A Systematic Review on Economic Evaluations of Comparisons Between CAR-T Therapies in Relapsed or Refractory Diffuse Large B-Cell Lymphoma

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Introduction

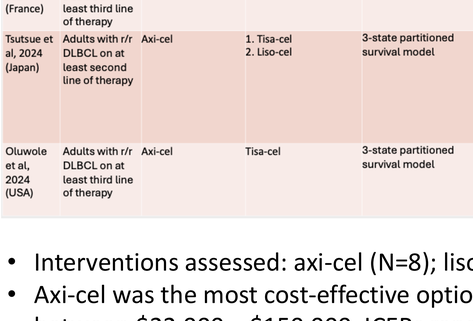
- Chimeric antigen receptor T-cell (CAR-T) therapies may provide significant value to patients with relapsed or refractory diffuse large B-cell lymphoma (r/r DLBCL).
- Prior studies have compared them to standard of care, but their value relative to each other is still unclear.
- We present a systematic review aimed at evaluating the current evidence on economic comparisons of CAR-T therapies for r/r DLBCL.

Methods

- This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance.
- **Data sources**
  - A comprehensive literature search was conducted in PubMed, Embase, and Scopus databases from inception to December 31st, 2024.
  - MeSH terms and keywords such as "CAR-T therapies", "B-cell lymphoma", "relapse", and "cost-effectiveness" were used, adapting search strings to the specific indexing systems of each database.
- **Eligibility criteria**
  - Studies must have focused on patients with relapsed /refractory B-Cell Lymphoma
  - Studies were included only if they were full economic evaluations. Key Parameters such as costs, effect measures, cost-effectiveness ratios, perspective, time horizon were evaluated.
  - Both the intervention and comparator had to include a CAR-T therapy. All available CAR-T therapies were eligible.
  - Studies were excluded if they were primary studies (eg, editorials, conference abstracts) or partial economic evaluations.
- **Data collection**
  - Data extraction and risk of bias assessment were independently performed by two authors using the Quality of Health Economic Studies (QHES) standardized framework.
  - Extracted data included the following: (1) study characteristics; (2) patient characteristics; (3) CAR-T type (intervention, comparator and dosing strategy); (4) setting; (5) model structure; (6) outcome measures (QALYs, LYs, ICERs, treatment found cost effective).

Results

Figure 1. Flow diagram of the study selection process.



- N=8 studies were extracted; N=5 were conducted in the US.
- All studies modeled patient who were on at least the 3rd line of therapy.
- Studies were conducted over a lifetime horizon with the majority (n=6) conducted using the payer's perspective.

Table 1. Summary of included studies

Author (Setting)	Disease Stage and Modeled Population	Intervention and Dosing Strategy	Comparator and Dosing Strategy	Model Structure	Time Horizon	Perspective	Evaluation Type	Base Case Results	Preferred Strategy
Joyner et al, 2022 (USA)[1]	Adults with r/r DLBCL on at least third line of therapy	Axicabtagene ciloleucel (axi-cel)	1. Lisocabtagene maraleucel (liso-cel) 2. Tisagenlecleucel (tisa-acel)	Decision-tree followed by partitioned survival model	Lifetime	Payer	Cost utility analysis (CUA)	Axi-cel vs liso-cel: 1. ICER- $8,946 2. INMB- $254,913 Axi-cel vs tisa-cel: 1. ICER- $24,506 2. NMB- $280,472 WTP threshold of $150,000	Axi-cel
Parker et al, 2023 (USA)[2]	Adults with r/r DLBCL on at least third line of therapy	Liso-cel	1. Axi-cel 2. Tisa-cel	3-state partitioned survival model	Lifetime	Payer	CUA	Liso-cel vs. axi-cel: INMB- $75,170 Liso-cel vs tisa-cel: INMB- $133,075 WTP threshold of $100,000	Liso-cel
Oluwole et al, 2022 (USA)[3]	Adults with r/r DLBCL on at least third line of therapy	Axi-cel	Liso-cel	3-state partitioned survival model	Lifetime	Payer	CUA	Axi-cel vs liso-cel: ICER- $7,843	Axi-cel
Liu et al, 2021 (USA)[4]	Adults with r/r DLBCL on at least third line of therapy	Axi-cel	Tisa-cel	3-state partitioned survival model	Lifetime	Payer	CUA	Axi-cel dominated tisa-cel with incremental costs and QALYs of -$1,407 and 2.31 respectively	Axi-cel
Bastos-Oreiro et al, 2022 (Spain)[5]	Adults with r/r DLBCL on at least third line of therapy	Axi-cel	Tisa-cel	3-state partitioned survival model	Lifetime	Health system	CUA	Axi-cel vs tisa-cel: 1. ICER- €10,999/LY 2. ICER- €13,049/QALY WTP thresholds of €22,000 – €60,000	Axi-cel
Ray et al, 2024 (France)	Adults with r/r DLBCL on at least third line of therapy	Axi-cel	Tisa-cel	3-state partitioned survival model	Lifetime	Health system	CUA	Axi-cel vs tisa-cel: ICER- €15,520 QALY	Axi-cel
Tsutsue et al, 2024 (Japan)	Adults with r/r DLBCL on at least second line of therapy	Axi-cel	1. Tisa-cel 2. Liso-cel	3-state partitioned survival model	Lifetime	Payer	CUA	Axi-cel vs. tisa-cel: ICER- $976.29 Axi-cel vs liso-cel: ICER - $242.0 WTP thresholds of $53,191.49	Axi-cel
Oluwole et al, 2024 (USA)	Adults with r/r DLBCL on at least third line of therapy	Axi-cel	Tisa-cel	3-state partitioned survival model	Lifetime	Payer	CUA	Axi-cel vs tisa-cel: ICER- $19,994 WTP threshold of $150,000	Axi-cel

- Interventions assessed: axi-cel (N=8); liso-cel (N=4); tisa-cel (N=7).
- Axi-cel was the most cost-effective option in N=7 studies under WTP thresholds between $22,000 – $150,000. ICERs ranged between -$609 – $24,506.
- Liso-cel was cost-effective option in one study, resulting in an ICER of $33,618.
- Models were most sensitive to parameters related to long-term survival (OS, PFS), pre-progression utilities, drug costs, hospitalization days and costs, and matching-adjusted indirect comparison (MAIC) methodology.

Results

Table 2. Summary of QHES instrument dimension scores.

QHES dimension	Author, publication year (reference)							
	Joyner et al, 2022 (1)	Parker et al, 2023 (2)	Oluwole et al, 2022 (3)	Liu et al, 2021 (4)	Bastos-Oreiro et al, 2022 (5)	Ray et al, 2024 (6)	Tsutsue et al, 2024 (7)	Oluwole et al, 2024 (8)
Was the study objective presented in a clear, specific, and measurable manner?	7	7	7	7	7	7	7	7
Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	4	4	4	4	4	4	4
Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	7	7	7	7	7	7	7	7
If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1	1	1	1	1	1	1	1
Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	9	9	9	9	9	9	9
Was incremental analysis performed between alternatives for resources and costs?	6	6	6	6	6	6	6	6
Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	5	5	5	5	5	5	5
Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given	7	7	7	7	7	7	7	7
Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	8	8	8	8	8	8	8
Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	6	6	6	6	6	6	6
Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	7	7	7	7	7	7	7
Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	8	8	8	8	8	8	8
Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	7	7	7	7	7	7	7
Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	6	6	6	6	6	6	6
Were the conclusions/recommendations of the study justified and based on the study results?	8	8	8	8	8	8	8	8
Was there a statement disclosing the source of funding for the study?	3	3	3	3	3	3	3	3

Conclusions

- Axi-cel may be the most cost-effective CAR-T therapy for r/r DLBCL over a lifetime horizon across the US, Spain, Japan, and France.
- Better axi-cel cost-effectiveness was partially driven by superior survival outcomes compared to other CAR-T therapies, despite costs being higher.
- Cost-effectiveness results can be highly sensitivity to MAIC adjustment methodologies.
- More direct head-to-head comparisons of these therapies is required to inform both future economic evaluation studies and pricing adjustments of these therapies.

Scan QR code for references

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