Poster
EE229

COST EFFECTIVENESS OF AXICABTAGENE CILOLEUCEL VERSUS TISAGENLECLEUCEL IN 3L+ RELAPSED/REFRACTORY LARGE B-CELL LYMPHOMA IN THE UNITED STATES: UTILIZING REAL-WORLD EVIDENCE OF CAR T-CELL THERAPIES

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BACKGROUND

- Axicabtagene ciloleucel (axi-cel) and tisagenlecleucel (tisa-cel) were the first two chimeric antigen receptor (CAR) T-cell therapies approved in the United States (US) for the treatment of adults with relapsed/refractory (R/R) large B-cell lymphoma (LBCL) after ≥2 prior systemic therapies[1,2]
- Cost effectiveness of axi-cel and tisa-cel based on Phase 2 clinical trials, ZUMA-1 and JULIET, respectively, has been previously explored[3]
- However, cost effectiveness of these treatments based on the real-world data remains limited
- A recent real-world evidence (RWE) meta-analysis evaluating progression-free survival (PFS), overall survival (OS), and adverse events favored axi-cel for PFS (HR: 0.67; 95% CI: 0.57, 0.78) and OS (HR: 0.60; 95% CI: 0.47, 0.77) versus tisa-cel[4]

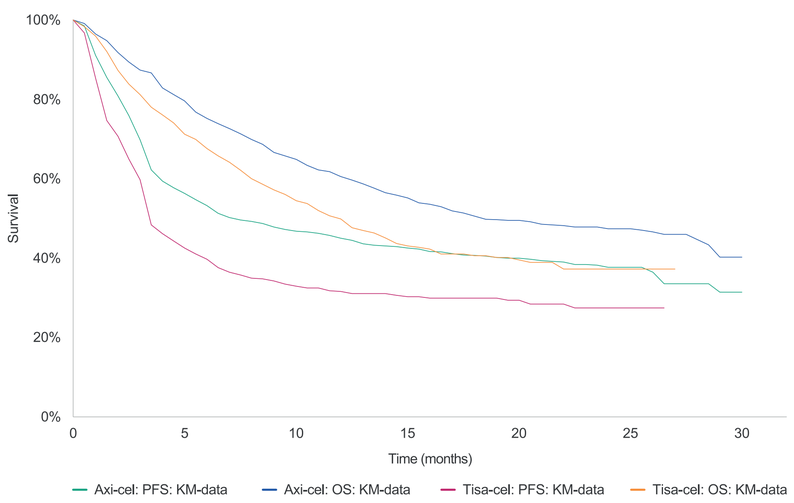
OBJECTIVES

The objective of this study was to assess the cost effectiveness of axi-cel and tisa-cel, utilizing RWE, in R/R LBCL after ≥2 prior systemic therapies in the US.[4]

METHODS

- RWE databases such as EMBASE and MEDLINE were searched using OVID on 29 November 2021 for outcomes of interest such as OS, PFS and duration of response. Searches were limited to the start of 2017 given that RWE could only be generated after the Food and Drug Administration (FDA) approval of CAR T for LBCL[4]
- Eligible studies reported on ≥10 patients with R/R LBCL treated with commercially available CAR T-cell therapies
- For the time-to-event outcomes, pseudo individual patient data (IPD) were reconstructed using the Guyot algorithm (Figure 1)[5]
- A partitioned survival model (PSM) approach was selected to project the clinical (disease progression and mortality) and economic consequences of therapy with axi-cel or tisa-cel in R/R LBCL patients using the pseudo IPD
- Patients initiated the model in the PFS state, transitioning to progressed disease and death states based on PFS and OS curves, respectively
- Costs were sourced from US databases and relevant literature and were discounted at an annual rate of 3%
- Within the PSM, two different approaches were used to model long-term health outcomes, namely:
  - A partitioned survival mixture cure model (PS-MCM)
  - A traditional standard parametric survival model
- The base case analysis used the PS-MCM to capture potential long-term responses associated with CAR T-cell therapies
- Standard parametric models were applied as a scenario analysis to test the robustness of the curve assumption

Figure 1. Axi-cel and tisa-cel Kaplan–Meier curves using pseudo IPD from RWE



Abbreviations: Axi-cel, axicabtagene ciloleucel; IPD, individual patient data; KM, Kaplan–Meier; OS, overall survival; PFS, progression-free survival; RWE, real-world evidence; Tisa-cel, tisagenlecleucel.

RESULTS

- Axi-cel was associated with an increase in life years (LYs) and quality-adjusted life years (QALYs) compared with tisa-cel: 2.00 (undiscounted) and 1.16 (discounted), respectively (Table 1)
- Axi-cel resulted in a total cost increase of $59,003 relative to tisa-cel, driven largely by differences in drug acquisition costs
- This led to an incremental cost-effectiveness ratio of $40,913/LY or $50,947/QALY

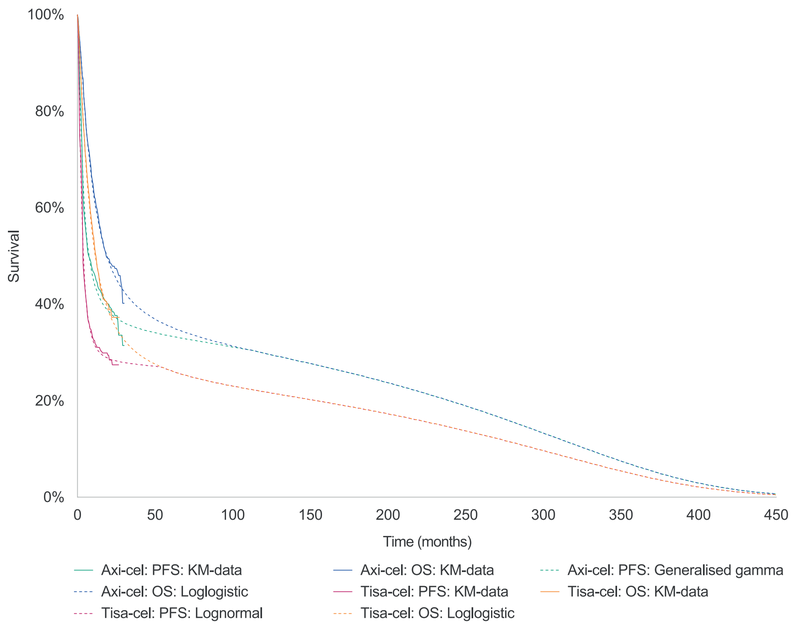
Table 1. Base case cost, effects and incremental outcomes

	Axi-cel	Tisa-cel	Incremental
Total undiscounted LYs	**8.16**	**6.15**	**2.00**
Pre-progression	7.71	5.75	1.95
Post-progression	0.45	0.40	0.05
Total discounted costs	**$675,087**	**$616,084**	**$59,003**
Treatment-related costs	$464,830	$401,361	$63,468
Stem cell transplant costs	$26,708	$18,227	$8,482
Hospitalization costs	$75,208	$97,375	-$22,167
Disease management costs	$56,119	$44,266	$11,853
Terminal care costs	$52,223	$54,856	-$2,633
Total discounted QALYs	**4.76**	**3.60**	**1.16**
Pre-progression	4.59	3.45	1.14
Post-progression	0.17	0.15	0.01
Total discounted LYs	**6.08**	**4.64**	**1.44**
Pre-progression	5.65	4.25	1.41
Post-progression	0.43	0.39	0.04
Costs per QALY gained			**$50,947**
Costs per LY gained			**$40,913**

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

- Following survival extrapolation, the estimated long-term OS and PFS curves for axi-cel and tisa-cel are presented (Figure 2). Axi-cel had a higher OS and PFS compared with tisa-cel over the full time-horizon of the model

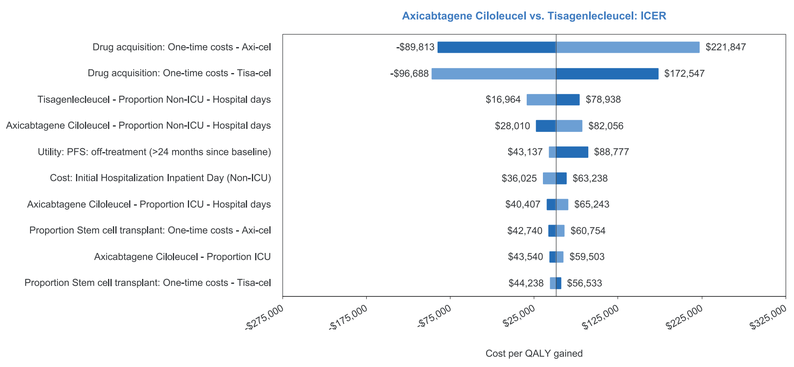
Figure 2. Treatment Kaplan–Meier and modeled long-term survival curves



Abbreviations: Axi-cel, axicabtagene ciloleucel; KM, Kaplan–Meier; 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 the cost per QALY gained, followed by the number of hospital days experienced by non-intensive care unit (ICU) patients (Figure 3)

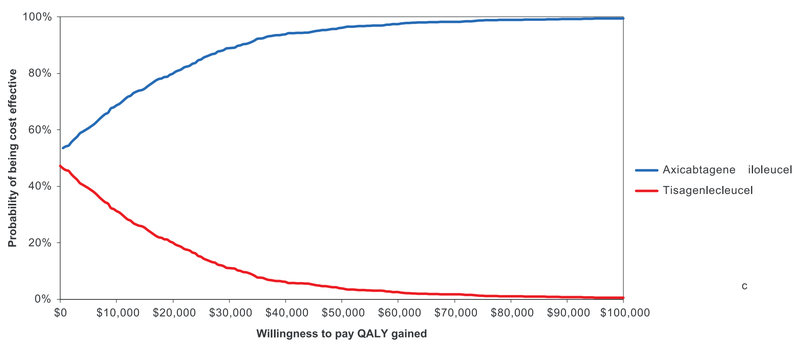
Figure 3. One-way sensitivity analysis – Tornado diagram of ICER



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.

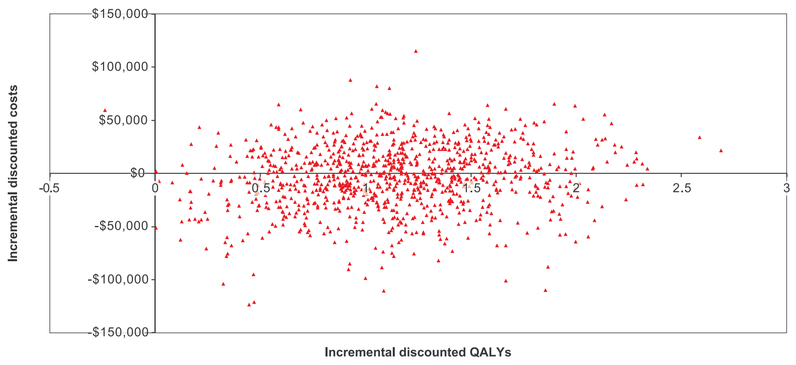
- Probabilistic sensitivity analysis (PSA) demonstrated that the ICER remained ≤$69,263 in 99% of simulations, which is below the often-cited cost-effectiveness threshold of $150,000/QALY

Figure 4. Cost-effectiveness acceptability curve



Abbreviations: QALY, quality-adjusted life year.

Figure 5. Cost-effectiveness plane of axi-cel versus 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
- A limitation of the analysis is that OS and PFS curves could only be fitted separately without capturing their structural relationship. In the instance of axi-cel, PFS was set equal to OS after 111 months, and for tisa-cel this was 54 months. This was implemented to avoid clinically implausible scenarios whereby PFS was greater than OS

CONCLUSIONS

- Over a lifetime horizon of 45 years, treatment of R/R LBCL with axi-cel was estimated to generate an additional 2.00 LYs (undiscounted) and 1.16 QALYs (discounted) compared with tisa-cel
- Treatment with axi-cel increased costs by $59,003 compared with tisa-cel. As such, axi-cel incurred a cost-effectiveness ratio of $50,947 when compared with tisa-cel
- With the incorporation of emerging RWE in 3L+ LBCL, axi-cel is still considered a cost-effective treatment compared with tisa-cel, from a US payer's perspective
- This study reinforces previous results from clinical trials, thus bolstering confidence in the cost effectiveness of axi-cel versus tisa-cel in current clinical practice

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DISCLOSURES

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