Abstract 7023

# Trends and Outcomes by Inpatient and Outpatient Infusion of Axicabtagene Ciloleucel (Axi-Cel) in the US for Patients With Relapsed/Refractory Large B-Cell Lymphoma

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## BACKGROUND

- Axicabtagene ciloleucel (axi-cel) is an autologous chimeric antigen receptor (CAR) T-cell therapy approved for adults with relapsed/refractory (R/R) large B-cell lymphoma (LBCL) after ≥1 prior line of therapy[1,2]
- In the pivotal ZUMA-7 trial of axi-cel in patients with R/R LBCL after 1 prior line of therapy[3,4]:
  - Both event-free and overall survival (OS) were superior to second-line standard of care
  - Cytokine release syndrome (CRS) occurred in 92% of patients (6% Grade ≥3), and neurologic events occurred in 60% (21% Grade ≥3)
- The risk of these commonly occurring CAR T-cell therapy–associated adverse events may deter centers from using axi-cel in an outpatient setting, though observational studies in individual centers have observed comparable safety and effectiveness between outpatient and inpatient care settings[5]
  - Improvements in adverse event management with prophylactic steroid use and early intervention may be associated with improved outcomes and increased feasibility of outpatient axi-cel administration[6]
- Additionally, preliminary results of the ZUMA-24 trial of outpatient axi-cel in R/R LBCL found no Grade ≥3 CRS, no Grade 5 neurologic events, a shorter median duration of hospitalization, and lower rates of intensive care unit admission than with previous clinical experience in the inpatient setting[7]
  - Efficacy outcomes were consistent with those in trials in the inpatient setting

## OBJECTIVE

- To evaluate real-world safety and effectiveness outcomes in patients with R/R LBCL by intention to treat with axi-cel in outpatient and inpatient settings

## METHODS

### Figure 1. Study Design and Analysis

**Data Source**

- Data collected from the CIBMTR observational database
- **Study population:** consenting adult patients with R/R LBCL after ≥1 prior line of therapy receiving axi-cel in the US (between July 2021 and November 2023)
  - Those with prior non-transplant cellular therapy, prior alloHCT, or unknown care setting intention were excluded

**Outcomes of Interest**

- **Safety:** CRS and ICANS,[a] hospitalization among patients intended for outpatient administration,[c] prolonged cytopenias, clinically significant infections, and causes of death including NRM
- **Effectiveness:** ORR, CRR, DOR, PFS, and OS

**Statistical Analysis**

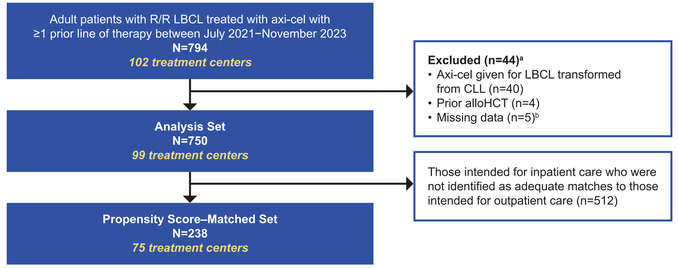
- Eligible patients intended for the outpatient setting were matched 1:1 to those intended for the inpatient setting by propensity score matching on age, sex, comorbidities, LDH, bulky disease, prior lines of therapy, chemosensitivity, and infusion year (**Figure S1**)[c]
- Univariable analysis and multivariable logistic regression were used to estimate differences in outcomes by intended care settings in the propensity score–matched dataset[c]

[a] CRS was graded per Lee et al[8] and ICANS was graded per ASTCT consensus criteria.[9] [b] Criteria for hospitalization after axi-cel infusion among patients intended for outpatient care was at the discretion of the institution. [c] ECOG PS was captured but not considered in the PSM due to small sample size (n=2/119 patients with ECOG PS ≥2 intended for outpatient care). [d] Variables considered for the multivariable analysis were cardiac comorbidities, arrhythmia, diabetes requiring non-dietary treatment in 4 weeks prior to infusion, mild hepatic comorbidities, obesity during pre-infusion workup, psychiatric disturbance requiring consult/treatment in 4 weeks prior to infusion, pulmonary comorbidities (moderate/severe), and severely low BMI <20.5 kg/m$^2$.

alloHCT, allogeneic hematopoietic cell transplantation; ASTCT, American Society for Transplantation and Cellular Therapy; axi-cel, axicabtagene ciloleucel; BMI, body mass index; CIBMTR, Center for International Blood and Marrow Transplant Research; CRR, complete response rate; CRS, cytokine release syndrome; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; NRM, non-relapse mortality; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PSM, propensity score matching; R/R, relapsed/refractory; US, United States.

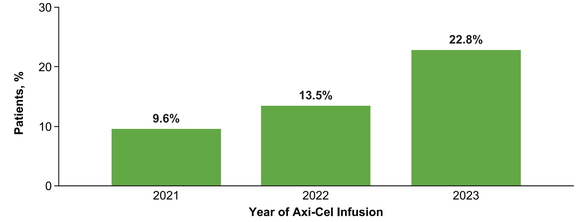
## RESULTS

### Figure 2. Analysis Population




[a] Reasons for exclusion are not mutually exclusive. [b] Missing data included the number of lines of prior therapy (n=2), comorbidity (yes/no, n=2), intended care setting (n=1).
AlloHCT, allogeneic hematopoietic cell transplantation; axi-cel, axicabtagene ciloleucel; CLL, chronic lymphocytic leukemia; LBCL, large B-cell lymphoma; R/R, relapsed/refractory.

### Figure 3. Patients Receiving Axi-Cel With Outpatient Intent by Year




Assessed prior to propensity score matching.
Axi-cel, axicabtagene ciloleucel.

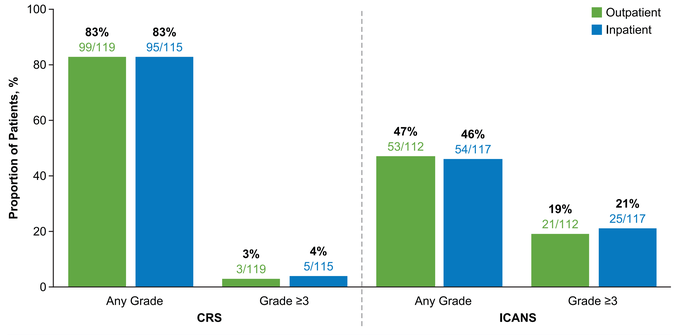
- An increasing trend in outpatient axi-cel administration was observed over time (**Figure 3**)

### Table 1. Baseline Characteristics by Intended Care Setting After Matching[a]

| Characteristic | Outpatient (N=119) | Inpatient (N=119) |
|---|---|---|
| **Median age, years (IQR)** | 63.4 (52.1–70.1) | 64.2 (55.5–72.2) |
| ≥65, n (%) | 52 (44) | 56 (47) |
| ≥70, n (%)[b] | 30 (25) | 42 (35) |
| **Male sex, n (%)** | 79 (66) | 78 (66) |
| **Race and Ethnicity, n (%)[b]** | | |
| Non-Hispanic White | 85 (71) | 79 (66) |
| Non-Hispanic Black | 9 (8) | 7 (6) |
| Hispanic or Latino | 10 (8) | 18 (15) |
| Other or not reported | 15 (13) | 15 (13) |
| **Clinically significant comorbidity, n (%)[c]** | 80 (67) | 73 (61) |
| **Bulky disease prior to infusion, n (%)[d]** | 3 (3) | 1 (<1) |
| **Elevated LDH prior to infusion, n (%)[e]** | 59 (50) | 63 (53) |
| **1 prior line of therapy, n (%)** | 87 (73) | 89 (75) |
| **Chemoresistant disease prior to infusion, n (%)** | 71 (60) | 75 (63) |
| **Lymphodepletion chemotherapy, n (%)[b]** | | |
| Cyclophosphamide + fludarabine | 96 (81) | 94 (79) |
| Single-agent bendamustine | 17 (14) | 21 (18) |
| Other | 6 (5) | 4 (3) |
| **Year of axi-cel infusion, n (%)** | | |
| 2021 | 7 (6) | 7 (6) |
| 2022 | 61 (51) | 62 (52) |
| 2023 | 51 (43) | 50 (42) |

[a] ECOG PS was captured but not considered in the PSM due to small sample size (n=2/119 patients with ECOG PS ≥2 intended for outpatient care). [b] Not included in PSM model. [c] Specific comorbidities included in the PS estimation included cardiac comorbidities, arrhythmia, diabetes requiring non-dietary treatment in 4 weeks prior to infusion, mild hepatic comorbidities, obesity during pre-infusion workup, psychiatric disturbance requiring consult/treatment in 4 weeks prior to infusion, pulmonary comorbidities (moderate/severe), and severely low BMI <20.5 kg/m$^2$. List of comorbidities defined per the HCT-specific comorbidity index[10] with the addition of low BMI. [d] Defined as largest size of nodal mass >10 cm. [e] Upper limit of normal LDH determined at each center.
BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; HCT, hematopoietic cell transplantation; LDH, lactate dehydrogenase; PS, performance status; PSM, propensity score matching.

### Figure 4. Incidence and Univariate Analysis of CRS and ICANS by Intended Care Setting



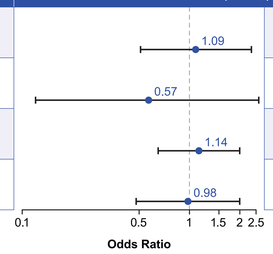

| Characteristic | CRS | | ICANS | |
|---|---|---|---|---|
| | Outpatient (N=119) | Inpatient (N=115) | Outpatient (N=112) | Inpatient (N=117) |
| **Median time from infusion to onset, days (IQR)** | 4 (3–7) | 4 (2–6) | 7 (5–9) | 7 (5–10) |
| **Median time from onset to resolution, days (IQR)** | 5 (4–6) | 6 (3–8) | 7 (3–10) | 5 (2–7) |
| **Event resolved, n (%)** | 99 (100) | 94 (99) | 49 (92) | 47 (87) |
| **Cumulative incidence by Week 3, % (95% CI)** | 82 (73–88) | 82 (73–88) | 46 (37–55) | 46 (36–55) |
| **Cumulative resolution by Week 3, % (95% CI)** | 98 (91–100) | 99 (88–100) | 89 (76–95) | 83 (69–91) |

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

- The incidence of CRS and immune effector cell-associated neurotoxicity syndrome (ICANS) was similar among intended treatment for inpatient and outpatient settings (**Figure 4**)
- No patient in any setting experienced Grade 5 CRS; 1 patient in each care setting experienced Grade 5 ICANS
- Between patients intended for outpatient and inpatient settings, respectively, similar rates of prolonged cytopenias (18%, 18%), clinically significant infections (59%, 47%), and 12-month non-relapse mortalities (6%, 4%) were observed
- Among patients intended for outpatient care, 50% were hospitalized within 3 days post-infusion, and the median duration of first admission was 9 days
- In a subset matched analysis among patients aged ≥70 years at infusion, outcomes were comparable between the intended care settings, except for a higher any-grade ICANS associated with the intended outpatient setting (Grade ≥3 ICANS was similar between groups)

### Figure 5. Multivariate Analysis of CRS and ICANS

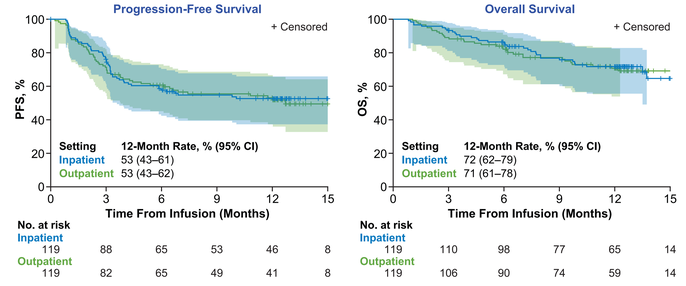
| Outcome | N Evaluable | Odds Ratio (95% CI) |
|---|---|---|
| **Any-grade CRS** | | |
| Inpatient | 115 | Reference |
| Outpatient | 119 | 1.09 (0.51–2.35) |
| **Grade ≥3 CRS** | | |
| Inpatient | 115 | Reference |
| Outpatient | 119 | 0.57 (0.12–2.60) |
| **Any-grade ICANS** | | |
| Inpatient | 117 | Reference |
| Outpatient | 112 | 1.14 (0.65–2.00) |
| **Grade ≥3 ICANS** | | |
| Inpatient | 117 | Reference |
| Outpatient | 112 | 0.98 (0.48–2.00) |




CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

- In the multivariate analyses, no associations were found between intended care setting and CRS nor ICANS (**Figure 5**)

### Figure 6. Efficacy Outcomes




| | Outpatient (N=119) | Inpatient (N=119) |
|---|---|---|
| **ORR, n/n (%)** CR rate | 92/118 (78) 80/118 (68) | 89/117 (76) 72/117 (62) |
| **Median DOR, months (95% CI)** 12-month rate, % (95% CI) | NR 64 (52–74) | NR 69 (58–78) |

CR, complete response; DOR, duration of response; ORR, objective response rate.

- Median follow-up among the 119 matched patients intended for outpatient care was 12.3 months (95% CI, 12.1–12.7)
  - Among those intended for inpatient care, median follow-up was 12.5 months (95% CI, 12.3–12.6)

## CONCLUSIONS

- In recent years, axi-cel has been administered more frequently in the outpatient setting, suggesting an increase in feasibility and comfort over time
- After matching on key factors, safety and effectiveness outcomes were comparable between patients with R/R LBCL treated with axi-cel intended for outpatient and inpatient settings
  - Rates of CRS and ICANS, both any-grade and Grade ≥3, were similar between intended settings
  - Safety outcomes remained comparable after multivariate assessment
- These findings corroborate prior real-world results[5] and support the consideration of axi-cel in appropriate outpatient settings

## PLAIN LANGUAGE SUMMARY

- **Axicabtagene ciloleucel (axi-cel)** is an "anticancer" **CAR T-cell therapy** made from a person's own immune cells. This one-time treatment is usually given to a person during a hospital stay. Doctors can also intend to give it without a hospital stay, which is called outpatient-intended treatment. In that case, the person must go to the hospital if certain side effects happen
- This **real-world study** looked at how safe and effective outpatient-intended axi-cel worked for people with a blood cancer called **large B-cell lymphoma**
- The number of people who got outpatient-intended axi-cel increased over time
- 50% of people who got outpatient-intended axi-cel needed to go to the hospital shortly after treatment
- The safety and effectiveness of axi-cel were similar in people who got it without a planned hospital stay and people who got it during a hospital stay

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

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- Dr. Pizzi was an employee of Kite when the study was conducted. Current affiliation: Sanofi

*This study is a collaboration between CIBMTR and Kite.*
CIBMTR® is a research collaboration between the Medical College of Wisconsin and NMDP℠

## DISCLOSURES

Full author disclosures are available through the virtual meeting platform.