Poster P1694

COST-EFFECTIVENESS OF AXICABTAGENE CILOLEUCEL VS. TISAGENLECLEUCEL FOR THE TREATMENT OF 3L+ RELAPSED/REFRACTORY LARGE B-CELL LYMPHOMA IN THE UNITED STATES: INCORPORATING LONGER SURVIVAL RESULTS

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BACKGROUND

- Axicabtagene ciloleucel (axi-cel) and tisagenlecleucel (tisa-cel) are the first two chimeric antigen receptor (CAR) T-cell therapies approved for the treatment of adults with relapsed/refractory (R/R) large B-cell lymphoma (LBCL) after ≥2 prior systemic therapies.[1,2] The safety and efficacy of axi-cel and tisa-cel in third-line or later (3L+) R/R LBCL patients were assessed in the open-label, single-arm, multi-center, Phase II trials, ZUMA-1 and JULIET, respectively.[3,4]
- Survival outcomes from the ZUMA-1 trial had previously been adjusted using a matching-adjusted indirect comparison (MAIC) approach to match the study population in JULIET.[5] After adjusting for differences in patient characteristics between trials, axi-cel was associated with a greater objective response rate (relative risk [RR]=1.61; 95% confidence interval [CI], 1.29 to 2.01) and complete response (RR=1.62; 95% CI, 1.16 to 2.27) than tisa-cel.[5]
- In a cost-utility analysis of ZUMA-1 and JULIET using shorter follow-up, axi-cel demonstrated greater life years (LYs), increased quality-adjusted life years (QALYs) and reduced costs vs. tisa-cel.[6] Since then, the two trials have published extended follow-up data, with ZUMA-1 reporting survival outcomes at a median follow-up of 51.1 months, and JULIET reporting survival outcomes at a median follow-up of 40.3 months.[7,8] The median overall survival (OS) from the two trials was reported as 25.8 and 11.1 months for axi-cel and tisa-cel, respectively.[7,8]

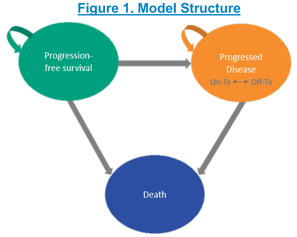
OBJECTIVES

- A cost-utility analysis was performed to compare axi-cel and tisa-cel in 3L+ R/R LBCL. This analysis utilized a previously conducted MAIC, along with the most recent 5-year follow-up survival data from the ZUMA-1 trial, and approximately 4-year follow-up data from the JULIET trial.[5,7,8]

METHODS

- A three-state (i.e., progression-free survival [PFS], progressed disease [PD], and death) partitioned survival model was developed using a United States (US) payer perspective over a lifetime time horizon (Figure 1).
- Patients entered the model in the PFS state. Transitions to the PD and death health states were managed by mixture-cure parametric models; OS was used to determine transitions to the death state.
- All costs in the model were reflective of 2022 US Dollars. Costs and outcomes were discounted at 3% per year.

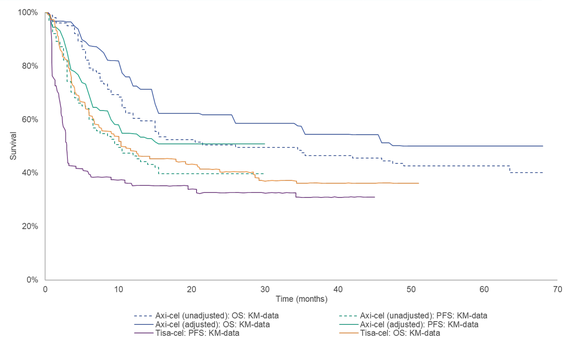
Figure 1. Model Structure



Abbreviations: Tx, treatment.

- Tisa-cel survival estimates were generated from the updated JULIET follow-up data.[8] The survival curves for axi-cel used a MAIC approach to account for the disparity in baseline patient characteristics between ZUMA-1 and JULIET patients.[5]
- The MAIC analysis assigned greater weights to ZUMA-1 trial patients that were more similar to JULIET patients.
- Therefore, ZUMA-1 patients with more favourable prognosis were upweighted owing to their similarity with JULIET patients.
- The previously published weights used to adjust the axi-cel survival curves were deemed appropriate for use with the updated 5-year ZUMA-1 data, since these new data used the same number of patients, with the same baseline characteristics, compared with the previous survival analysis.
- The adjusted ZUMA-1 population showed improved survival outcomes vs. the unadjusted ZUMA-1 population (Figure 2).

Figure 2. Tisa-cel, axi-cel unadjusted, and axi-cel MAIC-adjusted Kaplan–Meier curves



Abbreviations: Axi-cel, axicabtagene ciloleucel; KM, Kaplan–Meier; MAIC, matching-adjusted indirect comparison; OS, overall survival; PFS, progression-free survival; Tisa-cel, tisagenlecleucel.

RESULTS

- Axi-cel was associated with an increase in LYs and QALYs compared with tisa-cel: 3.11 and 2.82, respectively (Table 1).
- Axi-cel resulted in a total cost increase of $19,341 relative to tisa-cel, driven largely by differences in drug acquisition costs, despite higher post-progression costs for tisa-cel.
- This led to an incremental cost-effectiveness ratio of $6,223/LY or $6,847/QALY.

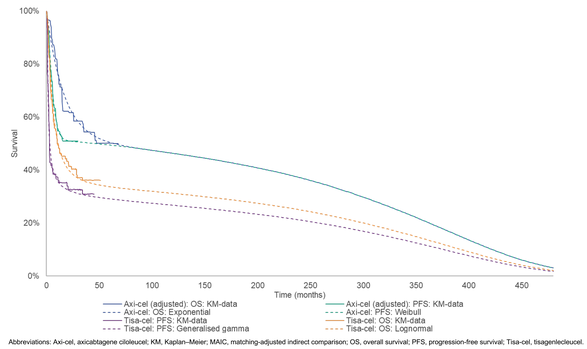
Table 1. Base case cost, effects and incremental outcomes

	Axi-cel	Tisa-cel	Incremental
Total undiscounted LYs	**13.88**	**9.38**	**4.51**
Pre-progression	13.45	7.84	5.61
Post-progression	0.43	1.53	-1.10
Total discounted costs	**$656,201**	**$636,860**	**$19,341**
Treatment-related costs	**$431,284**	**$402,516**	**$28,768**
Stem cell transplant costs	**$26,708**	**$18,227**	**$8,482**
Hospitalization costs	**$75,208**	**$97,375**	**-$22,167**
Disease management costs	**$77,317**	**$67,370**	**$9,947**
Pre-progression	*$67,400*	*$41,216*	*$26,185*
Post-progression	*$9,917*	*$26,155*	*-$16,238*
Terminal care costs	**$45,684**	**$51,373**	**-$5,689**
Total discounted QALYs	**7.66**	**4.84**	**2.82**
Pre-progression	*7.50*	*4.41*	*3.09*
Post-progression	*0.16*	*0.43*	*-0.27*
Total discounted LYs	**9.62**	**6.51**	**3.11**
Pre-progression	*9.21*	*5.42*	*3.79*
Post-progression	*0.42*	*1.09*	*-0.68*
Costs per QALY gained			**$6,847**
Costs per LY gained			**$6,223**

Abbreviations: Axi-cel, axicabtagene ciloleucel; LY, life year; QALY, quality-adjusted life year; Tisa-cel, tisagenlecleucel.

- Following MAIC adjustment, estimated long-term OS and PFS curves for axi-cel and tisa-cel were presented (Figure 3). The results demonstrated that axi-cel has greater OS and PFS compared with tisa-cel.

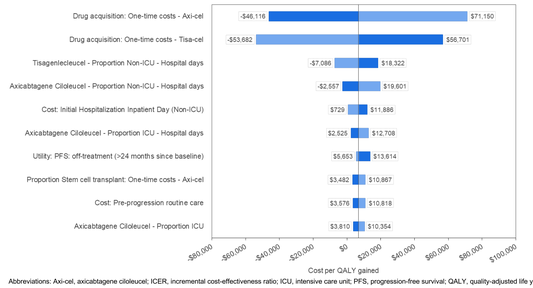
Figure 3. Treatment Kaplan–Meier and modeled long-term survival curves



Abbreviations: Axi-cel, axicabtagene ciloleucel; KM, Kaplan–Meier; MAIC, matching-adjusted indirect comparison; OS, overall survival; PFS, progression-free survival; Tisa-cel, tisagenlecleucel.

- One-way sensitivity analysis indicated that drug acquisition costs of CAR T-cell therapies had the greatest impact on costs per QALY gained, followed by length of non-intensive care unit inpatient stay, and cost of initial hospitalization inpatient days (Figure 4).

Figure 4. One-way sensitivity analysis – Tornado diagram of ICER

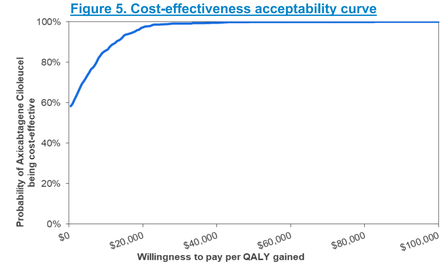


Abbreviations: Axi-cel, axicabtagene ciloleucel; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit; PFS, progression-free survival; QALY, quality-adjusted life year; Tisa-cel, tisagenlecleucel.

RESULTS (CONTINUED)

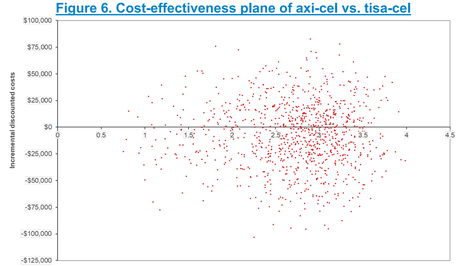
- Based on the probabilistic sensitivity analysis (PSA), axi-cel is cost-effective vs. tisa-cel across 1,000 model simulations. The cost-effectiveness acceptability curve (Figure 5) shows that the cost per QALY gained for axi-cel vs. tisa-cel was ≤$20,000 in 96.80% of simulations and ≤$25,000 in 99% of simulations.
- PSA scatterplot showcases that 100% of simulations were associated with an increase in QALYs for axi-cel compared with tisa-cel (Figure 6).

Figure 5. Cost-effectiveness acceptability curve



Abbreviations: QALY, quality-adjusted life year.

Figure 6. Cost-effectiveness plane of axi-cel vs. tisa-cel



Abbreviations: Axi-cel, axicabtagene ciloleucel; QALYs, quality-adjusted life years; Tisa-cel, tisagenlecleucel

- In all scenario analyses investigated, axi-cel remained cost-effective when compared with tisa-cel, assuming a commonly cited willingness-to-pay threshold of $150,000 per QALY gained.
- In this analysis, axi-cel was associated with a more substantial incremental QALY gain than in the previous model (+2.82 vs. +2.31 QALYs) but a higher incremental cost (+$19,341 vs. -$1,407).[6]
- A limitation of the model was that only observed differences in patient characteristics could be adjusted. Therefore, the MAIC results may be biased in the case where there were unobserved differences across trials.
- Use of real-world evidence should be employed to showcase how the two treatments compare in the general population.
- Furthermore, the clinical inputs for axi-cel, such as hospitalization use, stem cell transplant rates, and adverse event rates, were based on unadjusted ZUMA-1 data. This assumed that no differences in these inputs were expected after the MAIC.

CONCLUSIONS

- To our knowledge this is the first known study that presents an update to a previously published model to assess the cost-effectiveness of axi-cel vs. tisa-cel for treatment of R/R LBCL after ≥2 lines of systemic therapy, incorporating a more mature survival data cut for both axi-cel (60-month OS data) and tisa-cel (40.3-month OS and PFS data).
- This analysis indicates that axi-cel is a cost-effective treatment when compared with tisa-cel, for the treatment of 3L+ R/R LBCL from a US payer perspective, using a commonly cited threshold.
- The longer-term survival follow-up data from the ZUMA-1 and JULIET trials have provided more robust evidence for use in the survival analyses, thus reinforcing previous results and generating increased confidence in the findings.
- While limitations exist based on available prognostic factors, findings were robust to changes in key model assumptions as explored in scenario and sensitivity analyses.

REFERENCES

1. U.S. Food and Drug Administration. FDA approves CAR-T cell therapy to treat adults with certain types of large B-cell lymphoma. 2017. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-car-t-cell-therapy-treat-adults-certain-types-large-b-cell-lymphoma. Accessed on: 10 May 2023.
2. U.S. Food and Drug Administration. FDA approves tisagenlecleucel for adults with relapsed or refractory large B-cell lymphoma. 2018. Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tisagenlecleucel-adults-relapsed-or-refractory-large-b-cell-lymphoma. Accessed on: 10 May 2023.
3. Neelapu SS, Locke FL, Bartlett NL, Lekakis LJ, Miklos DB, Jacobson CA, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. The New England journal of medicine. 2017;377(26):2531-44.
4. Schuster SJ, Bishop MR, Tam CS, Waller EK, Borchmann P, McGuirk JP, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. New England Journal of Medicine. 2018;380(1):45-56.
5. Oluwole OO, Jansen JP, Lin VW, et al. Comparing Efficacy, Safety, and Preinfusion Period of Axicabtagene Ciloleucel versus Tisagenlecleucel in Relapsed/Refractory Large B Cell Lymphoma. Biol Blood Marrow Transplant. 2020 Sep;26(9):1581-1588. doi: 10.1016/j.bbmt.2020.06.008. PubMed PMID: 32561336.
6. Liu R, Oluwole OO, Diakite I, Botteman MF, Snider JT, Locke FL. Cost effectiveness of axicabtagene ciloleucel versus tisagenlecleucel for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy in the United States. J Med Econ. 2021;24(1):458-468. doi:10.1080/13696998.2021.1901721.
7. Neelapu SS, Jacobson CA, Ghobadi A, et al. 5-year follow-up supports curative potential of axicabtagene in refractory large b-cell lymphoma (ZUMA-1). Blood. 2023 Feb 23:blood.2022018893. doi: 10.1182/blood.2022018893. Epub ahead of print. PMID:36821768.
8. Schuster SJ, Tam CS, Borchmann P, et al. Long-term clinical outcomes of tisagenlecleucel in patients with relapsed or refractory aggressive B-cell lymphomas (JULIET): a multicentre, open-label, single-arm, phase 2 study. Lancet Oncol. 2021 Oct;22(10):1403-1415. doi: 10.1016/s1470-2045(21)00375-2. PubMed PMID: 34516954; eng.

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