CT-708

Systematic Literature Review of Clinical, Economic, and Health Related Quality of Life (HRQoL) Outcomes in Real-World Evidence (RWE) of Second-line or Higher (2L+) Relapsed/Refractory (R/R) Large B-Cell Lymphoma (LBCL) Patients Treated with Axicabtagene Ciloleucel (Axi-cel)

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PLAIN LANGUAGE SUMMARY

With axicabtagene ciloleucel (axi-cel), a CAR T therapy, now available to patients whose disease has relapsed (or not responded) after initial treatment, real-world evidence (RWE) helps inform its effectiveness, costs, and impact on quality of life when used in routine care. We reviewed recent studies and found that:

- In routine care, axi-cel works as well as in clinical trials, with serious side effects like systemic inflammatory response and neurologic issues less commonly observed than in trials. However, it will be important to continue assessing safety and effectiveness as additional data emerge.
- There isn't much data yet on the cost of using axi-cel earlier in treatment, but existing studies suggest most costs come from inpatient care during infusion. In some locations shorter inpatient stays and outpatient use may reduce costs, although some processes like safety monitoring would need to change.
- Data on patient-reported experiences after axi-cel is limited, but so far studies show quality of life drops at first but then improves, especially in physical, work, and social areas. Fatigue and financial worries may continue.

BACKGROUND

- Axi-cel is an autologous anti-CD19 chimeric antigen receptor T-cell (CAR T) therapy approved for relapsed/refractory (R/R) large B-cell lymphoma (LBCL), in second-line or later (2L+) patients.[1]
- RWE complements trial data by assessing outcomes in routine care, including long-term effectiveness, healthcare resource use (HCRU), costs, and health-related quality of life (HRQoL).
- As second-line (2L) or later (2L+) use of axi-cel expands, RWE is key to understanding its impact in broader clinical practice.

OBJECTIVES

With the approval of axi-cel for use in R/R 2L LBCL, emerging RWE is critical to understanding long-term clinical outcomes, HCRU, costs, and HRQoL. We conducted a systematic literature review (SLR) to summarize the growing RWE on axi-cel in 2L+ to treat patients with R/R LBCL.

METHODS

Systematic Literature Review

- Three PICOS were developed to capture clinical, economic, and HRQoL evidence for axi-cel in patients with R/R 2L+ LBCL. Systematic searches of MEDLINE, Embase, and CENTRAL identified English-language studies. Relevant conference proceedings were also reviewed.
- Three separate SLRs were conducted, with the clinical SLR covering January 2022 to August 2024 and the economic and HRQoL SLRs covering January 2022 to February 2025.
- HRQoL outcomes included data from both randomized and non-randomized trials, while clinical and economic outcomes focused on RWE.
- For **mixed cancer populations** an 80% LBCL threshold was applied for the HRQoL and economic studies, and 95% threshold for the clinical studies.
- For studies reporting outcomes for a population treated with **mixed interventions**, a 95% threshold was required for patients treated with axi-cel.
- Studies reporting exclusively on third-line or later (3L+) populations were excluded.
  - Studies were classified as 3L+ if they included patients with no prior line-of-therapy (LOT) details before 2L approval for axi-cel; required ≥1 prior LOT but were conducted pre-2L approval date; or explicitly described the population as 3L+.
- Study selection was performed at the publication level, with distinct studies identified through mapping; study names reflected registry or hospital name, location, author, and year.

Descriptive Summary

- No formal synthesis of results was conducted. Findings were summarized descriptively, with key patterns and trends identified, presented graphically and reported narratively.

Line of Therapy Cohort Definition

- **2L only:** Direct reporting of the proportion of 2L (has received one prior LOT) patients in the data.
- **2L+:** Clear identification of 2L+ status (two or more prior LOT) from study inclusion criteria; or inferred 2L+ status based on treatment approval dates relative to study recruitment periods.

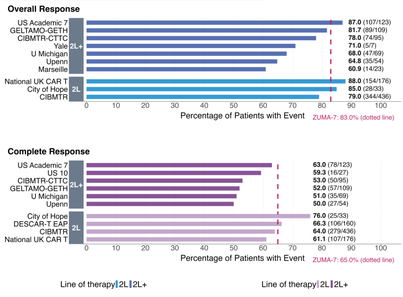
RESULTS

Evidence Base

- **Clinical SLR:** 24 records (21 unique studies) were identified for 2L/2L+ patients from 4,430 screened records.
- **Economic SLR:** 18 publications (11 unique studies) on cost and resource use included after screening 943 records. All studies described HCRU, however, only 3 studies reported direct costs.
- **HRQoL SLR:** 8 publications (4 unique studies) on HRQoL and patient reported outcomes (PRO) identified from 550 records and hand searches.

RESULTS

Figure 1. Response Outcomes



Clinical Outcomes

- Five studies reported 2L only results and 17 reported on the broader 2L+ population (one reported both).
- Overall response rates (**Figure 1**) in 2L only cohorts ranged from 79%–88% and were similar to ZUMA-7 (83%) [2], while 2L+ cohorts showed greater heterogeneity (61%–87%).
- Complete response rates (**Figure 1**) in 2L only patients (61%–76%) also aligned with ZUMA-7 (65%)[2].
- Any-grade cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were common, though grade ≥3 rates were generally numerically lower in the 2L only real-world studies than in ZUMA-7 (**Figure 2**).
- Infections and non-relapse mortality (NRM) were less frequently reported but aligned with trial data.
  - Four studies (three in 2L+ and one in 2L only) reported infection rates ranging from 27% to 78%, with the 2L CIBMTR study aligning closely with ZUMA-7 (44% vs 45%). [2]
  - NRM was infrequently reported, with only two 2L+ studies - GELTAMO-GETH (7%, n=169) and CIBMTR-CTTC (8%, n=95) - both showing lower rates than ZUMA-7 (13%). [2]

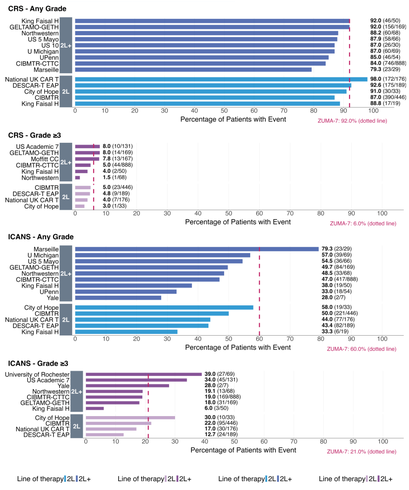
Economic Outcomes

- Most studies were conducted in the US (n=7) with retrospective designs (n=7), and the majority reported outcomes in 2L+ patients (n=7), including a mix of outpatient (n=3), inpatient (n=2), and combined settings (n=2).

Healthcare Resource Utilization

- All 11 studies reported HCRU outcomes, most commonly intensive care unit (ICU) stay (n=8), length of stay (LOS) (n=7), and inpatient stay (n=6), with median follow-up (mFU) ranging from 1.1 to 13.9 months.
- Post-infusion hospitalization rates varied widely (11%–96%) by care setting and admission definitions: 78%–95% in outpatient and 11%–96% in inpatient settings (mFU: 3–13.9 months).
- ICU admission rates ranged from 10%–24% in 2L+ patients (mFU: 5.9–13.9 months) and 20%–26% in 2L only patients (mFU: 1.1–10 months)
- ICU admission were observed more frequently among patients that were initially infused with axi-cel as inpatient (11%–20%) than outpatient (10%–13%).
- The LOS for all-cause hospitalization was reported in six 2L+ studies (LOS: 8.1–26 days; mFU: 3–13.9 months), with longer stays in inpatient-treated cohorts.

Figure 2. Safety Outcomes



CRS: Cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome

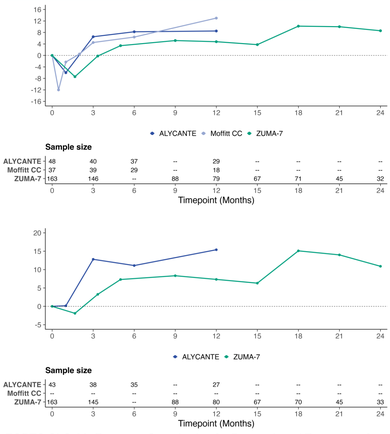
- ICU-specific LOS was reported in four studies (covering 2L only and 2L+) and ranged from 5 to 8 days (mFU: 1.1–13.9 months).
- Outpatient-treated patients had shorter overall LOS (5.5–8.1 days) than inpatient-treated patients (6.5–19.6 days), though variability in follow-up and limited AE-related LOS data limit comparability.

Direct Costs

- Direct costs of axi-cel infusion were reported in three studies with 2L+ patients - two outpatient administration and one mixed setting - with follow-up time ranging from 30 days to 7 months.
- In one study, mean total claim charges* for the CAR T infusion claim were higher for inpatient vs. outpatient administration ($2.53M vs. $1.55M), and mean reimbursed* CAR T infusion costs were ~24% lower in outpatients ($383K vs. $507K per patient per month).[3]
  - CAR T infusion costs or charges include all resources and expenses related to the index CAR T event, such as treatment, hospitalization, and physician fees.

**Claim charges reflect hospital accounting practices and may overstate costs, whereas reimbursed amounts, typically lower, provide a more accurate estimate of actual spending*

Figure 3. Change from Baseline in EORTC QLQ-C30 and EQ-5D-5L VAS Scores



HRQoL Outcomes

- Four PRO-focused studies were identified assessing HRQoL and symptom burden using global, subscale, and utility measures (e.g., EQ-5D), with EORTC QLQ-C30 as the most common (n=3). The evidence was broad in scope but limited in depth, with limited overlap across studies.
- QLQ-C30 global health scores and EQ-5D visual analogue scores declined early but improved beyond baseline, peaking between 12 to 18 months post-infusion (**Figure 3**).

EORTC QLQ-30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EQ-5D-5L: EuroQol 5-Dimension 5-Level questionnaire, assessing health status across five dimensions; VAS: Visual analogue scale

CONCLUSION

- This study presents a comprehensive and current real-world overview on clinical, cost, HCRU, and HRQoL outcomes in patients with R/R 2L+ LBCL treated with axi-cel.
- Axi-cel shows strong, durable responses with a safety profile comparable to clinical trials. However, continued assessment of safety and efficacy is needed as more data become available over time.
- RWE on HCRU and costs for axi-cel in R/R 2L+ LBCL is limited. Existing data suggest hospitalization during initial infusion drives costs. Inpatient costs may be lessened by either shorter inpatient stays or more outpatient use. The latter may require some changes to infrastructure or monitoring approaches.
- Patients receiving axi-cel often experience early declines in HRQoL with recovery over time, particularly physical, social, and daily activity functioning, though fatigue and financial burden may persist. Trial and limited RWE suggest that some patients achieve near-normal or better-than-baseline recovery, but more evidence and longer-term follow-up are needed to support this finding.

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DISCLOSURES

Dr. Lin holds advisory roles with Janssen, Sanofi, BMS, Regeneron, Genentech, Tessera, Legend, NexT Therapeutics; Steering committees for Janssen, Kite/Gilead; Research funding from Janssen, BMS; Scientific boards for NexImmune, Caribou; DSMB/EDMC for Pfizer. All funds to Mayo Clinic; no personal compensation.

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