.1)	90 (37.8)	4427 (39.9)
West, N (%)	8 (6.8)	1138 (12.0)	181 (14.4)	24 (10.1)	1351 (12.2)
Charlson Comorbidity Index score, mean (SD)	3.6 (2.3)	4.5 (3.0)	4.6 (3.1)	4.7 (2.9)	4.5 (3.0)

CAR indicates chimeric antigen receptor; SD, standard deviation.

the mean, median, standard deviation (SD), and range. The subgroup costs, by treatment, were also reported.

All the costs were inflated to 2019 first-quarter US dollars using the medical care component of the Consumer Price Index. All data transformations and statistical analyses were performed using SAS version 9.4 (SAS Institute; Cary, NC).

Results

A review of the prescribing information, summaries of drug characteristics, and clinical trials yielded a list of 23 neurologic AEs, which were further consolidated into 16 types of neurologic AEs consistent with ICANS. Of these AEs, 13 occur with CAR T-cell therapy, 5 with conventional immunochemotherapy, and 2 with both types of therapy. The final list of 11 neurologic AEs in the claims analysis was determined based on the availability of *ICD-9-CM* and *ICD-10-CM* diagnosis codes, and included encephalopathy, somnolence, mental status changes or disorientation, disturbances in attention, seizure, cerebral edema, speech disorder, aphasia, delirium, agitation or restlessness, and abnormal motor activity.

From the 3 claims databases, 87,187 patients with DLBCL were identified (18,980 from Optum; 37,142 from PharMetrics Plus; and 31,065 from MarketScan; **Figure 1**). After applying the study inclusion criteria, 11,480 patients remained (1203 from Optum; 5588 from PharMetrics Plus; and 4689 from MarketScan). A total of 11 potential duplicates were removed from the Optum database, 178 from PharMetrics Plus, and 193 from MarketScan.

The final sample consisted of a total of 11,098 patients with relapsed or refractory DLBCL, including 118 patients who received CAR T-cell therapy, 9483 who received high-intensity cytotoxic therapy, 1259 who received low-intensity cytotoxic therapy, and 238 who received targeted therapy (Figure 1 and **Table**).

A total of 299 (2.7%) patients had at least 1 neurologic AE during the 30-day postindex period, including 43 (36.4%) of the 118 patients who received CAR T-cell therapy, 197 (2.1%) of the 9483 patients who received high-intensity cytotoxic therapy, 44 (3.5%) of the 1259 patients who received low-intensity cytotoxic therapy, and 15 (6.3%) of the 238 patients who received targeted therapy. Of the 43 CAR T-cell therapy users who had at least 1 neurologic AE, 28% had encephalopathy. By contrast, in patients who received treatment with conventional immunotherapy, the rate of encephalopathy ranged from 0.6% to 4.2%.

The rates of other neurologic AEs were low, and each neurologic AE occurred in less than 10% of patients from each therapy group. Among the total population, patients with neurologic AEs were older and sicker than those without neurologic AEs (mean age, 65.3 years [SD, 13 years] vs 61.6 years [SD, 13.7 years]; mean CCI score, 5.9 [SD, 3.6] vs 4.5 [SD, 3]). Within the CAR T-cell therapy cohort, patients with neurologic AEs did not differ from those without neurologic AEs in patient demographics (age, sex, region) and CCI score (all $P > .05$).

The mean total healthcare costs were higher in patients with neurologic AEs versus patients without neurologic AEs across all the treatment groups (**Figure 2**). The mean total healthcare cost was $71,982 higher for patients with neurologic AEs than for patients without

neurologic AEs. Patients who received CAR T-cell therapy had the greatest cost difference between patients with and without any neurologic AEs ($143,309; 95% confidence interval, $5838-$280,779; **Figure 3**).

In patients with neurologic AEs, 70% of the healthcare costs were accrued in the inpatient setting. Among patients without neurologic AEs, 78% of the healthcare costs were for outpatient medical services. This trend was consistent for patients with encephalopathy, which was the most common neurologic event identified in patients who received CAR T-cell therapy in our study and in clinical trials (data not shown; **Figure 4**).

Discussion

Clinical trials have shown that CAR T-cell therapies were associated with consistent and durable remissions and greater survival rates than existing salvage chemotherapies for relapsed or refractory DLBCL.[18-20] Ongoing responses in 39 (39%) of the 101 patients at a median follow-up of 27.1 months were reported in the Safety and Efficacy of KTE-C19 in Adults with Refractory Aggressive Non-Hodgkin Lymphoma (ZUMA-1) phase 2 clinical trial of axicabtagene ciloleucel, and in 35 (35%) of the 99 patients at a median follow-up of 19.3 months in the Study of Efficacy and Safety of CTL019 in Adult DLBCL Patients (JULIET) phase 2 clinical trial of tisagenlecleucel.[18,19]

The results of a real-world study of patients with relapsed or refractory DLBCL suggest that the use of CAR T-cell therapies reduced healthcare utilization and costs in Medicare patients with multiple comorbidities[26]; however, it did not examine the rate of neurologic AEs or the costs associated with the management of neurologic AEs. It is important to understand the economic impact associated with therapy-related AEs.

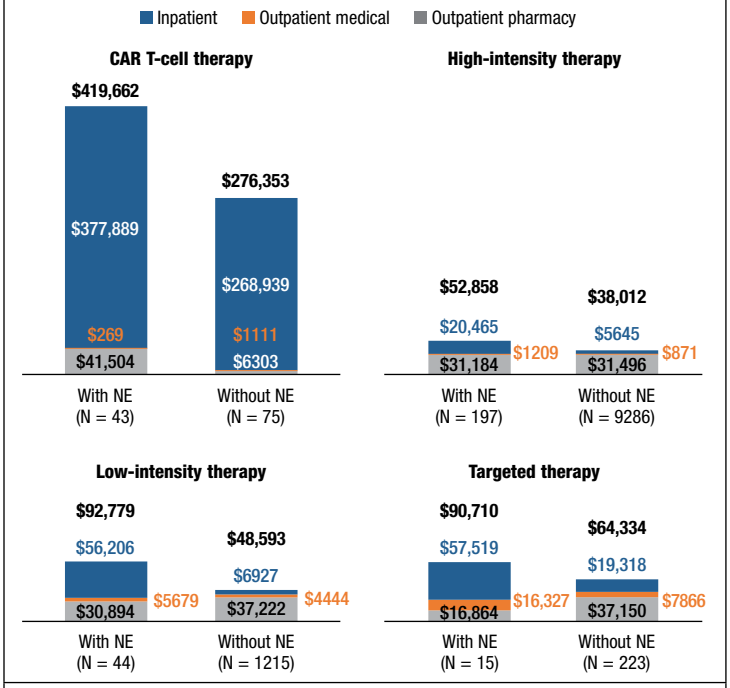
In our current retrospective analysis of 3 large claims databases, we found that patients who received treatment for relapsed or refractory DLBCL and had neurologic AEs incurred substantially higher costs than patients who did not have such events, regardless of the treatment used. Patients who received CAR T-cell therapy had the greatest cost differences between patients with and without any neurologic AEs, which may be driven by the major cost differences observed in patients with encephalopathy, the most common neurologic AEs in patients who receive CAR T-cell therapy.[18-20]

Our estimate of the cost of CAR T-cell therapy was less than the acquisition cost of CAR T-cell therapy (the current list price for axicabtagene ciloleucel and tisagenlecleucel is $373,000).[27] The Centers for Medicare & Medicaid Services' (CMS) current reimbursement policy sets a maximum inpatient payment of $186,500 per case.[27] This payment limit may explain the lower healthcare costs, particularly in patients who received CAR T-cell therapy and did not have neurologic AEs, that were observed in our study.

Other potential explanations for the lower cost for CAR T-cell therapy that we found include that patients in the study might have received discounted or free CAR T-cell therapy regimens as a part of clinical trials or as a managed access program. In addition, manufacturer prices paid by payers may reflect rebates. However, this information is not available in the data sets used in this study.

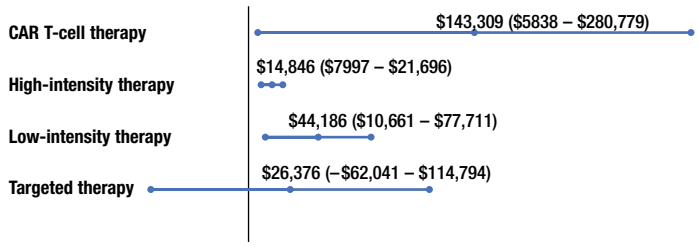
We conducted a sensitivity analysis that excluded patients who received CAR T-cell therapy and had healthcare costs of less than $186,500 (which was the

Figure 2 Patients with Neurologic Adverse Events Had Increased Healthcare Costs



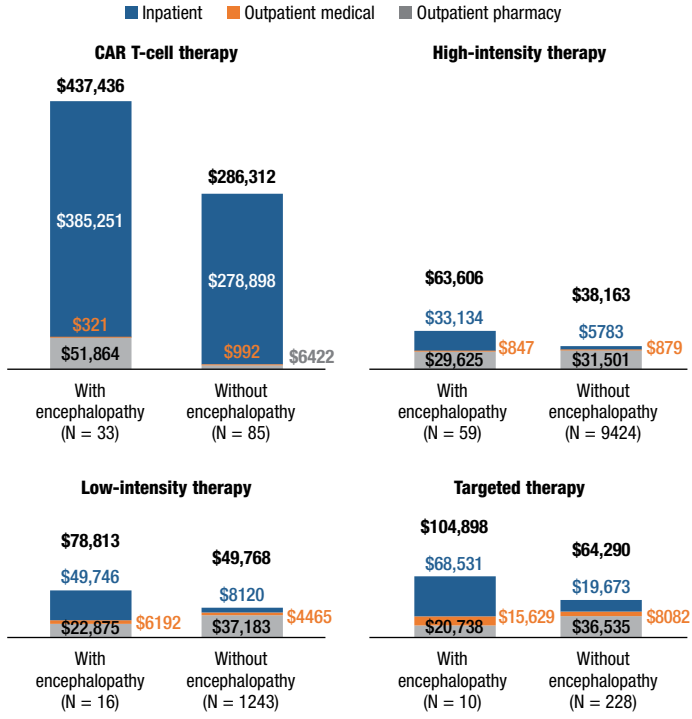
CAR indicates chimeric antigen receptor; NE, neurologic adverse event.

Figure 3 Difference in Mean Total Healthcare Costs Among Patients with versus without Neurologic Adverse Events, by Therapy Type



CAR indicates chimeric antigen receptor.

Figure 4 Mean Total Healthcare Costs of Patients with Encephalopathy, by Treatment Type



CAR indicates chimeric antigen receptor.

CMS' maximum reimbursement) because they likely had lower costs for the above reasons, and the results showed the same trend of greater costs in patients with neurologic AEs as patients without neurologic AEs.

Although we were unable to separate out the 2 commercially approved CAR T-cell therapies (ie, axicabtagene ciloleucel and tisagenlecleucel) in the claims data because of their shared *ICD-10-CM* coding, 6 recent real-world quasi head-to-head studies, including those from the United States, United Kingdom, France, and Germany, reported lower rates of neurologic AEs with tisagenlecleucel than with axicabtagene ciloleucel.[28-39]

For example, Pennisi and colleagues evaluated 49 patients with DLCBL who received treatment with CAR T-cell therapy from February 2018 through March 2019 and found no evidence of grade ≥3 ICANS that were associated with the use of tisagenlecleucel.[35,36] And in a recent review of CAR T-cell therapies, Abramson reported higher rates of ICANS, including more severe neurologic AEs, with axicabtagene ciloleucel than with tisagenlecleucel (64% with 28% severe vs 21% with 12% severe).[37] In addition, based on the retrospective analysis of data from 8 US academic centers, Riedell and colleagues reported lower rates of any neurologic AEs, including no evidence of grade ≥3 AEs, and lower rates of hospitalization associated with tisagenlecleucel than with axicabtagene ciloleucel.[29,34]

Several limitations of these published real-world studies should be noted, however, including small sample sizes, short follow-up durations, and differences in patient characteristics.[28-39] In the absence of results from larger, longer-term, propensity score–matched real-world studies, the evidence in those studies should be interpreted with caution.

Limitations

This study has several limitations. First, we cannot determine whether neurologic AEs were directly related to treatment, including whether they resulted from changes in treatment after the index treatment was initiated, from preexisting conditions that were exacerbated by current treatments, or from the residual effects of previous treatments.

Furthermore, the treatment patterns might have also changed over the study period, which was not accounted for in the analysis. We also did not identify which exact line of therapy a patient was receiving, because we would have had to require additional enrollment criteria to do so. Extending the enrollment length would have further limited the study sample size.

In this claims-based study, *ICD-9-CM* and *ICD-10-CM* codes were used to identify neurologic AEs, and these codes are not the same as the codes used in clinical trials. Thus, the specific AEs that were evaluated may not directly correspond to those in clinical trials. Neurologic AEs in the studies were confirmed through symptom observation and laboratory testing results, whereas the claims data used in this analysis were generated for reimbursement rather than research, and coding errors, misclassification, diagnostic uncertainty, and/or omissions could affect the reliability of the findings.

In this analysis, we focused on examining acute neurologic AEs in the 30-day postindex period. We considered examining a longer period, but we were limited by our sample size.

Moreover, there are no *ICD-9-CM* or *ICD-10-CM* diagnosis codes that are specific to relapsed DLBCL. However, consistent with previous work in the field,[8] we used the combination of diagnosis codes for DLBCL and treatments that are recommended for relapsed or refractory DLBCL to identify patients with relapsed or refractory DLBCL.

Finally, we could only identify possible duplicate records for patients based on the same age, sex, region, index date, and index treatment. However, because patients may have various insurance plans at different times, multiple records for the same patients may exist in several databases. We were not able to identify these patients in our study.

Conclusion

This is the first study of the economic burden of neurologic AEs associated with the treatment of relapsed or refractory DLBCL in a real-world setting, using data that reflect the current range of treatment options. Patients with relapsed or refractory DLBCL who have severe or life-threatening neurologic AEs incur substantially higher costs than patients without neurologic AEs, with the largest difference seen in patients who receive CAR T-cell therapy.

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Author Disclosure Statement

Dr Broder, Dr Yan, and Dr Chang are employees of Partnership for Health Analytic Research, which received funding from Novartis to conduct this research. Dr Ma, Dr Zhang, and Dr Eldjerou are employees and stockholders of Novartis. Dr Kuzan is an employee of Novartis.

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