Poster
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Real-world Impact of Time From Leukapheresis to Infusion (Vein-to-Vein Time) in Patients With Relapsed or Refractory Large B-cell Lymphoma Treated With Axicabtagene Ciloleucel

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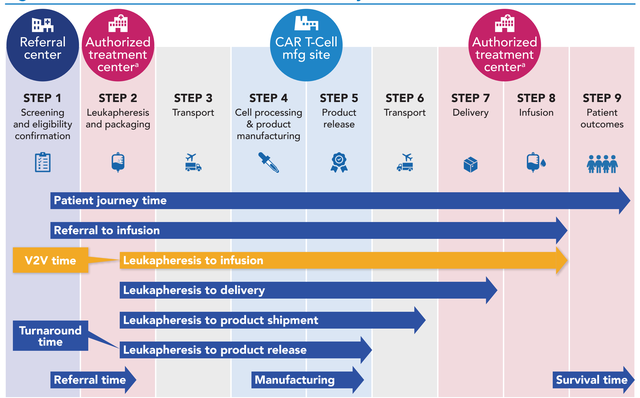
BACKGROUND

- Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved in the United States, as well as in multiple other countries worldwide, for the treatment of adults with relapsed or refractory (R/R) large B-cell lymphoma (LBCL) after ≥2 lines of systemic therapy and, recently in the United States and the European Union, for patients refractory to or who relapse within 12 months of first-line chemoimmunotherapy[1,2]
- Clinical trials of axi-cel have demonstrated favorable efficacy compared with standard of care for the treatment of R/R LBCL[3,4]
- Compared with other CAR T-cell products, axi-cel has a shorter median wait time from leukapheresis to infusion, referred to as vein-to-vein time (**Figure 1**)
  - Real-world data of axi-cel and tisagenlecleucel showed a median vein-to-vein time of 28 days for axi-cel versus 45 days for tisagenlecleucel,[5] while lisocabtagene maraleucel, in clinical trials, showed a median vein-to-vein time of 36-37 days[6-8]
- A study based on the JULIET trial suggested that reduced CAR T-cell treatment wait time is associated with increased efficacy[9]

Figure 1. Overview of CAR T-Cell Patient Journey



[a] Authorized Treatment Centers are also referred to as Qualified Treatment Centers.
CAR, chimeric antigen receptor; mfg, manufracturing; V2V, vein-to-vein.

OBJECTIVE

- To evaluate the impact of vein-to-vein time on real-world outcomes of axi-cel in R/R LBCL

METHODS

- In this analysis, vein-to-vein time refers to the time from leukapheresis to infusion for all patients in the study

Figure 2. Study Design

Data Source

- Retrospective observational data of patients receiving commercial axi-cel in the US after ≥2 lines of therapy identified between October 2017 and August 2020 using the CIBMTR registry

Endpoints of Interest

- **Effectiveness:** ORR, CR, DOR,[a] PFS, and OS
- **Safety:** CRS, ICANS, prolonged neutropenia, and prolonged thrombocytopenia[b]

Statistical Analysis

- Multivariable logistic and Cox regressions adjusted by key prognostic factors such as age, comorbidities, ECOG performance status, disease characteristics at diagnosis, and bridging therapy

[a] Among patients who achieved initial CR/PR. [b] Among patients who were alive at Day 30.
CIBMTR, Center for International Blood and Marrow Transplant Research; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; ICANS, immune effector cell-associated neurotoxicity syndrome; ORR, objective response rate; OS, overall survival; PFS, progression-free survival;; US, United States.

RESULTS

- Of 1497 patients with R/R LBCL treated with commercial axi-cel at 79 authorized treatment centers between October 2017 and August 2020, 1383 patients were included in the analysis (data cutoff date, May 4, 2022)
  - 114 patients were excluded from the analysis based on the following criteria: prior non-transplant cellular therapy (n=30), primary central nervous system lymphoma or other B-cell lymphoma (n=23), missing data on comorbidity (n=43), unknown or outlying date of leukapheresis (≤2 days before lymphodepleting chemotherapy or ≥144 days before infusion; n=13), and no follow-up (n=5)
- Overall, median vein-to-vein time for axi-cel was 27 days in this analysis (interquartile range, 26-32 days)

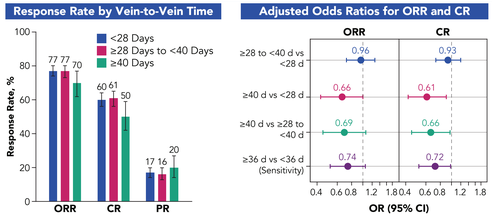
Table 1. Baseline Characteristics by Vein-to-Vein Time

	Vein-to-Vein Time		
	<28 Days n=697	≥28 to <40 Days n=533	≥40 Days n=153
Age ≥65 years at infusion, n (%)	239 (34)	217 (41)	65 (42)
Male sex, n (%)	455 (65)	348 (65)	91 (59)
Black or African American, n (%)	28 (4)	34 (6)	9 (6)
Hispanic or Latino, n (%)	76 (11)	56 (11)	18 (12)
High grade B-cell lymphoma, n (%)	115 (16)	96 (18)	20 (13)
Double/triple hit, n (%)[a]	106 (26)	87 (29)	18 (20)
ECOG PS ≥2 at infusion, n (%)	35 (5)	20 (4)	9 (6)
Chemoresistant prior to infusion, n (%)	469 (67)	355 (67)	101 (66)
No. of prior lines ≥3, n (%)[a,b]	485 (71)	361 (70)	118 (82)
Use of bridging therapy, n (%)[a]	132 (20)	109 (22)	65 (46)
Any comorbidities, n (%)[c]	479 (69)	382 (72)	125 (82)
Year of infusion: ≤2018, n (%)	210 (30)	155 (29)	30 (20)
Year of infusion: 2019, n (%)	324 (46)	252 (47)	69 (45)
Year of infusion: 2020, n (%)	163 (23)	126 (24)	54 (35)

[a] Percentages were based on non-missing cases. [b] Not including prior transplant. [c] Defined based on the hematopoietic cell transplant-specific comorbidity index[15]
ECOG PS, Eastern Cooperative Oncology Group performance status.

- Vein-to-vein times were consistent regardless of sex, race/ethnicity, disease histology, ECOG PS at infusion, or chemosensitivity (**Table 1**)
  - Patients with shorter vein-to-vein times appeared to be younger and less likely to have comorbidities
  - Patients with vein-to-vein time ≥40 days were more heavily pretreated and more likely to receive bridging therapy

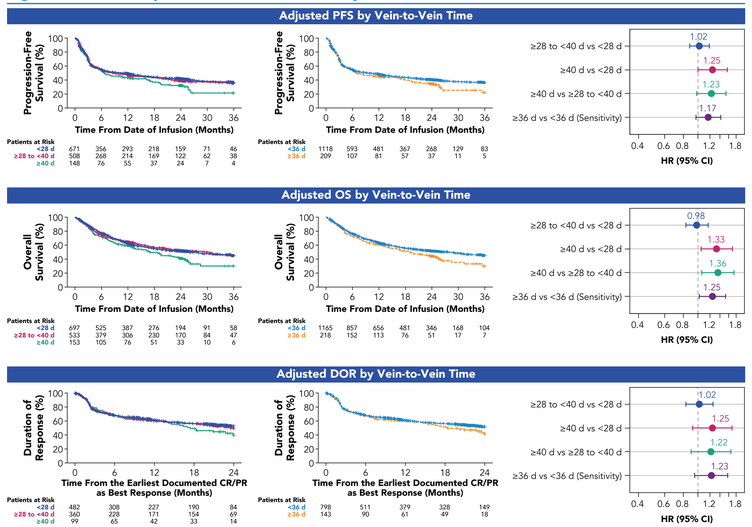
Figure 3. Axi-Cel Response Rate and Adjusted Odds Ratios of ORR and CR by Vein-to-Vein Time



Covariates for step-wise selection and multivariable adjustment: age, sex, race, ethnicity, ECOG performance status prior to infusion, comorbidities (pulmonary, cardiac/cerebrovascular/heart valve disease, hepatic, and renal), histologic transformation, disease characteristics at initial diagnosis (double/triple hit, disease stage, elevated LDH and >1 extranodal involvements), chemosensitivity prior to infusion, number of prior lines of therapy, prior HCT, year of infusion, time from initial diagnosis to infusion, and use of bridging therapy.
Axi-cel, axicabtagene ciloleucel; CR, complete response; d, day; ECOG, Eastern Cooperative Oncology Group; HCT, hematopoietic cell transplantation; LDH, lactate dehydrogenase; OR, odds ratio; ORR, objective response rate; PR, partial response.

- With a median follow-up of 24.2 months, complete response (CR) rates were 60%, 61%, and 50% (objective response rate 77%, 77%, and 70%) for patients with vein-to-vein time <28 days, ≥28 to <40 days, and ≥40 days, respectively (**Figure 3**)
- After other key prognostic factors were adjusted, patients with vein-to-vein time ≥40 days had a significantly lower CR rate compared with patients with shorter vein-to-vein time
  - ≥40 days versus <28 days: OR, 0.61 (95% CI, 0.42-0.90)
  - ≥40 days versus ≥28 to <40 days: OR, 0.66 (95% CI, 0.45-0.97)

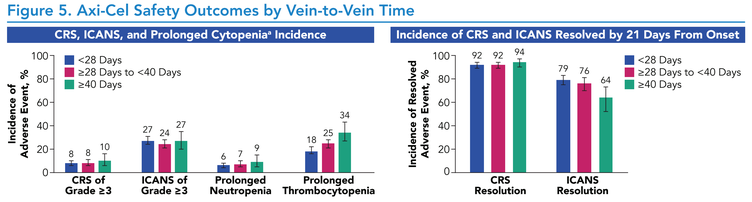
Figure 4. Axi-Cel Adjusted PFS, OS, and DOR by Vein-to-Vein Time[11,12]



For PFS, subsequent cellular therapy and hematopoietic cell transplantation were censored. Covariates for step-wise selection and multivariable adjustment: age, sex, race, ethnicity, ECOG performance status prior to infusion, comorbidities (pulmonary, cardiac/cerebrovascular/heart valve disease, hepatic, and renal), histologic transformation, disease characteristics at initial diagnosis (double/triple hit, disease stage, elevated LDH and >1 extranodal involvements), chemosensitivity prior to infusion, number of prior lines of therapy, prior HCT, year of infusion, time from initial diagnosis to infusion, and use of bridging therapy.
Axi-cel, axicabtagene ciloleucel; d, day; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HCT, hematopoietic cell transplantation; HR, hazard ratio; LDH, lactate dehydrogenase; OS, overall survival; PFS, progression-free survival.

- Adjusted progression-free survival (PFS), overall survival (OS), and duration of response (DOR) analyses based a stratified Cox model[10,11] were conducted to balance differences in baseline characteristics (**Figure 4**)
  - Sensitivity analyses comparing outcomes for patients with vein-to-vein time <36 days versus ≥36 days were also carried out to assess the validity of the vein-to-vein time categorization used in the primary analysis
- Among patients who achieved CR/partial response (PR) as best response, DOR at 12 months was 61% for patients with vein-to-vein time of <28 days, 60% for vein-to-vein time of ≥28 to <40 days, and 61% for vein-to-vein time of ≥40 days
  - Sensitivity analyses for DOR were consistent with the primary analyses
- Adjusted PFS and OS at 24 months appeared lower for patients with vein-to-vein time ≥40 days versus patients with vein-to-vein time of <28 days or ≥28 days to <40 days
  - Sensitivity analyses for OS and PFS were consistent with the primary analyses, with OS being significantly shorter for patients with vein-to-vein time ≥36 days compared with patients with vein-to-vein time <36 days (hazard ratio [HR], 1.25 [95% CI, 1.02-1.53])
- After other key prognostic factors were adjusted, patients with vein-to-vein time ≥ 40 days had a significantly lower OS compared with patients with shorter vein-to-vein time based on an unstratified Cox model
  - ≥40 days versus <28 days: HR, 1.33 (95% CI, 1.05-1.70)
  - ≥40 days versus ≥28 to <40 days: HR, 1.36 (95% CI, 1.06-1.74)

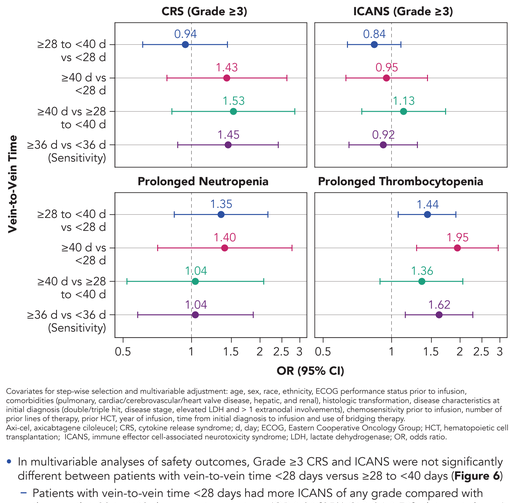
Figure 5. Axi-Cel Safety Outcomes by Vein-to-Vein Time



[a] Evaluated at Day 30.
Axi-cel, axicabtagene ciloleucel; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

- Grade ≥3 cytokine release syndrome (CRS),[13] immune effector cell-associated neurotoxicity syndrome (ICANS),[14] and prolonged neutropenia were consistent regardless of vein-to-vein time (**Figure 5**)
  - Patients with longer vein-to-vein time were increasingly more likely to experience prolonged thrombocytopenia
- Most CRS and ICANS were resolved by 21 days from onset regardless of vein-to-vein time

Figure 6. Multivariable Analyses of Axi-Cel Safety Outcomes



Covariates for step-wise selection and multivariable adjustment: age, sex, race, ethnicity, ECOG performance status prior to infusion, comorbidities (pulmonary, cardiac/cerebrovascular/heart valve disease, hepatic, and renal), histologic transformation, disease characteristics at initial diagnosis (double/triple hit, disease stage, elevated LDH and > 1 extranodal involvements), chemosensitivity prior to infusion, number of prior lines of therapy, prior HCT, year of infusion, time from initial diagnosis to infusion and use of bridging therapy.
Axi-cel, axicabtagene ciloleucel; CRS, cytokine release syndrome; d, day; ECOG, Eastern Cooperative Oncology Group; HCT, hematopoietic cell transplantation; ICANS, immune effector cell-associated neurotoxicity syndrome; LDH, lactate dehydrogenase; OR, odds ratio.

- In multivariable analyses of safety outcomes, Grade ≥3 CRS and ICANS were not significantly different between patients with vein-to-vein time <28 days versus ≥28 to <40 days (**Figure 6**)
  - Patients with vein-to-vein time <28 days had more ICANS of any grade compared with those with ≥28 to <40 days vein-to-vein time (OR 1.34 [95% CI 1.06-1.71]; data not shown)
- Among patients alive at Day 30, higher rates of prolonged thrombocytopenia compared with those with <28 days vein-to-vein time were seen in:
  - Patients with vein-to-vein time ≥28 to <40 days (OR 1.44 [95% CI 1.07-1.92])
  - Patients with vein-to-vein time ≥40 days (OR 1.95 [95% CI 1.29-2.95])

CONCLUSIONS

- In this real-world analysis, most patients with R/R LBCL received axi-cel infusion within 5 weeks after leukapheresis
- Shorter vein-to-vein time was associated with a favorable CR rate, OS, and reduced risk of prolonged thrombocytopenia even after adjustment of key prognostic factors; however, ICANS of any grade may be higher among patients with vein-to-vein time <28 days
- Overall, these findings demonstrate improvements in outcomes with shorter vein-to-vein times in patients treated with axi-cel
  - While the findings highlight the importance of shortening vein-to-vein times, additional studies are needed to identify factors that may lead to infusion delays

REFERENCES

1. YESCARTA® (axicabtagene ciloleucel) [Prescribing information]. Kite Pharma, Inc; 2022.
2. YESCARTA® (axicabtagene ciloleucel) [summary of product characteristics]. Amsterdam, The Netherlands: Kite Pharma EU B.V.; 2021.
3. Neelapu S, et al. *Blood Adv.* 2021;5:4149-4155.
4. Locke F, et al. *N Engl J Med.* 2022;386:640-654.
5. Riedell PA, et al. *Transplant Cell Ther.* 2022;S2666-6367:01474-01479.
6. Abramson JS, et al. *Lancet.* 2020;396:839-852.
7. Kamdar MK, et al. *Lancet.* 2022;399:2294-2308.
8. Sehgal A, et al. *Lancet Oncol.* 2022;23:1066-1077.
9. Chen AJ, et al. *Value Health.* 2022;25:1344-1351.
10. Sorror ML, et al. *Blood.* 2005;106(8): 2912-2919.
11. Chang IM, et al. *J Chronic Dis.* 1982;35:669-674.
12. Gail MH and Byar DP. *Biom J.* 1986;28:587-599.
13. CRS grade based on criteria from: Lee, D. W., et al. *Blood.* 2014;124(2):188-195.
14. ICANS grade based on criteria from: Lee, D. W., et al. *Biol Blood Marrow Transplant.* 2019;25(4):625-638.

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DISCLOSURES

Full author disclosures are available through the Quick Response (QR) code

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