Poster #207

Real-World Outcomes of Axicabtagene Ciloleucel for the Treatment of Relapsed/Refractory Secondary Central Nervous System Lymphoma

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BACKGROUND

- Outcomes for patients with secondary central nervous system lymphoma (SCNSL) are significantly worse than those with systemic large B-cell lymphoma (LBCL); median overall survival (OS) after diagnosis of SCNSL is ≤6 months, and there is no standard treatment[1]
- Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved in many countries for treating patients with relapsed and/or refractory (R/R) LBCL[2,3]
  - Axi-cel has demonstrated curative potential in the second-line (ZUMA-7) and third-line or later settings (ZUMA-1) for patients with R/R LBCL[4,5]
- Trials in CAR T-cell therapy to treat systemic LBCL have excluded patients with involvement of the central nervous system (CNS) due to safety concerns; however, early evidence is emerging from the real world, which suggests that patients have similar safety outcomes to systemic LBCL though potentially lower response rates and durability[6,7]
  - With 2 years of median follow-up, a Center for International Blood and Marrow Transplant Research (CIBMTR) study consisting of 144 patients with SCNSL who received CAR T-cell therapy reported 2-year PFS and OS rates of 21% and 34%, respectively; Grade ≥3 CRS and ICANS occurred in 12% and 24% of patients, respectively[7]
- These early data suggest that CAR T-cell therapies could have potential as a viable treatment for SCNSL; however, studies with further follow-up are needed to determine impact on long-term outcomes

OBJECTIVE

- To describe real-world effectiveness and safety outcomes of patients in the United States who received axi-cel for treating R/R SCNSL in the second-line or later setting

METHODS

Figure 1. Study Design

Data Source

- Data were collected from the CIBMTR registry
- Study population: Consenting adult patients with R/R active SCNSL who received axi-cel in 2L+ between 2018 and 2023 in the US and enrolled in the CIBMTR data registry; patients with primary CNS lymphoma and diseases other than LBCL were excluded
- Data cutoff was May 2024

Outcomes of Interest

- Effectiveness outcomes: ORR, CR rate, relapse, DOR, PFS, and OS
- Safety outcomes: CRS and ICANS per ASTCT consensus criteria,[a] other AEs, causes of death, and NRM

Statistical Analysis

- Descriptive statistics summarized baseline patient characteristics and outcomes in all patients
- Effectiveness and safety outcomes were assessed in all patients, and a sensitivity analysis was conducted by removing patients with only epidural space involvement as previous SCNSL studies have inconsistently included these cases
- Time-to-event outcomes with and without competing risks were analyzed using cumulative incidence and Kaplan-Meier functions, respectively

2L+, second line or later; AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; axi-cel, axicabtagene ciloleucel; CIBMTR, Center for International Blood and Marrow Transplant Research; CNS, central nervous system, CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; NRM, non-relapse mortality; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed and/or refractory; SCNSL, secondary central nervous system lymphoma; US, United States.

RESULTS

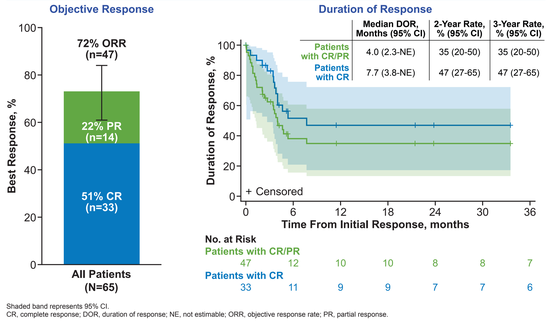
Table 1. Baseline Patient and Disease Characteristics

Characteristic	All Patients (N=65)	Patients Without Epidural Involvement (n=56)
Median age, years (range) ≥65, n (%)	62.8 (21-79) 29 (45)	62.8 (21-79) 25 (45)
Male sex, n (%)	43 (66)	36 (64)
ECOG performance status 0-1,[a] n (%)	49 (84)	43 (84)
Race/ethnicity[a] Non-Hispanic White, n (%) Non-Hispanic Black, n (%) Non-Hispanic Asian, n (%) Hispanic, n (%) Not reported, n	 39 (67) 4 (7) 7 (12) 8 (14) 7	 34 (68) 3 (6) 7 (14) 6 (12) 6
Clinically significant comorbidity,[b,c] n (%)	52 (80)	45 (80)
Disease type, n (%) Diffuse large B-cell lymphoma Primary mediastinal large B-cell lymphoma High grade B-cell lymphoma Burkitt lymphoma	 48 (74) 1 (2) 14 (22) 2 (3)	 41 (73) 1 (2) 12 (21) 2 (4)
Double-/triple-hit lymphoma at time of diagnosis,[a] n (%)	12 (24)	10 (24)
Stage III or IV organ involvement at initial diagnosis,[a] n (%)	51 (88)	45 (90)
Extranodal CNS involvement prior to infusion,[d] n (%) Brain Epidural space Cerebrospinal fluid Leptomeningeal Eyes or orbit Spinal cord CNS, not otherwise specified	 33 (51) 10 (15) 8 (12) 7 (11) 6 (9) 3 (5) 1 (2)	 33 (59) 1 (2)[e] 8 (14) 7 (13) 6 (11) 3 (5) 1 (2)
Median number of prior lines of therapy, n (IQR)	4 (3-5)	4 (2-5)
Prior ASCT, n (%)	12 (18)	9 (16)
Median time from leukapheresis to infusion, days (IQR)	28.0 (26.0-34.0)	27.5 (26.0-33.0)
Bridging therapy received,[a] n (%) Systemic[f] Radiation[f] Intrathecal[f] Surgery[f]	47 (75) 40 (63) 17 (27) 12 (19) 1 (2)	40 (73) 35 (64) 15 (27) 10 (18) 0

[a] Unknown or not reported was excluded from the denominator in percentage calculations. [b] Missing comorbidity data were considered as no comorbidity; if any individual comorbidity was present, it was considered as some clinically significant comorbidity. [c] Comorbidities were identified according to Sorror ML, et al. *Blood.* 2005;106:2912-2919.[8] [d] Not mutually exclusive. [e] One patient had leptomeningeal involvement. [f] Percentages based on number of patients who received bridging therapy.
ASCT, autologous stem cell transplantation; CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group.

- A total of 65 patients from 28 centers were included in the study (**Table 1**)
- The most common site of CNS involvement was the brain parenchyma (51%)

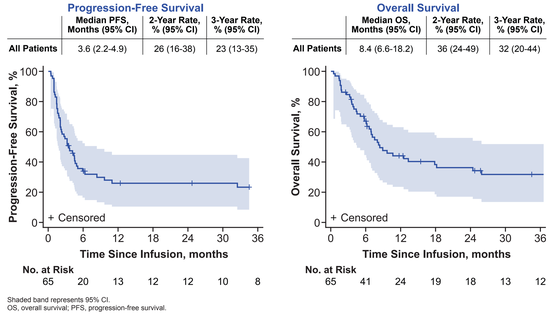
Figure 2. Response in All Patients



Shaded band represents 95% CI.
CR, complete response; DOR, duration of response; NE, not estimable; ORR, objective response rate; PR, partial response.

- Median follow-up for all patients was 48.2 months (95% CI, 24.7-48.9)
- Objective response occurred in 72% (complete response [CR] rate, 51%; partial response [PR] rate, 22%; **Figure 2**)
  - Among patients without epidural involvement, 71% had an objective response (CR rate, 52%; PR rate, 20%)
- Median duration of response (DOR) was 4.0 months (range, 2.3-not estimable [NE]); DOR at 3 years was 35% (95% CI, 20-50)
  - Median duration of complete response (DOCR) was 7.7 months (95% CI, 3.8-NE); DOCR at 3 years was 46% (95% CI, 26-64)
  - Among patients without epidural involvement, median DOR was 4.6 months (95% CI, 2.7-NE); DOR at 3 years was 36% (95% CI, 19-53)
- Cumulative incidence of relapse at 1 and 2 years was 66% (95% CI, 51-77) for all patients

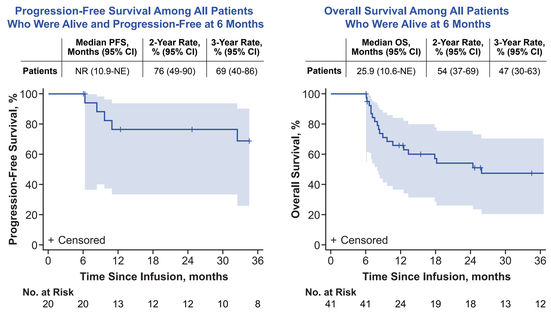
Figure 3. Progression-Free Survival and Overall Survival Among All Patients



Shaded band represents 95% CI.
OS, overall survival; PFS, progression-free survival.

- Median PFS was 3.6 months (95% CI, 2.2-4.9; **Figure 3**); PFS at 1 year was 26% (95% CI, 16-38)
  - Among patients without epidural involvement, median PFS was 3.7 months (95% CI, 2.2-5.9); PFS at 2 and 3 years was 26% (95% CI, 15-39) and 23% (95% CI, 12-36), respectively
- Median OS was 8.4 months (95% CI, 6.6-18.2); OS at 1 year was 44% (95% CI, 31-56)
  - Among patients without epidural involvement, median OS was 8.9 months (95% CI, 6.2-24.4); OS at 2 and 3 years was 37% (95% CI, 23-50) and 32% (95% CI, 19-45), respectively

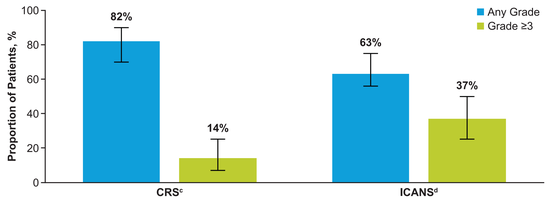
Figure 4. Progression-Free Survival and Overall Survival Among Patients Without Progression at 6 Months



Shaded band represents 95% CI.
NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival.

- Among all patients who were alive and without progression at 6 months, PFS at 2 and 3 years was 76% (95% CI, 49-90) and 69% (95% CI, 40-86), respectively (**Figure 4**)
  - OS at 2 and 3 years was 54% (95% CI, 37-69) and 47% (95% CI, 30-63), respectively
- Among all patients who were alive and without progression at 1 year, PFS at 2 and 3 years was 100% and 90% (95% CI, 47-99), respectively; OS at 2 and 3 years was 82% (59-93) and 72% (48-86), respectively

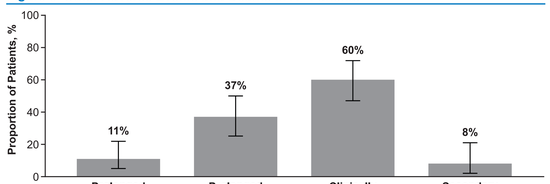
Figure 5. CRS and ICANS in All Patients[a,b]



Characteristic	All Patients (N=65)
CRS Median time from infusion to CRS onset, days (range) Median time from CRS onset to resolution, days (range) CRS resolved, n (%)	 3 (1-10) 6 (1-20) 52 (98)
ICANS Median time from infusion to ICANS onset, days (range) Median time from ICANS onset to resolution, days (range) ICANS resolved, n (%)	 6 (1-14) 10 (2-55) 33 (80)
Therapy given for treatment of CRS and/or ICANS, n (%) Corticosteroids Tocilizumab Anti-epileptics[e] Anakinra	 41 (63) 38 (58) 9 (14) 4 (6)

Error bars denote 95% CIs.
[a] CRS and ICANS were graded per ASTCT Consensus Criteria.[9] [b] Patients with missing data were excluded. [c] Any-grade CRS included 1 patient with undefined grade of CRS. [d] Any-grade ICANS included 2 patients with undefined grade of ICANS. [e] For ICANS only.
ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

Figure 6. Other Adverse Events and Deaths in All Patients



Characteristic	All Patients (N=65)
Deaths, n (%)	41 (63)
Primary cause of death among those who died during follow-up, n (%) Primary disease Infection Organ failure Malignancy Chronic GVHD	 32 (49) 4 (6) 2 (3) 2 (3) 1 (2)
Cumulative incidence of NRM at 3 years, % (95% CI)	12 (5-21)

Error bars denote 95% CIs.
[a] Prolonged neutropenia and prolonged thrombocytopenia are defined as present by Day 30 and was determined among patients who were alive on Day 30. [b] Includes infection that occurred after current or subsequent cellular therapy.
CT, computed tomography; GVHD, graft-versus-host disease; NRM, non-relapse mortality.

- Grade ≥3 CRS and ICANS occurred in 14% and 37% of all patients, respectively (**Figure 5**)
  - Among patients without epidural involvement, 82% had any-grade CRS (Grade ≥3 CRS, 15%) and 64% had any-grade ICANS (Grade ≥3 ICANS, 35%)
- The most common treatments of CRS and/or ICANS were corticosteroids (63%) and tocilizumab (58%); 98% of CRS and 80% of ICANS events resolved
- Prolonged neutropenia and thrombocytopenia (defined as present by Day 30), occurred in 11% and 37% of all patients, respectively (**Figure 6**)
- Among all patients, 3 developed one or more secondary malignancies, including acute myeloid leukemia, myelodysplasia, and sarcoma
- Safety outcomes were consistent among all patients and patients without epidural involvement

CONCLUSIONS

- With 4-year median follow-up, this is the longest reported follow-up of patients with R/R SCNSL treated with CAR T-cell therapy
- Across the study time period and with evolving management strategies, CRS and ICANS were managed primarily with corticosteroids and/or tocilizumab; almost all incidences of CRS and most incidences of ICANS resolved
- The effectiveness and safety outcomes observed in patients with R/R SCNSL, though encouraging and similar to previous reports,[6,7] demonstrated that further studies are needed to improve durability of response and optimize safety outcomes, as expected for this hard-to-treat population
- This study is limited by its relatively small sample size
- Patients with R/R SCNSL typically have poor prognoses; however, results herein support the potential use of axi-cel for treating patients with R/R SCNSL

PLAIN LANGUAGE SUMMARY

- Some people with a blood cancer called **large B-cell lymphoma (LBCL)** may also get cancer cells in the brain, spinal cord, or eyes. This is called **secondary central nervous system lymphoma (SCNSL)**. Among people with LBCL, people who also have SCNSL do not live as long as people without SCNSL
- SCNSL is harder to treat than LBCL because drugs have to cross the blood-brain or blood-retinal barrier to find and kill the cancer. New drugs to treat SCNSL are needed
- This study looked to see if **axicabtagene ciloleucel (axi-cel)** could work well and safely in people with SCNSL. Axi-cel is a type of anti-cancer drug made from a person's own immune cells
- Results showed that 72% of peoples' SCNSL went partially or completely away with axi-cel at first, but the cancer came back in most people within 1 year after getting axi-cel. Some people got severe side effects called **cytokine release syndrome (CRS**; 14% Grade ≥3) and **immune effector cell-associated neurotoxicity syndrome (ICANS**; 37% Grade ≥3), which happen with drugs like axi-cel
- This study showed that axi-cel can help people with SCNSL, but more studies are needed to improve how well and safely the drug works

Words in **bold text** are defined in the glossary that is accessible through the QR code

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DISCLOSURES

Full author disclosures are available through the virtual meeting platform.